Contrails

FOREWORD

This report was prepared by Wyandotte Chemicals Corporation under USAF Contract No. AF 33(616)-6749, Project No. 3044, "Aviation Lubricants," Task No. 73314, "Liquid and Solid Lubricants Development". The work was administered under the direction of **Directorate of Materials and Processes, Deputy for Technology,** Aeronautical Systems Division, with Mr. H. W. Adams of the Lubricants Section, Nonmetallic Materials Laboratory, acting as project engineer.

This report covers work conducted from 1 September 1960 to 31 August 1961 and is entitled Part II with subsequent reports to follow describing continued work on this program.

The work at Wyandotte Chemicals Corporation, designated Project 105R-919, was performed by Dr. P. T. Kan, Project Leader, Dr. J. D. Behun, Dr. S. M. Naqvi, Mrs. M. A. Jorgensen, Mrs. P. A. Gibson, Mr. Robert Gillmann and Mr. G. A. Spedding under the direction of Dr. John D. Behun and general supervision of Dr. C. T. Lenk and Mr. R. A. Graham. During the first quarter of this report period Dr. Kan was assigned as Project Leader while Dr. Behun, formerly Project Leader, continued to guide the direction of the program in the capacity of Section Head. During the last quarter of this report period responsibilities for general supervision of this program were assumed by Mr. W. W. Levis, Dr. D. R. Jackson and Dr. L. G. Lundsted.

Infrared and ultraviolet spectra were obtained by Wyandotte Chemicals Corporation, Analytical Research Department. Elemental analyses were performed by Spang Micro-Analytical Laboratories, Ann Arbor, Michigan.

The authors are grateful to Prof. R. Levine, University of Pittsburgh, and Prof. W. H. Urry, University of Chicago, for their consultation and valuable suggestions on this program.

Approved for Public Release

Contrails

ABSTRACT

Progress is reported on the synthesis and evaluation of new pyrazine derivatives for high temperature stable fluid applications. A variety of candidate products which were unsymmetrical 2,3-disubstituted- and 2,3,6-trisubstitutedpyrazines were prepared from the versatile starting compounds 2-chloro-3-methylpyrazine and 2-chloro-3,6-dimethylpyrazine. The substituents placed at the 2-position by nucleophilic displacement of the chlorine atom were various phenoxy, alkoxy, anilino and alkylamino radicals. Metalation of the methyl sites afforded the introduction of a number of other types of groups by arylation, aralkylation, alkylation, acylation and silylation reactions. A number of 2,6-disubstitutedpyrazines were prepared via oxidative demethylation of the corresponding intermediate 2,6-disubstituted-3-methylpyrazines. Some simple alkyl substituted pyrazines were also synthesized from the readily available starting compounds methylpyrazine, 2,5- and 2,6-dimethylpyrazines, and tetramethylpyrazine. Thus, a wide variety of pyrazine derivatives were obtained in good to excellent yields by the different synthetic routes.

The screening of pyrazine compounds prepared in this program for thermal and oxidative stability was continued. Based on these tests, classes of compounds containing undesirable linkages were bypassed and materials which showed promise were further screened under more severe conditions at higher temperatures. Correlations of the effect of variation in structure upon physical properties of the substituted pyrazines were made, based on the results of the more drastic screening. These correlations were utilized to guide the direction of the synthesis effort. As a consequence, a stepwise achievement of candidate products with further improved properties was realized.

PUBLICATION

This report has been reviewed and is approved:

FOR THE COMMANDER:

Marc P. Dunnam

MARC P. DUNNAM, Chief
Fuels and Lubricants Branch
Nonmetallic Materials Laboratory
Directorate of Materials and Processes

Approved for Public Release

Contrails

TABLE OF CONTENTS

	Page
INTRODUCTION.	1
DISCUSSION.	6
PROPERTIES OF PYRAZINE DERIVATIVES	6
Fluidity.	7
2-Phenoxy-3(and 6)-substitutedpyrazines and 2-Phenoxy-3,6-disubstitutedpyrazines	7
2-Amino-3-substitutedpyrazines and 2-Amino-3,6-disubstitutedpyrazines	11
2-Alkoxy-3-substitutedpyrazines and 2-Alkoxy-3,6-disubstitutedpyrazines.	12
Dialkylpyrazines and 1,4-Bis(alkylpyrazyl)butanes.	13
Conclusions Regarding Fluidity	14
Thermal Stability	15
2-Phenoxy-3(and 6)-substitutedpyrazines and 2-Phenoxy-3,6-disubstitutedpyrazines	16
2-Amino-3-substitutedpyrazines and 2-Amino-3,6-disubstitutedpyrazines	19
2-Alkoxy-3-substitutedpyrazines and 2-Alkoxy-3,6-disubstitutedpyrazines.	21
Dialkylpyrazines and 1,4-Bis(substitutedpyrazyl)butanes. . .	22
Conclusions Regarding Thermal Stability.	23
Oxidation Stability	24
2,3-Disubstitutedpyrazines	24
2,5- and 2,6-Disubstitutedpyrazines.	38
Conclusions Regarding Oxidative Stability.	38

Approved for Public Release

Contrails

TABLE OF CONTENTS (continued)

Page

SYNTHESIS OF PYRAZINE DERIVATIVES. 45

Initial Intermediates 45

2-Phenoxy-3-methylpyrazines and 2-Phenoxy-3,6-dimethylpyrazines. 45

2-Alkoxy-3-methylpyrazines and 2-Alkoxy-3,6-dimethylpyrazines. 53

2-Anilino-3-methylpyrazines and 2-Anilino-3,6-dimethylpyrazines. 55

2-Alkylamino-3-methylpyrazines and 2-Alkylamino-3,6-dimethylpyrazines. 64

Alkyl(methyl)pyrazines 68

Advanced Intermediates. 70

2-Phenoxy-3-methyl-6-substitutedpyrazines. 70

2-Alkoxy-3-methyl-6-substitutedpyrazines 75

2-Anilino-3-methyl-6-substitutedpyrazines and 2-Alkylamino-3-methyl-6-substitutedpyrazines. 77

Candidate Products. 79

2-Phenoxy-3-substitutedpyrazines and 2-Phenoxy-3,6-disubstitutedpyrazines 79

2-Phenoxy-6-substitutedpyrazines 86

2-Alkoxy-3-substitutedpyrazines and 2-Alkoxy-3,6-disubstitutedpyrazines. 87

2-Anilino-3-substitutedpyrazines and 2-Anilino-3,6-disubstitutedpyrazines 90

2-Anilino-6-substitutedpyrazines 95

2-Alkylamino-3-substitutedpyrazines and 2-Alkylamino-3,6-disubstitutedpyrazines 97

Approved for Public Release

Contrails

TABLE OF CONTENTS (continued)

	Page
Alkylpyrazines	100
Model Reactions	102
EXPERIMENTAL	107
I. INITIAL INTERMEDIATES	107
A. 2-Phenoxy-3-methylpyrazines and 2-Phenoxy-3,6-dimethylpyrazines	107
General Procedure	107
2-(o-i-Propylphenoxy)-3-methylpyrazine	107
2-(p-i-Propylphenoxy)-3-methylpyrazine	107
2-(p-Phenylphenoxy)-3-methylpyrazine	108
Selenium Dioxide Oxidation of the High-melting Isomer of 2-(p-Phenylphenoxy)-3-methylpyrazine, p-Phenylphenoxypyrazine	108
Attempted Selenium Dioxide Oxidation of the Low-melting Isomer of 2-(p-Phenylphenoxy)-3-methylpyrazine	109
p-Phenylene Bis-2-(3-methylpyrazyl) Ether	109
m-Phenylene Bis-2-(3-methylpyrazyl) Ether	110
m-Carbomethoxyphenol	110
2-(m-Carbomethoxyphenoxy)-3-methylpyrazine	111
Attempted Preparation of 2-Pentachlorophenoxy-3-methylpyrazine	111
Attempted Preparation of 2-(2,6-Di-t-butyl-4-methylphenoxy)-3-methylpyrazine	111
2-(2-Methyl-6-ethylphenoxy)-3-methylpyrazine	112
m-Trimethylsiloxybromobenzene	112
p-Trimethylsiloxybromobenzene	112

Approved for Public Release

Contrails

TABLE OF CONTENTS (continued)

	Page
(m-Trimethylsiloxy)trimethylsilylbenzene	112
(p-Trimethylsiloxy)trimethylsilylbenzene	113
m-Trimethylsilylphenol	113
p-Trimethylsilylphenol	113
2-(m-Trimethylsilylphenoxy)-3-methylpyrazine	113
2-(p-Trimethylsilylphenoxy)-3-methylpyrazine	113
2-(p-t-Butylphenoxy)-3,6-dimethylpyrazine	114
2-(p-Phenylphenoxy)-3,6-dimethylpyrazine	114
B. 2-Alkoxy-3-methylpyrazines and 2-Alkoxy-3,6-dimethylpyrazines	114
2-(2,2-Dimethylpentoxy)-3-methylpyrazine	114
2-(2,2,4-Trimethylpentoxy)-3-methylpyrazine	115
2-[1-(3-Hydroxy-2,2,4,4-tetramethylcyclobutoxy)] -3-methylpyrazine	115
Bis-{3-[2-(3-methylpyrazoxy)] -2,2,4,4-tetramethyl-1-cyclobutoxy}dimethylsilane	116
2-(2,2-Dimethylpentoxy)-3,6-dimethylpyrazine	116
2-(2,2,4-Trimethylpentoxy)-3,6-dimethylpyrazine	117
C. 2-Anilino-3-methylpyrazines and 2-Anilino-3,6-dimethylpyrazines	117
General Procedure	117
2-(N-Methylanilino)-3-methylpyrazine, Interaction of N-Methylaniline with 2-Chloro-3-methylpyrazine in Presence of Zinc Chloride	118
2-(N-Methylanilino)-3-methylpyrazine, Interaction of 2-Anilino-3-methylpyrazine with Methyl Iodide	118
N-Butylaniline	119

Approved for Public Release

Contrails

TABLE OF CONTENTS (continued)

Page

2-(N-Butylanilino)-3-methylpyrazine, Interaction of N-Butylaniline and 2-Chloro-3-methylpyrazine 119

Attempted Preparation of 2-(N-Butylanilino)-3-methylpyrazine, Interaction of 2-Anilino-3-methylpyrazine with 1-Bromobutane. 120

2-(N-Butylanilino)-3-methylpyrazine, Interaction of 2-Anilino-3-methylpyrazine with Sodium Amide and 1-Bromobutane in Pyridine 120

2-(p-Pentylanilino)-3-methylpyrazine 121

2-(p-Dodecylanilino)-3-methylpyrazine. 121

Attempted Preparation of 2-(N-Ethyl-p-pentylanilino)-3-methylpyrazine, Interaction of 2-(p-Pentylanilino)-3-methylpyrazine with Ethyl Bromide. 122

N-Ethyl-p-pentylaniline. 122

Attempted Preparation of 2-(N-Ethyl-p-pentylanilino)-3-methylpyrazine, Interaction of 2-Chloro-3-methylpyrazine with N-Ethyl-p-pentylaniline 122

Attempted Preparation of N,N-Di[2-(3-methylpyrazyl)] aniline, Interaction of 2-(N-Methylanilino)-3-methylpyrazine with 2-Chloro-3-methylpyrazine ("Direct" Method). 122

Attempted Preparation of N,N-Di-[2-(3-methylpyrazyl)] - aniline, Interaction of 2-Anilino-3-methylpyrazine with 2-Chloro-3-methylpyrazine ("Pyridine Solvent" Method). . . . 123

Attempted Preparation of N,N'-Diphenyl-N,N'-di-[2-(3-methylpyrazyl)] -1,2-diaminoethane, Interaction of 2-Anilino-3-methylpyrazine with 1,2-Dibromoethane ("Pyridine Solvent" Method). 123

N,N'-Diphenyl-N,N'-di-[2-(3-methylpyrazyl)] -1,2-diaminoethane 123

2-(N-Methylanilino)-3,6-dimethylpyrazine and 2-Anilino-3,6-dimethylpyrazine 123

Approved for Public Release

Contrails

TABLE OF CONTENTS (continued)

Page

2-Anilino-3,6-dimethylpyrazine 125

2-(p-Pentylanilino)-3,6-dimethylpyrazine 125

D. 2-Alkylamino-3-methylpyrazines and 2-Alkylamino-3,6-dimethylpyrazines 125

General Procedure. 125

2-(N-n-Hexylamino)-3-methylpyrazine. 125

2-(2-Ethylhexylamino)-3-methylpyrazine 126

Attempted Preparation of N,N-Di-[2-(3-methylpyrazyl)] hexylamine. 126

2-(N,N-Di-n-butylamino)-3-methylpyrazine 126

2-(N,N-Di-n-pentylamino)-3-methylpyrazine. 126

2-(N,N-Di-n-hexylamino)-3-methylpyrazine 127

2-(N-n-Hexyl-N-n-octylamino)-3-methylpyrazine. 127

2-(n-Hexylamino)-3,6-dimethylpyrazine. 128

2-(N,N-Di-n-butylamino)-3,6-dimethylpyrazine 128

Attempted Preparation of 2-(N,N-Di-n-butylamino)-3,6-dimethylpyrazine, Interaction of Di-n-butylamine with Sodium Hydride and 2-Chloro-3,6-dimethylpyrazine. 129

2-(N,N-Di-i-butylamino)-3,6-dimethylpyrazine 129

2-(N,N-Di-n-pentylamino)-3,6-dimethylpyrazine. 129

2-(N,N-Di-n-hexylamino)-3,6-dimethylpyrazine 130

E. x-Alkyl-x'-methylpyrazines. 130

General Procedure. 130

2-n-Heptyl-5-methylpyrazine. 131

Approved for Public Release

Contrails

TABLE OF CONTENTS (continued)

	Page
2-n-Heptyl-6-methylpyrazine.	132
2-n-Nonyl-5-methylpyrazine	132
2-n-Nonyl-6-methylpyrazine	132
2-n-Heptyl-3,5,6-trimethylpyrazine and 2,5-Di-n-heptyl-3,6-dimethylpyrazine	132
II. ADVANCED INTERMEDIATES	133
A. 2-Phenoxy-3-methyl-6-substitutedpyrazines	134
2-Phenoxy-3-methyl-6-benzylpyrazine.	134
2-(p-Nonylphenoxy)-3-methyl-6-benzylpyrazine	134
2-(p-Nonylphenoxy)-3-methyl-6-(p-phenoxybenzyl)pyrazine. . .	134
Attempted Preparation of 2-(p-Nonylphenoxy)-3-methyl-6-[p-(p'-phenyldimethylsilylphenoxy)benzyl]pyrazine	134
2-(p-Nonylphenoxy)-3-methyl-6-(2-trimethylsilylethyl)-pyrazine	135
2-(p-Nonylphenoxy)-3-methyl-6-(5-nonyl)pyrazine.	136
2-(p-Nonylphenoxy)-3-methyl-6-(2-phenylethyl)pyrazine. . . .	136
2-(p-Nonylphenoxy)-3-methyl-6-tridecylpyrazine	136
B. 2-Alkoxy-3-methyl-6-substitutedpyrazines.	137
2-(2,2-Dimethylpentoxy)-3-methyl-6-(n-heptyl)pyrazine. . . .	137
2-(2,2-Dimethylpentoxy)-3-methyl-6-(n-pentyl)pyrazine and 2-(2,2-Dimethylpentoxy)-3-methyl-6-(5-nonyl)pyrazine	137
C. 2-Anilino-3-methyl-6-substitutedpyrazines	138
2-(N-Methylanilino)-3-methyl-6-(5-nonyl)pyrazine	138
2-(N-Methylanilino)-3-methyl-6-(n-heptyl)pyrazine.	138

Approved for Public Release

Contrails

TABLE OF CONTENTS (continued)

Page

D. 2-Alkylamino-3-methyl-6-substitutedpyrazines. 139

2-(N,N-Di-n-pentylamino)-3-methyl-6-(n-heptyl)pyrazine . . . 139

2-(N,N-Di-n-hexylamino)-3-methyl-6-(n-heptyl)pyrazine. . . . 139

III. CANDIDATE PRODUCTS 139

A. 2-Phenoxy-3-substitutedpyrazines and 2-Phenoxy-3,6-disubstitutedpyrazines. 139

General Procedure. 139

2-Phenoxy-3-(p-phenylbenzyl)pyrazine 140

2-(p-Nonylphenoxy)-3-benzylpyrazine. 140

2-(p-Nonylphenoxy)-3-(p-phenoxybenzyl)pyrazine 140

p-Phenyldimethylsilylchlorobenzene 140

p-Phenyldimethylsilylbromobenzene. 141

Attempted Preparation of 2-Phenoxy-3-(p-phenyldimethylsilylbenzyl)pyrazine, 2-Phenoxy-3-benzylpyrazine 141

Attempted Preparation of 2-(p-Nonylphenoxy)-3-(p-phenyldimethylsilylbenzyl)pyrazine, 2-(p-Nonylphenoxy)-3-benzylpyrazine 142

Attempted Preparation of 2-Phenoxy-3-(p-trimethylsilylmethylbenzyl)pyrazine. 142

2-Phenoxy-3-tridecylpyrazine 142

2-Phenoxy-3-(5-nonyl)pyrazine. 142

Attempted Preparation of 2-Phenoxy-3-(tributylmethyl)pyrazine 143

2-(p-Phenylphenoxy)-3-(5-nonyl)pyrazine. 143

2-(m-Phenoxyphenoxy)-3-(5-nonyl)pyrazine 143

Approved for Public Release

Contrails

TABLE OF CONTENTS (continued)

	Page
2-(2-Methyl-6-ethylphenoxy)-3-(5-nonyl)pyrazine.	144
2-(p-Nonylphenoxy)-3-pentylpyrazine.	144
2-(p-t-Butylphenoxy)-3-(5-nonyl)pyrazine	144
2-(p-Nonylphenoxy)-3-tridecylpyrazine.	144
2-(p-Nonylphenoxy)-3-(2-phenylethyl)pyrazine	144
2-(m-Phenoxyphenoxy)-3-(2-trimethylsilylethyl)pyrazine . . .	145
2-(p-t-Butylphenoxy)-3-(2-trimethylsilylethyl)pyrazine . . .	145
2-(p-t-Butylphenoxy)-3-(2-phenylethyl)pyrazine	145
2-Phenoxy-3-pyrazinoic Acid Monohydrate.	145
Phenylhydrazone of 2-Phenoxy-3-benzoylpyrazine and 1,3-Diphenylpyrazolo[2,3-b]pyrazine.	146
2-(p-Nonylphenoxy)-3-pentyl-6-(5-nonyl)pyrazine.	146
B. 2-Phenoxy-6-substitutedpyrazines.	147
General Procedure.	147
2-Phenoxy-6-benzylpyrazine	147
2-Phenoxy-6-benzoylpyrazine.	147
Phenylhydrazone of 2-Phenoxy-6-benzoylpyrazine	147
2-(p-Nonylphenoxy)-6-benzylpyrazine.	148
2-(p-Nonylphenoxy)-6-(p-phenoxybenzyl)pyrazine	148
2-(p-Nonylphenoxy)-6-(5-nonyl)pyrazine	148
2-(p-Nonylphenoxy)-6-(2-phenylethyl)pyrazine	149
2-(p-Nonylphenoxy)-6-tridecylpyrazine.	149

Approved for Public Release

Contrails

TABLE OF CONTENTS (continued)

Page

Attempted Interaction of Pyrazine with Selenium Dioxide in Pyridine. 149

C. 2-Alkoxy-3-substitutedpyrazines and 2-Alkoxy-3,6-disubstitutedpyrazines. 149

General Procedure. 149

2-(2,2-Dimethylpentoxy)-3-(n-pentyl)pyrazine and 2-(2,2-Dimethylpentoxy)-3-(5-nonyl)pyrazine 149

2-(2,2,4-Trimethylpentoxy)-3-(n-pentyl)pyrazine and 2-(2,2,4-Trimethylpentoxy)-3-(5-nonyl)pyrazine 150

2-(2,2-Dimethylpentoxy)-3,6-di(n-heptyl)pyrazine 150

2-(2,2-Dimethylpentoxy)-3-(n-pentyl)-6-(n-heptyl)pyrazine. . 151

D. 2-Anilino-3-substitutedpyrazines and 2-Anilino-3,6-disubstitutedpyrazines. 151

General Procedure. 151

2-(N-Methylanilino)-3-benzylpyrazine 151

2-(N-Methylanilino)-3-(p-phenoxybenzyl)pyrazine. 152

2-(N-Methylanilino)-3-(2-trimethylsilylethyl)pyrazine. . . . 152

2-(N-Methylanilino)-3-tridecylpyrazine 152

2-(N-Butylanilino)-3-pentylpyrazine and 2-(N-Methylanilino)-3-(5-nonyl)pyrazine, Interaction of 2-(N-Methylanilino)-3-methylpyrazine with Excess Sodium Amide and 1-Bromobutane. 152

2-(N-Butylanilino)-3-(n-pentyl)pyrazine, Interaction of 2-Anilino-3-methylpyrazine with Sodium Amide and 1-Bromobutane in Pyridine 153

2-(N-Methylanilino)-3-(2-phenylethyl)pyrazine. 153

2-Anilino-3-(n-pentyl)pyrazine 154

Approved for Public Release

Contrails

TABLE OF CONTENTS (continued)

	Page
2-(N-Butyl-p-pentylanilino)-3-(n-pentyl)pyrazine	154
2-(N-Methylanilino)-3-(n-hexyl)pyrazine	154
2-(N-Methylanilino)-3-(9-heptadecyl)pyrazine	155
2-(N-n-Hexylanilino)-3-(n-heptyl)pyrazine	155
2-(N-Methylanilino)-3-(n-pentyl)-6-(5-nonyl)pyrazine	155
2-(N-Methylanilino)-3-(n-pentyl)-6-(n-heptyl)pyrazine	155
E. 2-Anilino-6-substitutedpyrazines	156
2-(N-Methylanilino)-6-(5-nonyl)pyrazine	156
F. 2-Alkylamino-3-substitutedpyrazines and 2-Alkylamino-3,6-disubstitutedpyrazines	156
General Procedure	156
2-(N,N-Di-n-butylamino)-3-(n-pentyl)pyrazine and 2-(N,N-Di-n-butylamino)-3-(5-nonyl)pyrazine	156
2-(N,N-Di-n-pentylamino)-3-(n-pentyl)pyrazine	157
2-(N-n-Butyl-N-n-hexylamino)-3-(5-nonyl)pyrazine	157
2-(N,N-Di-n-hexylamino)-3-(n-heptyl)pyrazine	157
2-(N-n-Hexyl-N-n-octylamino)-3-(n-nonyl)pyrazine	157
2-(N,N-Di-n-hexylamino)-3-(n-pentyl)-6-(n-heptyl)pyrazine	158
Attempted Preparation of 2-(N,N-Di-n-pentylamino)-3-(n-pentyl)-6-(n-heptyl)pyrazine	158
G. Alkylpyrazines	158
General Procedure	158
2-n-Heptyl-5-n-pentylpyrazine	158
2-n-Heptyl-5-n-nonylpyrazine	159

Approved for Public Release

Contrails

TABLE OF CONTENTS (continued)

Page

2-n-Heptyl-6-n-pentylpyrazine 159

2-n-Heptyl-6-n-nonylpyrazine 159

2,5-Di-n-nonylpyrazine 159

2,6-Di-n-nonylpyrazine 160

2,5-Di-(5-nonyl)pyrazine 160

2-n-Pentyl-6-(5-nonyl)pyrazine and 2,6-Di-(5-nonyl)-pyrazine 160

1,4-Bis[2-(5-n-heptylpyrazyl)]butane 161

1,4-Bis[2 (6-n-heptylpyrazyl)]butane 161

1,4-Bis[2-(5-n-nonylpyrazyl)]butane. 161

1,4-Bis[2-(6-n-nonylpyrazyl)]butane. 162

IV. MODEL REACTIONS. 162

Attempted Preparation of (Phenyldimethylsilylmethyl)-pyrazine, Treatment of Pyrazylmethylsodium with Phenyldi-methylsilane 162

(Phenyldimethylsilylmethyl)pyrazine. 162

Attempted Interaction of Pyrazylmethylsodium with Dimethyl-dichlorosilane 163

Attempted Reaction of Methylpyrazine with 1,2-Diphenyl-tetramethyldisilane and Lithium. 163

Attempted Preparation of p-Phenyldimethylsilylbenzyl-pyrazine, Benzylpyrazine and Benzhydrylpyrazine. 164

Attempted Amination of (p-Chlorobenzyl)trimethylsilane . . . 164

(5-Nonyl)pyrazine and (Tributyl)methylpyrazine 165

(2-Phenylethyl)pyrazine. 165

Approved for Public Release

Contrails

TABLE OF CONTENTS (continued)

	Page
n-Pentylpyrazine	165
Phenacylpyrazine	166
SUMMARY AND CONCLUSIONS	167
APPENDIX - INFRARED SPECTRA	172
INDEX OF INFRARED SPECTRA	173
BIBLIOGRAPHY	230

Approved for Public Release

Contrails

LIST OF TABLES

Table No.		Page
1	Classification of Pyrazine Derivatives	5
2	Thermal Stability of 2-Phenoxy-3(or 6)-substitutedpyrazines. . .	25
3	Thermal Stability of 2-Phenoxy-3,6-disubstitutedpyrazines. . . .	28
4	Thermal Stability of 2-Amino-3-substitutedpyrazines.	30
5	Thermal Stability of 2-Amino-3,6-disubstitutedpyrazines.	32
6	Thermal Stability of 2-Alkoxy-3(and 3,6-di)-substituted-pyrazines.	33
7	Thermal Stability of Dialkyl Pyrazines	35
8	Thermal Stability of 1,4-Bis(substitutedpyrazyl)butanes and of Mil-L-9236 Fluids.	36
9	Oxidative Stability of Pyrazine Derivatives (2,3-Disubstituted-pyrazines)	40
10	Oxidative Stability of Pyrazine Derivatives (2,5- and 2,6-Di-substitutedpyrazines) and Mil-L-9236 Fluids.	43
11	Lubricity of Pyrazine Derivatives and Mil-L-9236 Fluids.	44
12	2-Phenoxy-3-methylpyrazines and 2-Phenoxy-3,6-dimethylpyrazines.	46
13	2-Alkoxy-3-methylpyrazines and 2-Alkoxy-3,6-dimethylpyrazines. .	54
14	2-Anilino-3-methylpyrazines.	57
15	2-Anilino-3,6-dimethylpyrazines.	63
16	2-(N-Alkylamino)-3-methylpyrazines	65
17	2-N-Alkylamino-3,6-dimethylpyrazines	67
18	Alkyl(methyl)pyrazines	69
19	2-Phenoxy-3-methyl-6-substitutedpyrazines.	71
20	2-Alkoxy-3-methyl-6-substitutedpyrazines	76

Approved for Public Release

Contrails

LIST OF TABLES (continued)

Table No.		Page
21	2-Anilino-3-methyl-6-substitutedpyrazines and 2-Alkylamino-3-methyl-6-substitutedpyrazines	78
22	2-Phenoxy-3-benzylpyrazines	80
23	2-Phenoxy-3-alkylpyrazines	83
24	2-Phenoxy-6-substitutedpyrazines	88
25	2-Alkoxy-3-substitutedpyrazines and 2-Alkoxy-3,6-disubstitutedpyrazines	89
26	2-Anilino-3-substitutedpyrazines	92
27	Ultraviolet Spectra	96
28	2-Alkylamino-3-substitutedpyrazines	98
29	Alkylpyrazines	101

Approved for Public Release

Contrails

Approved for Public Release

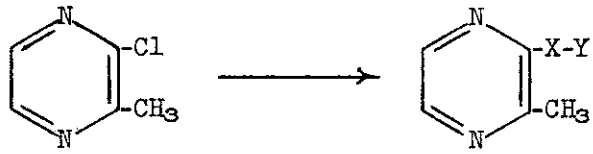
Contrails

INTRODUCTION

The objective of this program is the preparation of new pyrazine derivatives for gas turbine lubricant applications.

The theoretical foundation for consideration of pyrazine derivatives for prospective use in this application is discussed in detail in an earlier report (1) describing the initial phase of this program. Briefly, it is based upon the generally high thermal stability associated with aromatic compounds and the desirable properties of known pyrazine derivatives. Not the least of the considerations in undertaking this program has been the recent availability of highly versatile pyrazine starting materials which were expected to allow the introduction of a variety of substituents on the pyrazine nucleus. The proper substituents and their optimum arrangement were hoped to afford materials to meet the target requirements. Results obtained in the initial period of this study gave encouragement to the possibility of achievement of this program's objectives. Therefore, this investigation has continued generally along the initially proposed lines.

The original approach selected has been the development of various synthetic routes for unsymmetrically di- and tri-substituted pyrazines with substituents selected for their expected contribution to desirable properties. Simultaneously, it was proposed to determine the physical properties of the resulting pyrazine compounds to guide the continuing synthesis effort. Starting with 2-chloro-3-methylpyrazine in the initial phase of this program (1), success was met in the displacement of the chlorine radical by various nucleophilic displacement reagents, such as phenols, thiophenols, and anilines. The preparation of silylpyrazines was also accomplished by a magnesium coupling reaction between 2-chloro-3-methylpyrazine and a chlorosilane. Further modifications of these intermediates on the methyl



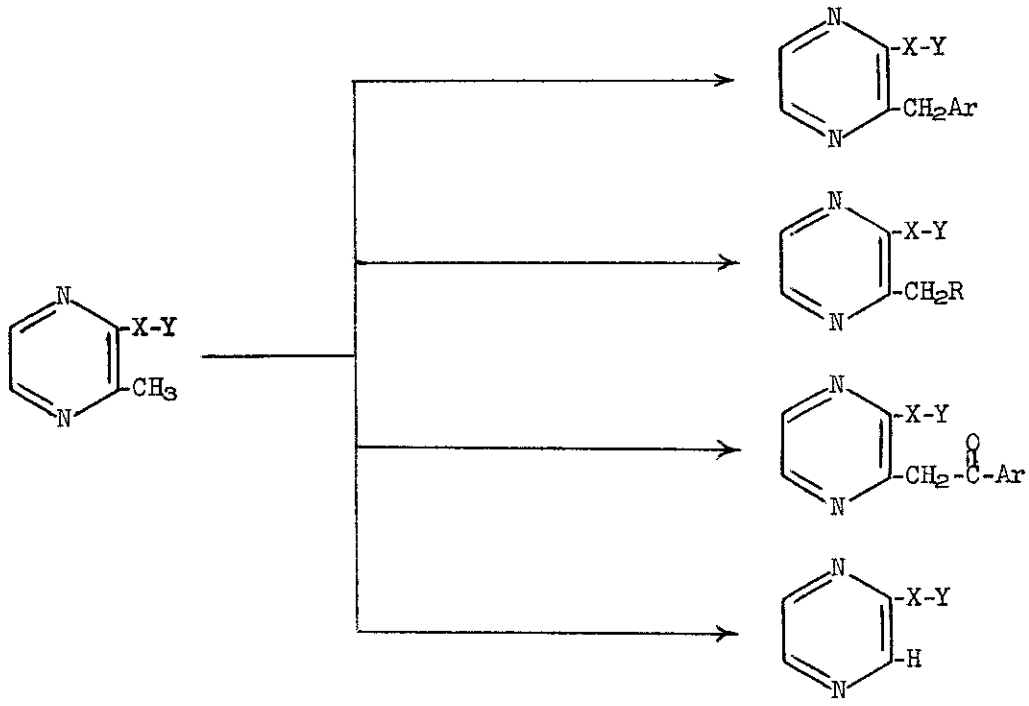
where X = O, S, $\overset{H}{\underset{|}{N}}$, Si
Y = phenyl and substituted phenyl

Manuscript released by the authors 14 November 1961 for publication as an ASD Technical Report.

Approved for Public Release

Contrails

site were also successful to give phenylated, alkylated, acylated, and demethylated products. Simultaneously, a parallel study of the physical properties, such as thermal and oxidative stabilities, and fluid characteristics, with different linkages could be established. Based on the results of such a study, some highly undesirable linkages have been eliminated at an early date and the synthetic efforts were thus directed towards most fruitful areas in leading to final products with the desired properties.

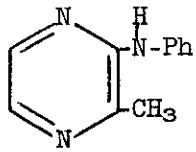


Based on the previous reported stability studies (1) of 2-substituted-3-methylpyrazines, the 2-thiophenoxy-3-methylpyrazines generally underwent decomposition at below 500°F. Members of the 2-phenoxy-, 2-anilino, and 2-silyl-3-methylpyrazine classes, however, showed good thermal stability at 500°F. Specifically, the representatives of the 2-phenoxy-3-methylpyrazine class were readily available due to ease of preparation. Extension in synthetic scope for this class of compound was undertaken to include new members with different substituents.

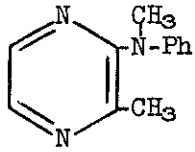
The 2-anilino-3-methylpyrazine class of compounds, although thermally stable, suffered the disadvantage of being mostly solid derivatives (1). This was attributed to hydrogen bonding and association due to the presence of a free N-H group in the molecule. However, when the hydrogen was replaced by a methyl group, the resulting 2-(N-methylanilino)-3-methylpyrazine was a high fluid liquid. Therefore, some emphasis during the present report period was placed on the preparation of 2-(N-alkylanilino)-3-methylpyrazines.

Approved for Public Release

Contrails



m.p. 92-94°C

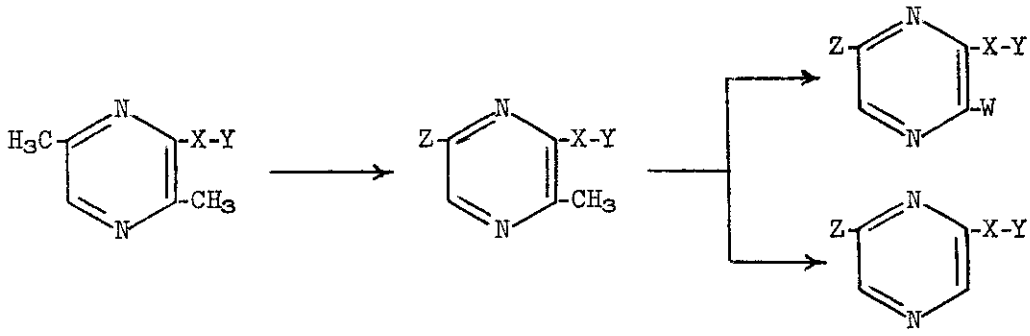


Viscosity 11.70 centistokes at 100°F

Two representatives of the 2-silyl-3-methylpyrazine class prepared so far exhibited good fluid properties. Inasmuch as the magnesium coupling method afforded these compounds in only moderate yields and the position of substitution was limited to the 2-position of the pyrazine nucleus, it was desirable to investigate other methods such as the "azomethine" addition reaction (3) for placing the silyl radical on other positions of the pyrazine nucleus. In addition, new classes of 2-substituted-3-methylpyrazines, the 2-substituent being alkoxy and alkylamino, were believed to be worthy of preparation, thus allowing their physical properties to be investigated and compared to their aromatic analogs.

Introduction of groups on the methyl site of 2-substituted-3-methylpyrazine via phenylation, alkylation, and acylation, to furnish 2,3-disubstitutedpyrazines has been accomplished previously (1). Optimum reaction conditions as well as scope of these reactions were deemed worthy of investigation for obvious reasons. Furthermore, the reactions involving the methyl site have been exclusively performed in a sodium amide-liquid ammonia system. Earlier attempts at variation of metalation agents and solvent media were unsuccessful. Further investigation of this type of reactions was of interest in order that the scope of the reaction might be broadened to allow utilization of reagents which are not compatible with liquid ammonia.

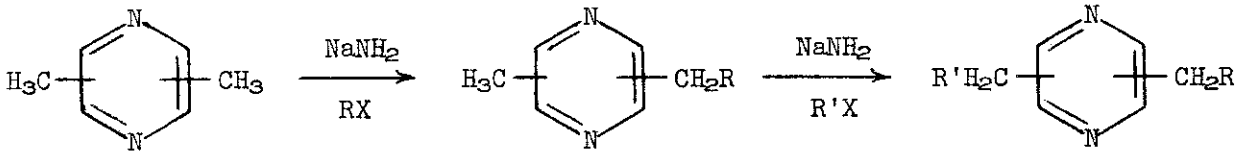
Starting with 2-chloro-3,6-dimethylpyrazine and performing a similar sequence of reactions to that with 2-chloro-3-methylpyrazine, only one representative of the 2,6-disubstituted-3-methylpyrazine group had previously been prepared (1). Preparation of additional members of this group would be of interest, since further reaction on the remaining methyl site of these compounds should lead to 2,3,6-trisubstitutedpyrazines and selenium dioxide demethylation to 2,6-disubstitutedpyrazines.



Approved for Public Release

Contrails

An additional preparative area of interest that was contemplated for investigation in the current report period was the simple alkylpyrazines. Conditions for the alkylation of methylpyrazine with alkyl halides in the presence of sodium amide and liquid ammonia have been developed (4) to furnish alkylpyrazines in up to 80% yield. Starting from the readily available 2,5- (and 2,6-)dimethylpyrazines and tetramethylpyrazine, various alkyl groups could conceivably be placed on these methyl sites to result in high molecular weight, fluid compounds.



As stated earlier, a number of pyrazine derivatives have demonstrated excellent thermal stability at 500°F as well as oxidative stability at 400°F. In order that further screening of various classes of compounds could be accomplished, thermal and oxidative stability tests at elevated temperatures were initiated. When sufficiently stable pyrazine derivatives were developed, a comparison of their physical properties to that of the Mil-L-9236 Base Stock and Formulation fluids was undertaken.

As a result of the vast number of widely different pyrazine derivatives which have been prepared and which are contemplated for the future, it has been necessary to classify these materials for convenience of reference. Thus, the pyrazine compounds are divided into major categories, groups, and classes based on their use and degree of substitution. This classification system is illustrated in Table 1 and will be followed in future reports on this program.

Approved for Public Release

Contrails

TABLE 1

CLASSIFICATION OF PYRAZINE DERIVATIVES

Major Categories	Groups	Classes
Starting Materials		2-Chloro-3-methylpyrazine 2-Chloro-3,6-dimethyl-pyrazine Methylpyrazine 2,5-Dimethylpyrazine 2,6-Dimethylpyrazine Tetramethylpyrazine
Initial Intermediates	2-Substituted-3-methyl-pyrazines	e.g., 2-Phenoxy-3-methyl-pyrazines, 2-anilino-3-methylpyrazines, etc.
	2-Substituted-3,6-di-methylpyrazines	e.g., 2-Phenylmercapto-3,6-dimethylpyrazines, 2-silyl-3,6-dimethylpyrazines, etc.
Advanced Intermediates	2-Substituted-x-methyl-x'-substitutedpyrazines	e.g., 2-Phenoxy-3-methyl-6-alkylpyrazines, 2-anilino--3-methyl-6-phenylethyl-pyrazines, etc.
Candidate Products	Monosubstituted pyra-zines	e.g., Phenoxypyrazines
	2,3-Disubstituted-pyrazines	e.g., 2-Silyl-3-benzylpyra-zines, etc.
	2,6-Disubstituted-pyrazines	e.g., 2-Anilino-6-alkyl-pyrazines, etc.
	2,3,6-Trisubstituted-pyrazines	e.g., 2-Phenoxy-3,6-dialkyl-pyrazines, etc.
	2,3,5,6-Tetrasubstitu-tedpyrazines	e.g., Tetraalkylpyrazines

Approved for Public Release

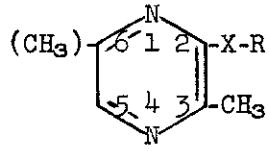
Contrails

DISCUSSION

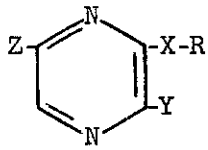
PROPERTIES OF PYRAZINE DERIVATIVES

The physical properties of the compounds being prepared are of prime importance to this program's objectives. Therefore, considerable emphasis has been placed upon the examination of properties of the intermediates as well as candidate products that have been synthesized to date. The properties which are significant for the intended application of these materials are fluidity, thermal stability, oxidative stability and lubricity. Measurements on these properties have been made and are described below. Each property is considered separately and some interpretation of the effect of structure variations upon this property is attempted in order to help guide the future synthesis effort.

In our preceding report (1), major emphasis was devoted to a study of the properties of the initial intermediates (for which synthetic routes were being developed). These intermediates contained substituents at the 2-position of the pyrazine nucleus linked by the hetero-atoms, O, S, N and Si, along with methyl groups at either the 3- or the 3- and 6-positions.



Initial screening tests for thermal and oxidative stability helped to eliminate the sulfur hetero-atom linkage from futher consideration at an early stage in the synthesis program. The intermediates from the remaining acceptable classes have now been further modified at the methyl sites to provide advanced intermediates and candidate products (see Introduction).



These resultant materials have been examined to determine the effect of these modifications on the different properties. Of considerable significance is the fact that these higher molecular weight materials possess sufficiently high boiling points to be tested for their thermal and oxidative stability at higher temperatures.

In the consideration of the properties below, attention is given to the effects arising from the different type of substituents as well as to the relative positions occupied by these substituents on the pyrazine nucleus. For the purpose of

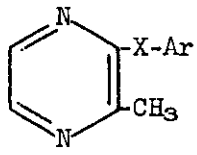
Approved for Public Release

Contrails

organization, the different classes of compounds are considered separately and comparisons are made within each class and then between the classes as a whole.

Fluidity

The term fluidity as it is used here applies to the liquid character of the materials in question. An effort is made below to interpret to what extent the type of the substituent influences the fluidity of the molecule. For example, from a comparison of the initial intermediates in the previous report (1) some conclusions were drawn regarding the tendency of each general class of intermediate to form either crystalline or liquid materials, and as to whether the liquids tended to be highly mobile or viscous. The different classes of intermediates were 2-(phenoxy, mercapto, amino and silyl)-3-methylpyrazines. The phenoxy compounds were generally moderately viscous liquids; the corresponding mercapto compounds tended to be more crystalline solids; the arylamino derivatives which contained a free N-H were solids, whereas, similar compounds with N-CH_3 were liquids and finally the silyl intermediates were mobile fluids. This general relationship is illustrated below.



$X = Si(CH_3)_3 \langle N(CH_3) \langle O$ $\qquad$ $S \langle NH$

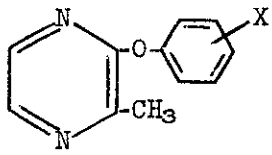
liquids, viscosity ⟶ $\qquad$ solids, m.p. ⟶

In the following discussion, these and other intermediates will be considered but emphasis will be placed on the effect upon fluidity produced by conversion of the intermediates to candidate products with different substituents. Interpretation will be given to the influence of the substituents within each class of intermediate and candidate products as well as to a further comparison of the different classes.

2-Phenoxy-3(and 6)-substitutedpyrazines and 2-Phenoxy-3,6-disubstitutedpyrazines. As concluded from our earlier studies (1), the 2-phenoxy-3-methylpyrazine initial intermediates were generally liquid materials. However, the secondary substituent on the phenoxy group was found to influence the liquid character of these compounds in a manner shown by the relationship below.

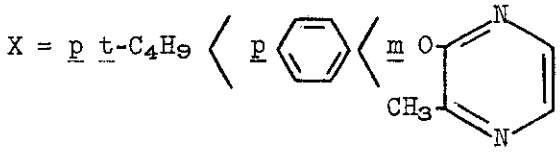
Approved for Public Release

Contrails



X = p CH_3 < m OCH_3 < m O- < p $C_{12}H_{25}$ < o

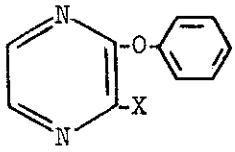
liquids, viscosity ⟶



X = p t-C_4H_9 < p < m O

crystalline solids, m.p. ⟶

Having modified these intermediates further at the methyl site to provide 2-phenoxy-3-substitutedpyrazine candidate products, a comparison of the effect of the various substituents placed on the methyl site can now be made. The viscosities (ranging from 21 to 4178 centistokes at 100°F) and/or melting points of these compounds are shown in Table 2 (see p. 25). When the phenoxy group was unsubstituted the effect of the 3-substituent upon the fluidity of this class of materials followed the order shown below.



X = $CH(C_4H_9)_2$ < CH_2- < CH_2-O- < CH_2-

liquids, viscosity ⟶

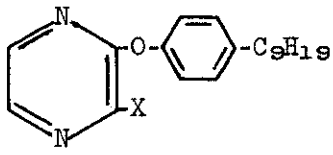
X = $(CH_2)_{12}$-CH_3 < CH_2-CH_2-

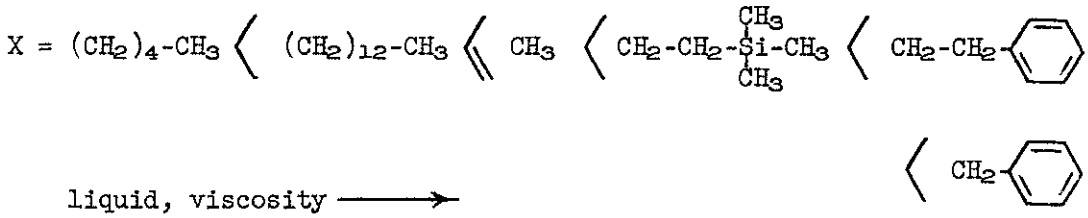
solids, melting point ⟶

When the 2-phenoxy group was substituted with a p-t-nonyl substituent and the methyl group was modified with a series of substituents similar to that above, a somewhat similar order of fluidity was observed. Note should be taken of the

Approved for Public Release

Contrails

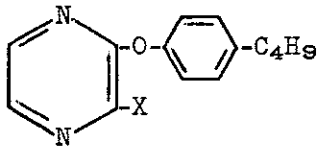


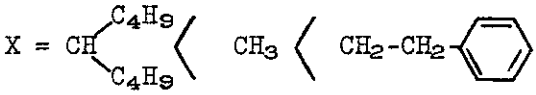


liquid, viscosity ⟶

positions occupied in this order by the two substituents that provided solid derivatives in the preceding sequence (namely, the β-phenylethyl and the n-tridecyl groups). These relatively large substituents appear to contribute to the crystallinity of the smaller molecule of the former series whereas they have less drastic effects on the viscosity of the larger molecule of the latter series.

A further comparison of the effect of some of these same substituents in the 3-position is evident in three examples of compounds where the 2-phenoxy group is substituted with a p-t-butyl function. Although two of these compounds are solids, the order of their melting points corresponds well with the above sequence.



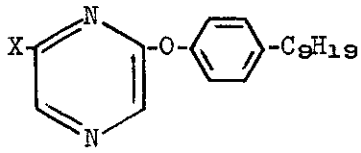


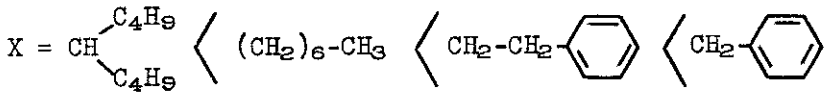
liquid, solids, melting point ⟶

It is interesting to compare the fluid properties of the series of 2-p-nonylphenoxy-3-substitutedpyrazines to a series of their positional isomers, the 2-p-nonylphenoxy-6-substitutedpyrazines. The 2,6-compounds are all liquids which exhibit the same general order of fluidity as shown by their corresponding 2,3-isomers.

Approved for Public Release

Contrails

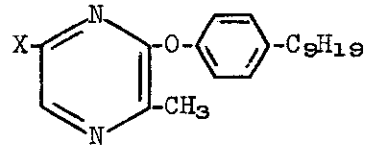


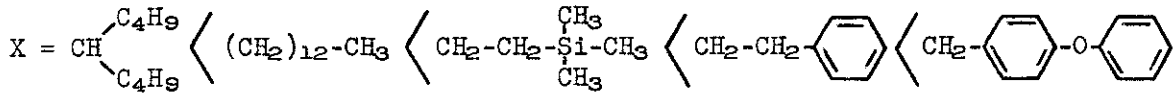


liquids, viscosity ⟶

Based on the above discussion, several generalizations regarding the effect of structure upon the fluid properties of the 2-phenoxy-3- and 6-substitutedpyrazines can be concluded. The 2,6-compounds display slightly lower viscosities than their corresponding 2,3-isomers. The type of substituents on the 3-position show a consistent order of influence on fluidity which is not greatly altered by the secondary substituent on the phenoxy group. That is, aliphatic groups in the 3(or 6)-position generally lower the viscosity of the parent compound and this effect is more pronounced with smaller aliphatic groups. The β-trimethylsilylethyl group shows about the same effect on viscosity as does a methyl group. Aromatic substituents on the 3-methyl site generally increase viscosity and tend to favor crystallinity. The p-biphenyl group appears to have the greatest effect in this direction of all the aromatic substituents that have been studied. The m-phenoxybenzyl, benzyl and β-phenylethyl groups show diminished influences on viscosity, in approximately that order. Thus, as one might expect, the best fluid properties in this series have been achieved by the introduction of optimum sized aliphatic groups on the 2-phenoxy substituent and at the 3(or 6)-position.

Some interesting comparisons can be made between the above 2-phenoxy-3(and 6)-substitutedpyrazines and the related series of 2-phenoxy-3,6-disubstitutedpyrazines (Table 3, p. 28). Most of the compounds prepared and examined in this family have an unsubstituted 3-methyl group and so these compounds are most closely related to the 2-phenoxy-6-substitutedpyrazines. The order of fluidity of a series of 2-(p-nonylphenoxy)-3-methyl-6-substitutedpyrazines is shown below. This order is similar to the orders shown by the corresponding 2-(p-nonylphenoxy)-3-(and 6)-substitutedpyrazines. The viscosities of the individual 2,3,6-compounds are generally





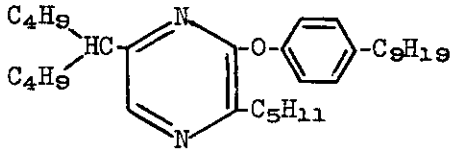
liquids, viscosity ⟶

Approved for Public Release

Contrails

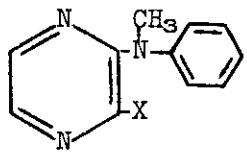
higher than their 2,6-homologs and in some cases higher than their 2,3-homologs. Thus, the added methyl group appears to result in a small viscosity increase although it does not seriously alter the magnitude of the effects of the other substituents.

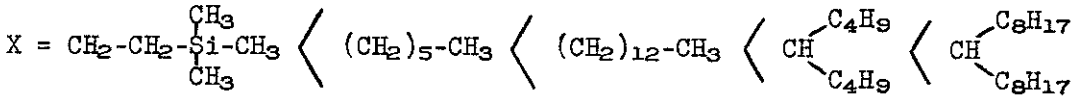
One representative of a 2-phenoxy-3,6-disubstitutedpyrazine where the substituents on the 3- and 6-positions are aliphatic groups, namely, 2-(p-nonylphenoxy)-3-pentyl-6-(5-nonyl)pyrazine, is available at this stage for a comparison with the above compounds. This highly substituted compound is a relatively fluid material



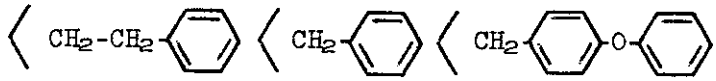
(88 centistokes at 100°F) in comparison with some equivalent molecular weight pyrazine derivatives containing aralkyl substituents.

2-Amino-3-substitutedpyrazines and 2-Amino-3,6-disubstitutedpyrazines. In the arylamino members of these classes, mention has already been made of the fact that intermediates containing the N-CH_3 function showed considerably improved fluid properties over the compounds having an N-H linkage. A number of 2-(N-methylanilino)-3-substitutedpyrazine candidate products were therefore prepared in an effort to achieve materials with good fluid properties. This family of compounds was found to possess the expected generally good fluid characteristics and exhibited considerably lower viscosities than their analogous 2-phenoxy-3-substitutedpyrazines (Table 4, p. 30). The variation of viscosities with the different substituents in the 3-position is shown below.





liquids, viscosity ⟶

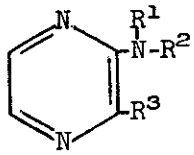


Approved for Public Release

Contrails

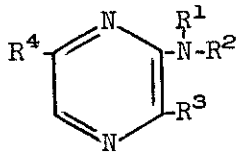
The order of the first four substituents differs slightly from that encountered with these same substituents in the phenoxypyrazines. However, the viscosities of these four compounds are relatively low (ranging from 18 to 39 centistokes at 100°F) and differ by only small amounts and so their order is not of great significance. However, it is significant that the viscosities of the compounds having aliphatic groups are considerably lower than those with the aromatic containing substituents (up to 3909 centistokes at 100°F); again showing the favorable effect of the aliphatic groups upon fluidity.

The general enhancement of liquid properties by the introduction of aliphatic groups is exemplified even more markedly in the low viscosities (ranging from 9 to 20 centistokes at 100°F) shown by all the members of a series of 2-dialkylamino-3-alkylpyrazines (Table 4, p. 31).



R^1, R^2, R^3 = aliphatic groups

A number of 2-amino-3,6-disubstitutedpyrazines have also been prepared in which the amino groups are either N-methylanilino or dialkylamino functions and where the 3- and 6-substituents are methyl or aliphatic groups. All of these compounds exhibited relatively low viscosities (Table 5, p. 32), with the purely aliphatic member having a relatively low viscosity (23 centistokes) in comparison to the arylamino compounds of equivalent molecular weight (23 to 39 centistokes).



R^1 = phenyl or aliphatic group
R^2 = methyl or aliphatic group
R^3 = methyl or aliphatic group
R^4 = aliphatic group

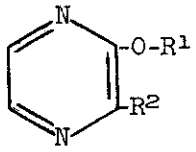
One representative which can be considered to be fully substituted with aliphatic groups, viz., 2-(N,N-dipentylamino)-3-pentyl-6-heptylpyrazine, also conformed to this pattern and displayed a low viscosity (23.22 centistokes at 100°F).

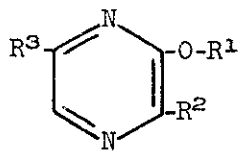
2-Alkoxy-3-substitutedpyrazines and 2-Alkoxy-3,6-disubstitutedpyrazines. Having observed the general moderately high viscosity of the phenoxypyrazines as well as their thermal instability (see p. 19), attention was turned to an examination of some analogous alkoxypyrazines. A series of 2-alkoxy-3-alkylpyrazines

Approved for Public Release

Contrails

and 2-alkoxy-3,6-dialkylpyrazines (Table 6, p. 33) were found to be good fluids with even lower viscosities (13 to 19 centistokes) than some of the comparable molecular weight 2-alkylamino-3-alkylpyrazines and 2-alkylamino-3,6-dialkylpyrazines.

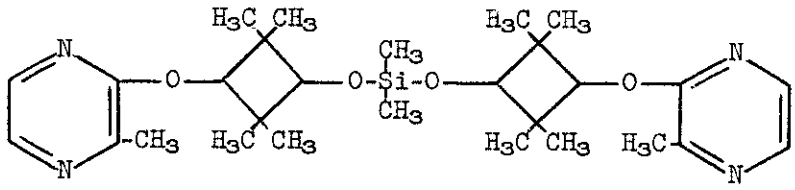




R^1, R^2, R^3 = aliphatic groups

The alkoxy groups in these compounds are 2,2-dimethylpentoxy and 2,2,4-trimethylpentoxy, which were selected because they have no hydrogen atoms attached to the carbon beta with respect to the oxygen and were expected to afford maximum thermal stability (see p. 22). The alkyl substituents in the 3- and 6-positions are similar to those in the other classes of compounds described above.

One compound from the class under consideration possesses a large bulky difunctional alkoxy group linked to two pyrazyl radicals, viz., bis-{3-[2-(3-methylpyrazoxy)]-2,2,4,4-tetramethyl-1-cyclobutoxy}dimethylsilane. This compound has a



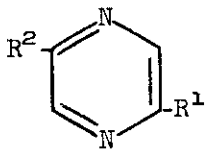
viscosity which is relatively high compared to the other members of this family (124.89 centistokes at 100°F) but which is low relative to some equivalent molecular weight phenoxypyrazines.

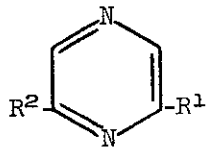
Based on the representatives of this family which have been prepared and examined, the alkoxypyrazines appear to afford materials with suitable fluid properties.

Dialkylpyrazines and 1,4-Bis(alkylpyrazyl)butanes. The desirable fluid properties found to be associated with the aliphatic substituents in all of the preceding classes prompted the preparation and examination of some simple alkylpyrazines. A series of 2,5- and 2,6-dialkylpyrazines with different aliphatic groups were found to be excellent liquid materials (Table 7, p. 35) with lower viscosities than any of the previously studied classes of pyrazine derivatives. The viscosities of the compounds examined ranged from 8 to 11 centistokes (at 100°F). One exception to this character was found in the case of the highly symmetrical compound 2,5-di(5-nonyl)pyrazine, which is a low-melting crystalline solid.

Approved for Public Release

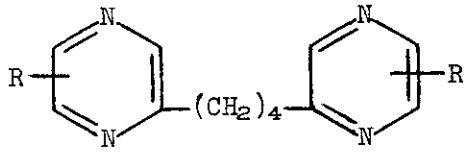
Contrails





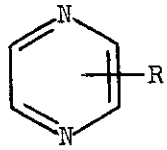
R^1, R^2 = aliphatic groups

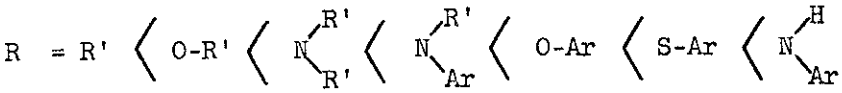
Since the dialkylpyrazines provided materials of exceptionally good fluid character, a small number of 1,4-bis(alkylpyrazyl)butanes was prepared in hopes of obtaining higher molecular weight (thus, higher boiling) derivatives which might also possess good fluid properties. The expected result was achieved only in part



since one of the members, 1,4-bis[2-(5-n-heptylpyrazyl)]butane, was a liquid (viscosity 23 centistokes at 100°F); while three other members were low-melting solids (m.ps. from 40 to 78°C). The tendency towards crystallinity of these compounds can be attributed to the larger straight chain substituents and to the more symmetrical structures.

Conclusions Regarding Fluidity. In conclusion, regarding fluidity of the pyrazine derivatives as a function of the substituents, a general order of substituent effect upon increasing fluidity (or decreasing viscosity) appears to be indicated as shown below. Thus, the alkylpyrazines appear to offer the best fluid





viscosity or crystallinity ⟶

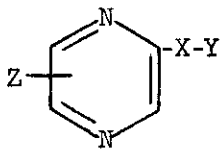
R' = alkyl group
Ar = aryl group

properties followed by the alkoxy, dialkylamino and N-alkyl-N-arylamino pyrazines in that sequence. The remaining phenoxy, thiophenoxy and anilinopyrazines offer little hope of providing materials having the required fluidity.

Approved for Public Release

Contrails

The di- and tri-substituted pyrazines which contain one of the hetero-atom linkages above also contain alkyl or aralkyl substituents. As pointed out earlier,



X = hetero-atoms, e.g., O, S, N
Y and Z = alkyl or aralkyl group

the aliphatic substituents provided better fluidity properties than any of the aralkyl groups, in any of the different classes. It is therefore concluded that the polyalkyl substituted pyrazines can be expected to offer the best possibility of achieving the fluidity properties necessary to meet the target requirements for this program.

Thermal Stability

If one property could be designated as the most important single feature which is desirable for the intended application, it would probably be thermal stability. This is because thermal stability is grossly related to another important property, oxidative stability (2); furthermore, one can also assume that once a suitable basic molecular skeleton of high thermal stability has been achieved, minor adjustments in structure can probably be made to improve the fluidity and other properties if necessary. For this reason close attention has been paid to the thermal stability of intermediates as well as candidate products synthesized in this program.

Most of the materials prepared in the initial period of this program (1) were relatively low molecular weight intermediates intended for subsequent conversion to candidate products; or they were model compounds prepared to demonstrate reaction feasibility and to study the physical properties associated with various linkages. Preliminary thermal stability studies were initiated on these materials in an effort to obtain a proper correlation of structure and properties and to screen out the most undesirable functionalities at an early stage. These compounds were tested at 500°F (for 9 hours, under N_2). The mercapto linkage to the pyrazine

Initial Intermediates Candidate Products

X = O, S, N-R'(H)

Approved for Public Release

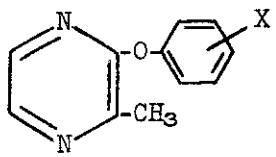
Contrails

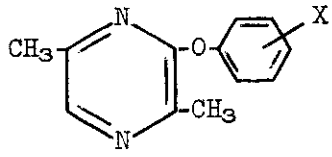
nucleus was found to be generally unstable (1). The intermediates containing the remaining linkages, which were stable at 500°F, have now been further modified to provide candidate products available for continued testing. The intermediates prepared in the initial period of this program were not tested at temperatures above 500°F due to their volatility at appreciably higher temperatures. Since the materials synthesized in the current period are higher molecular weight compounds, (thus higher boiling), testing has been continued at elevated temperatures (600° and 700°F). The target properties for materials arising from this project include good thermal stability at ambient temperatures of 500-550°F for prolonged periods of time. This requirement, therefore, demands that candidate products exhibit appropriate stability on exposure for shorter periods of time at elevated temperatures.

The thermal stability test was conducted by heating the sample (approximately 1-1.5 g.) contained in a glass tube (with a nitrogen atmosphere flowing over the sample at the rate of 2 liters per hour) at the desired temperature (500°, 600°, or 700°F) in an air-bath furnace for a 9-hour period. The sample was weighed before and after the test and the percent weight loss registered. Color change was also noted, along with change in viscosity at 100°F (or melting point for the solid samples) and any change in the infrared spectrum of the compound.

As in the case of fluidities, correlation of the effect of changes in structure upon thermal stability was attempted. Consequently, the results of the thermal stability tests have served as the most important single guide to the synthesis aspect of this program. The successful stepwise achievement of candidate products with continually improved properties has confirmed the soundness and validity of this approach.

2-Phenoxy-3(and 6)-substitutedpyrazines and 2-Phenoxy-3,6-disubstitutedpyrazines. A series of 2-phenoxy-3-methylpyrazines and a few 2-phenoxy-3,6-dimethylpyrazines were examined for their thermal stability at 500°F during the first-year period of this program (1). These compounds exhibited generally good to excellent stability at this temperature. Now that these initial intermediates have been





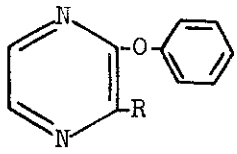
further modified at their methyl sites to provide higher molecular weight advanced intermediates and candidate products, testing was continued with the intention of determining the effect of the new substituents and in an effort to establish the stability of these classes of compounds at higher temperatures.

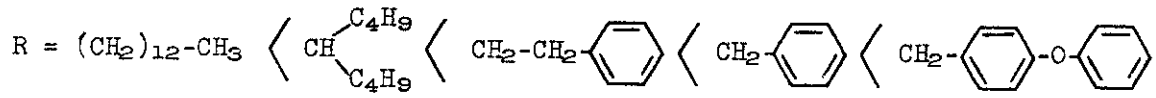
A series of 2-phenoxy-3-substitutedpyrazine candidate products derived from the appropriate 2-phenoxy-3-methylpyrazine intermediates is shown in Table 2 (p. 25). The first six members of this class have no secondary substituent on the

Approved for Public Release

Contrails

2-phenoxy group and have aralkyl or alkyl groups at the 3-position. Considerable difference in the stability of five of these compounds was observed at a test

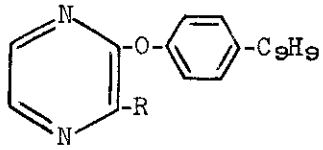


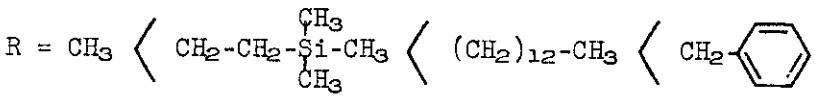


Extent of thermal decomposition at 500°F ⟶

temperature of only 500°F. The representatives bearing an aralkyl group in the 3-position were found to be less stable than those with corresponding alkyl groups. One member, 2-phenoxy-3-(p-phenylbenzyl)pyrazine was tested at 600°F and showed a high degree of instability.

Another series of 2-phenoxy-3-substitutedpyrazines which include enough members for a comparison of the effect of the substituents are the 2-(p-t-nonyl-phenoxy)-3-substitutedpyrazines (Table 2, p. 26). The members which have been tested at 500°F showed approximately the same order of influence as found in the above series. The 2-(p-t-nonylphenoxy)-3-substitutedpyrazines which were tested at





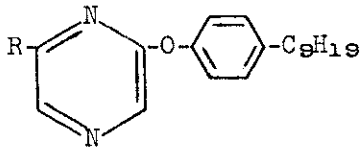
Extent of thermal decomposition at 500°F ⟶

600°F all exhibited significant instability at this temperature. Note should be taken of the fact that all of the compounds examined at 600°F showed the presence of carbonyl absorptions in their infrared spectra after the tests. The significance of this fact is discussed later in this section (see p. 19).

Approved for Public Release

Contrails

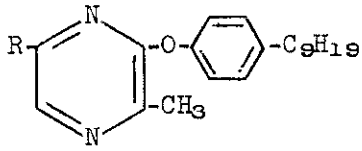
A group of compounds which are isomeric with the preceding series are the 2-(p-t-nonylphenoxy)-6-substitutedpyrazines. The four compounds of this class which



R = $(CH_2)_{12}$-CH_3, CH(C_4H_9)(C_4H_9), CH_2-CH_2-C_6H_5, CH_2-C_6H_5

were tested for thermal stability at 600°F exhibited no apparent improvement over their 2,3-isomers. Two of these compounds could not be examined for their viscosity after the test due to insufficient samples. The other two compounds whose viscosity after the test could be measured showed significant changes. All of these materials, however, exhibited the appearance of a carbonyl band in their infrared spectra after the tests. Thus, it appears that changing the relative positions of the substituents from 2,3- to 2,6- did not improve the thermal stability of the phenoxy substituted pyrazines.

A class of compounds which are homologous with the preceding series are the 2-(p-t-nonylphenoxy)-3-methyl-6-substitutedpyrazines shown in Table 3 (p. 28). These compounds differ from that above in having an additional methyl group at the 3-position and represent advanced intermediates which were intended to be used to prepare 2-phenoxy-3,6-disubstituted-candidate products. Examination of the thermal stability of this group of materials showed them to have approximately the same relative order of stability as the isomers of their homologs at 500°F. The alkyl substituted members displayed good stability at this temperature, however, the aralkyl substituted members did not. The compounds of this class all exhibited appreciable instability when tested at 600°F. The extent of the viscosity changes, however, indicated the same relative order of stability at 600°F as at 500°F. It



R = CH(C_4H_9)(C_4H_9) ≪ $(CH_2)_{12}$-CH_3 ≪ CH_2-CH_2-Si(CH_3)(CH_3)-CH_3 < CH_2-CH_2-C_6H_5 < CH_2-C_6H_4-O-C_6H_5

Extent of thermal decomposition at 500°F ⟶

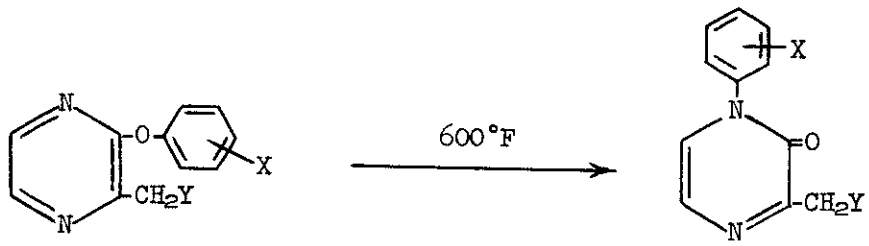
should be noted again, that after testing at 600°F, all of the compounds showed amide carbonyl absorption bands (5) in their infrared spectra.

Approved for Public Release

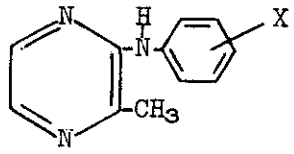
Contrails

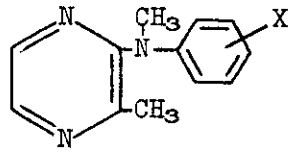
The results of the thermal stability tests on the phenoxypyrazines indicate that certain members possessed good to excellent stability at 500°F but none of the compounds could withstand the 600°F test conditions. Thus, 600°F appeared to be a ceiling temperature for the thermal stability of the phenoxypyrazines.

Although the exact chemical nature of the thermal decomposition of the phenoxy pyrazines has not yet been established, the appearance of the amide carbonyl bands in the infrared spectra is believed to provide a clue to the change which occurs. It has previously been reported that 2-phenoxypyridine undergoes a thermal rearrangement to N-phenyl-2-pyridone at elevated temperatures (6). It appears reasonable to suspect that a similar rearrangement may occur with the phenoxypyrazines. Work is currently in progress to investigate this possibility.



2-Amino-3-substitutedpyrazines and 2-Amino-3,6-disubstitutedpyrazines. In the previous report period a number of initial intermediates of the 2-anilino-3-methylpyrazine class were examined for their thermal stability. Some of the representatives showed good to excellent stability at 500°F but the principle disadvantage of these compounds was their tendency toward crystallinity. That is, most of the compounds having a secondary amino nitrogen (N-H) were crystalline solids. The notable exception to this tendency was the initial intermediate 2-(N-methylanilino)-3-methylpyrazine, which possesses a tertiary amino nitrogen by virtue of the N-CH_3 linkage as compared to the N-H group. This material was a highly mobile fluid. In



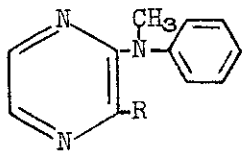


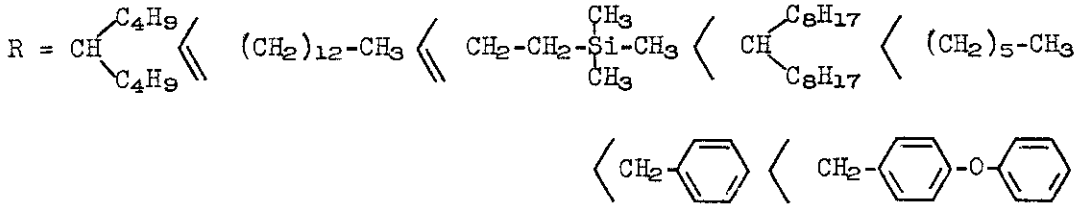
order to obtain candidate products with suitable fluid properties, therefore, emphasis was placed on preparing derivatives from the tertiary amine type of intermediates of this class.

A number of 2-(N-methylanilino)-3-substitutedpyrazine candidate products which have been prepared and examined for their thermal stability are shown at the head of Table 4 (p. 30). The effect of the 3-substituent upon the approximate order of stability is indicated below. The compounds containing aralkyl substituents were found to exhibit appreciable instability at even 500°F with the more highly aromatic

Approved for Public Release

Contrails

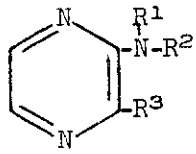




Extent of thermal decomposition at 500°, 600° or 700°F ⟶

substituent affording the most unstable product. The aliphatic substituents, again, as in the case of the phenoxypyrazines, provided derivatives with the highest order of stability within the class. The 2-(N-methylanilino)-3-alkylpyrazines which were tested at 600°F exhibited negligible decomposition under these conditions. The candidate products of this class tested at 700°F showed appreciable decomposition, however. Thus, the ceiling temperature for the thermal stability of such structures must be between 600° and 700°F. Two additional compounds with structures somewhat related to the above were examined, viz., 2-(N-n-butylanilino)-3-n-pentylpyrazine and 2-(N-n-butyl-p-pentylanilino)-3-pentylpyrazine, at 600° and 700°F respectively; the former was extremely stable whereas the latter was unstable under these respective conditions. These results suggest that substituting a N-butyl group for a N-methyl group might provide materials of approximately the same order of stability.

A number of 2-(N,N-dialkylamino)-3-alkylpyrazines were also prepared and tested. The representatives of this class of candidate products shown in Table 4 (p. 31) exhibited excellent stability at 600°F and some of them even displayed fair stability at 700°F. The ceiling for thermal stability of this class of compounds



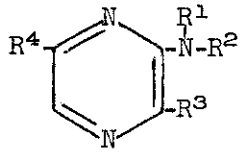
R^1, R^2, R^3 = alkyl groups

appears to approach 700°F more closely than that of the 2-(N-alkylanilino)-3-alkylpyrazines. Thus, substitution of alkyl groups on the 2-amino site as well as on the 3-position appears to favor more stable structures.

Approved for Public Release

Contrails

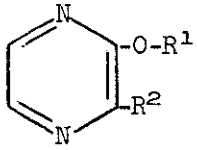
The 2-amino-3,6-disubstitutedpyrazines are structurally related to the foregoing materials. Some selected members of this category are listed in Table 5. The compounds are advanced intermediates (R^3 = methyl) or candidate products (R^3 = H or alkyl). The 2-positions are occupied either by a N-methylanilino group (R^1 = methyl, R^2 = phenyl) or a N,N-dialkylamino group (R^1 and R^2 = alkyl) and the 6-positions have alkyl groups (R^4 = alkyl). The compounds tested at 600°F displayed

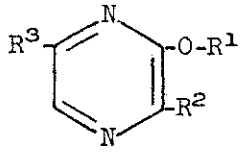


no significant decomposition under those conditions. When tested at 700°F, however, the N-methylanilino derivatives proved to be unstable; whereas, the N,N-dialkylamino compounds showed fair stability. Throughout the different classes of aminopyrazines, as in the case of the phenoxypyrazines, the aliphatic substituents appeared to afford enhancement of the thermal stability properties.

2-Alkoxy-3-substitutedpyrazines and 2-Alkoxy-3,6-disubstitutedpyrazines. As noted earlier (see p. 14 and p. 19), the phenoxypyrazines provided materials that were lacking in fluidity and in thermal stability. Therefore, attention was turned to the study of the analogous compounds, the alkoxypyrazines. Some representatives of the two subject classes of alkoxypyrazines are listed in Table 6 (p. 33).

The 2-alkoxy-3-alkylpyrazine candidate products which were tested at 600°F were found to be quite stable at this temperature, in contract to the corresponding phenoxypyrazines which were unstable at 600°F. The 2-alkoxy-3,6-dialkylpyrazines, which are higher boiling materials than their related 2,3-candidate products, were





R^1, R^2, R^3 = alkyl groups

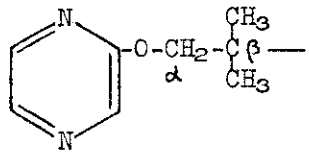
tested at the higher temperature of 700°F. At this temperature, significant thermal decomposition occurred and the stability of these materials under these conditions was considered, at best, only fair.

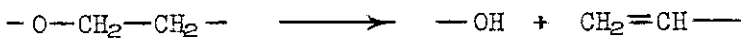
One high molecular weight advanced intermediate of this family which has been mentioned earlier in the discussion of fluidity, namely, bis{3-[2-(3-methylpyrazoxy)]-2,2,4,4-tetramethyl-1-cyclobutoxy}dimethylsilane was also examined for thermal stability at 700°F. This compound was found to be highly unstable under these conditions.

Approved for Public Release

Contrails

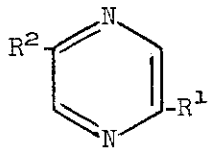
It should be noted that all of the alkoxy groups contained in the structures in Table 6 have methyl groups in beta positions with relation to the oxygen. This structural feature was adopted to avoid the common beta-elimination route of thermal decomposition (7).

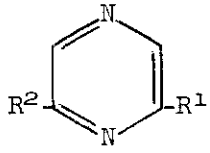




The thermal stability of the 2-alkoxy-3-alkylpyrazines and the 2-alkoxy-3,6-dialkylpyrazines seems to be of approximately the same order of magnitude as that of the 2-(N,N-dialkylamino)-3-alkylpyrazines and the 2-(N,N-dialkylamino)-3,6-dialkylpyrazines. The candidate products of these classes appear to have thermal stability ceilings somewhere between 600° and 700°F.

Dialkylpyrazines and 1,4-Bis(substitutedpyrazyl)butanes. By the observed improvement of both fluid and thermal stability properties associated with alkyl substituents, as described in the foregoing sections, the direction of the program was guided towards the nuclear alkylsubstituted pyrazines. A number of 2,5- and 2,6-dialkylpyrazines are listed in Table 7. (p. 35).





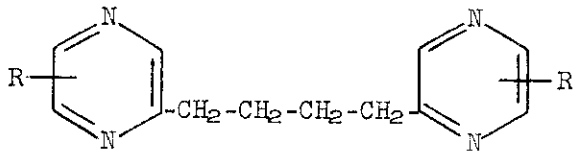
R^1 and R^2 = alkyl groups

The results of the thermal stability tests show these compounds to be highly stable materials at 700°F. The changes shown by these materials after exposure to that condition are relatively minor. Thus, it appears that the thermal stability ceiling for the dialkylpyrazines is above 700°F.

In order to provide higher molecular weight alkyl substituted pyrazines for high temperature testing, a few representative 1,4-bis(alkylpyrazyl)butanes (shown in Table 8, p. 36) were prepared and tested. In line with the above dialkylpyrazines, these high molecular weight derivatives also exhibited good thermal stability at 700°F. However, some of the representatives do not appear to hold up as well as the dialkylpyrazines.

Approved for Public Release

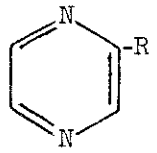
Contrails

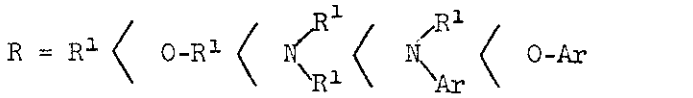


R = alkyl group

Conclusions Regarding Thermal Stability. Based on the above correlations, a sequential progression of improved thermal stability properties was realized in this program. The original proposition for the attainment of pyrazine derivatives with high thermal stability by the introduction of highly aromatic substituents (in some cases linked by hetero-atoms) on the pyrazine nucleus has now been found to be untenable. The most highly aromatic substituted pyrazines proved to be the least stable candidate products.

The order of influence of the substituent in the 2-position was found to be essentially that shown below. The phenoxy substituted pyrazines are apparently





Extent of thermal decomposition ⟶

R^1 = alkyl group
Ar = aryl groups

stable only up to approximately 600°F. No member of this family of pyrazine derivatives was found to be capable of enduring the thermal stability test at this temperature without undergoing a significant change in physical properties. The N-alkyl-N-arylamino pyrazines, N,N-dialkylamino pyrazines and alkoxy pyrazines were increasingly more stable in approximately that order. Compounds with these structural features seem to have their thermal stability limit somewhere between 600° and 700°F. The most thermally stable family of pyrazine derivatives found so far in this program were the nuclear alkyl substituted pyrazines. These materials were generally highly stable at the 700°F temperature test conditions.

Thus, the most promising candidate products found to date have been the dialkylpyrazines, whose thermal stability limit appears to be above 700°F. It is indeed fortunate that the same type of substituents which afforded the best fluidity

Approved for Public Release

Contrails

properties also gave materials with the best thermal stability. The parallel nature of the influence of substituents upon these two important properties offers realistic encouragement for the attainment of materials which can satisfy the target requirements.

Oxidation Stability

The intended application for materials arising from this program require use not only over a wide temperature range but also under oxidative environments. Such conditions demand that the candidate products possess good oxidative stability along with the previously discussed fluidity and thermal stability properties. Therefore, an effort was made to measure the oxidative stability of the compounds prepared in this program.

For this purpose, the thermal stability apparatus was modified by introducing a capillary tube bubbler which was immersed to the bottom of the sample. By means of this modification, compressed air was bubbled through the sample at a constant rate of 2.0 l./hr. The oxidative stability tests were carried out for 6 hours at constant temperatures of 400° and 500°F. Since volatilization losses were expected to be more severe under the oxidation test procedure than with the thermal stability test, no attempt was made to measure the weight losses occurring in the former case. The change in color, viscosity at 100°F or melting point and change in infrared spectrum were observed, as with the thermal stability tests.

This test was previously performed on a number of the intermediates and a few of the model compounds which were prepared in the initial period of this program (1). Those tests were carried out at 400°F and showed the pyrazine derivatives to exhibit generally good oxidative stability under such conditions. Testing at 500°F was initiated during the current period in order to determine the behavior of the newly prepared materials under more drastic conditions. For the purpose of establishing a basis for comparison of the oxidative stability of the pyrazine derivatives with a standard fluid, similar tests were also performed with Mil-L-9236 Base Stock and Formulation fluids (see Table 10, p. 43). The 9236 oil has been accepted by ASD as satisfying the specifications for a lubricant applicable at sustained 400°F ambient temperatures (8). Note should be made of the fact that it is the Formulation fluid (containing an antioxidant) which has qualified under these conditions and not the Base Stock; however, comparisons will be made of both of these materials with the candidate products synthesized in this program.

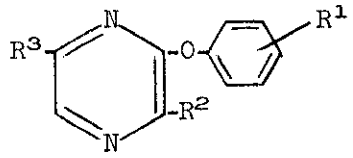
2,3-Disubstitutedpyrazines. Candidate products belonging to this group which have been tested for oxidative stability are listed in Table 9 (p. 40). The number of compounds tested is not as extensive as that examined for thermal stability, however, representatives of each of the most promising classes from the standpoint of thermal stability and fluidity have been included.

Approved for Public Release

AFML-TR-60-838 Pt II

TABLE 2

THERMAL STABILITY OF 2-PHENOXY-3(OR 6)-SUBSTITUTEDPYRAZINES



R^1	R^2	R^3	Micro B.P.* °F	Test Temp., °F	Wt. Loss %	Color Change	Viscosity at 100°F (centistokes) Before	After	IR Change
H	CH_2-C$_6$H$_5$	H	665	500	0.99	Darkened	45.10	53.58	No
H	CH_2-C$_6$H$_4$-C$_6$H$_5$	H	630	600	5.8	Blackened	4178.6	Glass	Yes
H	CH_2-C$_6$H$_4$-O-C$_6$H$_5$	H	630	500	1.22	Blackened	640.14	1013.33	No
H	CH_2CH_2-C$_6$H$_5$	H	677	500	0.13	Sl. darkened	65-65.5[a]	62-64[a]	No
H	$CH(C_4H_9)_2$	H	637	500	1.01	Sl. darkened	21.38	22.00	No
H	$(CH_2)_{12}$-CH_3	H	730	500	0.29	V. sl. yellowed	43-45[a]	43-45[a]	Slight
p-C$_6$H$_5$	CH_3	H	754	500	0.15	V. sl. yellowed	113.0-114.5[a]	113.0-114.5[a]	No
p-C$_6$H$_5$	$CH(C_4H_9)_2$	H	690	500 600	0.21 1.46	Sl. darkened Sl. darkened	69-70.5[a] 69-70.5[a]	68.70[a] 61-64.5[a]	No Carbonyl(M)[b]
m-O-C$_6$H$_5$	CH_2-CH_2-Si(CH_3)$_2$-CH_3	H	738	500 600	0.36 2.9	None Darkened	60.16 60.16	60.86 85.84	No Carbonyl(W)[b]

Approved for Public Release

Controls

TABLE 2 (continued)

THERMAL STABILITY OF 2-PHENOXY-3(OR 6)-SUBSTITUTEDPYRAZINES

R^1	R^2	R^3	Micro B.P.* °F	Test Temp., °F	Wt. Loss %	Color Change	Viscosity at 100°F (centistokes) Before	Viscosity at 100°F (centistokes) After	IR Change
o,o CH_3,C_2H_5	$CH(C_4H_9)_2$	H	675	600	1.1	Darkened	42.15	59.85	Carbonyl(S)[b]
p t-C_4H_9	CH_2-CH_2-	H	660	600	6.01	Darkened	105-105.5°	85-90°	Carbonyl(W)[b]
p t-C_4H_9	$CH(C_4H_9)_2$	H	695	600	0.67	V. sl. darkened	103.27	123.88	Carbonyl(W)[b]
p t-C_9H_{19}	CH_3	H	674	500 600	0.33 2.6	Sl. darkened Darkened	97.10 109.41	97.10 135.44	No Carbonyl(W)[b]
p t-C_9H_{19}	CH_2-	H	670	500	0.19	Sl. darkened	484.12	642.46	No
p t-C_9H_{19}	CH_2-CH_2-	H	675	600	2.99	Darkened	364.00	920.71	Carbonyl(M)[b]
p t-C_9H_{19}	CH_2-CH_2-$Si(CH_3)_2$-CH_3	H	710	500	0.28	Sl. darkened	124.18	128.41	No
p t-C_9H_{19}	$(CH_2)_4$-CH_3	H	685	600	0.93	Darkened	109.08	145.62	Carbonyl(M)[b]
p t-C_9H_{19}	$(CH_2)_{12}$-CH_3	H	695	500 600	0.02 1.29	None Darkened	100.26 100.26	103.43 121.72	No Carbonyl(M)[b]
m CO_2CH_3	CH_3	H	585	600	32.5	Blackened	74[a]	Charred	Yes
p t-C_9H_{19}	H	CH_2-	655	600	5.3	Blackened	473.20	c	Carbonyl(S)[b]

Approved for Public Release

TABLE 2 (continued)

THERMAL STABILITY OF 2-PHENOXY-3(OR 6)-SUBSTITUTEDPYRAZINES

R^1	R^2	R^3	Micro B.P.* °F	Test Temp., °F	Wt. Loss %	Color Change	Viscosity at 100°F (centistokes) Before	After	IR Change
p t-C_9H_{19}	H	CH_2-CH_2-⬡	670	600	3.9	Blackened	362.18	c	Carbonyl(M)[b]
p t-C_9H_{19}	H	$CH(C_4H_9)_2$	645	600	2.1	Blackened	87.26	187.96	Carbonyl(M)[b]
p t-C_9H_{19}	H	$(CH_2)_{12}$-CH_3	615	600	2.4	Blackened	101.92	167.06	Carbonyl(M)[b]

[a] These are melting points, °C.

[b] W, M and S denote weak, medium and strong respectively.

[c] Insufficient sample for measurement after test.

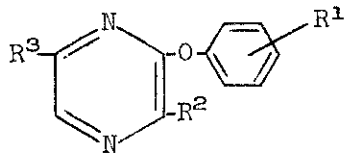
* Some of the values for the micro-boiling point are believed to be not true boiling points due to the high temperature which these materials were exposed to (up to 830°F) and thus they may only reflect the boiling points of the lowest boiling thermal decomposition products.

Approved for Public Release

Contents

TABLE 3

THERMAL STABILITY OF 2-PHENOXY-3,6-DISUBSTITUTEDPYRAZINES



R^1	R^2	R^3	Micro B.P.* °F	Test Temp., °F	Wt. Loss %	Color Change	Viscosity at 100°F (centistokes) Before	Viscosity at 100°F (centistokes) After	IR Change
H	CH_3	CH_3	547	500	0.74	Sl. yellowed	8.65	8.65	No
H	CH_3	CH_2-C$_6$H$_5$	682	500	0.82	Darkened	41.29	45.23	No
o C$_6$H$_5$	CH_3	CH_3	688	500	0.15	Sl. darkened	278.46 71-73[a]	289.38 70-73[a]	No
p t-C_9H_{19}	CH_3	CH_3	687	500	0.41	Sl. darkened	140.02	140.37	No
p t-C_9H_{19}	CH_3	CH_2-C$_6$H$_4$-O-C$_6$H$_5$	610	600	3.5	Blackened	138.32[c]	655.20[c]	Carbonyl(M)[b]
p t-C_9H_{19}	CH_3	CH_2-CH_2-C$_6$H$_5$	635	500 600	0.03 3.73	Darkened Darkened	373.10 373.10	383.02 1008.28	No Carbonyl(W)[b]
p t-C_9H_{19}	CH_3	CH_2-CH_2-Si(CH_3)$_2$-CH_3	707	500 600	0.27 2.39	None Sl. darkened	111.52 111.52	111.87 178.01	No Carbonyl(M)[b]
p t-C_9H_{19}	CH_3	$CH(C_4H_9)_2$	660	500 600	0.21 1.83	Sl. yellowed Sl. darkened	70.79 70.79	70.79 100.53	No Carbonyl(M)[b]

Approved for Public Release

TABLE 3 (continued)

THERMAL STABILITY OF 2-PHENOXY-3,6-DISUBSTITUTEDPYRAZINES

R^1	R^2	R^3	Micro B.P.* °F	Test Temp., °F	Wt. Loss %	Color Change	Viscosity at 100°F (centistokes) Before	After	IR Change
p t-C_9H_{19}	CH_3	$(CH_2)_{12}$-CH_3	650	500	0.08	None	110.47	111.52	No
				600	1.45	Darkened	110.47	155.50	Carbonyl(S)[b]
p t-C_9H_{19}	$(CH_2)_4$-CH_3	$CH(C_4H_9)_2$	655	600	0.87	Darkened	88.35	131.99	Carbonyl(S)[b]

[a] These are melting points, °C.

[b] W, M and S denote weak, medium and strong respectively.

[c] This viscosity was measured at 70°C.

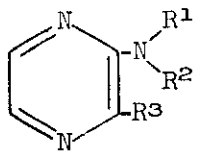
* Some of the values for the micro-boiling point are believed to be not true boiling points due to the high temperature which these materials were exposed to (up to 830°F) and thus they may only reflect the boiling points of the lowest boiling thermal decomposition products.

Approved for Public Release

Contents

TABLE 4

THERMAL STABILITY OF 2-AMINO-3-SUBSTITUTEDPYRAZINES



R^1	R^2	R^3	Micro B.P.* °F	Test Temp., °F	Wt. Loss %	Color Change	Viscosity at 100°F (centistokes) Before	After	IR Change
CH_3		CH_2-	702	500	1.14	Sl. darkened	91.68	96.72	No
CH_3		CH_2- -O-	715	500	0.25	Sl. darkened	3909.47	7397.56	No
CH_3		CH_2-CH_2-	670	700	39.60	Blackened	73.97	a	Yes
CH_3		CH_2-CH_2-$\overset{CH_3}{\underset{CH_3}{Si}}$-$CH_3$	625	500 600	0.25 1.75	None Sl. darkened	17.57 17.57	17.57 18.18	No No
CH_3		$(CH_2)_5$-CH_3	668	700	20.7	Darkened	27.41	72.39	Yes
CH_3		$CH(C_4H_9)_2$	683	600	1.4	Sl. darkened	39.33	40.43	No
CH_3		$(CH_2)_{12}$-CH_3	735	600	1.0	Sl. darkened	29.41	28.76	No
CH_3		$CH(C_8H_{17})_2$	706	700	22.1	Darkened	39.99	57.39	Yes

Approved for Public Release

TABLE 4 (continued)

THERMAL STABILITY OF 2-AMINO-3-SUBSTITUTEDPYRAZINES

R^1	R^2	R^3	Micro B.P.* °F	Test Temp., °F	Wt. Loss %	Color Change	Viscosity at 100°F (centistokes) Before	Viscosity at 100°F (centistokes) After	IR Change
$(CH_2)_3$-CH_3		$(CH_2)_4$-CH_3	660	600	0.7	Sl. darkened	29.37	29.37	No
$(CH_2)_3$-CH_3	p -C_5H_{11}	$(CH_2)_4$-CH_3	690	700	21.2	Blackened	89.96	a	Yes
$(CH_2)_3$-CH_3	$(CH_2)_3$-CH_3	$(CH_2)_4$-CH_3	600	600	2.9	Sl. darkened	9.08	9.26	No
$(CH_2)_3$-CH_3	$(CH_2)_5$-CH_3	$CH(C_4H_9)_2$	695	600	1.25	Sl. darkened	20.14	20.71	No
				700	23.5	Darkened	20.14	22.16	Slight
$(CH_2)_4$-CH_3	$(CH_2)_4$-CH_3	$(CH_2)_4$-CH_3	620	600	3.9	Sl. darkened	11.70	11.77	No
$(CH_2)_5$-CH_3	$(CH_2)_5$-CH_3	$(CH_2)_6$-CH_3	675	700	39.8	Darkened	13.89	18.31	Yes
$(CH_2)_5$-CH_3	$(CH_2)_7$-CH_3	$(CH_2)_8$-CH_3	660	700	30.7	Blackened	19.54	30.85	Yes

[a] Insufficient sample for measurement after test.

* Some of the values for the micro-boiling point are believed to be not true boiling points due to the high temperature which these materials were exposed to (up to 830°F) and thus they may only reflect the boiling points of the lowest boiling thermal decomposition products.

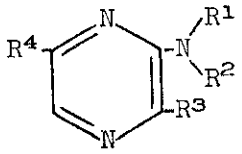
Approved for Public Release

AD No. 60-838 Pt II

Approved for Public Release

TABLE 5

THERMAL STABILITY OF 2-AMINO-3,6-DISUBSTITUTEDPYRAZINES



R^1	R^2	R^3	R^4	Micro B.P.* °F	Test Temp., °F	Wt. Loss %	Color Change	Viscosity at 100°F (centistokes) Before	After	IR Change
CH_3		CH_3	$CH(C_4H_9)_2$	690	700	32.0	Blackened	23.47	a	Yes
CH_3		$(CH_2)_4$-CH_3	$(CH_2)_6$-CH_3	715	700	35.3	Blackened	24.1	b	Yes
CH_3		$(CH_2)_4$-CH_3	$CH(C_4H_9)_2$	723	600 700	0.58 28.2	Sl. darkened Darkened	39.33 39.33	40.31 a	No Yes
CH_3		H	$CH(C_4H_9)_2$	690	600	4.3	Darkened	29.99	30.60	Very slight
$(CH_2)_5$-CH_3	$(CH_2)_5$-CH_3	$(CH_2)_4$-CH_3	$(CH_2)_6$-CH_3	680	700	34.1	Darkened	23.22	28.50	Yes

[a] Due to high weight loss of this sample, insufficient quantity remained for viscosity measurement after the test.

[b] Sample too viscous to be measured.

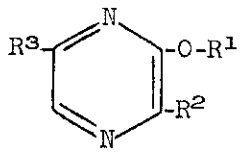
* Some of the values for the micro-boiling point are believed to be not true boiling points due to the high temperature which these materials were exposed to (up to 830°F) and thus they may only reflect the boiling points of the lowest boiling thermal decomposition products.

Confidential

Approved for Public Release

TABLE 6

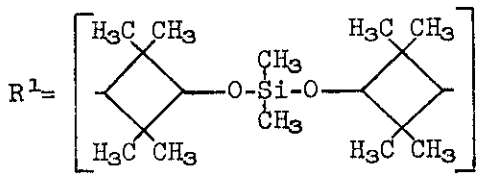
THERMAL STABILITY OF 2-ALKOXY-3(AND 3,6-DI)-SUBSTITUTEDPYRAZINES



R^1	R^2	R^3	Micro B.P.* °F	Test Temp., °F	Wt. Loss %	Color Change	Viscosity at 100°F (centistokes) Before	Viscosity at 100°F (centistokes) After	IR Change
$CH_2-\overset{CH_3}{\underset{CH_3}{C}}-C_3H_7$	$CH(C_4H_9)_2$	H	605	600	1.8	Sl. darkened	13.16	13.89	No
$CH_2-\overset{CH_3}{\underset{CH_3}{C}}-CH_2-\overset{CH_3}{\underset{H}{C}}-CH_3$	$CH(C_4H_9)_2$	H	605	600	1.7	Sl. darkened	12.80	13.16	No
$CH_3-\overset{CH_3}{\underset{CH_3}{C}}-C_3H_7$	CH_3	$(CH_2)_6-CH_3$	615	600	2.4	Yellowed	11.06	11.88	No
$CH_2-\overset{CH_3}{\underset{CH_3}{C}}-C_3H_7$	$(CH_2)_4-CH_3$	$(CH_2)_6-CH_3$	685	700	19.0	Blackened	15.74	32.27	Yes
$CH_2-\overset{CH_3}{\underset{CH_3}{C}}-C_3H_7$	$(CH_2)_6-CH_3$	$(CH_2)_6-CH_3$	710	700	25.6	Blackened	18.97	53.09	Yes

TABLE 6 (continued)

THERMAL STABILITY OF 2-ALKOXY-3(AND 3,6-DI)-SUBSTITUTEDPYRAZINES

R^1	R^2	R^3	Micro B.P.* °F	Test Temp., °F	Wt. Loss %	Color Change	Viscosity at 100°F (centistokes) Before	Viscosity at 100°F (centistokes) After	IR Change
	CH_3	H bis	675	700	59.4	Blackened	124.89	Charred	Yes

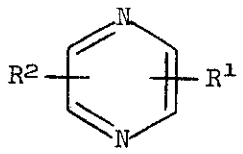
* Some of the values for the micro-boiling point are believed to be not true boiling points due to the high temperature which these materials were exposed to (up to 830°F) and thus they may only reflect the boiling points of the lowest boiling thermal decomposition products.

Approved for Public Release

Approved for Public Release

TABLE 7

THERMAL STABILITY OF DIALKYL PYRAZINES



R^1	R^2	Micro B.P.* °F	Test Temp., °F	Wt. Loss %	Color Change	Viscosity at 100°F (centistokes) Before	Viscosity at 100°F (centistokes) After	IR Change
2-$(CH_2)_6$-CH_3	5-$(CH_2)_8$-CH_3	685	700	10.2	V. sl. darkened	8.40	8.65	No
2-$(CH_2)_6$-CH_3	6-$(CH_2)_8$-CH_3	675	700	3.4	Sl. yellowed	7.94	8.19	No
2-$(CH_2)_8$-CH_3	5-$(CH_2)_8$-CH_3	720	700	6.1	Darkened	10.82	11.06	No
2-$(CH_2)_8$-CH_3	6-$(CH_2)_8$-CH_3	715	700	6.6	Sl. yellowed	9.93	9.95	No
2-$CH(C_4H_9)_2$	5-$CH(C_4H_9)_2$	640	600	1.4	Sl. darkened	39-41[a]	37-40[a]	No

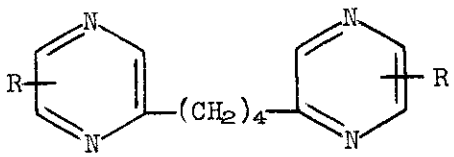
[a] These are melting points, °C.

* Some of the values for the micro-boiling point are believed to be not true boiling points due to the high temperature which these materials were exposed to (up to 830°F) and thus they may only reflect the boiling points of the lowest boiling thermal decomposition products.

Approved for Public Release

TABLE 8

THERMAL STABILITY OF 1,4-BIS(SUBSTITUTEDPYRAZYL)BUTANES AND OF MIL-L-9236 FLUIDS

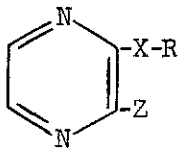


R	Micro B.P.* °F	Test Temp., °F	Wt. Loss %	Color Change	Viscosity at 100°F (centistokes) Before	Viscosity at 100°F (centistokes) After	IR Change
5-$(CH_2)_6$-CH_3	770	700	5.6	Darkened	72.5-74.0[a]	68-69.5[a]	No
6-$(CH_2)_6$-CH_3	695	700	8.5	Blackened	23.23	24.58	No
5-$(CH_2)_8$-CH_3	710	700	4.7	Darkened	78-79[a]	70-73[a]	Yes
6-$(CH_2)_8$-CH_3	740	700	5.6	Darkened	30.48	31.22	Yes
Mil-L-9236 Base Stock	720	700	15.2	Sl. darkened	15.35	18.94	No
Mil-L-9236 Formulation	720	700	15.1	Darkened	16.17	19.72	No

[a] These are melting points, °C.

* Some of the values for the micro-boiling point are believed to be not true boiling points due to the high temperature which these materials were exposed to (up to 830°F) and thus they may only reflect the boiling points of the lowest boiling thermal decomposition products.

Contrails



X = O, $\overset{CH_3}{N}$, $\overset{R^1}{N}$ (R^1 = alkyl)
R = alkyl or aryl group
Z = alkyl or CH_2-CH_2-$\overset{CH_3}{\underset{CH_3}{Si}}$-$CH_3$ group

One phenoxypyrazine, i.e., 2-phenoxy-3-(5-nonyl)pyrazine, exhibited relatively good oxidative stability at 500°F, under abnormally severe conditions. Testing of other representatives phenoxypyrazines was not continued due to the observed thermal instability of such compounds at 600°F (see p. 19). Based on the good oxidative stability of the above compound, some modification of these structures should be considered in an effort to increase their thermal stability.

At one point during the current period of this program the 2-(N-alkylanilino)-3-alkylpyrazines showed promise of affording materials of high thermal stability and acceptable fluidity. Therefore, fairly extensive examination of the oxidative stability of some representatives of this class was performed. The initial intermediate 2-(N-methylanilino)-3-methylpyrazine was tested at 400°F and displayed fair oxidative stability (better than Mil-L-9236 Base Stock but not as good as Mil-L-9236 Formulation, see Table 9). The compound was retested at a higher air-flow rate and the results were practically identical, thus showing that the original air-flow rate was sufficiently fast so that it did not limit the rate of oxidation. The compound 2-(N-methylanilino)-3-(2-silylethyl)pyrazine was found to be highly susceptible to oxidation at 400°F. The addition of a commercial anti-oxidant to this compound failed to improve its oxidative stability significantly. The compound 2-(N-methylanilino)-3-(5-nonyl)pyrazine exhibited fairly good stability approximately comparable to Mil-L-9236 Formulation fluid based on the percent viscosity increase at 500°F. The homologous compound 2-(N-methylanilino)-3-tridecylpyrazine displayed very poor oxidative stability at 500°F suggesting that the longer straight chain alkyl group is an undesirable structural feature.

A compound from this same class which showed sufficient promise to be given some special attention was 2-(N-butylanilino)-3-(n-pentyl)pyrazine. This candidate product, in its raw form, exhibited oxidative stability fairly comparable to the Mil-L-9236 Formulation fluid. In an effort to further stabilize this material towards oxidation, it was formulated with some additives which have been successful in stabilizing some ester based fluids (9). Four different combinations of additives were formulated with this compound by ASD personnel. Although all of these additives appeared to produce the desired effect to a small extent, no drastically increased oxidative stability was achieved. One additional member of this class, 2-(N-butyl-p-pentylanilino)-3-(n-pentyl)pyrazine, was examined and was found to be oxidatively unstable at 500°F.

Approved for Public Release

Contrails

Three 2-(N,N-dialkylamino)-3-alkylpyrazines were tested and exhibited good oxidative stability at 500°F. These compounds showed percent viscosity changes which were approximately equivalent to or less than that displayed by the Mil-L-9236 Formulation fluid. It should be noted that in all cases the absolute viscosity changes are smaller with the pyrazine derivatives.

One 2-alkoxy-3-alkylpyrazine candidate product was examined for its oxidative stability at 500°F. This compound, 2-(2,5-dimethylpentoxy)-3-(5-nonyl)pyrazine, showed an even smaller viscosity change (percent as well as absolute) than the Mil-L-9236 Formulation fluid. Thus, this class of compound appears to afford materials of sufficiently promising oxidative stability to be further investigated.

2,5- and 2,6-Disubstitutedpyrazines. Only one compound bearing some of the same type of substituents as described above but being isomeric by virtue of having these substituents on different positions was tested. This compound was 2-(N-methylanilino)-6-(5-nonyl)pyrazine (Table 10), which is isomeric with the corresponding 2,3-compound. The 2,6-isomer appeared to be less oxidatively stable. Further examples of isomeric compounds will have to be tested to determine the general merit of the different relative positions in contributing to oxidative stability.

The remaining three candidate products in Table 10 are alkyl substituted pyrazines. The two compounds which are liquids and thus can be compared to the 9236 standards in viscosity changes displayed oxidative stability superior to the Base Stock fluid and have an apparent stability on the order of the Formulation fluid.

Conclusions Regarding Oxidative Stability. The examples of pyrazine derivatives tested for oxidative stability were not as extensive as that examined for thermal stability. Thus, it was not possible to correlate the oxidative stabilities of the different classes of candidate products with general structures. Most of the pyrazine derivatives exhibited oxidative stability superior to that of the 9236 Base Stock fluid and comparable or better than the 9236 Formulation fluid. It would appear from these results that the pyrazine nucleus enhances the oxidative stability of these molecules to a degree comparable to that which the additive stabilizes the ester Base Stock fluid. This leads one to suspect that the pyrazine nucleus may be functioning as a built-in oxidation inhibitor.

The notable exceptions to the generally good oxidative stability of the pyrazine derivatives were compounds in which the 3-position was substituted with a trimethylsilylethyl and tridecyl group respectively. Further representative structures containing such substituents will have to be tested to determine whether they are inherently oxidatively unstable groups.

Note should be made of the fact that the one phenoxy substituted pyrazine tested displayed unusually high oxidative stability. If the thermal stability of such structures could be increased by some structural modification, useful materials for the desired application might be realized.

Approved for Public Release

Contrails

In general, the results of the oxidative stability tests performed to date with the various pyrazine derivatives give encouragement to the possibility of achieving materials in this program which can satisfy the oxidative stability requirements.

Lubricity

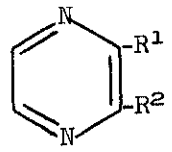
In the preceding report (1) some study of the lubricity behavior of pyrazine derivatives was initiated to ascertain what wear characteristics might be associated with these structures. Although only a few initial intermediates were tested, the results were considered to be encouraging, since no deleterious effect due to the pyrazine structure was detected.

One candidate product, 2-(N-butylanilino)-3-pentylpyrazine, (a sample of which was submitted to ASD for preliminary evaluation) was tested for lubricity during the current reporting period. The result of this test is listed in Table 11 and compared to results with Mil-L-9236 fluids. This pyrazine derivative appeared to have lubricity characteristics better than Mil-L-9236 Base Stock and comparable to Mil-L-9236 Formulation.

Approved for Public Release

TABLE 9

OXIDATIVE STABILITY OF PYRAZINE DERIVATIVES (2,3-DISUBSTITUTEDPYRAZINES)



R^1	R^2	Test Temp., °F	Color Change	Viscosity at 100°F (centistokes) Before	After	% Increase	IR Change
O-⬡	$CH(C_4H_9)_2$	500[a]	Blackened	21.38	26.38	23	No
	CH_3	400	Blackened	10.78	13.12	22	No
	CH_3	400[b]	Blackened	10.78	13.19	22	No
	$CH_2-CH_2-Si(CH_3)_3$	400[c]	Blackened	17.57	23.11	32	No
	$CH_2-CH_2-Si(CH_3)_3$	400[d]	Blackened	17.57	29.50	68	No
	$CH(C_4H_9)_2$	400 500	Darkened Blackened	39.33 39.33	44.61 70.42	13 79	No Slight

Approved for Public Release

Contents

TABLE 9 (continued)

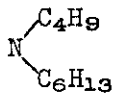
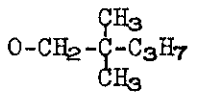
OXIDATIVE STABILITY OF PYRAZINE DERIVATIVES (2,3-DISUBSTITUTEDPYRAZINES)

R^1	R^2	Test Temp., °F	Color Change	Viscosity at 100°F (centistokes) Before	After	% Increase	IR Change
	$(CH_2)_{12}$-CH_3	500	Blackened	27.41	~ 390	~1350	Slight
	$(CH_2)_4$-CH_3	400	Darkened	29.37	31.95	9	No
		500	Blackened	29.37	42.52	45	Slight
(+1% PANA)[e]	$(CH_2)_4$-CH_3	500	Blackened	32.57	44.98	38	No
(+1% PANA and 1% 5,10,10)[e]	$(CH_2)_4$-CH_3	500	Blackened	33.18	46.70	41	No
(+1% GEIGY)[e]	$(CH_2)_4$-CH_3	500	Blackened	33.06	46.21	39	No
(+1% GEIGY + 1% PANA)[e]	$(CH_2)_4$-CH_3	500	Blackened	32.94	44.98	36	No
	$(CH_2)_4$-CH_3	500	Blackened	89.96	f	--	Slight

Approved for Public Release

TABLE 9 (continued)

OXIDATIVE STABILITY OF PYRAZINE DERIVATIVES (2,3-DISUBSTITUTEDPYRAZINES)

R^1	R^2	Test Temp., °F	Color Change	Viscosity at 100°F (centistokes) Before	After	% Increase	IR Change
$N(C_4H_9)_2$	$(CH_2)_4$-CH_3	500	Blackened	9.08	15.99	76	Slight
$N(C_5H_9)_2$	$(CH_2)_4$-CH_3	500	Blackened	11.70	21.51	84	Slight
	$CH(C_4H_9)_2$	500	Blackened	20.14	33.19	65	Slight
	$CH(C_4H_9)_2$	500	Blackened	13.16	20.44	55	Yes

[a] This test was carried out for a 7-hr. period instead of the standard 6 hrs.

[b] This test was carried out with a 50% higher rate of air flow.

[c] This test was stopped after only 2.25 hrs. due to plugging of capillary by decomposition products.

[d] A 0.5% by weight of American Cyanamid "Antioxidant 2246" (2,2'-methylene-bis(4-methyl-6-t-butyl-phenol)) was added to this compound and the test time was only 3.75 hrs. due to plugging of capillary.

[e] These formulations were prepared at ASD.

[f] The recovered sample was too viscous to obtain a measurement.

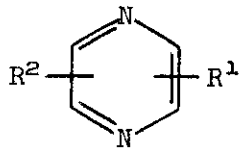
Approved for Public Release

AMRL TR 60-838 Pt II

Approved for Public Release

TABLE 10

OXIDATIVE STABILITY OF PYRAZINE DERIVATIVES
(2,5- AND 2,6-DISUBSTITUTEDPYRAZINES) AND MIL-L-9236 FLUIDS



R^1	R^2	Test Temp., °F	Color Change	Viscosity at 100°F (centistokes) Before	After	% Increase	IR Change
2-N-(CH3)-pyrrolyl	6-$CH(C_4H_9)_2$	500[a]	Blackened	29.99	58.75	96	No
2-$CH(C_4H_9)_2$	5-$CH(C_4H_9)_2$	500	Blackened	39-41[b]	30-35[b]	--	Yes
2-$(CH_2)_8$-CH_3	5-$(CH_2)_8$-CH_3	500	Darkened	8.40	18.31	118	Slight
[2-$(CH_2)_2$	6-$(CH_2)_8$-CH_3]$_2$ 1,4-bis[2-(6-heptylpyrazyl)] butane	500	Blackened	23.23	47.07	103	Slight
Mil-L-9236 Base Stock		400[c]	V. sl. yellowed	15.35	27.20	72	Yes
		500	Darkened	15.35	55.06	258	Yes
Mil-L-9236 Formulation		400[c]	V. sl. darkened	16.17	16.31	1	No
		500	Blackened	16.17	28.02	73	Yes

[a] This test was stopped after only 4 hrs. due to plugging of capillary by decomposition products.

[b] These are melting points, °C.

[c] These results are representative of an average of several repeat tests.

Contrails

TABLE 11

LUBRICITY* OF PYRAZINE DERIVATIVES
AND MIL-L-9236 FLUIDS

Compound	Average Scar Diam., mm.
1. 2-(N-Butylanilino)-3-pentylpyrazine	0.70
2. Mil-L-9236 Base Stock	1.03
3. Mil-L-9236 Formulation	0.71

* Shell four-ball wear test at 400°F, 600 rpm, 40-kg. load and one-hour duration.

Approved for Public Release

Contrails

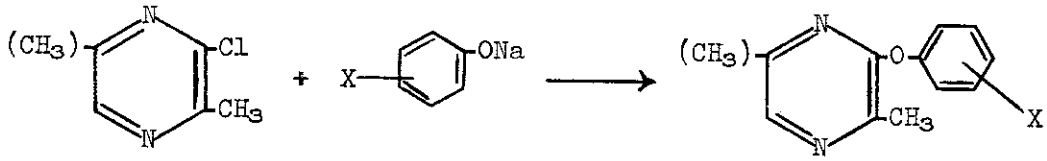
SYNTHESIS OF PYRAZINE DERIVATIVES

The original proposed routes to substituted pyrazine derivatives via two key starting compounds, namely, 2-chloro-3-methylpyrazine and 2-chloro-3,6-dimethylpyrazine, have been established and the results were reported in the initial phase of this program (1). As a consequence, methods have been developed for the preparation of a variety of mono-, di- and trisubstituted pyrazines. Simultaneously, thermal and oxidative screening tests of these compounds were performed to determine the physical properties associated with various linkages. Guided by the results of these tests, the synthetic approach of this program has consisted of the incorporation of substituents onto the pyrazine nucleus to provide compounds with improved stability and fluid properties. During the second contractual year of this program, in addition to the continued preparation of new members of each established class of compounds, the synthetic scope has been broadened to include the preparation of derivatives containing new linkages as well as the preparation of a number of model compounds to determine the feasibility of reaction path. The purpose of this multi-pronged approach was to explore and take full advantage of the versatility of the pyrazine nucleus. As a result, a stepwise achievement of materials with further improved properties and a logical elimination of undesirable linkages was realized.

The following discussion of the synthesis of pyrazine derivatives will follow the outline of the classification of pyrazine compounds stated in the Introduction (p. 5), for the purpose of clarity.

Initial Intermediates

2-Phenoxy-3-methylpyrazines and 2-Phenoxy-3,6-dimethylpyrazines. Various reaction conditions have been investigated previously for the preparation of this class of compounds (1). The sodium alkoxide method (1) was found most satisfactory and provided the necessary high reflux temperature during the interaction of 2-chloro-3-methyl-(or 3,6-dimethyl)pyrazine with the appropriate sodium phenoxide to achieve good yields in these reactions. The representatives thus synthesized are tabulated in Table 12. The first two members, namely,



2-(o-i-propylphenoxy)-3-methylpyrazine and 2-(p-i-propylphenoxy)-3-methylpyrazine, were prepared in the customary manner in 78% and 86% yield, respectively. It is interesting to note that the o-isomer is a liquid at room temperature while the p-isomer is a low-melting solid.

Approved for Public Release

Contrails

TABLE 12

2-PHENOXY-3-METHYLPYRAZINES AND 2-PHENOXY-3,6-DIMETHYLPYRAZINES

Phenol	Product	% Yield
1. o-i-Propylphenol	2-(o-i-Propylphenoxy)-3-methylpyrazine	78
2. p-i-Propylphenol	2-(p-i-Propylphenoxy)-3-methylpyrazine	86
3. p-Phenylphenol	2-(p-Phenylphenoxy)-3-methylpyrazine	
	Isomer I, m.p. 113-114.5°C	68
	Isomer II, m.p. 75-76°C	10
4. Hydroquinone	p-Phenylene Bis-2-(3-methylpyrazyl) Ether	
	Isomer I, m.p. 185.5-186°C	8[a], 36[b]
	Isomer II, m.p. 127-128°C	20[a], 37[b]
	Isomer III, m.p. 150.5-152°C	4[a], 0[b]
5. Resorcinol	m-Phenylene Bis-2-(3-methylpyrazyl) Ether	79
6. m-Carbomethoxyphenol	2-(m-Carbomethoxyphenoxy)-3-methylpyrazine	71[c]
7. Pentachlorophenol	---	--
8. 2,6-Di-t-butyl-4-methylphenol	---	--
9. 2-Methyl-6-ethylphenol	2-(2-Methyl-6-ethylphenoxy)-3-methylpyrazine	59[c]
10. m-Trimethylsilylphenol	2-(m-Trimethylsilylphenoxy)-3-methylpyrazine	23
11. p-Trimethylsilylphenol	2-(p-Trimethylsilylphenoxy)-3-methylpyrazine	27
12. p-t-Butylphenol	2-(p-t-Butylphenoxy)-3,6-dimethylpyrazine	80

Approved for Public Release

Contrails

TABLE 12 (continued)

2-PHENOXY-3-METHYLPYRAZINES AND 2-PHENOXY-3,6-DIMETHYLPYRAZINES

Phenol	Product	% Yield
13. p-Phenylphenol	2-(p-Phenylphenoxy)-3,6-dimethylpyrazine	67

---

[a] This reaction was carried out at 173-177°C during a 39.5-hour period.

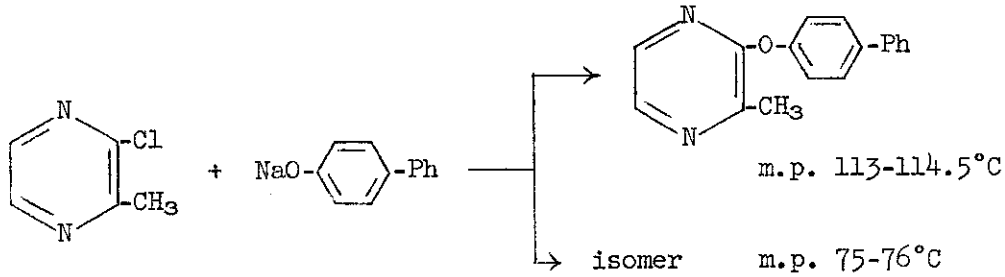
[b] This reaction was carried out at 170-180°C during a 6-day period.

[c] The sodium salt of this phenol was prepared by the interaction of the phenol with sodium methoxide in methanol and dried overnight in vacuum oven at 40°C.

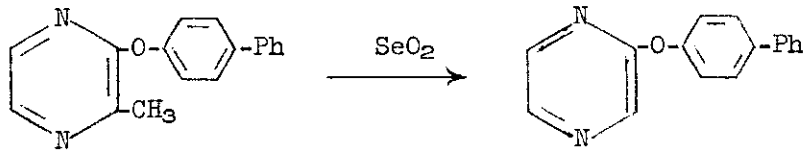
Approved for Public Release

Contrails

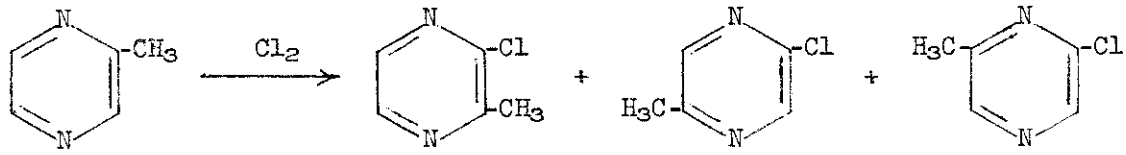
A previously reported reaction between sodium p-phenylphenoxide (obtained via the sodium ethoxide method) and 2-chloro-3-methylpyrazine (Reaction 3, Table 12) gave a presumed quantitative yield of 2-(p-phenylphenoxy)-3-methylpyrazine, m.p. 73-104°C (1). Upon further purification of this crude material by repeated recrystallizations and elution chromatography of the remaining mother liquor, two isomeric compounds were isolated. The major product (m.p. 113-114°C) was obtained in 68% over-all yield, in addition to a 10% yield of a lower melting isomer (m.p. 75-76°C). The infrared spectra of both isomers



contained no free hydroxy bands (5) in the 3650-3590 cm.-1 region. Monopicrate derivatives were prepared for both isomers and they again were shown to be isomeric. However, treatment of the higher melting isomer with selenium dioxide in pyridine afforded the expected p-phenylphenoxypyrazine in 72% yield. Similar oxidation of the lower melting isomer over extended time periods furnished only



starting material, identified by its picrate derivative. Inasmuch as the starting 2-chloro-3-methylpyrazine, which was obtained from the chlorination of methylpyrazine by chlorine under polar conditions (10), was reported to be contaminated with small amounts of 2-chloro-5-methylpyrazine (11) or 2-chloro-6-methylpyrazine (12), it was most likely that these two different melting isomers

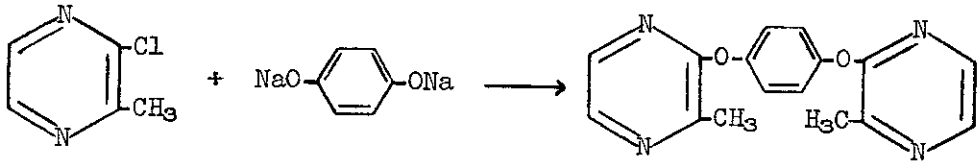


were position isomers arising from the starting mixed ring chlorinated methylpyrazines. The high-melting isomer, being the major product, is tentatively assigned as the desired 2-(p-phenylphenoxy)-3-methylpyrazine. The lower melting isomer then would be either the 2,5- or 2,6-compound.

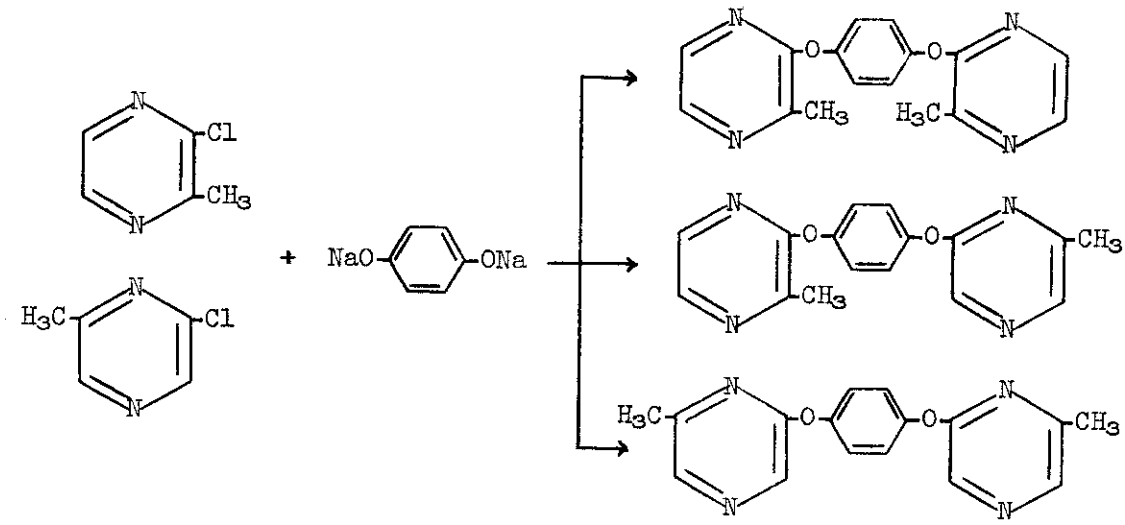
Approved for Public Release

Contrails

When 2-chloro-3-methylpyrazine was allowed to interact with the disodium salt of hydroquinone (Reaction 4, Table 12), three different melting solids (I, 8%, m.p. 185.5-186°C; II, 20%, m.p. 127-128°C; III, 4%, m.p. 150.5-152°C) were obtained by careful elution chromatographic separation. The empirical



formulas of all three compounds were shown by elemental analysis to correspond to that of the desired product, p-phenylene bis-2-(3-methylpyrazyl) ether. Based on the method of synthesis and the nature of the hetero-linkage of this product as contrasted to that of the 2-anilino-3-methylpyrazines (1), the possibility of tautomerism was ruled out, since there were no enolizable hydrogens present in the molecule. Furthermore, the infrared spectra of these three compounds, which were different and contained no OH and/or NH bands, did not show appreciable change when their chloroform solutions were allowed to stand for one week. Therefore, it was concluded that these compounds were also position isomers. Similar to the case of 2-(p-phenylphenoxy)-3-methylpyrazine described earlier, dipicrate derivatives of these three isomers were prepared and likewise shown to be isomeric. On a repeated preparation of p-phenylene bis-2-(3-methylpyrazyl) ether under extended reaction periods, only two isomers (isomers I and II, Reaction 4, Table 12) were isolated and each was obtained in over 35% yield. Based on the above mentioned fact that the starting 2-chloro-3-methylpyrazine was contaminated with some 2,5- or 2,6-isomer, three different possible structures could be written for the reaction products starting from a mixture of two different ring chlorinated methylpyrazines. Additional chemical evidences are

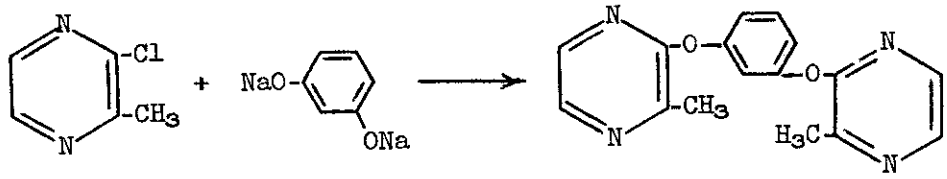


Approved for Public Release

Contrails

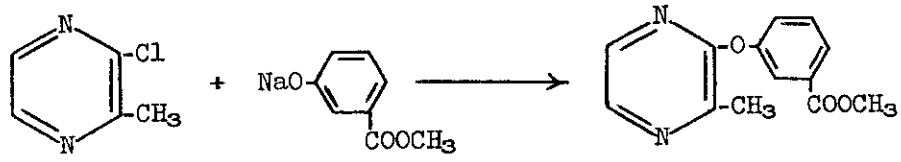
needed for the definite assignment of structure to each individual isomer. At this stage, it should be pointed out the possibility existed that the pyrazine derivatives prepared to date derived from 2-chloro-3-methylpyrazine could contain other position isomers. The standard purification method for these liquid derivatives has been by distillation and this method presumably is not sufficiently effective for the separation of position isomers which could possess similar boiling ranges.

The reaction of the disodium salt of resorcinol with 2-chloro-3-methylpyrazine (Reaction 5, Table 12) was attempted earlier to afford a 32% yield of the desired m-phenylene bis-2-(3-methylpyrazyl) ether, in addition to a 1% yield of the mono-coupling product, 2-(m-hydroxyphenoxy)-3-methylpyrazine (1). Since only one di-coupling product was obtained in this reaction and the yield was moderate, it was of interest to repeat this reaction in an effort to improve the yield and to observe whether isomer materials would be obtained. Identical reaction conditions



as in the preparation of p-phenylene bis-2-(3-methylpyrazyl) ether were employed. Workup of the reaction product mixture furnished the known m-phenylene bis-2-(3-methylpyrazyl) ether exclusively in 79% yield. It was noteworthy that in the interaction of disodium salts of diprotic phenols with 2-chloro-3-methylpyrazine, an extended reaction time was necessary to bring about the desired coupling in good yield.

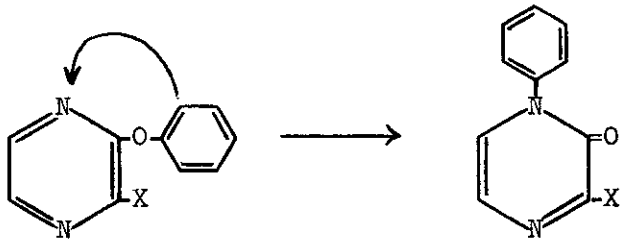
Another initial intermediate of the phenoxypyrazine class, 2-(m-carbomethoxyphenoxy)-3-methylpyrazine, was prepared in 71% yield by treatment of sodium m-carbomethoxyphenoxide with 2-chloro-3-methylpyrazine (Reaction 6, Table 12). This product was synthesized to determine the effect of an ester substituent upon stability (although it appeared as a low-melting solid). The starting m-carbomethoxyphenol was obtained in 80% yield by the interaction of m-hydroxybenzoic acid with methanol in chloroform in the presence of sulfuric acid.



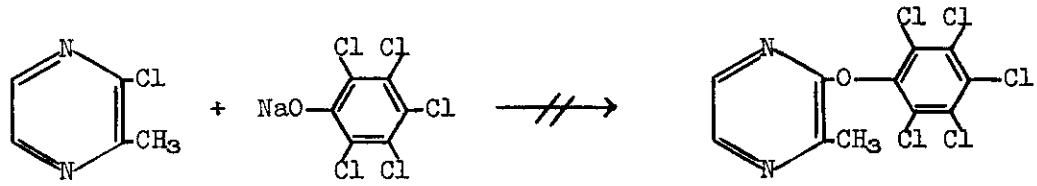
Approved for Public Release

Contrails

A number of candidate products of the 2-phenoxy-3-substitutedpyrazine class of compounds appeared to have undergone a structural rearrangement when subjected to thermal stability screening tests at 600°F for 9 hours (see p. 19). It was of interest to investigate whether this rearrangement occurred via an attack of the ortho-position of the phenoxy group on the ring nitrogen atom in the pyrazine nucleus. Efforts, therefore, were made to prepare 2-phenoxy-3-methylpyrazines in which the ortho-positions of the phenoxy moiety were blocked by substituents.



The interaction of sodium pentachlorophenoxide with 2-chloro-3-methylpyrazine (Reaction 7, Table 12) under extended time periods gave only recovered starting materials. The failure of this reaction might be explained on the basis that a strong electron-withdrawing effect was exerted on the aromatic nucleus by the five chlorine atoms in pentachlorophenol, and as a result the pentachlorophenoxide ion was too poor a nucleophile to displace the chlorine atom of 2-chloro-3-methylpyrazine. Next, an attempt was made to prepare 2-(2,6-di-t-butyl-4-methylphenoxy)-3-methylpyrazine. It was known (13) that sodium 2,6-di-t-butyl-4-methylphenoxide could not be prepared by the sodium methoxide method due to

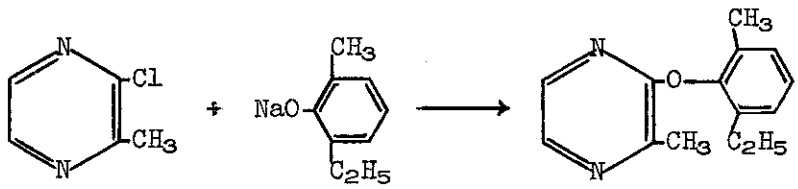


the bulkiness of the t-butyl groups substituted at the ortho-positions. It was logical, then, to attempt to make the corresponding lithium salt of the phenol via lithium methoxide in methanol. However, when 2,6-di-t-butyl-4-methylphenol was interacted with an equimolar quantity of lithium methoxide and then excess 2-chloro-3-methylpyrazine (Reaction 8, Table 12), only starting materials were recovered. Inasmuch as no desired product was isolated, it was suspected that the lithium methoxide did not react with the phenol to form the corresponding lithium salt. The recovered 2-chloro-3-methylpyrazine was then redistilled in an effort to isolate any 2-methoxy-3-methylpyrazine (1), which possessed similar boiling range as that of the 2-chloro-3-methylpyrazine and might have resulted from the interaction of 2-chloro-3-methylpyrazine with lithium methoxide. Upon redistillation, only 2-chloro-3-methylpyrazine was obtained.

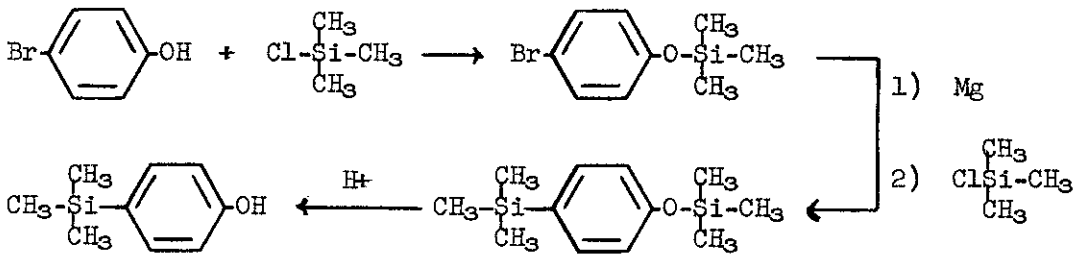
Approved for Public Release

Contrails

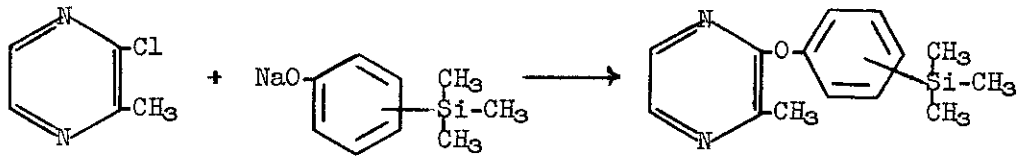
Next, the preparation of a 2-(di-ortho-substitutedphenoxy)-3-methylpyrazine was attempted with 2-methyl-6-ethylphenol, a compound containing two less bulky ortho-substituents. Indeed, the reaction of sodium 2-methyl-6-ethylphenoxide with excess 2-chloro-3-methylpyrazine (Reaction 9, Table 12) proceeded in the usual manner to furnish the desired 2-(2-methyl-6-ethylphenoxy)-3-methylpyrazine in 59% yield.



Efforts to prepare 2-silylphenoxy-3-methylpyrazines were initiated. A literature survey indicated the compounds p-(and m-)trimethylsilylphenol have been prepared via several similar routes (14,15). The synthesis of both 2-(m- and p-trimethylsilylphenoxy)-3-methylpyrazine (Reaction 10 and 11, Table 12) was undertaken with the aid of these phenols. The sequence of reactions to



prepare the silylsubstituted phenols is illustrated using the p-isomer. Each step was accomplished in yields ranging from 50 to 90%. The resulting silylphenols were extremely acid-sensitive and they were employed immediately after their isolation to react with sodium methoxide to form the corresponding sodium phenoxide. When these sodium salts were allowed to interact with 2-chloro-3-methylpyrazine in the usual manner, the desired 2-(m- and p-trimethylsilylphenoxy)-3-methylpyrazines were obtained in only moderate yields (23 to 27%). The hydrolytic instability of the phenols may be responsible for the relatively low yields obtained in these reactions.

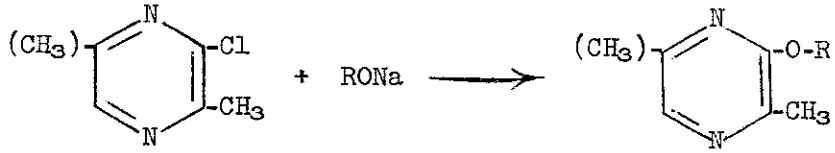


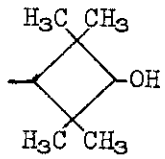
Approved for Public Release

Contrails

Two new representatives of the 2-phenoxy-3,6-dimethylpyrazine class of compounds were prepared in good yield employing the sodium alkoxide method. 2-(p-t-Butylphenoxy)-3,6-dimethylpyrazine, obtained in 80% from the interaction of sodium p-t-butylphenoxide and 2-chloro-3,6-dimethylpyrazine (Reaction 12, Table 12), is a moderately fluid liquid, while the corresponding 2-(p-t-butylphenoxy)-3-methylpyrazine, prepared earlier, is a solid, m.p. 61-63.5°C (1). Treatment of sodium p-phenylphenoxide with 2-chloro-3,6-dimethylpyrazine (Reaction 13, Table 12) afforded the desired 2-(p-phenylphenoxy)-3,6-dimethylpyrazine in 67% yield.

2-Alkoxy-3-methylpyrazines and 2-Alkoxy-3,6-dimethylpyrazines. The next class of initial intermediates whose synthesis is to be considered is the 2-alkoxy-3-methyl- (and -3,6-dimethyl)pyrazines. One member of this class, namely, 2-methoxy-3-methylpyrazine, was obtained earlier as a side product from the attempted preparation 2-phenyldimethylsiloxy-3-methylpyrazine by the interaction of 2-chloro-3-methylpyrazine with sodium phenyldimethylsiloxide in the presence of methanol (1). Subsequently, the observed instability of the phenoxypyrazines at 600°F (see p. 19) has prompted the investigation of the synthesis of their aliphatic analogs as well as the determination of the physical properties of these compounds. With this aim, a number of 2-alkoxy-3-methyl- (and -3,6-dimethyl)pyrazines were prepared and the results are listed in Table 13. The preparation of the intermediate sodium alkoxide involved the treatment of excess starting alcohol with metallic sodium. The rate of formation of the sodium salt (as judged by the rate of disappearance of metallic sodium) appeared to be slow, and the use of benzene or toluene as solvent failed to improve the rate of reaction to any appreciable extent. Subsequently, the sodium alkoxide was treated in situ with excess 2-chloro-3-methyl- (and -3,6-dimethyl)pyrazine to afford the desired product. Yields from these reactions were in general quite high, ranging from 64 to 87%. In the case of 2-(2,2,4-trimethylpentoxy)-3-methylpyrazine (Reaction 2, Table 13), the preparation of the intermediate, sodium 2,2,4-trimethyl-1-pentoxide, was also attempted by the sodium methoxide method (1), but the yield of the desired pyrazine compound was lower (34%) than that obtained from the direct sodium metal method (88%).



Where R = $-CH_2C(CH_3)_2CH_2CH_2CH_3$, $-CH_2C(CH_3)_2CH(CH_3)CH_3$, 

Approved for Public Release

Contrails

TABLE 13

2-ALKOXY-3-METHYLPYRAZINES AND 2-ALKOXY-3,6-DIMETHYLPYRAZINES

Alcohol	Product	% Yield
1. 2,2-Dimethyl-1-pentanol	2-(2,2-Dimethylpentoxy)-3-methylpyrazine	68[a]
2. 2,2,4-Trimethyl-1-pentanol	2-(2,2,4-Trimethylpentoxy)-3-methylpyrazine	34[b], 88[a]
3. 2,2,4,4-Tetramethyl-1,3-cyclobutanediol	2-[1-(3-Hydroxy-2,2,4,4-tetramethylcyclobutoxy)] -3-methylpyrazine	64[a]
4. 2-[1-(3-Hydroxy-2,2,4,4-tetramethylcyclobutoxy)] -3-methylpyrazine	Bis-{3-[2-(3-methylpyrazoxy)] -2,2,4,4-tetramethyl-1-cyclobutoxy}dimethylsilane	69[c]
5. 2,2-Dimethyl-1-pentanol	2-(2,2-Dimethylpentoxy)-3,6-dimethylpyrazine	83[a], 83[a]
6. 2,2,4-Trimethyl-1-pentanol	2-(2,2,4-Trimethylpentoxy)-3,6-dimethylpyrazine	64[a]

[a] The sodium salt of this alcohol was prepared by refluxing a mixture of the excess alcohol and sodium.

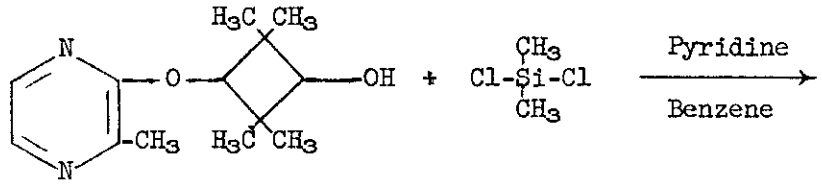
[b] The sodium methoxide method (1) was employed to prepare the sodium salt of this alcohol.

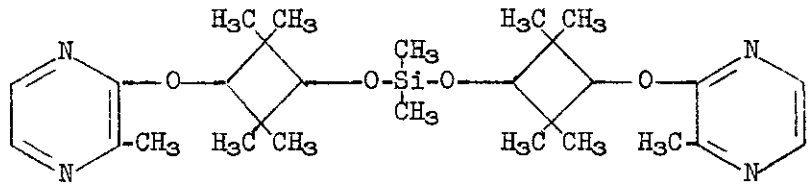
[c] This product was prepared by the interaction of the alcohol with dimethyldichlorosilane in benzene.

Approved for Public Release

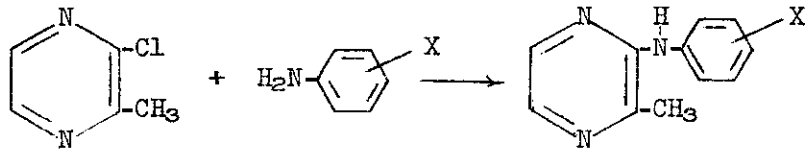
Contrails

A silicon-containing alkoxypyrazine derivative was also prepared (Reaction 4, Table 13) by further reaction of one of the alkoxy initial intermediates. This involved the treatment of 2-[1-(3-hydroxy-2,2,4,4-tetramethylcyclobutoxy)]-3-methylpyrazine with one half of an equivalent of dimethyldichlorosilane in benzene. Pyridine was also added to precipitate the hydrogen chloride formed during the reaction. Thus, the desired bis-{3-[2-(3-methylpyrazoxy)]-2,2,4,4-tetramethyl-1-cyclobutoxy}dimethylsilane was obtained in 69% yield. It should be pointed out that the choice of aliphatic alcohols in all instances was guided by the fact that they possess no β-hydrogens with respect to the oxygen function.





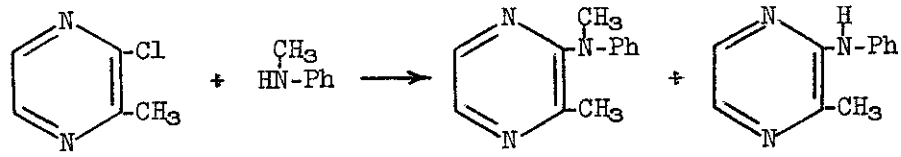
2-Anilino-3-methylpyrazines and 2-Anilino-3,6-dimethylpyrazines. A number of representatives of the 2-anilino-3-methylpyrazine class of compounds have been prepared by the general method of heating 2-chloro-3-methylpyrazine with an excess of an aniline at reflux temperature for a short period of time (1). This method, designated as the "Direct" method, was found to be most satisfactory for



the preparation of representatives with the general structure indicated above, in which the exocyclic nitrogen function is secondary. This method was also employed previously (1) to prepare 2-(N-methylanilino)-3-methylpyrazine by the interaction of 2-chloro-3-methylpyrazine with excess N-methylaniline. However, the isolation of the desired product was always accompanied with significant quantities of cleavage product 2-anilino-3-methylpyrazine. The amount of side product obtained appeared to be proportional to the temperature employed during reaction. At this point, candidate products derived from 2-(N-methylanilino)-3-methylpyrazine had shown stabilities as well as fluid properties superior to those derived from 2-phenoxy-3-methylpyrazine intermediates (see p. 19). Thus,

Approved for Public Release

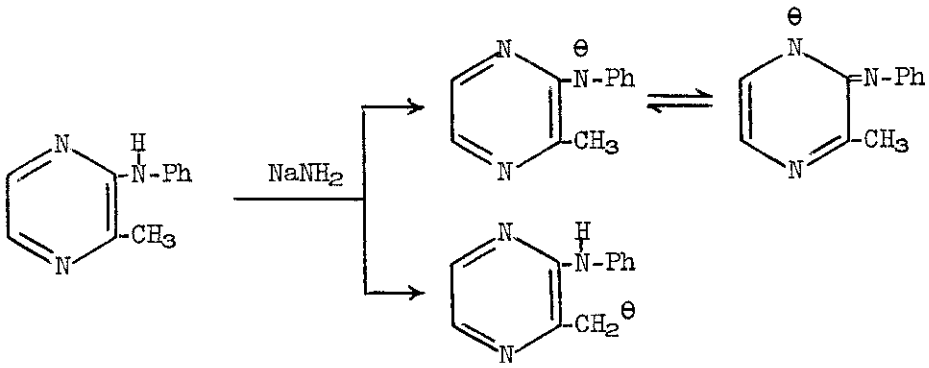
Contrails



synthetic effort toward the anilinopyrazines was intensified with the preparation of additional representatives either by the established "Direct" procedure with or without modifications, or by new procedures, and the results are summarized in Table 14.

In Reaction 1, Table 14, the effect of a catalyst was investigated for the preparation of 2-(N-methylanilino)-3-methylpyrazine by the "Direct" method. Zinc chloride has been used in the alkylation of aniline with an alkyl halide to give N-alkylanilines (16). It was reported that the reaction can be accelerated with this catalyst and yields of the products were generally quite high. Thus, two attempts were made to couple N-methylaniline with 2-chloro-3-methylpyrazine in the presence of zinc chloride (Reaction 1, Table 14). However, no great improvement in yield was observed and the desired 2-(N-methylanilino)-3-methylpyrazine was obtained in yields of 31% and 50%, along with 33% and 22% of the cleavage product, 2-anilino-3-methylpyrazine, respectively.

A different approach to this compound was then attempted (Reaction 2, Table 14). This method involved the alkylation of 2-anilino-3-methylpyrazine (1) with methyl iodide and sodium amide in the presence of pyridine (the "Pyridine Solvent" method). There were two potential complications present in using this method. The first was the competing anion formation on the 3-methyl site; the second was the possible ring alkylation due to the tautomerization of the NH group (1). A molar ratio of 2 to 2 to 1 of 2-anilino-3-methylpyrazine to sodium amide to methyl iodide was employed in an effort to avoid the first complication



and displace only what was expected to be the most acidic hydrogen, that at the amino site. Pyridine was used as a solvent to improve the solubility of the starting 2-anilino-3-methylpyrazine and thus facilitate its anion formation.

Approved for Public Release

Contrails

TABLE 14

2-ANILINO-3-METHYLPYRAZINES

	Reactants	Product	% Yield
1.	N-Methylaniline and 2-Chloro-3-methylpyrazine[a,c]	2-(N-Methylanilino)-3-methylpyrazine	50, 31
		2-Anilino-3-methylpyrazine	22, 33
2.	2-Anilino-3-methylpyrazine and Methyl Iodide[b]	2-(N-Methylanilino)-3-methylpyrazine	81
3.	2-N-Butylaniline and 2-Chloro--3-methylpyrazine[a]	2-(N-Butylanilino)-3-methylpyrazine	18
		2-Anilino-3-methylpyrazine	16
4.	2-Anilino-3-methylpyrazine and 1-Bromobutane[b]	2-(N-Butylanilino)-3-methylpyrazine	65
5.	p-Pentylaniline and 2-Chloro-3-methylpyrazine[a]	2-(p-Pentylanilino)-3-methylpyrazine	86
6.	p-Dodecylaniline and 2-Chloro-3-methylpyrazine[a]	2-(p-Dodecylanilino)-3-methylpyrazine	77
7.	N-Ethyl-p-pentylaniline and 2-Chloro-3-methylpyrazine[a]	2-(p-Pentylanilino)-3-methylpyrazine	37
8.	2-(p-Pentylanilino)-3-methylpyrazine and Ethyl Bromide[b]	---	--
9.	2-(N-Methylanilino)-3-methylpyrazine and 2-Chloro-3-methylpyrazine[a]	---	--
10.	2-Anilino-3-methylpyrazine and 2-Chloro-3-methylpyrazine[b]	---	--
11.	2-Anilino-3-methylpyrazine and 1,2-Dibromoethane[b]	---	--

Approved for Public Release

Contrails

TABLE 14 (continued)

2-ANILINO-3-METHYLPYRAZINES

Reactants	Product	% Yield
12. 2-(N-Methylanilino)-3-methylpyrazine and 1,2-Dibromoethane[d]	N,N'-Diphenyl-N,N'-di[2-(3-methylpyrazyl)]-1,2-diaminoethane	29

[a] The "Direct" method was employed.

[b] The "Pyridine Solvent" method was employed.

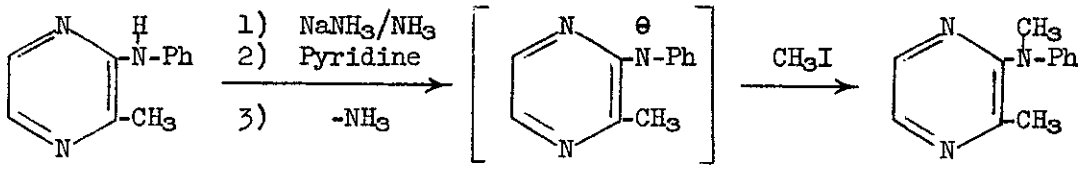
[c] This reaction was run in the presence of zinc chloride.

[d] The "Alkylation" method (see p. 70) was employed.

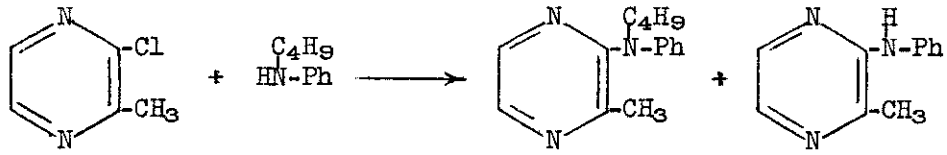
Approved for Public Release

Contrails

The product obtained from this reaction was the desired 2-(N-methylanilino)-3-methylpyrazine (81%), together with the recovery of 42% of the starting 2-anilino-3-methylpyrazine. The identity of the desired product was confirmed by comparison of physical properties, infrared and ultraviolet spectra ((1) also see p. 96) with those of an authentic sample prepared by the direct coupling of 2-chloro-3-methylpyrazine with N-methylaniline.



Employing the "Direct" method, 2-chloro-3-methylpyrazine was interacted with a two-fold excess of N-butylaniline (17), under various conditions. When the reaction was first performed using a 5-hour reaction time at 210°C (identical to the conditions used for the preparation of 2-(N-methylanilino)-3-methylpyrazine (1)), essentially no reaction had taken place and only starting materials were recovered. When the reaction time was lengthened to 23 hours, the reaction temperature rose to 250°C and the reaction mixture decomposed into an intractable tar. In the next attempt, a reaction time of 13.5 hours was employed (Reaction 3, Table 14); the desired 2-(N-butylanilino)-3-methylpyrazine was obtained in 18% yield together with 16% of the cleavage product, 2-anilino-3-methylpyrazine. Two subsequent attempts were made by heating a mixture of

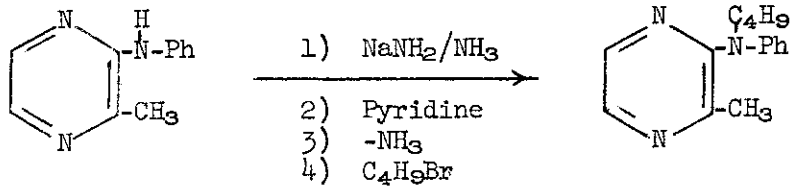


1-bromobutane and 2-anilino-3-methylpyrazine (1) in an effort to prepare 2-(N-butylanilino)-3-methylpyrazine in good yield, but in both cases only the starting materials were recovered.

The next logical choice for the preparation of this compound appeared to be the "Pyridine Solvent" method which involved the alkylation of 2-anilino-3-methylpyrazine (1) with 1-bromobutane and sodium amide (2 to 1 to 2) in pyridine. This reaction (Reaction 4, Table 14) was performed under essentially the same conditions as that for the alkylation of 2-anilino-3-methylpyrazine with methyl iodide described earlier (see p. 56). From this reaction there were obtained 65% of 2-(N-butylanilino)-3-methylpyrazine and 50% of recovered 2-anilino-3-pyrazine.

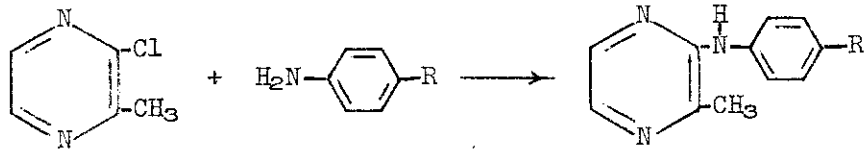
Approved for Public Release

Contrails



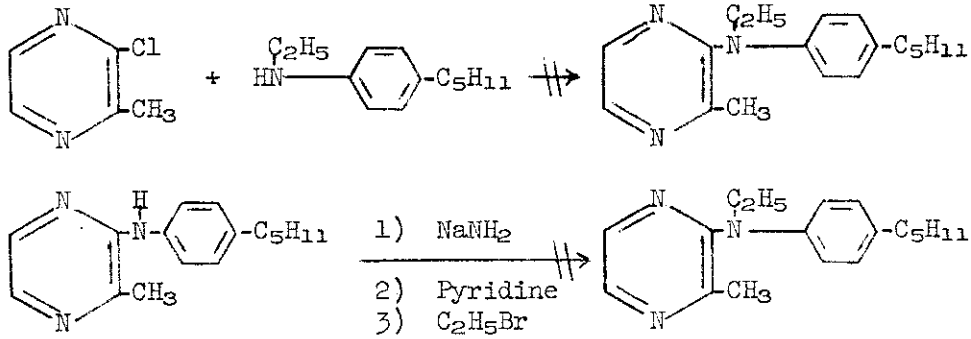
Thus, the "Pyridine Solvent" method of preparing 2-(N-alkylanilino)-3-methylpyrazines should be the future method of choice since it has the following advantages over the "Direct" method of using 2-chloro-3-methylpyrazine and an N-alkylaniline; a) higher yields of product, b) no cleavage side product, and c) allowing the introduction of large alkyl groups.

Two additional initial intermediates, namely, 2-(p-pentylanilino)-3-methylpyrazine and 2-(p-dodecylanilino)-3-methylpyrazine, were prepared by the "Direct" method in 86 and 77% yield, respectively (Reactions 5 and 6, Table 14). Both compounds were extremely viscous materials and will be further reacted in an effort to obtain liquid candidate products.



where R = $-C_5H_{11}$ and $-C_{12}H_{25}$

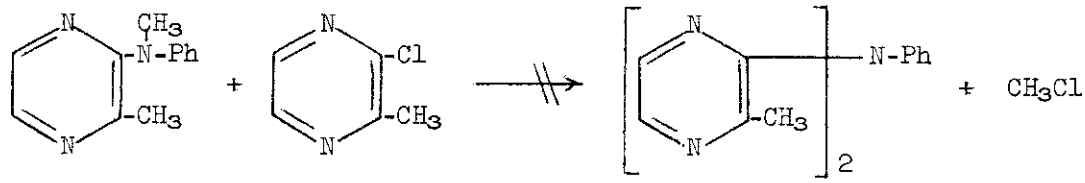
Next, N-ethyl-p-pentylaniline was treated with 2-chloro-3-methylpyrazine in an effort to prepare 2-(N-ethyl-p-pentylanilino)-3-methylpyrazine (Reaction 7, Table 14). However, only the cleaved product, 2-(p-pentylanilino)-3-methylpyrazine (37%), was isolated. Alkylation of 2-(p-pentylanilino)-3-methylpyrazine with sodium amide and ethyl bromide in pyridine (Reaction 8) was also unsuccessful. The reason for the failure of the second attempt is not known.



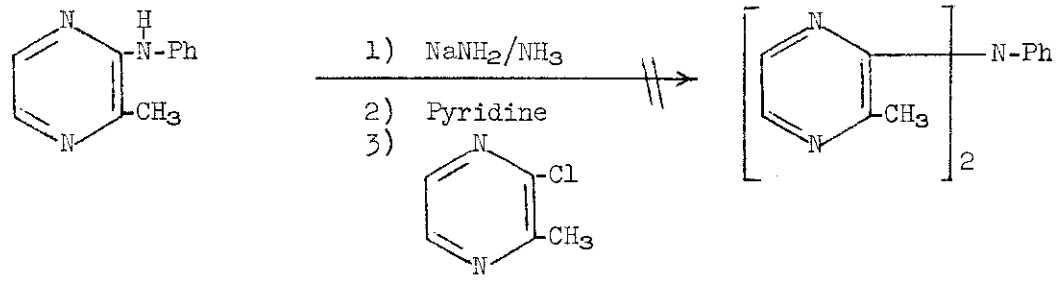
Approved for Public Release

Contrails

A considerable amount of effort was devoted earlier (1) to the attempted preparation of N,N-di[2-(3-methylpyrazine)]aniline. The best yield obtained so far for this compound has been 15%, by the direct coupling of aniline and 2-chloro-3-methylpyrazine. Two different methods were subsequently investigated for the preparation of this material. One method involved heating equimolar quantities of 2-(N-methylanilino)-3-methylpyrazine and 2-chloro-3-methylpyrazine (Reaction 9, Table 14). Inasmuch as the treatment of 2-chloro-3-methylpyrazine at elevated temperatures with an N-alkylaniline resulted in the formation of 2-anilino-3-methylpyrazine (1), it was hoped that the displacement of the methyl group on the nitrogen might be effected with 2-chloro-3-methylpyrazine to form the desired N,N-di[2-(3-methylpyrazyl)]aniline. However, from this reaction only



starting materials were recovered. Another method for the attempted preparation of this product involved the treatment of 2-anilino-3-methylpyrazine with sodium amide and reaction of the resulting intermediate with 2-chloro-3-methylpyrazine in pyridine (Reaction 10, Table 14) employing the same reaction conditions described for the successful N-alkylation of 2-anilino-3-methylpyrazine. No product was isolated from this reaction and only starting materials were recovered.

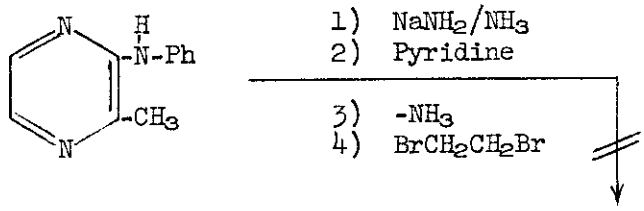


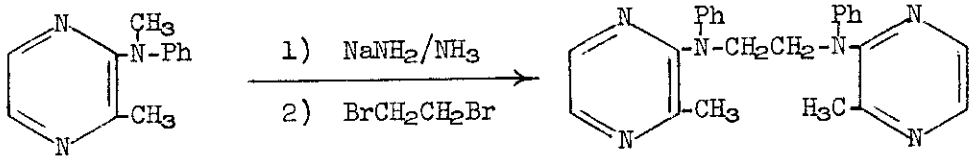
With the development of the "Pyridine Solvent" method, conditions for the preferential N-alkylation on the exocyclic nitrogen function of 2-anilino-3-methylpyrazine with an alkyl halide have been worked out as discussed in detail earlier. It was of interest to start with an alkyl dihalide under similar conditions in an effort to prepare N-alkyl bridged bis(anilinopyrazines). With this aim, 2-anilino-3-methylpyrazine was interacted with 1,2-dibromoethane under the "Pyridine Solvent" conditions (Reaction 11, Table 14). However, only starting 2-anilino-3-methylpyrazine was recovered in this instance. The desired product, N,N'-diphenyl-N,N'-di[2-(3-methylpyrazyl)]-1,2-diaminoethane, which was not obtained from the above mentioned reaction, was actually prepared by the

Approved for Public Release

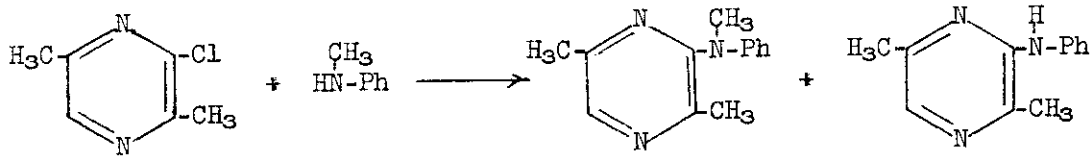
Contrails

interaction of 2-(N-methylanilino)-3-methylpyrazine with 1,2-dibromoethane and sodium amide in liquid ammonia (Reaction 12, Table 14). Inasmuch as the formation of the product involved an unusual displacement of the methyl group on the amino site and only the elemental analysis as well as molecular weight determination supported the assigned structure, further work is needed in order to gain some insight to the nature of the reaction and to conclusively establish the structure of the product.





The "Direct" procedure found to be successful for the preparation of 2-anilino-3-methylpyrazine was applied next to the preparation of 2-anilino-3,6-dimethylpyrazines and the results are listed in Table 15. Analogously, this method consisted of the interaction of an aniline with 2-chloro-3,6-dimethylpyrazine at reflux temperature for an appropriate period of time. The first four reactions listed in Table 15 concerned the preparation of 2-(N-methylanilino)-3,6-dimethylpyrazine under various conditions. However, in each case a varying amount of side product, 2-anilino-3,6-dimethylpyrazine, was also isolated. Results to date suggest that up to approximately 50% yield of the desired 2-(N-methylanilino)-3,6-dimethylpyrazine can be obtained under these conditions by the "Direct" method. It should be pointed out that the side product 2-anilino-3,6-dimethylpyrazine isolated from the above reactions melted at 79-80°C initially. However,



upon standing at room temperature for a 3-month period, the compound's melting point rose to 89-91°C and showed no depression when admixed with a sample of 2-anilino-3,6-dimethylpyrazine (m.p. 88-89°C) prepared from the interaction of aniline with 2-chloro-3,6-dimethylpyrazine (described below). This behavior of undergoing a change in melting point upon standing is analogous to the observed tautomerism exhibited by 2-anilino-3-methylpyrazine (1). At this stage, lack of

Approved for Public Release

TABLE 15

2-ANILINO-3,6-DIMETHYLPYRAZINE

Aniline Reactants	Reaction Max. Temp., °C	Reaction Time, Hrs.	Products (% Yield)
1. N-Methylaniline[a]	215	9	2-(N-Methylanilino)-3,6-dimethylpyrazine (30) and 2-Anilino-3,6-dimethylpyrazine (8)
2. N-Methylaniline[a]	225	9.4	" (33) " (44)
3. N-Methylaniline[a]	223	9.75	" (48) " (21)
4. N-Methylaniline[b]	212	12.25	" (34) " (41)
5. Aniline[a]	222	0.8	2-Anilino-3,6-dimethylpyrazine (86)
6. p-Pentylaniline[a]	240	1.1	2-(p-Pentylanilino)-3,6-dimethylpyrazine (88)

[a] The molar ratio of the aniline to 2-chloro-3,6-dimethylpyrazine was 2 to 1.

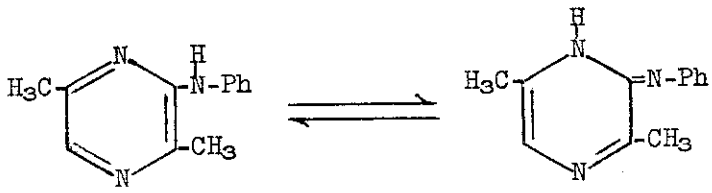
[b] The molar ratio of the aniline to 2-chloro-3,6-dimethylpyrazine was 3 to 1.

Approved for Public Release

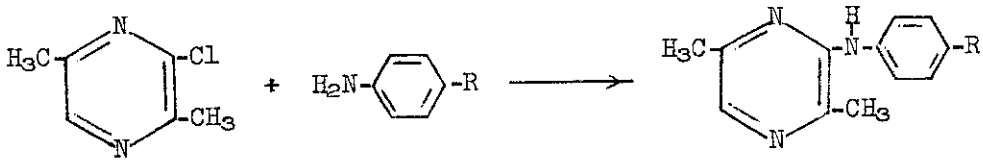
Confidential

Contrails

sufficient evidence prohibits the assignment of definite structures to these tautomers.

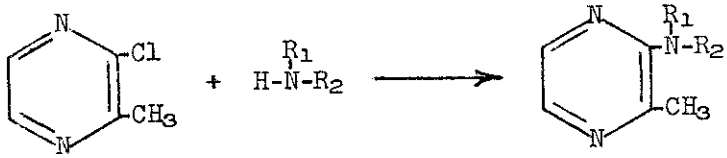


The last two reactions (5 and 6) listed in Table 15 describe the preparation of two additional representatives, (2-anilino-3,6-dimethylpyrazine and 2-(p-pentylanilino)-3,6-dimethylpyrazine). It can be seen that only a short reaction time was needed and the yield of the desired product was excellent in both cases.



where R = -H and $-C_5H_{11}$

2-Alkylamino-3-methylpyrazines and 2-Alkylamino-3,6-dimethylpyrazines. Candidate products derived from the 2-anilino-3-methylpyrazines, whose syntheses were discussed in the previous section, have displayed good thermal and oxidative stabilities based on preliminary test results (see p. 20). It was of interest to consider the preparation of the corresponding alkyl analogs, namely, the alkylaminopyrazines, for comparison. A number of the 2-alkylamino-3-methylpyrazines were thus synthesized employing the "Direct" method (see p. 55) and the results are summarized in Table 16.



where R_1 = H , H , n-C_4H_9, n-C_5H_{11}, n-C_6H_{13}

and R_2 = n-C_6H_{13}, CH_2-CH(C_2H_5)-C_4H_9, n-C_4H_9, n-C_5H_{11}, n-C_6H_{13}

In general, it appeared that the yield of product is directly proportional to the maximum temperature achieved during the reaction and the total reaction time. However, some reaction temperatures were limited by virtue of the low-boiling point of the reactant, and extended reaction periods did not effect a substantial temperature increase in such mixtures (e.g., Table 16, Reactions 4 and 5), although they did increase the yield somewhat. It is interesting to

Approved for Public Release

Contrails

TABLE 16

2-(N-ALKYLAMINO)-3-METHYLPYRAZINES

Amine Reactant	Reaction: Max. Temp., °C	Reaction: Time, Hrs.	Product, (% Yield)
1. n-Hexylamine[a]	165	8	2-n-Hexylamino-3-methylpyrazine (80)
2. 2-Ethylhexylamine[a]	218	24	2-(2-Ethylhexylamino)-3-methylpyrazine (78)
3. n-Hexylamine[c]	195	4.9	2-n-Hexylamino-3-methylpyrazine (31)
4. Di-n-butylamine[b]	168	33.6	2-(N,N-Di-n-butylamino)-3-methylpyrazine (39)
5. Di-n-butylamine[a]	161	8.3	2-(N,N-Di-n-butylamino)-3-methylpyrazine (10)
6. Di-n-pentylamine[b]	193	24.9	2-(N,N-Di-n-pentylamino)-3-methylpyrazine (40)
7. Di-n-pentylamine[a]	183	5.5	2-(N,N-Di-n-pentylamino)-3-methylpyrazine (13)
8. Di-n-hexylamine[b]	247	4.3	2-(N,N-Di-n-hexylamino)-3-methylpyrazine (71)
9. Di-n-hexylamine[a]	245	4.9	2-(N,N-Di-n-hexylamino)-3-methylpyrazine (74)

[a] The molar ratio of 2-chloro-3-methylpyrazine to the amine was 1 to 3.

[b] The molar ratio of 2-chloro-3-methylpyrazine to the amine was 1 to 2.

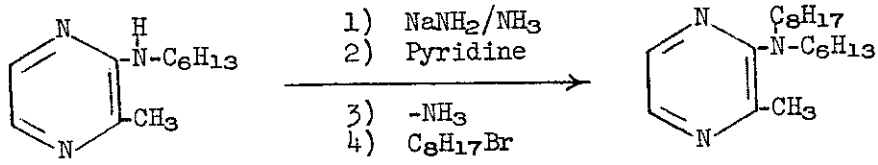
[c] The molar ratio of 2-chloro-3-methylpyrazine to the amine was 2 to 1.

Approved for Public Release

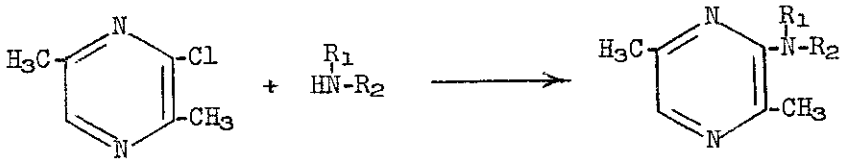
Contrails

note the increase in yield corresponding to the increasing molecular weight of the homologous series of dialkylamines in the series of reactions carried out with short reaction times (compounds 5, 7 and 8). Monoalkylamines appeared to couple more readily with 2-chloro-3-methylpyrazines at lower temperatures than dialkylamines of comparable molecular weight (Table 16, reaction 1 vs. 5). It should also be pointed out that no cleavage products were obtained from these coupling reactions of dialkylamines and 2-chloro-3-methylpyrazine. In Reaction 3 (Table 16), an excess of 2-chloro-3-methylpyrazine to n-hexylamine (2 to 1) was employed in an attempt to prepare N,N-di-[2-(3-methylpyrazyl)] hexylamine, but the product obtained was the mono-coupling product, 2-n-hexylamino-3-methylpyrazine, in 31% yield.

The "Pyridine Solvent" method, which has been successfully developed for the synthesis of 2-(N-alkylanilino)-3-methylpyrazines (see p. 56), was employed to prepare an unsymmetrically substituted dialkylaminopyrazine. Thus, 2-(n-hexylamino)-3-methylpyrazine was treated with 1-bromooctane and sodium amide (2 to 1 to 2) in pyridine to furnish the desired 2-(N-n-hexyl-N-n-octylamino)-3-methylpyrazine in 74% yield. The successful application of this method to the alkylaminopyrazines again demonstrated its synthetic versatility.



As with the case of the N-alkylamino-3-methylpyrazines, the N-alkylamino-3,6-dimethylpyrazines were synthesized by the condensation of alkylamines with 2-chloro-3,6-dimethylpyrazine at elevated temperatures ("Direct" method). In some instances, the maximum temperature reached during the reaction was not sufficiently high by virtue of the low-boiling point of the reactant to result in good yield of the product. This difficulty was circumvented by performing the reaction in a sealed steel bomb under increased pressure conditions. The results of these runs are listed in Table 17.



where R_1 = H , n-C_4H_9, i-C_4H_9, n-C_5H_{11}, n-C_6H_{13}
R_2 = C_6H_{13}, n-C_4H_9, i-C_4H_9, n-C_5H_{11}, n-C_6H_{13}

For comparison purpose, the preparation of 2-(N,N-di-n-butylamino)-3,6-dimethylpyrazine was attempted under various conditions (Reactions 2, 3, 4, and 5, Table 17). The molar ratio of reactants in these runs was held constant to study the effect of variation in reaction time and temperature upon the yield of

Approved for Public Release

Contrails

TABLE 17

2-N-ALKYLAMINO-3,6-DIMETHYLPYRAZINES

	Amine Reactant	Reaction Max. Temp., °C	Reaction Time, Hrs.	Product (% Yield)
1.	n-Hexylamine[a]	195	12.5	2-(n-Hexylamino)-3,6-dimethylpyrazine (46)
2.	Di-n-butylamine[a]	171	42.25	2-(N,N-Di-n-butylamino)-3,6-dimethylpyrazine (34)
3.	Di-n-butylamine[a,b]	200	2.25	" (19)
4.	Di-n-butylamine[a,b,c]	250	4	" (71)
5.	Di-n-butylamine[a,b,d]	260	4	" (66)
6.	Di-i-butylamine[a,b,e]	260	4	2-(N,N-Di-i-butylamino)-3,6-dimethylpyrazine (35)
7.	Di-n-pentylamine[a]	201	25.75	2-(N,N-Di-n-pentylamino)-3,6-dimethylpyrazine (41)
8.	Di-n-pentylamine[a,b,c]	260	3.5	" (55)
9.	Di-n-hexylamine[a]	252	7.3	2-(N,N-Di-n-hexylamino)-3,6-dimethylpyrazine (59)

[a] The molar ratio of 2-chloro-3,6-dimethylpyrazine to the amine was 1 to 2.

[b] This reaction was performed in a sealed steel bomb.

[c] In this run, the line joining the pressure gauge to the steel bomb was plugged due to formation of solid amine hydrochloride. No reliable pressure reading could be obtained.

[d] The max. pressure achieved during reaction was 95 lb./in.^{2}

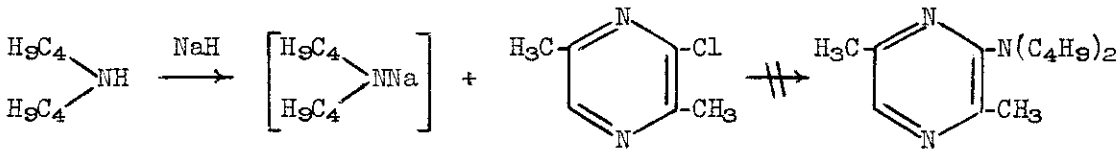
[e] The max. pressure achieved during reaction was 150-160 lb./in.^{2}

Approved for Public Release

Contrails

product. As expected, in run 2, where the reaction was performed at atmospheric pressure and the maximum temperature attained was only 171°C during a 42.25-hour period, the yield of the desired product was low, only 34%. The next attempt (Reaction 3) was performed in a sealed steel bomb to effect higher reaction temperature (200°C). However, the low yield (19%) obtained from this reaction indicated either the time or temperature, or both, were not sufficiently drastic. However, in runs 4 and 5, when the reaction temperature was maintained at 250 to 260°C in a steel bomb during a 4-hour period, the desired 2-(N,N-di-n-butylamino)-3,6-dimethylpyrazine was obtained in 71-66% yield. Similar behavior was also observed in the preparation of 2-(N,N-di-n-pentylamino)-3,6-dimethylpyrazine (Reactions 7 and 8, Table 17). When di-n-hexylamine was employed as the amine reactant (Reaction 9, Table 17), a sufficiently high reflux temperature (252°C) was achieved during reaction without the aid of a sealed vessel. Although a relatively longer reaction time was needed, the product, 2-(N,N-di-n-hexylamino)-3,6-dimethylpyrazine was prepared in 59% yield.

The preparation of 2-(N,N-di-n-butylamino)-3,6-dimethylpyrazine was also attempted by the condensation of the sodium salt of di-n-butylamine with 2-chloro-3,6-dimethylpyrazine under various conditions. The intermediate sodium di-n-butylamine was prepared by heating a mixture of sodium hydride and di-n-butylamine



(1 to 2) at 173-184°C until the evolution of gas was completed. However, subsequent interaction of this presumed sodium salt of the amine with 2-chloro-3,6-dimethylpyrazine at various temperatures failed to yield the desired product.

Alkyl(methyl)pyrazines. In the various classes of 2-substituted-3-methylpyrazine intermediates synthesized so far during this program, the 2-substituent has been linked by a hetero-atom, such as O, S, N and Si, to the pyrazine nucleus. The original contention was that the hetero-atom linkage would provide the necessary flexibility to result in liquid pyrazine derivatives. Another means to achieve fluidity, it was found, was to place long alkyl chains directly on the pyrazine nucleus. Therefore, it was of interest to prepare high molecular weight simple alkylpyrazines in order that their physical properties could be investigated.

Alkylation of methylpyrazine with a variety of alkyl halides in the presence of sodium amide and liquid ammonia have resulted in alkylpyrazines in high yields (4). Similar alkylations of 2,5-(and 2,6-)dimethylpyrazine and tetramethylpyrazine were attempted and conditions have now been worked out to give monoalkylated products in excellent yields. The results are given in Table 18.

Approved for Public Release

TABLE 18

ALKYL(METHYL)PYRAZINES

	Pyrazine Reactant	Alkyl Halide	Product (% Yield)
1.	2,5-Dimethylpyrazine[a]	1-Bromohexane	2-n-Heptyl-5-methylpyrazine (89)
2.	2,5-Dimethylpyrazine[a,b]	1-Bromohexane	2-n-Heptyl-5-methylpyrazine (69) 2,5-Dimethyl-3-[5-(2-methylpyrazylmethyl)]-pyrazine (Trace)
3.	2,5-Dimethylpyrazine[c]	1-Bromohexane	2-n-Heptyl-5-methylpyrazine (40)
4.	2,6-Dimethylpyrazine[a]	1-Bromohexane	2-n-Heptyl-6-methylpyrazine (80)
5.	2,6-Dimethylpyrazine[a,b]	1-Bromohexane	2-n-Heptyl-6-methylpyrazine (88)
6.	2,5-Dimethylpyrazine[a]	1-Bromooctane	2-n-Nonyl-5-methylpyrazine (90)
7.	2,6-Dimethylpyrazine[a]	1-Bromooctane	2-n-Nonyl-6-methylpyrazine (95)
8.	Tetramethylpyrazine[d]	1-Bromohexane	2-n-Heptyl-3,5,6-trimethylpyrazine (42) 2,5-Di-n-heptyl-3,6-dimethylpyrazine (26)

[a] A molar ratio of 2 to 2 to 1 of the pyrazine compound to sodium amide to alkyl halide was employed.

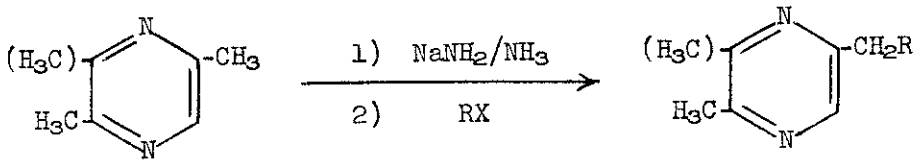
[b] The run was performed in a 6-mole scale.

[c] A molar ratio of 2 to 4 to 1 of the pyrazine compound to sodium amide to alkyl halide was employed.

[d] A molar ratio of 1 to 2 to 2 of the pyrazine compound to sodium amide to alkyl halide was employed.

Approved for Public Release

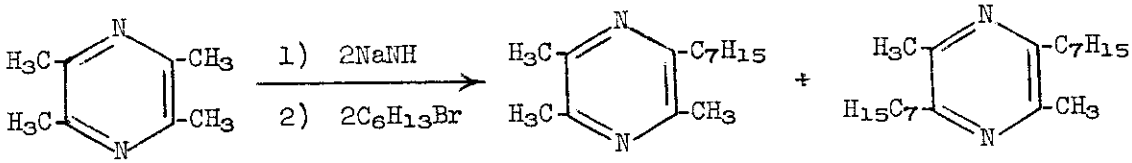
Contrails



where R = $-C_6H_{13}$ and $-C_8H_{17}$

The importance of employing a correct molar ratio of reactants to obtain the desired product in good yield was demonstrated in Reactions 1 and 3. In Reaction 1, where 2,5-dimethylpyrazine was treated with sodium amide and 1-bromohexane (2 to 2 to 1), the monoalkylated compound, 2-n-heptyl-5-methylpyrazine, was obtained in 89% yield. When a large excess of sodium amide was employed as in the case of Reaction 3, the yield of the desired product was reduced to 40%. Thus, the molar ratio of 2 to 2 to 1 of the dimethylpyrazine compound to sodium amide to alkyl halide was adapted as standard conditions for the monoalkylation of dimethylpyrazine. As seen in Table 18, the yields from these reactions (Reactions 3 to 7) were excellent (80-95%).

A study of the conditions for the alkylation of tetramethylpyrazine was also initiated. A molar ratio of 1 to 2 to 2 of tetramethylpyrazine to sodium amide to alkyl halide was used to favor polyalkylation. Indeed, from this reaction a monoalkylated compound, tentatively assumed to be 2-n-heptyl-3,5,6-trimethylpyrazine, was obtained as the major product in 42% yield, together with a 26% of the dialkylated material, 2,5-di-n-heptyl-3,6-dimethylpyrazine.



Advanced Intermediates

By definition (see p. 5), compounds in this category consist of the 2,6-disubstituted-3-methylpyrazines. These compounds were synthesized to serve as intermediates for the preparation of 2,6-disubstituted-(and 2,3,6-trisubstituted)-pyrazines; or, if possessing good thermal and oxidative stabilities, to serve as candidate products themselves. Furthermore, the routes developed for the preparation of the advanced intermediates may eventually be applied to the synthesis of tetrasubstitutedpyrazines from tetramethylpyrazine.

2-Phenoxy-3-methyl-6-substitutedpyrazines. Based on the methods of synthesis, compounds in this class can be divided into two types, namely, the 2-phenoxy-3-methyl-6-benzylpyrazines and 2-phenoxy-3-methyl-6-alkylpyrazines. The former were obtained by the "benzyne" arylation (1) of 2-phenoxy-3,6-dimethylpyrazine with aryl halides in the presence of sodium amide and liquid ammonia; the latter were prepared by the alkylation of 2-phenoxy-3,6-dimethylpyrazine with appropriate

Approved for Public Release

TABLE 19

2-PHENOXY-3-METHYL-6-SUBSTITUTEDPYRAZINES

	2-Phenoxy-3,6-dimethylpyrazine	Aryl or Alkyl Halide	Product (% Yield)
1.	2-Phenoxy-3,6-dimethylpyrazine[a]	Bromobenzene	2-Phenoxy-3-methyl-6-benzylpyrazine (41)
2.	2-(p-Nonylphenoxy)-3,6-dimethylpyrazine[a]	Bromobenzene	2-(p-Nonylphenoxy)-3-methyl-6-benzylpyrazine (58)
3.	2-(p-Nonylphenoxy)-3,6-dimethylpyrazine[a]	p-Bromophenyl Phenyl Ether	2-(p-Nonylphenoxy)-3-methyl-6-(p-phenoxybenzyl)pyrazine (49)
4.	2-(p-Nonylphenoxy)-3,6-dimethylpyrazine[a]	p-Phenyldimethylsilylphenyl p-Bromophenyl Ether	- - -
5.	2-(p-Nonylphenoxy)-3,6-dimethylpyrazine[b]	Chloromethyltrimethylsilane	2-(p-Nonylphenoxy)-3-methyl-6-(2-trimethylsilylethyl)pyrazine (28) 2-(p-Nonylphenoxy)-3-methyl-6-[2-(3,6-dimethylpyrazylmethyl)]pyrazine (50)
6.	2-(p-Nonylphenoxy)-3,6-dimethylpyrazine[c]	Chloromethyltrimethylsilane	2-(p-Nonylphenoxy)-3-methyl-6-(2-trimethylsilylethyl)pyrazine (44)
7.	2-(p-Nonylphenoxy)-3,6-dimethylpyrazine[d]	1-Bromobutane	2-(p-Nonylphenoxy)-3-methyl-6-(5-nonyl)-pyrazine (58, 80)
8.	2-(p-Nonylphenoxy)-3,6-dimethylpyrazine[c]	Benzyl Chloride	2-(p-Nonylphenoxy)-3-methyl-6-(2-phenylethyl)pyrazine (54)
9.	2-(p-Nonylphenoxy)-3,6-dimethylpyrazine[c]	n-Dodecyl Bromide	2-(p-Nonylphenoxy)-3-methyl-6-tridecylpyrazine (66)

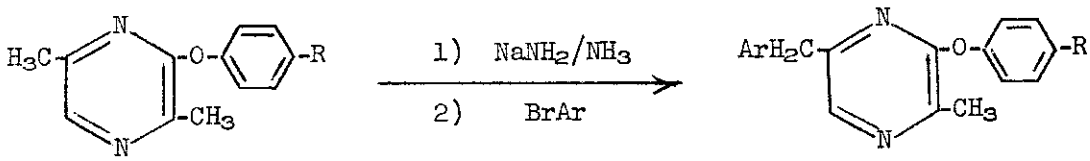
The molar ratio of sodium amide to pyrazine compounds to aryl (or alkyl) halide employed for the above runs is indicated as follows: [a]8 to 2 to 1; [b]2 to 2 to 1; [c]1 to 1 to 1; and [d]3 to 1 to 3.

Approved for Public Release

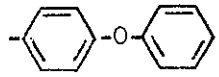
Contrails

alkyl halides under similar conditions. Results from these preparations are summarized in Table 19.

2-(p-Nonylphenoxy)-3-methyl-6-(p-phenoxybenzyl)pyrazine, a product obtained from Reaction 3 (Table 19), was prepared in 46% yield previously (1). The molar ratio of the reactants for this reaction was 4 to 2 to 1 (sodium amide to 2-(p-nonylphenoxy)-3,6-dimethylpyrazine to p-bromophenyl phenyl ether). The repeated preparation of this compound as well as two other new representatives (Reactions 3, 1 and 2 respectively, Table 19) were attempted by using an 8 to 2 to 1 molar ratio of the corresponding reactants as that described above. The yields from these reactions ranged from 41 to 58%. Apparently, the increased amount of sodium amide employed did not seem to alter the yield of product to any significant



where R = -H , $-C_8H_{19}$, $-C_9H_{19}$

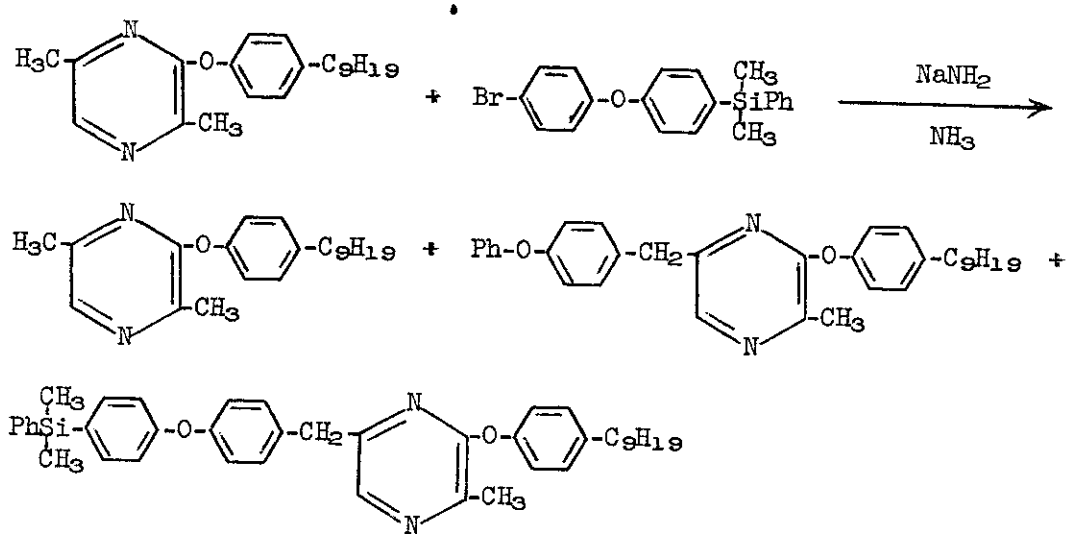
Ar = $-C_6H_5$, $-C_6H_5$, 

extent. Inasmuch as there were two methyl sites in the starting 2-phenoxy-3,6-dimethylpyrazines available for reaction, arylation could conceivably take place either at the 3-methyl or the 6-methyl site. Further evidences, obtained from the reactions of these 2-phenoxy-3-methyl-6-benzylpyrazines with selenium dioxide, indicated the 6-methyl site was attacked by the aryl halide. The proof of structure of these materials is discussed in detail under the section describing the 2,6-disubstitutedpyrazines (see p. 86).

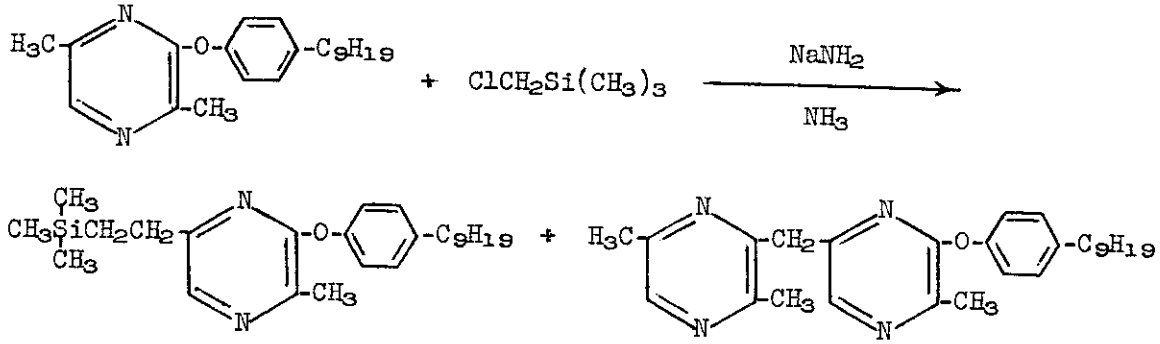
The interaction of 2-phenoxy-3-methylpyrazine with p-phenyldimethylsilylphenyl p-bromophenyl ether and sodium amide in liquid ammonia, resulting in a silyl substituted 2-phenoxy-3-benzylpyrazine, was accomplished previously (1). This phenylation was now repeated employing 2-(p-nonylphenoxy)-3,6-dimethylpyrazine in place of 2-phenoxy-3-methylpyrazine (Reaction 4, Table 19). However, based on the results of elemental analysis of a high-boiling fraction, it was concluded that a mixture of starting 2-(p-nonylphenoxy)-3,6-dimethylpyrazine, the cleavage product, 2-(p-nonylphenoxy)-3-methyl-6-(p-phenoxybenzyl)pyrazine, and a small amount of the desired 2-(p-nonylphenoxy)-3-methyl-6-[p-(p'-phenyldimethylsilylphenoxy)benzyl]pyrazine was obtained.

Approved for Public Release

Contrails



An alkylated representative of this class, 2-(p-nonylphenoxy)-3-methyl-6-(2-trimethylsilylethyl)pyrazine, was prepared by the interaction of 2-(p-nonylphenoxy)-3,6-dimethylpyrazine with chloromethyltrimethylsilane and sodium amide in liquid ammonia. Initially, the reaction was attempted employing a molar ratio of 2 to 2 to 1 (sodium amide to 2-(p-nonylphenoxy)-3,6-dimethylpyrazine to chloromethyltrimethylsilane) of reactants and a 2-hour reaction time (Reaction 5, Table 19). The desired alkylated product was obtained in 28% yield, together with a 50% yield of a coupling product, 2-(p-nonylphenoxy)-3-methyl-6-[2-(3,6-dimethylpyrazylmethyl)]pyrazine. This coupling product probably resulted via a nucleophilic



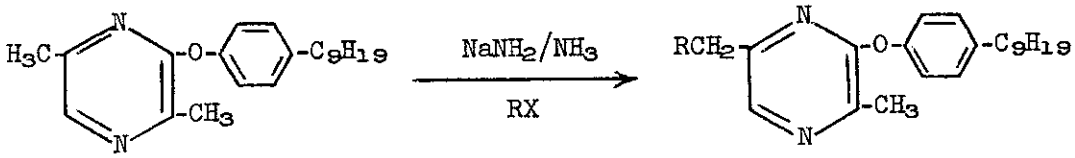
displacement of the p-nonylphenoxy group in 2-(p-nonylphenoxy)-3,6-dimethylpyrazine by the anion of another molecule of 2-(p-nonylphenoxy)-3,6-dimethylpyrazine. An analogous reaction was observed earlier when 2-thiophenoxy-3-methylpyrazine was phenylated under the "benzyne" conditions with bromobenzene and a presumed self-coupling product of the starting material, 2-thiophenoxy-3-(3-methyl-2-pyrazylmethyl)pyrazine was obtained in low yield (1). One method of circumventing the formation of the self-coupling product was to employ an equivalent amount of sodium amide and a shorter reaction time. Therefore, the preparation of

Approved for Public Release

Contrails

2-(p-nonylphenoxy)-3-methyl-6-(2-trimethylsilylethyl)pyrazine was repeated using a 1 to 1 to 1 molar ratio of reactants and 1-hour reaction time (Reaction 6, Table 19). The desired alkylated product was, indeed, obtained in higher yield (44%) and none of the self-coupling product was isolated.

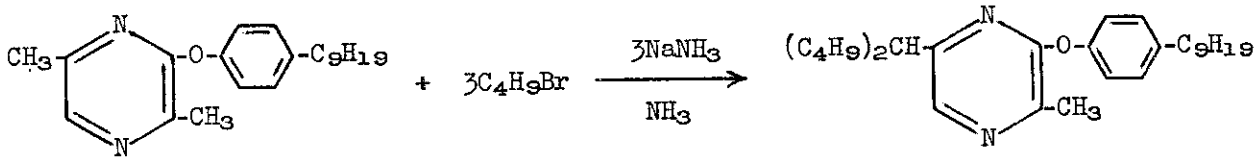
Therefore, employing the conditions developed above for monoalkylation, 2-(p-nonylphenoxy)-3,6-dimethylpyrazine was treated with benzyl chloride and n-dodecyl bromide (Reactions 8 and 9) to afford the desired 2-(p-nonylphenoxy)-3-methyl-6-(2-phenylethyl)pyrazine and 2-(p-nonylphenoxy)-3-methyl-6-tridecylpyrazine in 54% and 66% yield, respectively. The assignments of structures for both



where RX = $PhCH_2Cl$ and n-$C_{12}H_{25}Br$

products were based on results of selenium dioxide demethylation (see p.87). It was interesting to note that both of these products were high molecular weight fluids.

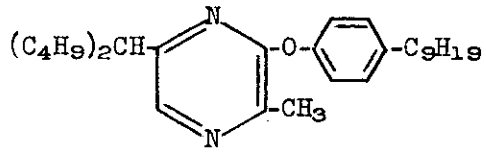
Next, conditions for polyalkylation on the methyl site of 2-(p-nonylphenoxy)-3,6-dimethylpyrazine were investigated. As a result, 2-(p-nonylphenoxy)-3-methyl-(5-nonyl)pyrazine, a fluid liquid, was prepared in 58-80% yield by the interaction of 2-(p-nonylphenoxy)-3,6-dimethylpyrazine with a three-fold excess of 1-bromobutane and sodium amide (Reaction 7, Table 19). Based on the results of elemental analysis of this material, which indicated the introduction of two butyl groups on



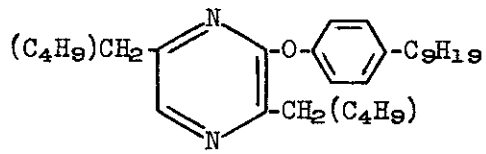
2-phenoxy-3,6-dimethylpyrazine, three possible structures could be written. Structure C was eliminated by virtue of the fact that 2-(p-nonylphenoxy)-3-methylpyrazine could not be dialkylated with excess 1-bromobutane and sodium amide. The product obtained from this reaction was the monoalkylated material, 2-(p-nonylphenoxy)-3-pentylpyrazine (see p. 82). Essentially the same degree of steric inhibition was present in 2-(p-nonylphenoxy)-3,6-dimethylpyrazine as well. Structure B was ruled out based on results of selenium dioxide oxidation of this compound (see p. 87) to a demethylated product. From this reaction a quantitative amount of reduced selenium was recovered and there was no carbonyl band present in the infrared spectrum of the oxidized product. Therefore, structure A is the logical choice for this material.

Approved for Public Release

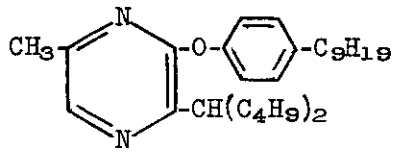
Contrails



A

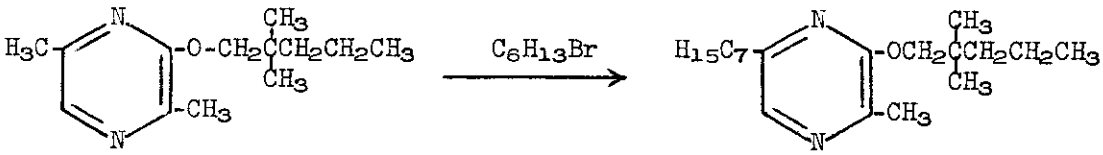


B



C

2-Alkoxy-3-methyl-6-substitutedpyrazines. Previously, it was found that using a molar ratio of 2 to 2 to 1 of sodium amide to dimethylpyrazine to alkyl halide for the alkylation of dimethylpyrazines, the desired monoalkylated alkyl-(methyl)pyrazines could be obtained in over 90% yield (see p. 68). Subsequently, the dialkylation conditions for the synthesis of 2-phenoxy-3-methyl-6-substituted-pyrazine was developed by using a molar ratio of 3 to 1 to 3 of sodium amide to 2-phenoxy-3,6-dimethylpyrazine to alkyl halide (see p. 74). The above mentioned conditions were applied to the mono- and di-alkylation of the 2-alkoxy-3,6-di-methylpyrazines and the results are listed in Table 20. Thus, 2-(2,2-dimethyl-pentoxy)-3,6-dimethylpyrazine, whose synthesis has been described earlier, was further reacted at the 6-methyl site with two different alkyl halides. When the reaction was performed using 1-bromohexane as the alkyl halide and under mono-alkylation conditions (Reaction 1, Table 20), the product, 2-(2,2-dimethylpentoxy)-3-methyl-6-(n-heptyl)pyrazine, was obtained in 73-82% yield. When 1-bromobutane was used as the alkyl halide and the reaction was performed under dialkylation conditions (Reaction 2, Table 20), both the mono- and dialkylated products were obtained in nearly equivalent yields (41% and 46%, respectively). The assignments of structure for these products were based only on analogy to the 2-phenoxy-3-methyl-6-substitutedpyrazines.



Approved for Public Release

Approved for Public Release

TABLE 20

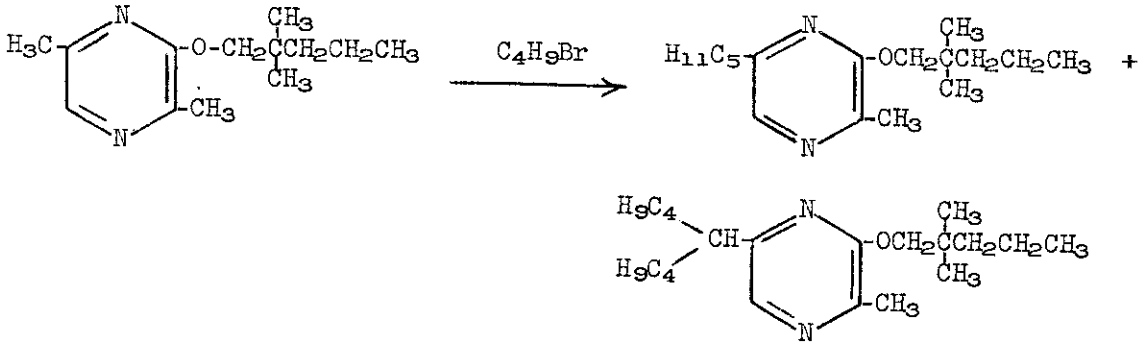
2-ALKOXY-3-METHYL-6-SUBSTITUTEDPYRAZINES

2-Alkoxy-3,6-dimethylpyrazines	Alkyl Halide	Product (% Yield)
1. 2-(2,2-Dimethylpentoxy)-3,6-dimethylpyrazine[a]	1-Bromohexane	2-(2,2-Dimethylpentoxy)-3-methyl-6-(n-heptyl)pyrazine (73, 82)
2. 2-(2,2-Dimethylpentoxy)-3,6-dimethylpyrazine[b]	1-Bromobutane	2-(2,2-Dimethylpentoxy)-3-methyl-6-(n-pentyl)pyrazine (41) 2-(2,2-Dimethylpentoxy)-3-methyl-6-(5-nonyl)pyrazine (46)

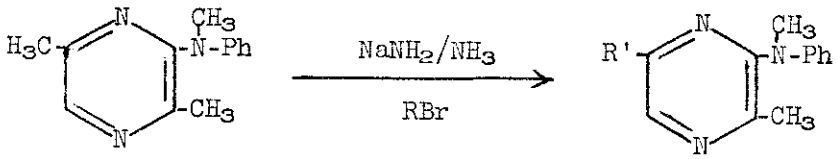
[a] The molar ratio of sodium amide to pyrazine compound to alkyl halide was 2 to 2 to 1.

[b] The molar ratio of sodium amide to pyrazine compound to alkyl halide was 3 to 1 to 3.

Contrails



2-Anilino-3-methyl-6-substitutedpyrazines and 2-Alkylamino-3-methyl-6-substitutedpyrazines. These derivatives were obtained from the alkylation of the corresponding 2-anilino- (or 2-alkylamino)-3,6-dimethylpyrazines. Due to similarity in reaction conditions, the synthesis of these two classes of compounds is most conveniently discussed together at this point. The results are tabulated in Table 21. Reaction 1 describes the preparation of 2-(N-methylanilino)-3-methyl-6-(5-nonyl)-pyrazine in 60-73% yield by the interaction of 2-(N-methylanilino)-3,6-dimethylpyrazine with a three-fold excess of 1-bromobutane and sodium amide. The structure of this material was confirmed by elemental analysis and selenium dioxide demethylation to the corresponding 2-(N-methylanilino)-6-(5-nonyl)pyrazine (see p. 95). Similarly, under monoalkylation conditions, 2-(N-methylanilino)-3-methyl-6-(n-heptyl)pyrazine was prepared in 43% yield by the treatment of 2-(N-methylanilino)-3,6-dimethylpyrazine with equimolar quantities of 1-bromohexane and sodium amide in liquid ammonia (Reaction 2). When the above preparation was repeated using a 2 to 2 to 1 ratio of 2-(N-methylanilino)-3,6-dimethylpyrazine to sodium amide to 1-bromohexane, the desired product was obtained in 58% yield. Employing the pyrazine compound in excess was expected to minimize the possibility of polyalkylation.



where R = $-C_4H_9$, $-C_6H_{13}$
R' = $-CH(C_4H_9)_2$, $-C_7H_{15}$

The molar ratio of 2 to 2 to 1 of the corresponding reactants mentioned above was also adopted for the monoalkylation of 2-(N,N-di-n-pentylamino)-3,6-dimethylpyrazine and 2-(N,N-di-n-hexylamino)-3,6-dimethylpyrazine (Reactions 3 and 4). In the first instance, the desired 2-(N,N-di-n-pentylamino)-3-methyl-6-(n-heptyl)-pyrazine was obtained in 84% yield. The lower yield (36%) of product in the second case when the reaction was performed under similar conditions might be attributed to the insolubility of the starting 2-(N,N-di-n-hexylamino)-3,6-dimethylpyrazine in liquid ammonia. When the same reaction was repeated under conditions

Approved for Public Release

Contrails

TABLE 21

2-ANILINO-3-METHYL-6-SUBSTITUTEDPYRAZINES
AND 2-ALKYLAMINO-3-METHYL-6-SUBSTITUTEDPYRAZINES

Pyrazine Reactant	Alkyl Halide	Product (% Yield)
1. 2-(N-Methylanilino)-3,6-dimethylpyrazine	1-Bromobutane	2-(N-Methylanilino)-3-methyl-6-(5-nonyl)pyrazine (60[a], 73[a])
2. 2-(N-Methylanilino)-3,6-dimethylpyrazine	1-Bromohexane	2-(N-Methylanilino)-3-methyl-6-(n-heptyl)pyrazine (43[b], 58[c])
3. 2-(N,N-Di-n-pentylamino)-3,6-dimethylpyrazine	1-Bromohexane	2-(N,N-Di-n-pentylamino)-3-methyl-6-(n-heptyl)-pyrazine (84[c])
4. 2-(N,N-Di-n-hexylamino)-3,6-dimethylpyrazine	1-Bromohexane	2-(n,N-Di-n-hexylamino)-3-methyl-6-(n-heptyl)-pyrazine (36[c], 67[c,d])

---

[a] The molar ratio of sodium amide to pyrazine compound to alkyl halide of 3 to 1 to 3 was employed.

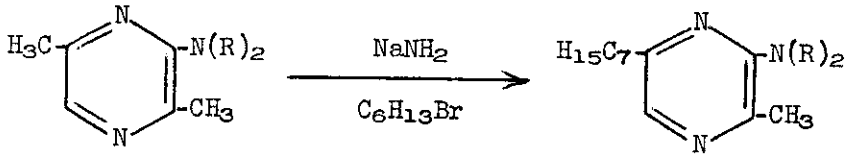
[b] The molar ratio of 1 to 1 to 1 of the corresponding reactants stated in (a) was employed.

[c] The molar ratio of 2 to 2 to 1 of the corresponding reactants stated in (a) was employed.

[d] This run was performed under the conditions described in the "Pyridine Solvent" method.

Approved for Public Release

Contrails



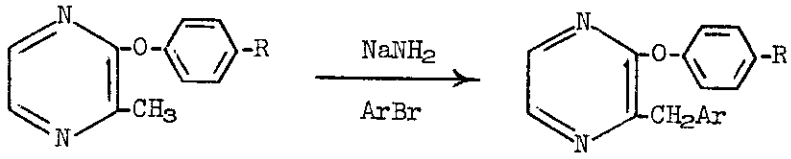
where R = $-C_5H_{11}$ and $-C_6H_{13}$

described in the "Pyridine Solvent" method (see p. 59), the yield of the product rose to 67%. The assignment of structures for these products was based on analogy to the 2-anilino-3-methyl-6-substitutedpyrazines.

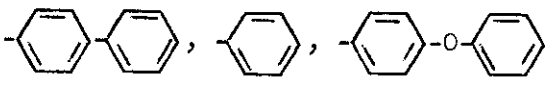
Candidate Products

Representatives in this category consisted of fully substituted pyrazine derivatives, in the sense that all of the potentially reactive sites of the appropriate pyrazine starting material have been substituted or displaced. The lower molecular weight materials in this category might be considered model candidate products which were prepared to demonstrate reaction feasibility. Those products which have sufficient molecular weight and show good fluid properties and other desirable characteristics have been or will be evaluated for the proposed application.

2-Phenoxy-3-substitutedpyrazines and 2-Phenoxy-3,6-disubstitutedpyrazines. Utilizing previously prepared 2-phenoxy-3-methylpyrazines, studies of reactions on the methyl site were continued. Phenylation of representatives of this class of compounds via the "benzyne" conditions to give the desired phenylated products with yields up to 58% was reported earlier (1). During the current period, this reaction was extended to include other 2-phenoxy-3-methylpyrazines as well as different phenylating reagents for reaction on the methyl site. The results of these reactions are summarized in Table 22. Reactions 1, 2 and 3 were performed by using the "one flask" method (18). In this procedure a 4 to 2 to 1 molar ratio of sodium amide to the pyrazine compound to aryl halide was employed. Yields (51 and 49%, respectively) obtained from Reactions 1 and 2 were quite respectable for this type of arylation. The lower yield (24%) obtained from Reaction 3 might be explained on the basis of steric hindrance offered by the bulky 2-substituent in 2-(p-nonylphenoxy)-3-methylpyrazine as well as of the large "benzyne" reagent, p-bromophenyl phenyl ether.



where R = H , $-C_9H_{19}$, $-C_9H_{19}$

and Ar = 

Approved for Public Release

Contrails

TABLE 22

2-PHENOXY-3-BENZYLPYRAZINES

	2-Phenoxy-3-methylpyrazine	Aryl Halide	Product (% Yield)
1.	2-Phenoxy-3-methylpyrazine[a]	4-Bromobiphenyl	2-Phenoxy-3-(p-phenylbenzyl)pyrazine (51)
2.	2-(p-Nonylphenoxy)-3-methylpyrazine[a]	Bromobenzene	2-(p-Nonylphenoxy)-3-benzylpyrazine (49)
3.	2-(p-Nonylphenoxy)-3-methylpyrazine[a]	p-Bromophenyl Phenyl Ether	2-(p-Nonylphenoxy)-3-(p-phenoxybenzyl)-pyrazine (24)
4.	2-Phenoxy-3-methylpyrazine[b]	p-Phenyldimethylsilylchlorobenzene	2-Phenoxy-3-benzylpyrazine (58)
5.	2-Phenoxy-3-methylpyrazine[b]	p-Phenyldimethylsilylbromobenzene	2-Phenoxy-3-benzylpyrazine (50) 1,3-Diphenyltetramethyldisiloxane (60)
6.	2-(p-Nonylphenoxy)-3-methylpyrazine[b]	p-Phenyldimethylsilylbromobenzene	2-(p-Nonylphenoxy)-3-benzylpyrazine (30)
7.	2-Phenoxy-3-methylpyrazine[a]	(p-Chlorobenzyl)-trimethylsilane	Crude mixture of 2-phenoxy-3-methylpyrazine and 2-phenoxy-3-(p-methylbenzyl)-pyrazine (?)

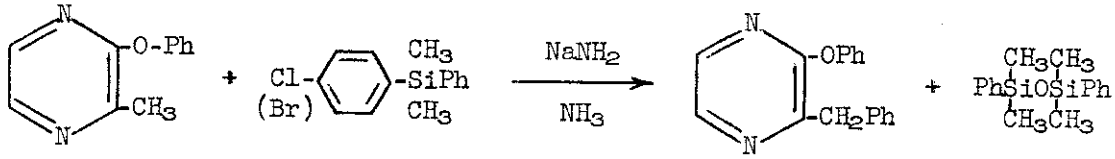
[a] A molar ratio of 4 to 2 to 1 of sodium amide to pyrazine compound to aryl halide was employed.

[b] A molar ratio of 5 to 2 to 1 of the corresponding reactants mentioned in (a) was employed.

Approved for Public Release

Contrails

The previously attempted phenylation of 2-phenoxy-3-methylpyrazine with m-phenyldimethylsilylchlorobenzene and sodium amide in liquid ammonia resulted in the cleavage of the phenyldimethylsilyl group under these conditions (1). Since 2-phenoxy-3-benzylpyrazine was isolated as the only product from this reaction and the silicon-containing fragment was lost in the workup, it was of interest to study further reactions of this type so that the true nature of the cleavage might be established. With this aim, arylation of 2-phenoxy-3-methylpyrazines with a number of silicon-containing aryl halides was continued and the results are summarized in Reactions 4, 5, 6 and 7 of Table 22. Phenylation of 2-phenoxy-3-methylpyrazine with p-phenyldimethylsilylchlorobenzene and p-phenyldimethylsilylbromobenzene via the "benzyne" conditions were attempted (Reactions 4 and 5, Table 22), and in each instance the known 2-phenoxy-3-benzylpyrazine (1) was isolated in 58% and 50% yield, respectively. In addition, a 60% yield of crude 1,3-diphenyltetramethyldisiloxane was obtained in the latter case. Similarly, the interaction of 2-(p-nonylphenoxy)-3-methylpyrazine with p-phenyldimethylsilylbromobenzene



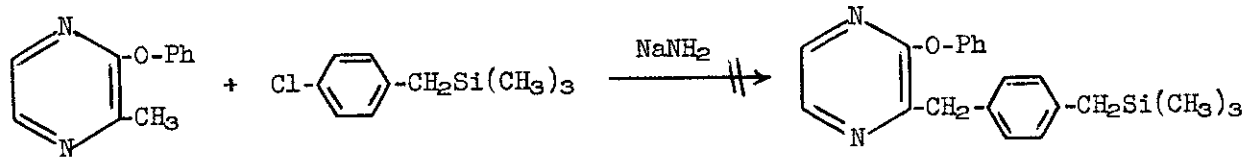
(Reaction 6, Table 22) afforded the cleavage product 2-(p-nonylphenoxy)-3-benzylpyrazine (see p. 80) in 30% yield. The cleavage of aryl-silicon bond by acidic reagents is well known (19). Furthermore, Hauser and Hance reported (20) the cleavage of tetraphenylsilane by nucleophilic reagents such as potassium amide in liquid ammonia to give a 62% yield of benzene in one hour. Whether the cleavage of the silicon-aryl bond observed in the attempted preparation of silicon-containing pyrazines took place during the reaction in the presence of excess sodium amide and liquid ammonia or during the quenching of the reaction by ammonium chloride (strong acid in liquid ammonia) is not certain at this stage. Studies of the amination of the starting p-phenyldimethylsilylbromobenzene in sodium amide and liquid ammonia under various conditions should shed some light into the nature of this cleavage.

The above efforts in the attempted synthesis of silicon-containing 2,3-disubstitutedpyrazines by the phenylation of 2-phenoxy-3-methylpyrazine with silyl-substituted halobenzene via the "benzyne" conditions resulted in the cleavage of the silicon-aryl bond. Therefore, a new phenylation agent, (p-chlorobenzyl)trimethylsilane (21), was prepared from p-chlorobenzylmagnesium chloride and trimethylchlorosilane in 62.5%. This arylating agent was expected to be stable in the sodium amide-liquid ammonia system, inasmuch as it did not contain a silicon-aryl bond. Two runs were attempted wherein 2-phenoxy-3-methylpyrazine was treated with (p-chlorobenzyl)trimethylsilane in the presence of sodium amide and liquid ammonia (Reaction 7, Table 22), but the starting 2-phenoxy-3-methylpyrazine was recovered in 75% and 81% respectively, in each instance. In addition, a small amount of material which was presumed to be a mixture of starting 2-phenoxy-3-methylpyrazine and the desilylated 2-phenoxy-3-(p-methylbenzyl)pyrazine was

Approved for Public Release

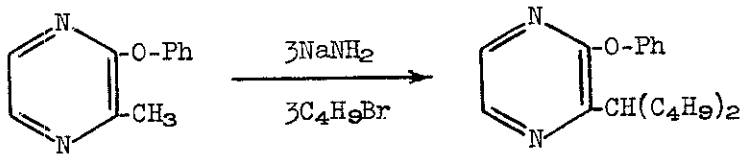
Contrails

isolated from the first run. The cleavage of the benzyl-silicon bond under the above conditions was demonstrated by the attempted amination of (p-chlorobenzyl)-trimethylsilane which will be discussed later (see p. 104).



The next 2-phenoxy-3-substitutedpyrazines to be discussed will be the 2-phenoxy-3-alkylpyrazines. These compounds were prepared by the interaction of a 2-phenoxy-3-methylpyrazine with an alkyl halide and sodium amide in liquid ammonia and the results are given in Table 23.

In Reaction 2, Table 23, the original intention of using three-fold excess of 1-bromobutane and sodium amide with respect to the pyrazine compound was to prepare 2-phenoxy-3-(tributyl)methylpyrazine. However, the product isolated was the di-alkylated compound, 2-phenoxy-3-(5-nonyl)pyrazine, in 74% yield. Employing a larger excess of 1-bromobutane and sodium amide (six-fold excess of each) did not alter the reaction to any extent, inasmuch as 2-phenoxy-3-(5-nonyl)pyrazine was again obtained in 75% yield (Reaction 2, Table 23). A stepwise alkylation was also attempted by the interaction of 2-phenoxy-3-(5-nonyl)pyrazine with one equivalent each of 1-bromobutane and sodium amide, but only starting material was recovered in this instance. It appeared that the steric requirements for three butyl groups at the methyl site of 2-phenoxy-3-methylpyrazine were too severe to be accommodated.



Therefore, with the conditions developed above, a number of dialkylations were carried out. In Table 23, when 1-bromobutane was employed as the alkyl halide, a molar ratio of 3 to 3 to 1 (sodium amide to 1-bromobutane to 2-substituted-3-methylpyrazine) was used to effect dialkylation, if possible. In all other cases a molar ratio of 1 to 1 to 1 (sodium amide to alkyl halide to 2-substituted-3-methylpyrazine) was employed to favor monoalkylation. The yields from these reactions ranged from good to excellent. It is noteworthy that the alkylation of 2-(p-nonylphenoxy)-3-methylpyrazine with excess 1-bromobutane (Table 23, Reaction 6) did not furnish the desired dialkylated product, 2-(p-nonylphenoxy)-3-(5-nonyl)-pyrazine; rather, the monoalkylated material, 2-(p-nonylphenoxy)-3-pentylpyrazine was obtained in 50% yield. Thus, the size of a p-substituent on the phenoxy moiety appears to affect the degree of substitution at the methyl site of 2-phenoxy-3-methylpyrazines.

Approved for Public Release

Contrails

TABLE 23

2-PHENOXY-3-ALKYLPYRAZINES

	2-Phenoxy-3-methylpyrazine	Alkyl Halide	Product (% Yield)
1.	2-Phenoxy-3-methylpyrazine	n-Dodecyl Bromide	2-Phenoxy-3-tridecylpyrazine (59[a])
2.	2-Phenoxy-3-methylpyrazine	1-Bromobutane	2-Phenoxy-3-(5-nonyl)pyrazine (74[b], 75[c])
3.	2-(p-Phenylphenoxy)-3-methylpyrazine	1-Bromobutane	2-(p-Phenylphenoxy)-3-(5-nonyl)pyrazine (71[b])
4.	2-(m-Phenoxyphenoxy)-3-methylpyrazine	1-Bromobutane	2-(m-Phenoxyphenoxy)-3-(5-nonyl)pyrazine (59[b])
5.	2-(2-Methyl-6-ethylphenoxy)-3-methylpyrazine	1-Bromobutane	2-(2-Methyl-6-ethylphenoxy)-3-(5-nonyl)pyrazine (91[b])
6.	2-(p-Nonylphenoxy)-3-methylpyrazine	1-Bromobutane	2-(p-Nonylphenoxy)-3-pentylpyrazine (50[b])
7.	2-(p-t-Butylphenoxy)-3-methylpyrazine	1-Bromobutane	2-(p-t-Butylphenoxy)-3-(5-nonyl)pyrazine (86[b])
8.	2-(p-Nonylphenoxy)-3-methylpyrazine	n-Dodecyl Bromide	2-(p-Nonylphenoxy)-3-tridecylpyrazine (86[a])
9.	2-(p-Nonylphenoxy)-3-methylpyrazine	Benzyl Chloride	2-(p-Nonylphenoxy)-3-(2-phenylethyl)pyrazine (36[a])
10.	2-(m-Phenoxyphenoxy)-3-methylpyrazine	Chloromethyltrimethylsilane	2-(m-Phenoxyphenoxy)-3-(2-trimethylsilylethyl)-pyrazine (61[a])
11.	2-(p-t-Butylphenoxy)-3-methylpyrazine	Chloromethyltrimethylsilane	2-(p-t-Butylphenoxy)-3-(2-trimethylsilylethyl)-pyrazine (53[a])

Approved for Public Release

Contrails

TABLE 23 (continued)

2-PHENOXY-3-ALKYLPYRAZINES

2-Phenoxy-3-methylpyrazine	Alkyl Halide	Product (% Yield)
12. 2-(p-t-Butylphenoxy)-3-methylpyrazine	Benzyl Chloride	2-(p-t-Butylphenoxy)-3-(2-phenylethyl)pyrazine (47[a])

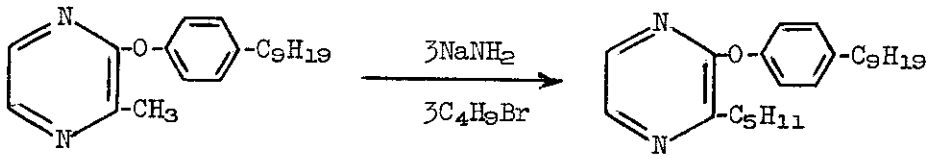
[a] A molar ratio of 1 to 1 to 1 of sodium amide to pyrazine compound to alkyl halide was employed.

[b] A molar ratio of 3 to 1 to 3 of the reactants mentioned in (a) was employed.

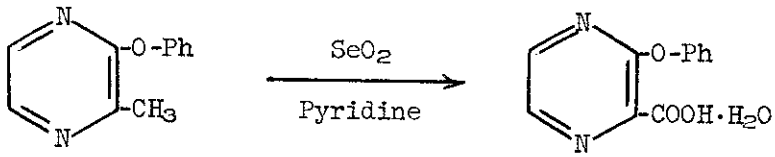
[c] A molar ratio of 6 to 1 to 6 of the reactants mentioned in (a) was employed.

Approved for Public Release

Contrails

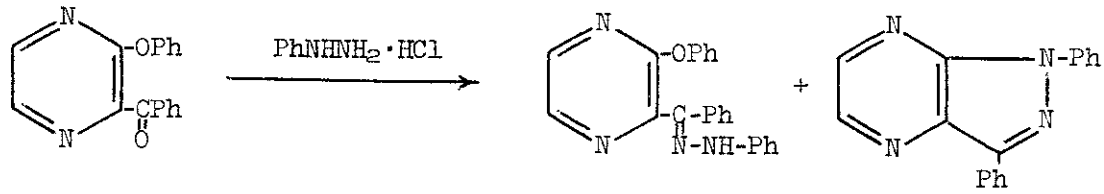


The study of the selenium dioxide oxidation of 2-phenoxy-3-methylpyrazine in an effort to obtain 2-phenoxy-3-pyrazinoic acid in good yield was continued. The best previous yield of the acid was 9%, using dioxane as solvent (1). The reaction conditions were further modified by using pyridine as solvent and employing a



six-hour refluxing period (the usual refluxing period of 19 to 24 hours resulted in decarboxylation of the acid to phenoxypyrazine (1)). From the product mixture there was isolated 20% of desired crude 2-phenoxy-3-pyrazinoic acid, presumably as the monohydrate. In addition, a 46% yield of a mixture of 2-phenoxy-3-methylpyrazine and 2-phenoxypyrazine was obtained.

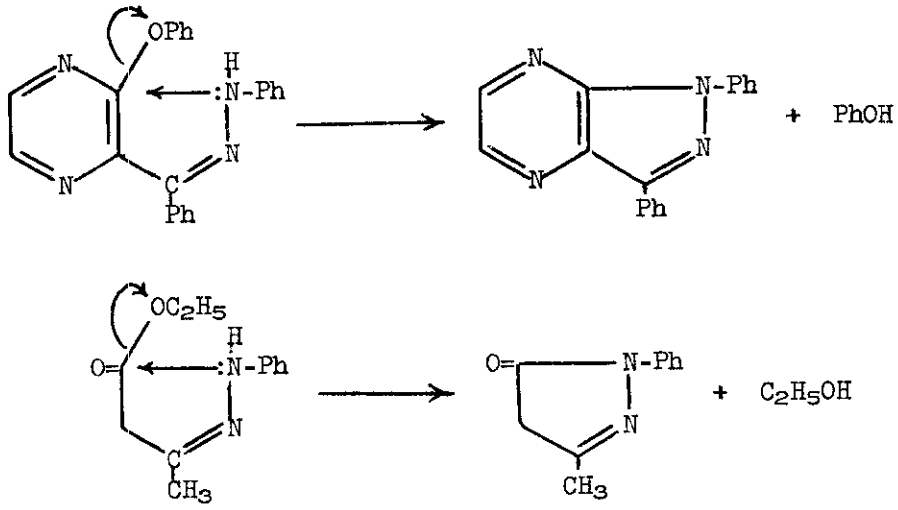
The compound, 2-phenoxy-3-benzoylpyrazine, was prepared earlier by the selenium dioxide oxidation of 2-phenoxy-3-benzylpyrazine (1). This pyrazyl ketone derivative was then treated with phenylhydrazine hydrochloride in ethanol in an effort to prepare its phenylhydrazone, inasmuch as a solid derivative from 2-phenoxy-3-benzoylpyrazine was needed for comparison to that derived from 2-phenoxy-6-benzoylpyrazine (see p. 87). In this attempt two different substances were isolated from the ethanol solution. The first material was identified as 1,3-diphenylpyrazolo[2,3-b]-pyrazine, m.p. 124.5-125°C, on the basis of its elemental analysis and infrared spectrum which did not show any N-H absorption bands (5). Concentration of the mother liquor from which the 1,3-diphenylpyrazolo[2,3-b]pyrazine was isolated gave the desired phenylhydrazone of 2-phenoxy-3-benzoylpyrazine, m.p. 136-137.5°C. Actually, the formation of 1,3-diphenylpyrazolo[2,3-b]pyrazine should not be



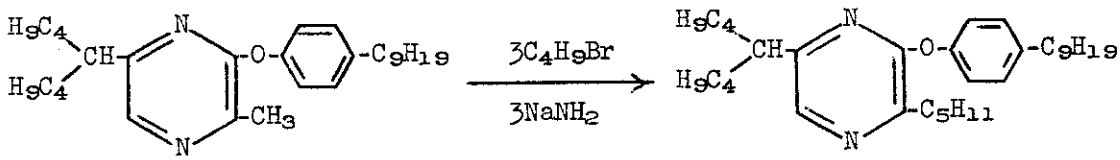
entirely unexpected, since analogous behavior can be found in the reaction of the structurally similar β-ketoesters with phenylhydrazine. These compounds can form the intermediate phenylhydrazone which can be isolated, but the phenylhydrazones are easily converted to the pyrazolones with the elimination of ethanol by warming.

Approved for Public Release

Contrails



Only one member from the 2-phenoxy-3,6-disubstituted group of candidate products was synthesized in this quarter. 2-(p-Nonylphenoxy)-3-pentyl-6-(5-nonyl)-pyrazine was prepared in 60% yield by the alkylation of 2-(p-nonylphenoxy)-3-methyl-6-(5-nonyl)pyrazine (see p. 74) with excess 1-bromobutane in sodium amide



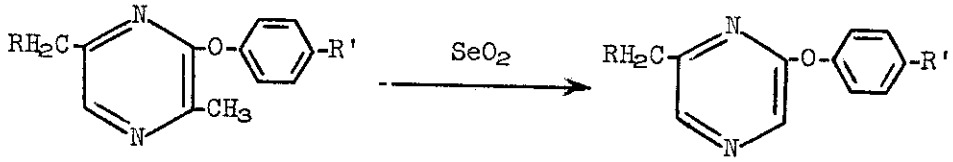
and liquid ammonia. Analogous to the alkylation of 2-(p-nonylphenoxy)-3-methylpyrazine with 1-bromobutane (see p. 82), only one butyl group could be placed on the 3-methyl site.

2-Phenoxy-6-substitutedpyrazines. The general method of preparing 2,3-disubstitutedpyrazines from 2-chloro-3-methylpyrazine by the displacement of the chlorine atom with a nucleophile followed by substitution at the 3-methyl site with an appropriate reagent could not be adopted for the preparation of 2,6-disubstitutedpyrazines, since the necessary starting 2-chloro-6-methylpyrazine was not available. However, with the development of the selenium dioxide oxidation method, which was applied successfully for the preparation of monosubstitutedpyrazines from 2-substituted-3-methylpyrazines (1), it was of interest to subject a number of 2,6-disubstituted-3-methylpyrazines (see p. 70) to this oxidation. The resulting 2,6-disubstitutedpyrazines would allow a comparison of their physical properties, viz., thermal and oxidative stabilities, and fluidity, to that of the known 2,3-isomers. Furthermore, the 2,6-disubstitutedpyrazines would be expected to possess different infrared spectra, boiling points, refractive indexes, etc., as compared to the corresponding 2,3-compounds. Comparison of these properties would eliminate the possibility that the starting materials could be the isomeric 2,3-disubstituted-6-methylpyrazines instead of the 2,6-disubstituted-3-methylpyrazines.

Approved for Public Release

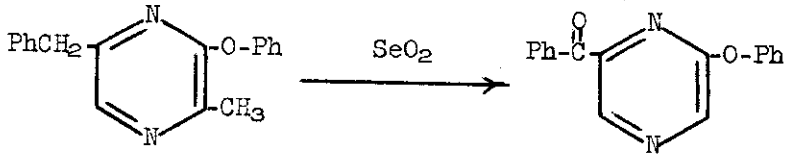
Contrails

With these aims, a number of previously prepared 2-phenoxy-3-methyl-6-substituted-pyrazines (see p. 71) were treated with selenium dioxide in pyridine and the results are summarized in Table 24.



In all the reactions listed in Table 24, oxidation was evidenced by the isolation of reduced selenium in above 76% yield in each case. The basis for the assignment of 2,6-structures instead of the 2,3-structures for all oxidation products was that the infrared spectra of the demethylated products showed distinct differences in the region of 6-9μ as compared to that of the corresponding authentic 2,3-disubstitutedpyrazines prepared earlier. In addition, with the exception of Reaction 2 in Table 24, no carbonyl absorption (that would indicate oxidation at sites other than the methyl) could be detected from the infrared spectra of the product mixtures. A control experiment was also performed by refluxing equimolar amounts of pyrazine and selenium dioxide in pyridine for a period of 96 hours, and no reduced selenium was obtained. The assignment of the 2,6-structures also seems more likely from steric considerations since the methyl group on the 6-position would be expected to be more available for substitution as compared to the methyl group on the 3-position of the 2-substituted-2,6-dimethylpyrazines.

In Reaction 2 (Table 24), 2-phenoxy-6-benzoylpyrazine was obtained from a one-step oxidation of 2-phenoxy-3-methyl-6-benzylpyrazine. Subsequently, interaction of 2-phenoxy-6-benzoylpyrazine with phenylhydrazine hydrochloride gave a hydrazone, m.p. 129-130.5°C, as the only product (the phenylhydrazone of the 2,3-compound melted at 136-137.5°C, see page 85). Thus, with the preparation of two different hydrazones from the 2,3- and the 2,6-compound and the formation of the pyrazolopyrazine from the 2,3-compound, the structure of 2-phenoxy-6-benzoylpyrazine was unequivocally established.



2-Alkoxy-3-substitutedpyrazines and 2-Alkoxy-3,6-disubstitutedpyrazines. Employing the conditions developed for the alkylation of 2-phenoxy-3-methylpyrazines (see p. 82), the corresponding 2-alkoxy-3-methylpyrazines and 2-alkoxy-3-methyl-6-substitutedpyrazines were interacted with an alkyl halide and sodium amide in liquid ammonia to furnish the desired candidate products. The results are listed in Table 25. When the molar ratio of reactants was 3 to 1 to 3 of sodium amide to the pyrazine compound to alkyl halide, a condition which provided

Approved for Public Release

Contrails

TABLE 24

2-PHENOXY-6-SUBSTITUTEDPYRAZINES

2-Phenoxy-3-methyl-6-substitutedpyrazine	Reaction Time (Hrs.)	Product (% Yield)
1. 2-Phenoxy-3-methyl-6-benzylpyrazine[a]	22	2-Phenoxy-6-benzylpyrazine (53)
2. 2-Phenoxy-3-methyl-6-benzylpyrazine[b]	114	2-Phenoxy-6-benzoylpyrazine (24)
3. 2-(p-Nonylphenoxy)-3-methyl-6-benzylpyrazine[a]	22	2-(p-Nonylphenoxy)-6-benzylpyrazine (30)
4. 2-(p-Nonylphenoxy)-3-methyl-6-(p-phenoxybenzyl)pyrazine[a]	22	2-(p-Nonylphenoxy)-6-(p-phenoxybenzyl)pyrazine (33)
5. 2-(p-Nonylphenoxy)-3-methyl-6-(5-nonyl)pyrazine[b]	42	2-(p-Nonylphenoxy)-6-(5-nonyl)pyrazine (44)
6. 2-(p-Nonylphenoxy)-3-methyl-6-(2-phenylethyl)pyrazine[a]	92	2-(p-Nonylphenoxy)-6-(2-phenylethyl)pyrazine (75)
7. 2-(p-Nonylphenoxy)-3-methyl-6-tridecylpyrazine[a]	36	2-(p-Nonylphenoxy)-6-tridecylpyrazine (68)

[a] Equivalent amounts of selenium dioxide and the pyrazine compound was employed.

[b] Excess selenium dioxide was employed.

Approved for Public Release

Contrails

TABLE 25

2-ALKOXY-3-SUBSTITUTEDPYRAZINES
AND 2-ALKOXY-3,6-DISUBSTITUTEDPYRAZINES

	Pyrazine Reactant	Alkyl Halide	Product (% Yield)
1.	2-(2,2-Dimethylpentoxy)-3-methylpyrazine[a]	1-Bromobutane	2-(2,2-Dimethylpentoxy)-3-(n-pentyl)pyrazine (44) 2-(2,2-Dimethylpentoxy)-3-(5-nonyl)pyrazine (13)
2.	2-(2,2,4-Trimethylpentoxy)-3-methylpyrazine[a]	1-Bromobutane	2-(2,2,4-Trimethylpentoxy)-3-(n-pentyl)pyrazine (62) 2-(2,2,4-Trimethylpentoxy)-3-(5-nonyl)pyrazine (15)
3.	2-(2,2-Dimethylpentoxy-3-methyl-6-(n-heptyl)pyrazine[b]	1-Bromohexane	2-(2,2-Dimethylpentoxy)-3,6-di(n-heptyl)pyrazine (31)
4.	2-(2,2-Dimethylpentoxy)-3-methyl-6-(n-heptyl)pyrazine[a]	1-Bromobutane	2-(2,2-Dimethylpentoxy)-3-(n-pentyl)-6-(n-heptyl)-pyrazine (47)

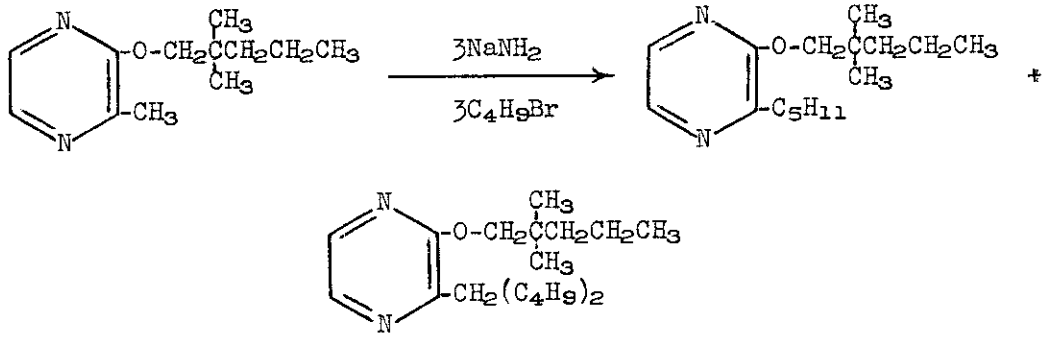
[a] A molar ratio of 3 to 1 to 3 of sodium amide to the pyrazine compound to alkyl halide was employed.

[b] A molar ratio of 1 to 1 to 1 of the corresponding reactants mentioned in (a) was employed.

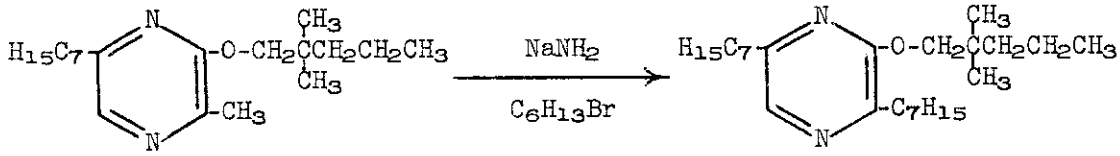
Approved for Public Release

Contrails

dialkylated products earlier (see p. 82), the products obtained were both the mono- and dialkylated compounds in two instances (Reactions 1 and 2, Table 25), the monoalkylated compound being the major product. In Reaction 4 (Table 25), under similar conditions, only the monoalkylated product was isolated in 47% yield. As in



the case of the attempted dialkylation of 2-(p-nonylphenoxy)-3-methylpyrazine (see p. 82), the steric requirement of these alkoxy groups substituted at the 2-position of the pyrazine nucleus makes dialkylation of the 3-methyl site unfavorable. Even under monoalkylation conditions, whereas the molar ratio of reactants was 1 to 1 to 1 (Reaction 3, Table 25), the desired monoalkylated compound was obtained only in 31% yield. Additional work is now in progress to determine the experimental conditions in an effort to obtain optimum yield of this class of compounds.



2-Anilino-3-substitutedpyrazines and 2-Anilino-3,6-disubstitutedpyrazines. Three general procedures were adapted for the preparation of this class of candidate products. They are described as follows.

1. The "Arylation" Method. This method involved the treatment of the 2-substituted-3-methylpyrazine with sodium amide in liquid ammonia to form the intermediate 2-substituted-3-pyrazylmethyl anion. This intermediate was in turn reacted in situ with the "benzyne" formed by the interaction of an aryl halide with sodium amide in liquid ammonia. The resulting compound was designated as a 2-substituted-3-benzylpyrazine. The theoretical considerations as well as practical applications of this method have been discussed in detail earlier ((1), also see p. 79).

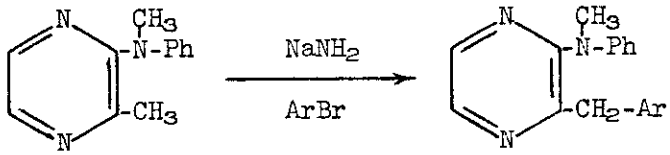
Approved for Public Release

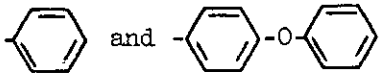
Contrails

2. The "Alkylation" Method. This method is similar to the "arylation" method with the exception that an alkyl halide was used in place of the aryl halide. This method has been successfully applied to the synthesis of a number of advanced intermediates as well as candidate products (see pp. 74 and 82). Depending on the molar ratio of reactants employed, the methyl site could be preferentially mono- or dialkylated in most cases.

3. The "Pyridine Solvent" Method. This method is essentially a modified "alkylation" procedure for the introduction of alkyl groups either on the exocyclic amino site, or on both the amino and the methyl site of 2-anilino-3-methylpyrazines. The detailed experimental conditions for N-alkylation of 2-anilino-3-methylpyrazines as well as the potential complications present in this type of reactions were discussed in detail under the synthesis of 2-anilino-3-methylpyrazines (see p. 59).

With the three general procedures mentioned above at hand, a number of 2-anilino-3-substitutedpyrazines were prepared and the results are listed in Table 26. Reactions 1 and 2 described the synthesis of two 2-anilino-3-benzylpyrazines in moderately good yields by the "Arylation" method. The products, namely 2-(N-methylanilino)-3-benzylpyrazine and 2-(N-methylanilino)-3-(p-phenoxybenzyl)pyrazine, represent the first two liquid 2-anilino-3-substitutedpyrazines prepared in this program. It is noteworthy that previously reported phenylations of 2-anilino-3-methylpyrazine with a two-fold excess of bromobenzene gave a mixture of two crystalline compounds, believed to be tautomeric forms of 2-anilino-3-benzhydrylpyrazine, in low yield (1).



where Ar =  and

Reactions 3, 4, 5, 6, 8, 9, 11 and 12 were performed under the "alkylation" conditions. In Reactions 5, 6, 9, 11 and 12 a molar ratio of 3 to 1 to 3 of sodium amide to the pyrazine compound to alkyl halide was employed in an effort to effect dialkylation, if possible. In Reactions 3, 4 and 8 a molar ratio of 1 to 1 to 1 of the above mentioned reactants was employed to favor monoalkylation.

In the case of the interaction of 2-(N-methylanilino)-3-methylpyrazine with excess 1-bromobutane and sodium amide (Reaction 5, Table 26), the desired 2-(N-methylanilino)-3-(5-nonyl)pyrazine was obtained in only 28% yield. The major product, obtained in 53% yield, is believed to be 2-(N-butylanilino)-3-pentylpyrazine. The two products exhibited different physical properties (viz., boiling

Approved for Public Release

Contrails

TABLE 26

2-ANILINO-3-SUBSTITUTEDPYRAZINES

	2-Anilino-3-methylpyrazine	Aryl or Alkyl Halide	Product (% Yield)
1.	2-(N-Methylanilino)-3-methylpyrazine[a]	Bromobenzene	2-(N-Methylanilino)-3-benzylpyrazine (49)
2.	2-(N-Methylanilino)-3-methylpyrazine[a]	4-Bromophenyl Phenyl Ether	2-(N-Methylanilino)-3-(p-phenoxybenzyl)pyrazine (48)
3.	2-(N-Methylanilino)-3-methylpyrazine[b]	Chloromethyltrimethylsilane	2-(N-Methylanilino)-3-(2-trimethylsilylethyl)pyrazine (48)
4.	2-(N-Methylanilino)-3-methylpyrazine[b]	n-Dodecyl Bromide	2-(N-Methylanilino)-3-tridecylpyrazine (52)
5.	2-(N-Methylanilino)-3-methylpyrazine[c]	1-Bromobutane	2-(N-Butylanilino)-3-pentylpyrazine (53) 2-(N-Methylanilino)-3-(5-nonyl)pyrazine (28)
6.	2-(N-Methylanilino)-3-methylpyrazine[c]	1-Bromobutane	2-(N-Butylanilino)-3-pentylpyrazine (94)
7.	2-Anilino-3-methylpyrazine[c,d]	1-Bromobutane	2-(N-Butylanilino)-3-pentylpyrazine (68)
8.	2-(N-Methylanilino)-3-methylpyrazine[b]	Benzyl Chloride	2-(N-Methylanilino)-3-(2-phenylethylpyrazine (73)
9.	2-Anilino-3-methylpyrazine[c]	1-Bromobutane	2-Anilino-3-(n-pentyl)-pyrazine (15)
10.	2-(p-Pentylanilino)-3-methylpyrazine[c,d]	1-Bromobutane	2-(N-Butyl-p-pentylanilino)-3-(n-pentyl)pyrazine (71)
11.	2-(N-Methylanilino)-3-pyrazine[c]	1-Bromopentane	2-(N-Methylanilino)-3-(n-hexyl)pyrazine (54) 2-Anilino-3-methylpyrazine (25)
12.	2-(N-Methylanilino)-3-methylpyrazine[c]	1-Bromooctane	2-(N-Methylanilino)-3-(9-heptadecyl)pyrazine (69)

Approved for Public Release

Contrails

TABLE 26 (continued)

2-ANILINO-3-SUBSTITUTEDPYRAZINES

2-Anilino-3-methylpyrazine	Aryl or Alkyl Halide	Product (% Yield)
13. 2-Anilino-3-methyl-pyrazine[c,d]	1-Bromohexane	2-(N-Hexylanilino)-3-(n-heptyl)pyrazine (53)

[a] A molar ratio of 4 to 2 to 1 of sodium amide to pyrazine compound to aryl halide was employed.

[b] A molar ratio of 1 to 1 to 1 of the corresponding reactants mentioned in (a) was employed.

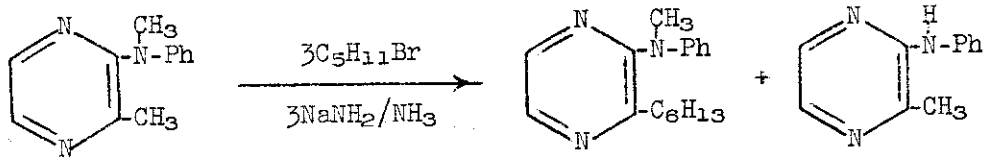
[c] A molar ratio of 3 to 1 to 3 of the corresponding reactants mentioned in (a) was employed.

[d] This reaction was performed under the conditions described in the "Pyridine Solvent" method.

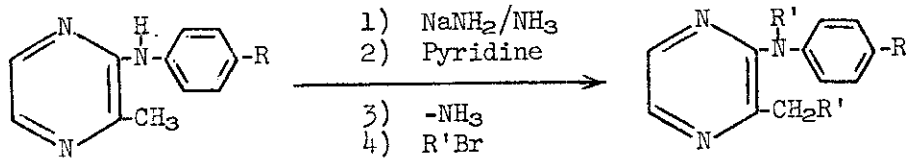
Approved for Public Release

Contrails

point and viscosity) as well as different infrared spectra. The formation of the major product, 2-(N-butylanilino)-3-pentylpyrazine, was unexpected, inasmuch as it involved the displacement of the methyl group from the amino site with a butyl group. When this reaction was repeated on a larger scale (Table 26, Reaction 6), the presumed 2-(N-butylanilino)-3-(n-pentyl)pyrazine was obtained exclusively in 94% yield. The structure of this material is, however, not yet certain at this point. This displacement of the methyl group with a butyl group appeared to be similar to the observed displacement of a methyl group in 2-(N-methylanilino)-3-methylpyrazine by 1,2-dibromoethane in the presence of sodium amide and liquid ammonia to give N,N'-diphenyl-N,N'-di[2-(3-methylpyrazyl)]-1,2-diaminoethane (see p. 61). A reaction, which appears to be related to the above type of displacement, was observed in the interaction of 2-(N-methylanilino)-3-methylpyrazine with excess 1-bromopentane and sodium amide in liquid ammonia (Table 26 , Reaction 11). In addition to the isolation of 54% of alkylated product, there was also obtained 25% of 2-anilino-3-methylpyrazine. The formation of the 2-anilino-3-methylpyrazine would involve the displacement of the amino methyl group by a hydrogen.



Alkylations performed on the methyl site of 2-anilino-3-methylpyrazine class of compounds have so far been limited to 2-(N-methylanilino)-3-methylpyrazine, a compound possessing no enolizable hydrogen on the amino function. With the recent development of the "Pyridine Solvent" method, it was of interest to apply this technique to the simultaneous alkylation of both the amino function and the methyl site of 2-anilino-3-methylpyrazines, inasmuch as it has already been demonstrated (see p. 59) that preferential monoalkylation at the amine function of 2-anilino-3-methylpyrazine could be effected in pyridine. Thus, three such attempts were made (Table 26, Reactions 7, 10 and 13), using two different 2-anilino-3-methylpyrazines. The molar ratio of alkyl halide and sodium amide with respect to the pyrazine



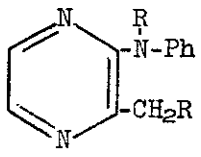
where R = -H , -H , $-C_5H_{11}$
R' = $-C_4H_9$, $-C_6H_{13}$, $-C_4H_9$

compound was 3 to 3 to 1 to favor polyalkylation. Yields of 53-71% for the desired dialkylated product were obtained. The structures of the products were established by the following evidence: (1) elemental analysis confirmed the placement of two alkyl groups on the molecule; (2) the absence of N-H absorption bands in the infrared spectra of these compounds, thus, excluding the possibility of dialkylation

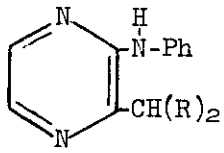
Approved for Public Release

Contrails

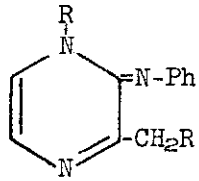
occurring at the methyl site (structure B); and (3) the ultraviolet spectra of these products (see Table 27) correlated well with that of the 2-(N-methylanilino)-3-methylpyrazine, prepared by the coupling of 2-chloro-3-methylpyrazine with N-methylaniline, thus eliminating another possible structure (C) which could arise



A



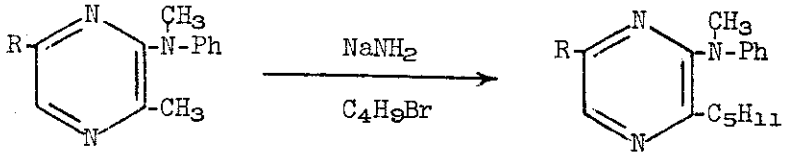
B



C

from ring nitrogen alkylation and methyl alkylation. Based upon the above evidence, structure A must be favored over structures B and C for these products.

Two advanced intermediates, namely, 2-(N-methylanilino)-3-methyl-6-(5-nonyl)-pyrazine and 2-(N-methylanilino)-3-methyl-6-(n-heptyl)pyrazine (see p. 78), were treated with 1-bromobutane and sodium amide in liquid ammonia under the conditions described in the "Alkylation" procedure. Three-fold excess of 1-bromobutane and sodium amide was employed in the former case, but the product obtained was the monoalkylated compound, 2-(N-methylanilino)-3-(n-pentyl)-6-(5-nonyl)pyrazine, in 41% yield. In the latter reaction equimolar quantities of reactants were used, and likewise, the monoalkylated material, 2-(N-methylanilino)-3-(n-pentyl)-6-(n-heptyl)-pyrazine, was afforded in only 25% yield. However, the feasibility of reaction path has been demonstrated and work is in progress to determine the optimum conditions as well as the scope of these reactions.



where R = $-CH(C_4H_9)_2$ and $-n-C_7H_{15}$

2-Anilino-6-substitutedpyrazines. Employing the selenium dioxide oxidation method, which has been successfully applied to the synthesis of 2-phenoxy-6-substitutedpyrazines (see p. 87), 2-(N-methylanilino)-3-methyl-6-(5-nonyl)pyrazine was converted to 2-(N-methylanilino)-6-(5-nonyl)pyrazine in 71% yield. The structure of this 2,6-disubstituted product is indicated by a comparison of its properties as well as infrared spectrum with that of the previously prepared (see p. 92) isomeric 2,3-disubstituted compound.

Approved for Public Release

Contrails

TABLE 27

ULTRAVIOLET SPECTRA

(In Ethanol)

Compound	Max. (mμ)	Mol. Ext. Coeff.
1. 2-(N-Methylanilino)-3-methylpyrazine[a]	238; 280; 332	7,820; 8,480; 6,630
2. 2-(N-Methylanilino)-3-methylpyrazine[b]	240; 280; 335	7,030; 8,480; 6,720
3. 2-(N-Butylanilino)-3-methylpyrazine[a]	245; 273; 337	8,480; 11,600; 7,200
4. 2-(N-Methylanilino)-3-(5-nonyl)-pyrazine[c]	240; 281; 340	10,000; 8,540; 7,170
5. 2-(N-Butylanilino)-3-pentylpyrazine[c]	261; 338	38,900; 7,420
6. 2-(N-Butylanilino)-3-pentylpyrazine[b]	244; 289; 348	7,410; 8,380; 6,950
7. 2-(N-Butyl-p-pentylanilino)-3-pentylpyrazine[b]	245; 285; 332	9,180; 9,830; 6,680
8. 2-Anilino-3-methylpyrazine[a]	269; 333	18,000; 6,600
9. 2-(p-Pentylanilino)-3-methylpyrazine[a]	273; 340	20,900; 7,520

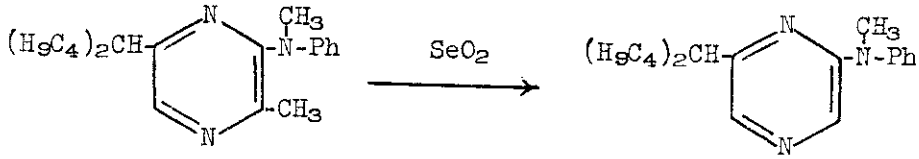
[a] This compound was prepared by the "Direct" method.

[b] This compound was prepared by the "Pyridine Solvent" method.

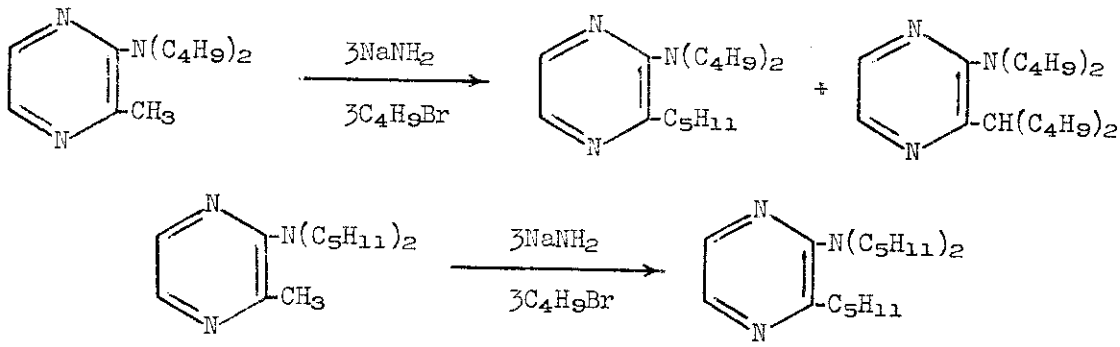
[c] This compound was prepared by the "Alkylation" method.

Approved for Public Release

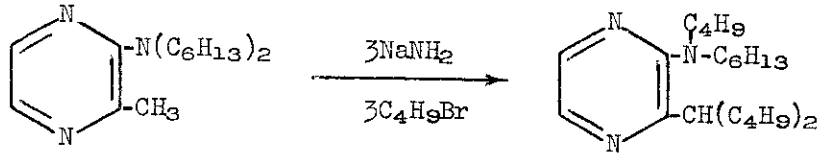
Contrails



2-Alkylamino-3-substitutedpyrazines and 2-Alkylamino-3,6-disubstitutedpyrazines. The conditions adopted for the preparation of this class of compounds were analogous to that described for the 2-anilino-3-substituted(and -3,6-disubstituted)-pyrazines. The "Alkylation" procedure (see p. 91) was used for C-alkylations on the methyl site of the starting 2-alkylamino-3-methylpyrazines. When a simultaneous C- and N-alkylation was desired, the "Pyridine Solvent" procedure (see p. 59) was found to be the method of choice. The results of the preparation of 2,3-disubstituted compounds are listed in Table 28. In Reaction 1 (Table 28), when the N-alkyl groups in the starting 2-alkylamino-3-methylpyrazine were n-butyl, the interaction of this material with 1-bromobutane under dialkylation conditions gave two products, namely, the mono- and dialkylated compounds. The monoalkylated product was obtained as the major component. When the N-alkyl groups in the starting material were n-pentyl (Reaction 2, Table 28), the reaction underwent exclusively monoalkylation under identical conditions as that described in the first case (Reaction 1).



In Reaction 3 (Table 28), the interaction of 2-(N,N-di-n-hexylamino)-3-methylpyrazine with 1-bromobutane gave a product (68% yield) which tentatively was assigned the structure of 2-(N-n-butyl-N-n-hexylamino)-3-(5-nonyl)pyrazine, based on the results of elemental analysis. A repeated run under identical conditions again furnished the same product in 77% yield. This unexpected product would be formed by the displacement of one hexyl group by a butyl group. Displacement of an amino methyl group by other alkyl groups under similar reaction conditions was



Approved for Public Release

Contrails

TABLE 28

2-ALKYLAMINO-3-SUBSTITUTEDPYRAZINES

2-Alkylamino-3-methylpyrazine	Alkyl Halide	Product (% Yield)
1. 2-(N,N-Di-n-butylamino)-3-methylpyrazine[a,c]	1-Bromobutane	2-(N,N-Di-n-butylamino)-3-(n-pentyl)pyrazine (38) 2-(N,N-Di-n-butylamino)-3-(5-nonyl)pyrazine (16)
2. 2-(N,N-Di-n-pentylamino)-3-methylpyrazine[a,c]	1-Bromobutane	2-(N,N-Di-n-pentylamino)-3-(n-pentyl)pyrazine (83)
3. 2-(N,N-Di-n-hexylamino)-3-methylpyrazine[a,c]	1-Bromobutane	2-(N-n-Butyl-N-n-hexylamino)-3-(5-nonyl)pyrazine (68, 77)
4. 2-(N-n-Hexylamino)-3-methylpyrazine[b,c]	1-Bromohexane	2-(N,N-Di-n-hexylamino)-3-(n-heptyl)pyrazine (66)
5. 2-(N-n-Hexylamino)-3-methylpyrazine[b,c]	1-Bromooctane	2-(N-n-Hexyl-N-n-octylamino)-3-(n-nonyl)pyrazine (77)

[a] The "Alkylation" method was used for the preparation of this compound.

[b] The "Pyridine Solvent" method was used.

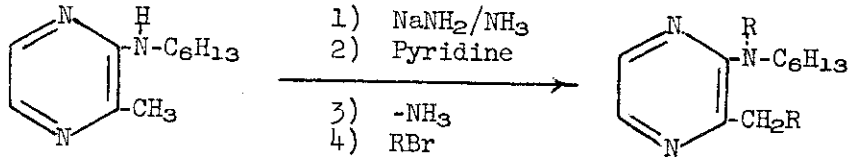
[c] A molar ratio of 3 to 1 to 3 of sodium amide to the pyrazine compound to alkyl halide was employed.

Approved for Public Release

Contrails

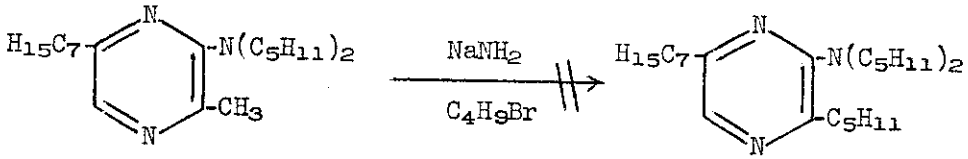
observed earlier in two instances (see pp. 61 and 94). The mechanism for these unusual displacement reactions on the amino position is not clear, and additional work is in progress in order to gain some insight into the nature of the reaction and to conclusively establish the structure of the products.

The next two reactions (Reactions 4 and 5, Table 28) described the preparation of two additional representatives of this class. The products, 2-(N,N-di-n-hexylamino)-3-(n-heptyl)pyrazine and 2-(N-n-hexyl-N-n-octylamino)-3-(n-nonyl)pyrazine, were obtained by the treatment of 2-(N-n-hexylamino)-3-methylpyrazine with the appropriate alkyl halides under the reaction conditions described in the "Pyridine Solvent" procedure in 66% and 77% yield, respectively.

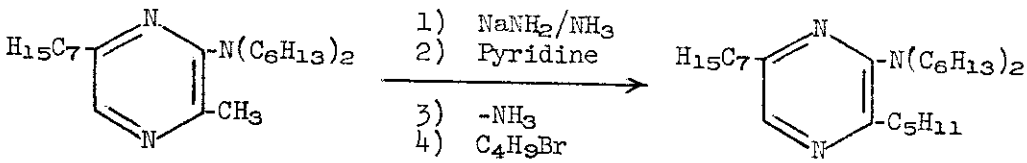


where R = $-C_6H_{13}$ and $-C_8H_{17}$

An initial attempt employing the "Alkylation" procedure to prepare a 2-alkylamino-3,6-disubstitutedpyrazine was not successful. This involved the interaction of 2-(N,N-di-n-pentylamino)-3-methyl-6-(n-heptyl)pyrazine with equimolar quantities of sodium amide and 1-bromobutane. From this run 84% of the starting pyrazine compound was recovered. The failure of this reaction to occur could possibly be due



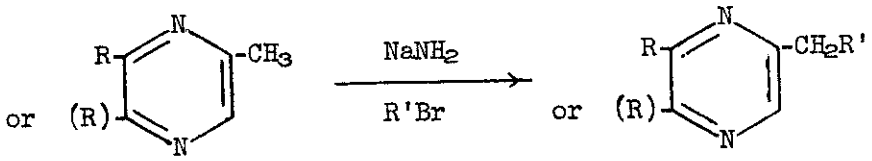
to the insolubility of the starting 2-(N,N-di-n-pentylamino)-3-methyl-6-(n-heptyl)-pyrazine in liquid ammonia, inasmuch as the starting material appeared as a white precipitate when added to the sodium amide suspension in liquid ammonia and very little red color (characteristic of the formation of the pyrazylmethyl anion) could be observed. Next, 2-(N,N-di-n-hexylamino)-3-methyl-6-(n-heptyl)pyrazine was interacted with three-fold excess of sodium amide and 1-bromobutane using the "Pyridine Solvent" method. The desired trisubstituted compound, 2-(N,N-di-n-hexylamino)-3-(n-pentyl)-6-(n-heptyl)pyrazine, was obtained in 37% yield. It should be pointed out that this reaction was performed under dialkylation conditions and only the monoalkylated product was isolated.

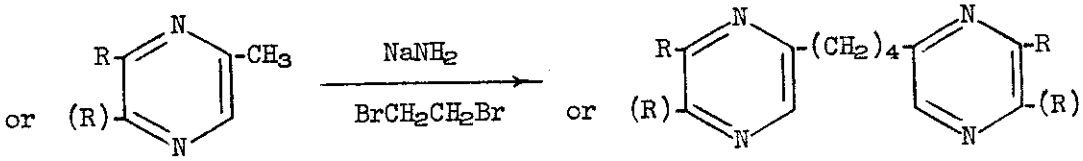


Approved for Public Release

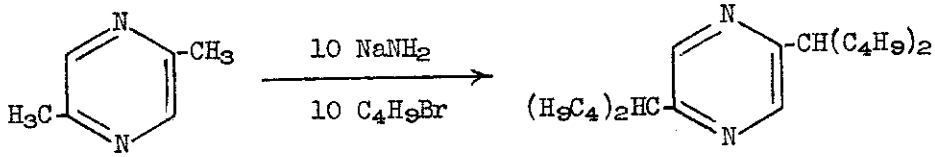
Contrails

Alkylpyrazines. A number of candidate products of the alkylpyrazine group were prepared employing the "Alkylation" procedure, the conditions of which have been discussed in detail under the section of alkyl(methyl)pyrazines (p. 68). These compounds were prepared either by a one step alkylation of a dimethylpyrazine, or by alkylation of a previously obtained alkyl(methyl)pyrazine intermediate to furnish the substituted dialkylpyrazines in excellent yield. These results are given in Table 29. Reactions 1 to 6 and 9 to 12 (Table 29) were performed by using a molar ratio of 2 to 2 to 1 (sodium amide to pyrazine compound to alkyl halide). In all cases it was presumed that the methyl instead of the methylene position of the starting alkyl(methyl)pyrazine was attacked. This assumption is based on the anticipated relative reactivity of the methyl hydrogen and methylene hydrogen with respect to bases such as sodium amide (the methyl hydrogen would be expected to be more acidic). Additional work is in progress to prove unequivocally the structures of these products.





The alkylation of a dimethylpyrazine with a large excess of sodium amide and 1-bromobutane was also attempted in an effort to effect polyalkylations at both methyl positions in one step. When 2,5-dimethylpyrazine was reacted with a ten-fold excess of sodium amide and 1-bromobutane, the tetraalkylated compound, 2,5-di-(5-nonyl)pyrazine, was obtained in 64% yield (Reaction 7, Table 29). A similar



reaction was also carried out with 2,6-dimethylpyrazine (Reaction 8, Table 29). However, the desired 2,6-di-(5-nonyl)pyrazine was obtained as the minor product in only 10% yield, along with 31% of the trialkylated compound, 2-(n-pentyl)-6-(5-nonyl)pyrazine.

Approved for Public Release

Contrails

TABLE 29

ALKYLPYRAZINES

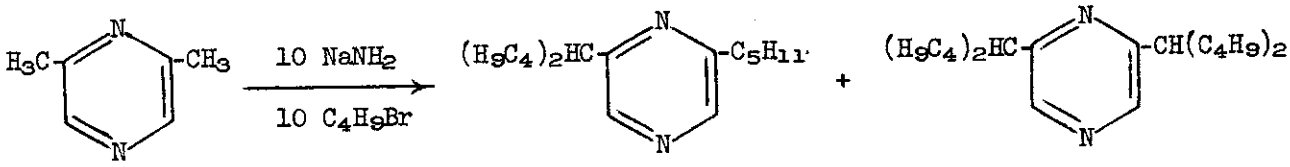
	Pyrazine Reactant	Alkyl Halide	Product (% Yield)
1.	2-n-Heptyl-5-methylpyrazine[a]	1-Bromobutane	2-n-Heptyl-5-n-pentylpyrazine (86)
2.	2-n-Heptyl-5-methylpyrazine[a]	1-Bromooctane	2-n-Heptyl-5-n-nonylpyrazine (93, 85)
3.	2-n-Heptyl-6-methylpyrazine[a]	1-Bromobutane	2-n-Heptyl-6-n-pentylpyrazine (91)
4.	2-n-Heptyl-6-methylpyrazine[a]	1-Bromooctane	2-n-Heptyl-6-n-nonylpyrazine (88)
5.	2-n-Nonyl-5-methylpyrazine[a]	1-Bromooctane	2,5-Di-n-nonylpyrazine (82)
6.	2-n-Nonyl-6-methylpyrazine[a]	1-Bromooctane	2,6-Di-n-nonylpyrazine (87)
7.	2,5-Dimethylpyrazine[b]	1-Bromobutane	2,5-Di-(5-nonyl)pyrazine (64)
8.	2,6-Dimethylpyrazine[b]	1-Bromobutane	2-n-Pentyl-6-(5-nonyl)pyrazine (31) 2,6-Di-(5-nonyl)pyrazine (10)
9.	2-n-Heptyl-5-methylpyrazine[a]	1,2-Dibromoethane	1,4-Bis[2-(5-n-heptylpyrazyl)]-butane (62)
10.	2-n-Heptyl-6-methylpyrazine[a]	1,2-Dibromoethane	1,4-Bis[2-(6-n-heptylpyrazyl)]-butane (53, 57)
11.	2-n-Nonyl-5-methylpyrazine[a]	1,2-Dibromoethane	1,4-Bis[2-(5-n-nonylpyrazyl)]-butane (44)
12.	2-n-Nonyl-6-methylpyrazine[a]	1,2-Dibromoethane	1,4-Bis[2-(6-n-nonylpyrazyl)]-butane (56)

[a] A molar ratio of 2 to 2 to 1 of sodium amide to the pyrazine compound to alkyl halide was employed.

[b] A molar ratio of 10 to 1 to 10 of the reactants mentioned in (a) was employed.

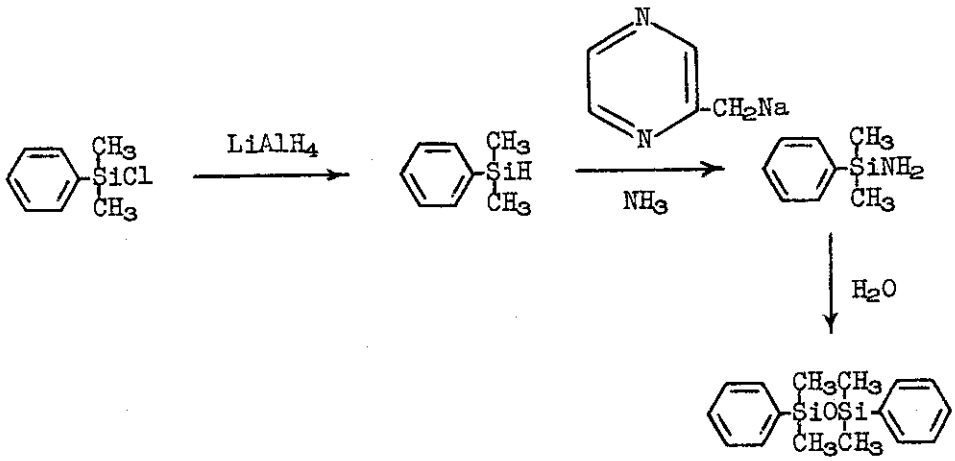
Approved for Public Release

Contrails



Model Reactions

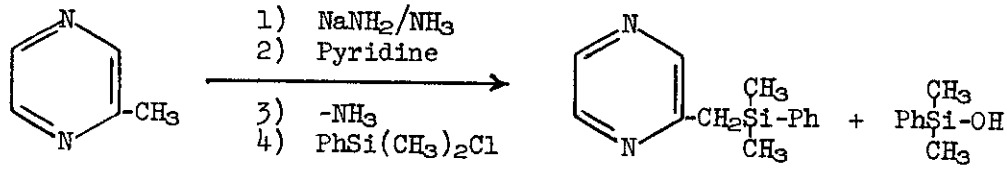
In order to improve fluid properties of the pyrazine derivatives, efforts to synthesize silicon-containing pyrazines were continued. The introduction of a silyl radical on the methyl site of methylpyrazine was attempted earlier using phenyldimethylethoxysilane and phenyldimethyl-(1-piperidyl)silane with pyrazylmethylsodium (1). However, no coupling product was obtained. In another attempt to prepare such a structure, phenyldimethylsilane (22), obtained from the lithium aluminum hydride reduction of phenyldimethylchlorosilane, was allowed to interact with excess pyrazylmethylsodium in liquid ammonia. The only materials isolated were 87% of starting methylpyrazine and 65% of 1,3-diphenyltetramethyldisiloxane. The latter compound apparently resulted from the displacement of hydrogen on the starting silane by the amide ion and subsequent hydrolysis of the phenyldimethylaminosilane.



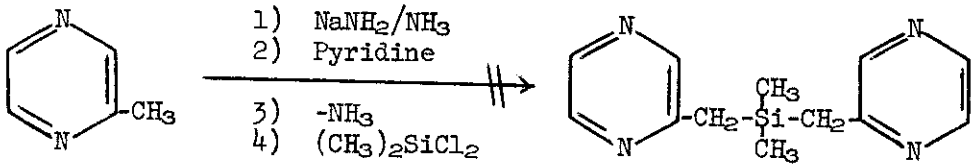
Next the silylation of methylpyrazine was attempted with phenyldimethylchlorosilane by using the "Pyridine Solvent" method. This method involved the treatment of methylpyrazine with sodium amide in liquid ammonia to form the intermediate, pyrazylmethylsodium, in the usual manner. Subsequently, the liquid ammonia was displaced with pyridine, thus allowing the reaction of the intermediate pyrazylmethylsodium with reagents which are not compatible with liquid ammonia. In the above described manner, the desired (phenyldimethylsilylmethyl)pyrazine was obtained in 40% yield, together with a 19% yield of phenyldimethylsilanol.

Approved for Public Release

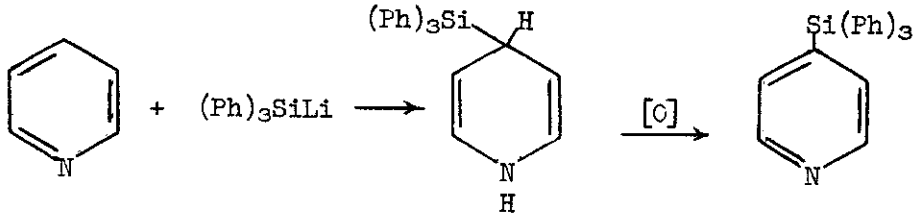
Contrails



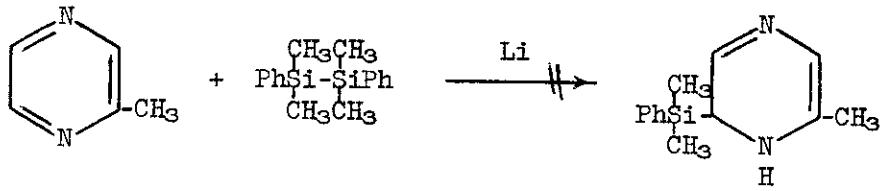
A similar silylation of methylpyrazine was attempted with a difunctional silane, namely, dimethyldichlorosilane, in an effort to link two pyrazylmethyl radicals with a silicon atom. The reaction was performed under various conditions, but no desired product was obtained as indicated by an extensive tar formation in each case.



The preparation of two representatives from the class of 2-silyl-3-methylpyrazines was described in the previous report (1). These compounds possessed good fluid properties but were obtained in only moderate yields. It was, therefore, of interest to investigate other methods of synthesis of this class of compounds. Gilman and co-workers (3) reported the "azomethine addition" of triphenylsilyllithium to pyridine, and oxidation of the resulting dihydropyridine derivative to the corresponding silylpyridine in good yield. This method, when applied to pyrazine



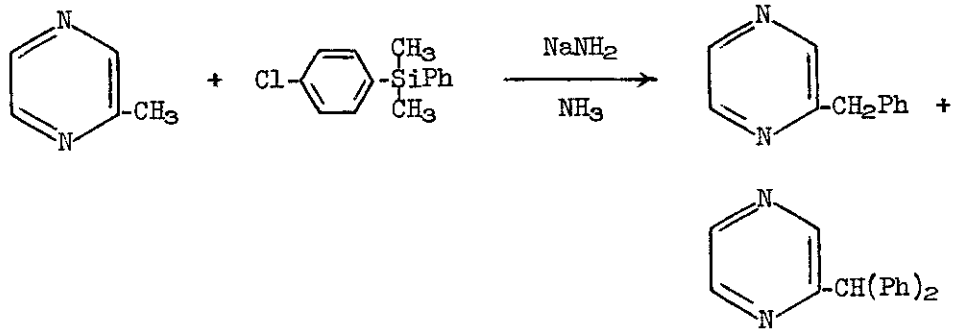
compounds, would seem particularly attractive, inasmuch as it permits the placement of the silyl group on any of the four available positions of the pyrazine nucleus. Therefore, 1,2-diphenyltetramethyldisilane (23) was interacted with methylpyrazine and lithium in an effort to prepare x-phenyldimethylsilyl-2-methyldihydropyrazine. However, none of the desired dihydropyrazine derivative was isolated. There was recovered only 62% of methylpyrazine and 74% of 1,2-diphenyltetramethyldisilane.



Approved for Public Release

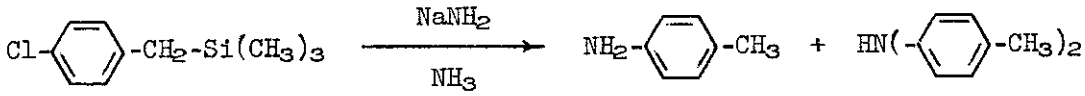
Contrails

The previously reported attempts at arylation of 2-phenoxy-3-methylpyrazine with a number of silyl substituted halobenzenes in the presence of sodium amide and liquid ammonia have resulted in the cleavage of the aryl-silicon bond ((1), also see p. 81) in each instance. A similar reaction was then attempted using methylpyrazine and p-phenyldimethylsilylchlorobenzene. From this reaction there was isolated 48%



of benzylpyrazine together with a small amount of benzhydrylpyrazine. These results again supported the earlier observation of the instability of the aryl-silicon bond under the sodium amide and liquid ammonia reaction conditions.

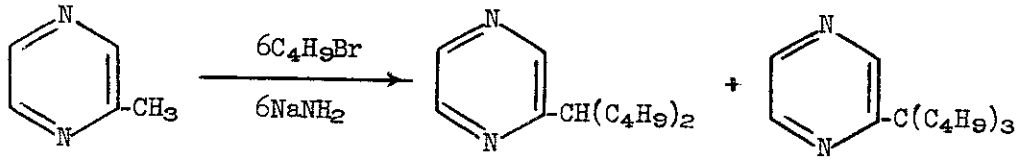
Next, the attempted arylation of 2-phenoxy-3-methylpyrazine by using (p-chlorobenzyl)trimethylsilane in sodium amide and liquid ammonia was also reported to be unsuccessful (see p. 82). The cleavage of the benzyl-silicon bond under these conditions was demonstrated by the attempted amination of (p-chlorobenzyl)trimethylsilane in sodium amide and liquid ammonia, from which a 36% of p-toluidine and 28% of presumed di-(p-tolyl)amine were isolated.



The earlier described alkylation of 2-phenoxy-3-methylpyrazine with excess sodium amide and 1-bromobutane in liquid ammonia gave exclusively the dialkylated compound, 2-phenoxy-3-(5-nonyl)pyrazine, in good yield (see p. 83). The trialkylated compound, 2-phenoxy-3-(tributylmethyl)pyrazine, could not be obtained either by employing a larger excess of sodium amide and 1-bromobutane, or by attempting to further alkylate 2-phenoxy-3-(5-nonyl)pyrazine. Therefore, a study of the alkylation of the simpler compound, methylpyrazine, was undertaken. When methylpyrazine was treated with a six-fold excess of 1-bromobutane and sodium amide, employing the same conditions for the preparation of 2-phenoxy-3-(5-nonyl)pyrazine, the dialkylated product, (5-nonyl)pyrazine, was obtained in 45% yield. In addition, there was also isolated 5% of the trialkylated compound, (tributyl)methylpyrazine.

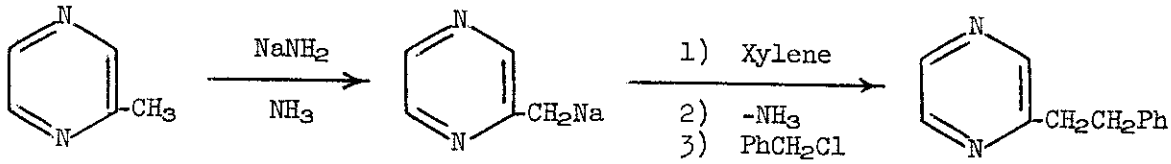
Approved for Public Release

Contrails



It appeared that with butyl bromide as the alkylating agent, the steric conditions at the methyl site, even in the absence of an adjacent bulky group, are such as to make trialkylation extremely difficult.

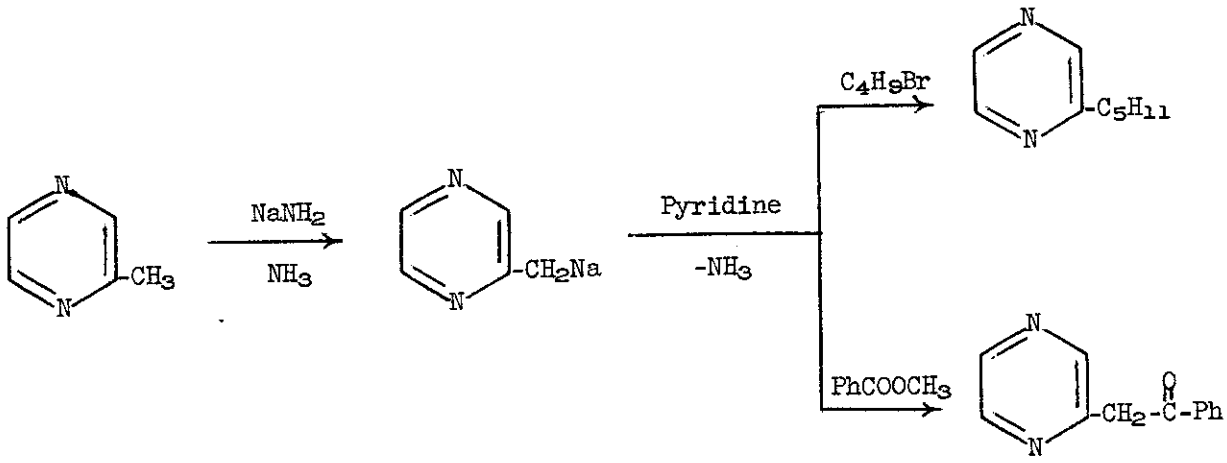
The studies on the metalation of the methyl site in methylpyrazine were continued. The performance of reactions on the methyl site in systems other than sodium amide and liquid ammonia is desirable, since this will allow reactions with reagents which are not compatible with liquid ammonia. A previous unsuccessful attempt was made to perform the metalation with a different reagent, sodium hydride, in tetrahydrofuran (1). One method considered in the current period to circumvent the difficulty of metalating the methyl site in other systems was to first treat methylpyrazine with sodium amide in liquid ammonia to form the intermediate, pyrazylmethylsodium by the standard method. Subsequently, the liquid ammonia could be displaced with a different solvent and the resulting mixture allowed to condense with the proper agent to undergo the desired alkylations, acylations, etc. In the above described manner, pyrazylmethylsodium was prepared by the interaction of methylpyrazine with sodium amide in liquid ammonia. The liquid ammonia was then displaced by xylene and treatment of the resulting mixture with benzyl chloride afforded (2-phenylethyl)pyrazine (4) in 21% yield. The moderate yield of the product was believed probably to be due to the insolubility of pyrazylmethylsodium in xylene. Therefore, the alkylation of methylpyrazine with 1-bromobutane was next attempted in pyridine. The procedure was



similar to that above except that the ammonia was now displaced with pyridine. The molar ratio of sodium amide to methylpyrazine to 1-bromobutane was 2 to 2 to 1. This ratio was found earlier to favor monoalkylation in liquid ammonia (4). The desired n-pentylpyrazine was, indeed, obtained in 50% yield. Similarly, the acylation of methylpyrazine with methylbenzoate in pyridine at room temperature afforded phenacylpyrazine in 73% yield.

Approved for Public Release

Contrails



Approved for Public Release

Contrails

EXPERIMENTAL

I. INITIAL INTERMEDIATES

A. 2-Phenoxy-3-methylpyrazines and 2-Phenoxy-3,6-dimethylpyrazines

General Procedure. A general procedure is given below for the preparation of this class of compounds. Unless indicated otherwise, the reaction conditions and methods of workup described in detail under this general procedure are followed for the preparation of each member of this class. Modifications in reaction conditions and workup, if any, are given under each individual compound. In a typical reaction, sodium methoxide (0.2 mole) was prepared by dissolving 4.6 g. (0.2 g. atom) of sodium in 150 ml. of methanol. To this solution, under nitrogen, was added 0.2 mole of the corresponding phenol. The methanol was removed first by distillation at atmospheric pressure then at reduced pressure with the aid of a warm-water bath until the mixture turned into a viscous paste. To this mixture was then added 150 ml. of 2-chloro-3-methylpyrazine and low-boiling materials were removed by distillation of the resulting solution to a pot temperature of 175°C. When 2-chloro-3,6-dimethylpyrazine was employed, the distillation was continued until a pot temperature of 190°C was reached. The mixture was refluxed at this temperature for 24 hours. The precipitated salt was removed by filtration and washed with chloroform or ether. The filtrate and washings were combined and stripped of solvent at reduced pressure and the remaining liquid was distilled to obtain the desired product.

2-(o-i-Propylphenoxy)-3-methylpyrazine. Employing the general procedure described above, this compound was prepared by the reaction of 0.2 mole of sodium methoxide, 27.2 g. (0.2 mole) of o-i-propylphenol and 150 ml. of 2-chloro-3-methylpyrazine in 78.4% yield (35.8 g.), b.p. 71°C at 0.2 mm. to 92°C at 0.15 mm. The fraction, b.p. 90-92°C at 0.15 mm., n_D^{25} 1.5527, was analyzed.

Anal. Calc'd. for $C_{14}H_{16}N_2O$: C, 73.65; H, 7.07; N, 12.27.
Found: C, 73.50; H, 7.17; N, 12.35.

2-(p-i-Propylphenoxy)-3-methylpyrazine. The general procedure described above was employed using 0.2 mole of sodium methoxide, 27.2 g. (0.2 mole) of p-i-propylphenol and 150 ml. of 2-chloro-3-methylpyrazine. The desired product, b.p. 96-98°C at 0.18 mm., obtained in 85.7% yield (33.9 g.), solidified partially on standing.

Anal. Calc'd. for $C_{14}H_{16}N_2O$: C, 73.65; H, 7.07; N, 12.27.
Found: C, 73.77; H, 7.12; N, 12.22.

Approved for Public Release

Contrails

2-(p-Phenylphenoxy)-3-methylpyrazine. In this run, sodium ethoxide was used in place of sodium methoxide as described in the general procedure, (p. 107). Thus, 85.1 g. (0.5 mole) of p-phenylphenol was interacted with 0.5 mole of sodium ethoxide and 250 ml. of 2-chloro-3-methylpyrazine. Upon removal of solvent and excess 2-chloro-3-methylpyrazine from the reaction product mixture by distillation, the remaining material (130.1 g.) solidified upon standing, m.p. 73-104°C. Repeated recrystallizations of this crude material from ether gave 82.3 g. of purified 2-(p-phenylphenoxy)-3-methylpyrazine, m.p. 112-114°C; a sample was further recrystallized from ether, m.p. 113-114.5°C for elemental analysis.

Anal. Calc'd. for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68.
Found: C, 78.48; H, 5.41; N, 10.78.

A monopicrate derivative was prepared in ethanol, m.p. 143-144°C.

Anal. Calc'd. for $C_{23}H_{17}N_5O_8$: C, 56.21; H, 3.49; N, 14.25.
Found: C, 56.15; H, 3.51; N, 14.29.

The mother liquor, from which the 82.3 g. of product was isolated, was evaporated to dryness leaving 23.2 g. of crystalline solid, m.p. 50-65°C. This wide melting solid was dissolved in petroleum ether and adsorbed on 400 g. of Merck alumina. Elution with a petroleum ether-benzene mixture (1:1) yielded an additional 6.9 g. of the desired crude 2-(p-phenylphenoxy)-3-methylpyrazine, m.p. 94-110°C. Further elution with petroleum ether-benzene (1:1) and benzene afforded 13.6 g. of a lower-melting solid, m.p. 62-75°C, which was purified by recrystallization from ether, m.p. 75-76°C. Although the infrared spectrum of this low-melting material showed distinct differences as compared to that of 2-(p-phenylphenoxy)-3-methylpyrazine (m.p. 113-114.5°C), its elemental analysis indicated that it possessed the same empirical formula as the desired product.

Anal. Calc'd. for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68.
Found: C, 77.96; H, 5.47; N, 11.04.
77.95 5.49 10.98.

A monopicrate of this low-melting isomer (m.p. 75-76°C) was prepared in ethanol, m.p. 140-141°C; when admixed with the monopicrate of the higher-melting product (m.p. 143-144°C) it was depressed to 123-133°C.

Anal. Calc'd. for $C_{23}H_{17}N_5O_8$: C, 56.21; H, 3.49; N, 14.25.
Found: C, 56.31; H, 3.50; N, 14.35.

From the above reaction a total of 89.2 g. (68%) of 2-(p-phenylphenoxy)-3-methylpyrazine and 13.6 g. (10.4%) of a low-melting isomer were obtained.

Selenium Dioxide Oxidation of the High-melting Isomer of 2-(p-Phenylphenoxy)-3-methylpyrazine, p-Phenylphenoxypyrazine. A mixture of 26.2 g. (0.1 mole) of 2-(p-phenylphenoxy)-3-methylpyrazine (m.p. 112-114°C) (see above)

Approved for Public Release

Contrails

23.1 g. (0.21 mole) of selenium dioxide, 100 ml. of pyridine and 5 ml. of water was refluxed for 16 hours. The mixture was filtered while hot to separate 12.6 g. (76%) of selenium. The filtrate was evaporated in vacuo to remove pyridine. The resulting partially solidified material was treated with 300 ml. of chloroform and digested on the steam bath almost to dryness. To this mixture was then added 100 ml. of ether and the mixture was again filtered. Concentration of the ether filtrate furnished 18 g. (72.5%) of p-phenylphenoxypyrazine, m.p. 113-118°C. The product was purified by filtration of its benzene solution through 200 g. of Merck alumina and recrystallization of the filtrate from a benzene-petroleum ether mixture, m.p. 119-120.5°C.

Anal. Calc'd. for $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.29.
Found: C, 77.66; H, 5.07; N, 11.20.

Attempted Selenium Dioxide Oxidation of the Low-melting Isomer of 2-(p-Phenylphenoxy)-3-methylpyrazine. A mixture of 3.4 g. (0.013 mole) of the low-melting isomer of 2-(p-phenylphenoxy)-3-methylpyrazine, m.p. 72-74°C (see p. 108), 2.9 g. (0.026 mole) of selenium dioxide, 100 ml. of pyridine and 5 ml. of distilled water was refluxed for 23 hours. It was observed that no reduced selenium was deposited at the end of this period and so mixture was then refluxed for an additional 96 hours. Filtration of the reaction mixture furnished 0.4 g. (20%) of reduced selenium. The pyridine was removed from the filtrate; the residue was treated with 10% sodium hydroxide and extracted with chloroform. Evaporation of the chloroform extracts gave 2.85 g. of solid, m.p. 62-68°C, which was purified by filtration of its benzene solution through a column of 50 g. of Merck alumina, m.p. 67-69°C. A monopicrate of this solid was prepared, m.p. 140-141°C, which did not depress when admixed with the picrate of starting low-melting isomer of 2-(p-phenylphenoxy)-3-methylpyrazine. Thus a total of 84% of starting low-melting isomer of 2-(p-phenylphenoxy)-3-methylpyrazine was recovered.

p-Phenylene Bis-2-(3-methylpyrazyl) Ether. (1) Employing the reaction conditions described in the general procedure (p. 107), 27.5 g. (0.25 mole) of hydroquinone was interacted with 0.5 mole of sodium methoxide and 250 ml. of 2-chloro-3-methylpyrazine and employing a reflux temperature of 173-177°C for 39.5 hours. Ether and 2-chloro-3-methylpyrazine were distilled off at reduced pressure to leave 33.4 g. of solid material. Repeated recrystallizations of this solid failed to yield any sharp-melting material. Therefore, the entire amount of solid was dissolved in benzene and adsorbed on 900 g. of Merck alumina. Elution with benzene gave 6.14 g. (8.4%) of solid (compound I), which melted over the range of 185.5-186°C after recrystallization from an ether-petroleum ether mixture. Further elution with benzene-ether mixture (4:1) furnished 14.77 g. (20%) of a lower-melting solid (compound II) which was purified by recrystallization from ether-petroleum ether mixture, m.p. 127-128°C. Finally, elution with chloroform gave 3.19 g. (4.4%) of a third compound which was purified in the same manner as described above, m.p. 150.5-152°C. The elemental analyses of these three different melting solids agreed well with the empirical formula for the desired p-phenylene bis-2-(3-methylpyrazyl) ether.

Approved for Public Release

Contrails

Anal. Calc'd. for $C_{16}H_{14}N_4O_2$: C, 65.29; H, 4.79; N, 19.04.
Found: Compound I: C, 65.21; H, 4.79; N, 18.82.
Compound II: C, 65.39; H, 4.82; N, 19.00.
Compound III: C, 65.35; H, 4.87; N, 19.16.

Dipicrate derivatives were prepared from compounds I, II and III; their melting ranges were 216-217°C, 154-160°C, and 157-158°C, respectively.

Anal. Calc'd. for $C_{28}H_{20}N_{10}O_{16}$: C, 44.69; H, 2.68; N, 18.16.
Found: Compound I-picrate: C, 44.71; H, 2.53; N, 18.61.
Compound II-picrate: C, 44.74; H, 2.69; N, 18.70.
Compound III-picrate: C, 44.72; H, 2.65; N, 18.65.

(2) The above reaction was repeated using a longer reaction time and on a larger scale. The disodium salt of hydroquinone, prepared from 46.0 g. (2.0 g. atom) of sodium in 500 ml. of methanol and 110.0 g. (1.0 mole) of hydroquinone in 400 ml. of methanol, was allowed to interact with 700 ml. of 2-chloro-3-methylpyrazine over a 6-day period at the refluxing temperature of the mixture (170-180°C). Upon cooling, 1500 ml. of ether was then added and the insoluble material was filtered. The residue was dissolved in 10% aqueous sodium hydroxide and extracted with chloroform to give 69.5 g. of solid, m.p. 163-186°C. The aqueous basic solution was then acidified to pH 4 and again extracted with chloroform to furnish an additional 37.0 g. of solid, m.p. 184-180°C. The original ether filtrate, which on standing gave 8.8 g. of solid, m.p. 164-179°C, was again filtered and the filtrate was distilled to remove excess starting 2-chloro-3-methylpyrazine to leave 169 g. of solid. Repeated recrystallization of this solid gave 109 g. of the crude low-melting isomer. The melting point of this material ranged from 112-135°C. From the workup a total of 105.3 g. (35.8%) of crude compound I and 109 g. (37.1%) of compound II were isolated.

m-Phenylene Bis-2-(3-methylpyrazyl) Ether (1). A quantity of disodium salt of resorcinol, prepared from 46 g. (2.0 g. atom) of sodium in 500 ml. of methanol and 110 g. (1.0 mole) of resorcinol, was allowed to interact with 500 ml. of 2-chloro-3-methylpyrazine over a 6-day period at the refluxing temperature of the mixture (175-185°C). Upon removal of solvent and excess 2-chloro-3-methylpyrazine by distillation of the reaction product mixture, the remaining material (232.5 g.) solidified completely, m.p. 125-138°C, after it was washed with a small amount of ether. The crude yield of the desired m-phenylene bis-2-(3-methylpyrazyl) ether was 79%, based on the 232.5 g. of solid isolated.

m-Carbomethoxyphenol. The method described for the preparation of o-carbomethoxyphenol by Clinton and Laskowski (24) was modified for the preparation of m-carbomethoxyphenol. A mixture of 13.8 g. (0.1 mole) of m-hydroxybenzoic acid, 9.6 g. (0.3 mole) of methanol, 10 ml. of concentrated sulfuric acid and 200 ml. of chloroform was heated under reflux for 24 hours. Upon cooling, the reaction mixture was washed successively with water, saturated sodium bicarbonate solution, and water. The chloroform solution was then dried over sodium sulfate and the solvent was removed from the mixture. Distillation of the remaining liquid gave

Approved for Public Release

Contrails

12.2 g. (80.3%) of crude m-carbomethoxyphenol, b.p. 154-156°C at 10 mm., which solidified upon standing, m.p. 59-66°C. The desired product was purified by recrystallization from an ether-petroleum ether mixture, m.p. 71-72.5°C.

Anal. Calc'd. for $C_8H_8O_3$: C, 63.15; H, 5.30.
Found: C, 63.61; H, 5.26.

2-(m-Carbomethoxyphenoxy)-3-methylpyrazine. A solution of 7.61 g. (0.05 mole) of m-carbomethoxyphenol (prepared above) in 15 ml. of methanol was treated with 0.05 mole of sodium methoxide in 20 ml. of methanol and 100 ml. of 2-chloro-3-methylpyrazine, employing the conditions described in the general procedure (p. 107). Distillation of the reaction product mixture gave 8.6 g. (70.5%) of 2-(m-carbomethoxyphenoxy)-3-methylpyrazine, b.p. 134°C at 0.55 mm. to 144°C at 0.60 mm., n_D^{25} 1.5650-1.5690. The product solidified on standing, m.p. 52-65°C, and was purified by recrystallization from an ether-petroleum ether mixture, m.p. 74°C.

Anal. Calc'd. for $C_{13}H_{12}N_2O_3$: C, 63.92; H, 4.95; N, 11.47.
Found: C, 63.79; H, 4.93; N, 11.33.

Attempted Preparation of 2-Pentachlorophenoxy-3-methylpyrazine. A quantity of 28.9 g. (0.10 mole) of sodium pentachlorophenoxide (supplied by Reichhold Chem., Inc., under the trade name of "Chlorophen") was dried overnight in vacuum oven at 120°C, and then was allowed to interact with 150 ml. of 2-chloro-3-methylpyrazine at its reflux temperature of 176°C for 120 hours. The mixture was cooled and an insoluble material was removed by filtration. The filtrate was distilled at 62°C at 12 mm. to recover 130 ml. of 2-chloro-3-methylpyrazine. The remaining material was digested in petroleum ether and filtered to recover 22 g. of starting sodium pentachlorophenoxide. The filtrate was again distilled to give an additional 10 ml. of 2-chloro-3-methylpyrazine and about 10 ml. of highly viscous residue. A total of 140 ml. (93.5%) of 2-chloro-3-methylpyrazine and 22 g. (76%) of sodium pentachlorophenoxide were recovered from the workup.

Attempted Preparation of 2-(2,6-Di-t-butyl-4-methylphenoxy)-3-methylpyrazine. Lithium methoxide (0.2 mole) was prepared by dissolving 1.38 g. (0.2 g. atom) of lithium wire in 300 ml. of methanol. To this solution was added 44 g. (0.2 mole) of 2,6-di-t-butyl-4-methylphenol and the resulting solution was stirred and refluxed for 2.5 hours. Excess methanol was removed *in vacuo* to leave a white powder. A quantity of 250 ml. of 2-chloro-3-methylpyrazine was then added, low-boiling material was removed by distillation to a pot temperature of 173°C, and the mixture was stirred and refluxed for 24 hours. The filtrate was then distilled to give 240 ml. (96%) of 2-chloro-3-methylpyrazine, b.p. 55°C at 10 mm. The residue from distillation was a dark brown solid. It was washed with a methanol-water mixture to leave 34 g. (77%) of starting 2,6-di-t-butyl-4-methylphenol, m.p. 69-71°C. Inasmuch as no desired product was isolated, it was suspected that the lithium methoxide did not react with the phenol to form the corresponding lithium phenoxide. The recovered 2-chloro-3-methylpyrazine (240 ml.) was then redistilled in an effort to isolate any 2-methoxy-3-methylpyrazine (1), which possesses a similar boiling range

Approved for Public Release

Contrails

to that of the 2-chloro-3-methylpyrazine and would result from the interaction of 2-chloro-3-methylpyrazine with lithium methoxide. However, upon redistillation, only 226 ml. of 2-chloro-3-methylpyrazine, b.p. 166-170°C, n_D^{25} 1.5269-1.5291, was recovered.

2-(2-Methyl-6-ethylphenoxy)-3-methylpyrazine. This material was prepared from 27.2 g. (0.2 mole) of 2-methyl-6-ethylphenol, 0.2 mole of sodium methoxide and 300 ml. of 2-chloro-3-methylpyrazine in 59.2% yield (27 g.), b.p. 99-102°C at 0.17 mm., n_D^{25} 1.5552. The product was further purified by redistillation, b.p. 100°C at 0.28 mm. to 99°C at 0.27 mm., n_D^{25} 1.5551.

Anal. Calc'd. for $C_{14}H_{16}N_2O$: C, 73.65; H, 7.07; N, 12.27.
Found: C, 73.54; H, 6.89; N, 12.16.

m-Trimethylsiloxybromobenzene. This compound was prepared following the procedure of Neville (14). To a solution of 86.5 g. (0.5 mole) of m-bromophenol in 90 ml. anhydrous benzene and 39.5 g. of pyridine was added 54.2 g. (0.5 mole) of trimethylchlorosilane in 50 ml. of benzene during a 1-hour period while maintaining the temperature between 10-12°C. The reaction mixture was further stirred for 3 hours at 10°C and left standing at room temperature for 62 hours. The precipitated pyridine hydrochloride was filtered off and the filtrate was distilled to give 111.5 g. (91%) of m-trimethylsiloxybromobenzene, b.p. 101-102°C at 11 mm., n_D^{25} 1.5149.

p-Trimethylsiloxybromobenzene (14). Employing identical reaction conditions and workup as described above for the preparation of the m-analog and substituting 86.5 g. (0.5 mole) of p-bromophenol for m-bromophenol, the desired p-trimethylsiloxybromobenzene was obtained in 90% yield (110.5 g.) from distillation, b.p. 118-119°C at 21 mm., n_D^{25} 1.5128 (Lit. b.p. 126°C at 25 mm., n_D^{25} 1.5123).

(m-Trimethylsiloxy)trimethylsilylbenzene (14). To a mixture of 50 ml. of tetrahydrofuran and 12.7 g. (0.47 g. atom) of magnesium turnings was added 3 ml. of methyl iodide and the mixture was warmed gently until the appearance of a grayish precipitate. To this was then added 75 ml. of tetrahydrofuran, followed by the addition of a solution of 111.5 g. (0.41 mole) of m-trimethylsiloxybromobenzene (see above) in 150 ml. of tetrahydrofuran over a 150-minute period while maintaining the temperature at 70°C. The resulting mixture was stirred and refluxed for an additional hour and then cooled to 10°C. To this was then added 54.2 g. (0.5 mole) of trimethylchlorosilane over an 1-hour period at 10°C. After the completion of addition the mixture was refluxed for 1 hour and then left standing for 15 hours at room temperature. The reaction mixture was filtered and the precipitate was washed with several portions of ether. Distillation of the combined filtrate and washings afforded 56.3 g. (50%) of (m-trimethylsiloxy)trimethylsilylbenzene, b.p. 77-78°C at 2 mm., n_D^{25} 1.4470.

Anal. Calc'd. for $C_{12}H_{22}OSi_2$: C, 60.43; H, 9.28; Si, 23.55.
Found: C, 60.38; H, 9.35; Si, 23.6.

Approved for Public Release

Contrails

(p-Trimethylsiloxy)trimethylsilylbenzene (14). A quantity of 12.1 g. (0.45 g. atom) of magnesium turnings in 125 ml. of tetrahydrofuran was allowed to interact with 110.5 g. (0.45 mole) of p-trimethylsiloxybromobenzene (see p. 112) in 150 ml. of tetrahydrofuran and 54.2 g. (0.5 mole) of trimethylchlorosilane, using identical reaction conditions and workup as described for the preparation of (m-trimethylsiloxy)trimethylsilylbenzene. Distillation of the product mixture gave 64 g. (59.6%) of (p-trimethylsiloxy)trimethylsilylbenzene, b.p. 132-134°C at 25 mm., n_D^{25} 1.4777 (Lit. b.p. 132°C at 25 mm., n_D^{25} 1.4794).

m-Trimethylsilylphenol (14). To a 56.3 g. (0.24 mole) quantity of (m-trimethylsiloxy)trimethylsilylbenzene (see p. 112) was added 18 ml. of 95% ethanol and one drop of concentrated hydrochloric acid while keeping the temperature of the mixture below 15°C. To this was then added 2 ml. of water and the mixture was shaken for 5 minutes, after which an additional 22 ml. of water was added and the resulting mixture became turbid. The mixture was left standing for 15 minutes and then washed with water twice. The organic layer was distilled to give 24.8 g. (58.3%) of m-trimethylsilylphenol, b.p. 62-65°C at 0.35 mm., n_D^{25} 1.4855.

p-Trimethylsilylphenol (14). Following the procedure for the preparation of m-trimethylsilylphenol described above 9.6 g. (0.04 mole) of (p-trimethylsiloxy)-trimethylsilylbenzene (see above) was hydrolyzed in ethanol and concentrated hydrochloric acid. After the reaction product mixture was washed with water, the remaining ethanol was removed *in vacuo* below room temperature to leave 5.1 g. (79% calculated as p-trimethylsilylphenol) of colorless solid. This material was extremely unstable in the presence of acid or heat, therefore its melting point was not determined. However, the infrared spectrum of this compound was consistent with the structure, p-trimethylsilylphenol.

2-(m-Trimethylsilylphenoxy)-3-methylpyrazine. Sodium m-trimethylsilylphenoxide, prepared from 0.15 mole of sodium methoxide and 24 g. (0.14 mole) of m-trimethylsilylphenol (see above) in methanol and dried overnight in vacuum oven at 40°C, was refluxed with 62.7 g. of 2-chloro-3-methylpyrazine at 174°C for 24 hours. Distillation of the reaction product mixture after the usual workup yielded 7.0 g. (23%) of the desired pure 2-(m-trimethylsilylphenoxy)-3-methylpyrazine, b.p. 90°C at 0.03 mm., n_D^{25} 1.5475.

Anal. Calc'd. for $C_{14}H_{18}N_2OSi$: C, 65.09; H, 7.02; N, 10.85; Si, 10.84.
Found: C, 65.04; H, 7.01; N, 11.12; Si, 10.96.

2-(p-Trimethylsilylphenoxy)-3-methylpyrazine. Sodium p-trimethylsilylphenoxide, prepared from 0.031 mole of sodium methoxide and 5.0 g. (0.031 mole) of p-trimethylsilylphenol (see above) in methanol and dried overnight in vacuum oven at 40°C, was allowed to interact with 25.6 g. of 2-chloro-3-methylpyrazine at 160-175°C for 24 hours. Distillation of the reaction product mixture after the usual workup gave 2.0 g. (27%) of pure 2-(p-trimethylsilylphenoxy)-3-methylpyrazine, b.p. 114-115°C at 0.3 mm., n_D^{25} 1.5504. This material solidified on standing, m.p. 62-63°C.

Approved for Public Release

Contrails

Anal. Calc'd. for $C_{14}H_{18}N_2OSi$: C, 65.09; H, 7.02; N, 10.85; Si, 10.84.
Found: C, 65.07; H, 7.12; N, 10.90; Si, 11.04.

2-(p-t-Butylphenoxy)-3,6-dimethylpyrazine. Employing the general procedure (p. 107) described for the preparation of this class of compounds, the interaction of 150 g. (1.0 mole) of p-t-butylphenol with 1.0 mole of sodium methoxide and 1,350 ml. of 2-chloro-3,6-dimethylpyrazine afforded 203.4 g. (79.5%) of the desired 2-(p-t-butylphenoxy)-3,6-dimethylpyrazine, b.p. 153°C at 6.0 mm. to 155°C at 4.0 mm., n_D^{25} 1.5448-1.5474. This material solidified on standing, m.p. 49-51°C.

Anal. Calc'd. for $C_{16}H_{20}N_2O$: C, 74.96; H, 7.86; N, 10.93.
Found: C, 74.98; H, 8.02; N, 11.04.

2-(p-Phenylphenoxy)-3,6-dimethylpyrazine. A quantity of 170 g. (1.0 mole) of p-phenylphenol was treated with 1.0 mole of sodium methoxide and 500 ml. of 2-chloro-3,6-dimethylpyrazine under the conditions described in the general procedure (p. 107). After removal of excess 2-chloro-3,6-dimethylpyrazine from the reaction product mixture by distillation, the remaining liquid was dissolved in 1500 ml. of ether and washed with 1500 ml. of 10% sodium hydroxide. The ether fraction was washed with water and dried over magnesium sulfate. Successive concentration of the ether solution and filtration afforded 185.7 g. (67.3%) of the desired 2-(p-phenylphenoxy)-3,6-dimethylpyrazine, m.p. 86-93°C. The product was recrystallized from an ether-chloroform mixture, m.p. 89.5-90°C.

Anal. Calc'd. for $C_{18}H_{16}N_2O$: C, 78.23; H, 5.84; N, 10.14.
Found: C, 78.12; H, 5.77; N, 10.22.

B. 2-Alkoxy-3-methylpyrazines and 2-Alkoxy-3,6-dimethylpyrazines

2-(2,2-Dimethylpentoxy)-3-methylpyrazine. A mixture of 46.4 g. (0.4 mole) of 2,2-dimethyl-1-pentanol,* 4.6 g. (0.2 g. atom) of sodium and 200 ml. of benzene was heated under reflux for 2 hours. At this point it was observed that not all the sodium had reacted. The benzene was then removed slowly by distillation over a 1-hour period, at the end of which time there was no sodium remaining in the mixture. A quantity of 200 ml. of 2-chloro-3-methylpyrazine was added to the viscous liquid and low-boiling materials were removed by distillation of the resulting solution to a pot temperature of 172°C. The reaction mixture was refluxed at this temperature for 16 hours, cooled, and insoluble material removed by filtration. Distillation of the filtrate gave 28.2 g. (67.8%) of 2-(2,2-dimethylpentoxy)-3-methylpyrazine, b.p. 72°C at 0.45 mm. to 77°C at 0.40 mm., n_D^{25} 1.4808-1.4815. The fraction, b.p. 72°C at 0.45 mm. to 74.5°C at 0.40 mm., n_D^{25} 1.4808, was shown to be pure product by elemental analysis.

Anal. Calc'd. for $C_{12}H_{20}N_2O$: C, 69.19; H, 9.68; N, 13.45.
Found: C, 69.32; H, 9.66; N, 13.62.

* The starting 2,2-dimethyl-1-pentanol was obtained from Eastman Kodak as a courtesy sample.

Approved for Public Release

Contrails

2-(2,2,4-Trimethylpentoxy)-3-methylpyrazine. (1) To a sodium methoxide solution, prepared from 6.9 g. (0.3 g. atom) of sodium and 100 ml. of methanol, was added 39.0 g. (0.3 mole) of 2,2,4-trimethyl-1-pentanol* and the resulting solution was first distilled between 65-130°C at atmospheric pressure and later at 50-65°C at 2 mm. to remove methanol. To the remaining white solid was added 200 ml. of 2-chloro-3-methylpyrazine and the mixture was refluxed at 172°C for 24 hours. Following the usual workup, distillation of the reaction product mixture gave 22.3 g. (33.5%) of 2-(2,2,4-trimethylpentoxy)-3-methylpyrazine, b.p. 82°C at 0.35 mm. to 83°C at 0.28 mm., n_D^{25} 1.4815-1.4832. The product was purified by redistillation, b.p. 72-75°C at 0.15 mm., n_D^{25} 1.4809.

Anal. Calc'd. for $C_{13}H_{22}N_2O$: C, 70.22; H, 9.98; N, 12.60.
Found: C, 70.01; H, 9.87; N, 12.74.

(2) The preparation of this compound was repeated employing a modified procedure to prepare the sodium salt of 2,2,4-trimethyl-1-pentanol. A mixture of 78.0 g. (0.60 mole) of 2,2,4-trimethyl-1-pentanol, 6.9 g. (0.3 g. atom) of sodium, and 200 ml. of benzene was refluxed for a 2.5-hour period. At the end of this period the surface of the sodium was coated with the sodium 2,2,4-trimethylpentoxide and conversion of the alcohol to the sodium salt appeared to be extremely slow. The benzene was then removed by distillation and the remaining mixture, which consisted of the alcohol, its sodium salt, and molten sodium was refluxed for 16 hours. The absence of sodium at this point indicated the formation of the desired sodium alkoxide was complete. To this mixture was then added 200 ml. of 2-chloro-3-methylpyrazine, and then the low-boiling materials were removed by distillation until a pot temperature of 174°C was attained. The resulting reaction mixture was refluxed at this temperature for 24 hours. After the usual workup, the reaction product mixture was distilled to furnish 58.5 g. (87.8%) of the desired 2-(2,2,4-trimethylpentoxy)-3-methylpyrazine, b.p. 77°C at 0.42 mm. to 80°C at 0.35 mm., n_D^{25} 1.4805-1.4811.

2-[1-(3-Hydroxy-2,2,4,4-tetramethylcyclobutoxy)]-3-methylpyrazine. To a solution of 144.2 g. (1.0 mole) 2,2,4,4-tetramethyl-1,3-cyclobutanediol** in 300 ml. of toluene was added 11.5 g. (0.5 g. atom) of sodium and the mixture was refluxed for a 3-hour period. At the end of this period, there was a considerable amount of unreacted sodium remaining in the reaction mixture. The mixture was cooled and to it was added an additional 72.1 g. (0.5 mole) of the diol, followed by 100 ml. of toluene. After the mixture was refluxed for an additional 15-hour period, there was still sodium remaining in the mixture. Toluene was then removed by distillation at atmospheric pressure and heating was continued until the

---

* The starting 2,2,4-trimethyl-1-pentanol was obtained from Eastman Kodak as a courtesy sample.

** The starting 2,2,4,4-tetramethyl-1,3-cyclobutanediol, m.p. 125-135°C, was obtained from Eastman Kodak as a courtesy sample and is a mixture of *cis* and *trans* isomers.

Approved for Public Release

Contrails

pot temperature reached 160°C. At this point the reaction mixture became partially solid and all the sodium appeared to have been reacted. The mixture was cooled to 60°C and a quantity of 300 ml. of 2-chloro-3-methylpyrazine was added. Low-boiling materials were removed by distilling the mixture to a pot temperature of 180°C. After the reaction mixture was stirred and refluxed at 180°C for 24 hours, it was cooled and filtered. The insoluble material was digested with hot methanol and again filtered to leave 19 g. (69%) of sodium chloride. The methanol filtrate was evaporated to recover 101 g. of starting 2,2,4,4-tetramethyl-1,3-cyclobutanediol, m.p. 104-123°C, identified by infrared comparison. The original filtrate of the reaction product mixture on standing gave an additional 24 g. of the starting diol, m.p. 105-125°C. The remaining liquid was then distilled to recover 224 ml. of 2-chloro-3-methylpyrazine, b.p. 63°C at 18 mm. to 70°C at 20 mm., and 75 g. (63.5%) of crude product, 2-[1-(3-hydroxy-2,2,4,4-tetramethylcyclobutoxy)]-3-methylpyrazine, b.p. 106°C at 0.38 mm. to 145°C at 0.28 mm. The crude product was redistilled to yield 44.5 g. (37.7%) of pure material, b.p. 100°C at 0.10 mm. to 103°C at 0.08 mm., n_D^{25} 1.5115.

Anal. Calc'd. for $C_{13}H_{20}N_2O_2$: C, 66.07; H, 8.53; N, 11.86.
Found: C, 66.15; H, 8.55; N, 11.94.

Therefore, from the above reaction a total of 135 g. (62.3%) of 2,2,4,4-tetramethyl-1,3-cyclobutanediol, 224 ml. (74.7%) of 2-chloro-3-methylpyrazine were recovered and 44.5 g. (37.7%) of the desired pure 2-[1-(3-hydroxy-2,2,4,4-tetramethylcyclobutoxy)]-3-methylpyrazine was obtained.

Bis-{3-[2-(3-methylpyrazoxy)]-2,2,4,4-tetramethyl-1-cyclobutoxy}dimethylsilane. To a solution of 23.6 g. (0.1 mole) of 2-[1-(3-hydroxy-2,2,4,4-tetramethylcyclobutoxy)]-3-methylpyrazine (see above) in 100 ml. of benzene and 8 g. (0.1 mole) of pyridine was introduced 6.5 g. (0.05 mole) of dimethyldichlorosilane over a 15-minute period. The resulting mixture was stirred and refluxed for 18 hours. Upon cooling, the insoluble pyridine hydrochloride (11.3 g., 98%) was filtered from the mixture and the filtrate was distilled in vacuo to remove benzene. The viscous residue was treated with ether and again filtered to remove the last trace of pyridine hydrochloride. Distillation of the ether filtrate afforded 18.2 g. (69%) of pure bis-{3-[2-(3-methylpyrazoxy)]-2,2,4,4-tetramethyl-1-cyclobutoxy}dimethylsilane, b.p. 187-191°C at 0.09 mm., n_D^{25} 1.4963.

Anal. Calc'd. for $C_{28}H_{44}N_4O_4Si$: C, 63.60; H, 8.39; N, 10.60; Si, 5.30.
Found: C, 63.12; H, 8.13; N, 10.91; Si, 5.02.

2-(2,2-Dimethylpentoxy)-3,6-dimethylpyrazine. (1) A mixture of 92.8 g. (0.8 mole) of 2,2-dimethyl-1-pentanol and 9.2 g. (0.4 g. atom) of sodium was stirred for 15 hours at room temperature and then was heated up to a pot temperature of 100°C. This temperature was maintained until all the sodium had been reacted. To this was added 200 ml. of 2-chloro-3,6-dimethylpyrazine and low-boiling material was removed by distilling the mixture to a pot temperature of

Approved for Public Release

Contrails

193°C. After refluxing the mixture for 24 hours, it was cooled, treated with ether, and filtered to remove the insoluble salt. Distillation of the ether solution gave 120 ml. of recovered 2-chloro-3,6-dimethylpyrazine, b.p. 73°C at 17 mm., and 76.6 g. (83.2%) of crude 2-(2,2-dimethylpentoxy)-3,6-dimethylpyrazine, b.p. 82°C at 0.75 mm. to 83°C at 0.60 mm., n_D^{25} 1.4835-1.4842.

(2) This reaction was repeated on a larger scale and employing a modified condition for the preparation of the sodium salt. A mixture of 696 g. (6.0 moles) of 2,2-dimethyl-1-pentanol and 69 g. (3.0 g. atoms) of sodium was heated at 100°C with stirring until all the sodium has been reacted. About 200 ml. of the excess 2,2-dimethyl-1-pentanol was removed by distillation. Upon cooling the mixture to 120°C, 1500 ml. of 2-chloro-3,6-dimethylpyrazine was added and the resulting mixture was refluxed at 193°C for 24 hours. Following the usual workup and distillation, a total of 572 g. (83%) of the desired 2-(2,2-dimethylpentoxy)-3,6-dimethylpyrazine was obtained in two fractions: (1) 21 g., b.p. 78-83°C at 0.70 mm., n_D^{25} 1.4887; and (2) 551 g., b.p. 83-85°C at 0.70 mm., n_D^{25} 1.4829. Fraction 2 was shown to be the pure product by elemental analysis.

Anal. Calc'd. for $C_{13}H_{22}N_2O$: C, 70.22; H, 9.98; N, 12.60.
Found: C, 70.44; H, 9.99; N, 12.50.

2-(2,2,4-Trimethylpentoxy)-3,6-dimethylpyrazine. Following the reaction conditions and workup described above under condition (1) for the preparation of 2-(2,2-dimethylpentoxy)-3,6-dimethylpyrazine, 2-(2,2,4-trimethylpentoxy)-3,6-dimethylpyrazine, b.p. 90-93°C at 0.05 mm., n_D^{25} 1.4832, was prepared in 64% yield (60.3 g.) from the interaction of 104 g. (0.8 mole) of 2,2,4-trimethyl-1-pentanol, 9.2 g. (0.4 g. atom) of sodium and 200 ml. of 2-chloro-3,6-dimethylpyrazine. The desired product was purified by redistillation, b.p. 95°C at 1.0 mm., n_D^{25} 1.4827.

Anal. Calc'd. for $C_{14}H_{24}N_2O$: C, 71.14; H, 10.23; N, 11.86.
Found: C, 70.98; H, 10.15; N, 11.99.

C. 2-Anilino-3-methylpyrazines and 2-Anilino-3,6-dimethylpyrazines

General Procedure. Two general procedures were employed for the preparation of this class of materials and they are described as follows.

1. The "Direct" Method. This method involved the heating of a two- to three-fold excess of an aniline with 2-chloro-3-methylpyrazine or 2-chloro-3,6-dimethylpyrazine at elevated temperatures. The maximum temperature attained and length of heating are given under the preparation of each individual compound. The mixture was cooled, poured into water, neutralized with sodium carbonate and made strongly basic with sodium hydroxide. The basic mixture was then extracted with ether or chloroform and the extracts were distilled to obtain the desired product.

Approved for Public Release

Contrails

2. The "Pyridine Solvent" Method. This method applied to the preparation of 2-(N-alkylanilino)-3-methylpyrazines and 2-(N-alkylanilino)-3,6-dimethylpyrazines from the corresponding 2-anilino-3-methylpyrazines and 2-anilino-3,6-dimethylpyrazines. A typical run was carried out by first adding 0.2 mole of a 2-(anilino)-3-methylpyrazine to a suspension of 0.2 mole of sodium amide in 300 ml. of liquid ammonia. The mixture was then stirred for 20 to 30 minutes and to it was introduced 250 ml. of anhydrous pyridine. The liquid ammonia was removed under a stream of nitrogen and with the aid of a warm-water bath. To this deep red mixture was added 0.1 mole of an alkyl halide during a 10-minute period while maintaining the temperature of the mixture at or slightly below room temperature with an ice bath. After the mixture was stirred for 18 hours at room temperature the reaction was quenched with the addition of 100 ml. of methanol. The solvent was removed in vacuo below room temperature. The residue was poured into water and extracted with ether. The ether extracts were distilled to yield the desired 2-(N-alkylanilino)-3-methylpyrazine.

2-(N-Methylanilino)-3-methylpyrazine (1), Interaction of N-Methylaniline with 2-Chloro-3-methylpyrazine in Presence of Zinc Chloride. (1) The "Direct" Method (p. 117) was employed here with the exception that a catalyst, zinc chloride, was added. A mixture of 2-chloro-3-methylpyrazine (128 g., 1.0 mole), N-methylaniline (214 g., 2.0 moles) and anhydrous zinc chloride (68.2 g., 0.5 mole) was heated for a 7-hour and 25-minute period during which time the temperature of the reaction mixture reached 200°C. Following the workup described for this method the combined ether fractions upon distillation gave 114 g. (53.3%) of crude recovered N-methylaniline, b.p. 74-78°C at 12 mm., n_D^{25} 1.5660; 62.5 g. (31.4%) of the crude desired 2-(N-methylanilino)-3-methylpyrazine, b.p. 92-100°C at 0.1 mm.; and 49.3 g. (33%) of the demethylated product, 2-anilino-3-methylpyrazine, b.p. 120-124°C at 0.15 mm. These products were confirmed by comparing their physical properties with those of the authentic compounds. A large quantity of intractable tar was left in the distillation pot.

(2) In another attempt when the same quantities of reactants were heated up to 209°C for a 6-hour period, 2-(N-methylanilino)-3-methylpyrazine was obtained in 50% yield (99.5 g.), b.p. 90-96°C at 0.1 mm., along with 23.5 g. (22%) of the demethylated product, 2-anilino-3-methylpyrazine, b.p. 120-125°C at 0.15 mm.

2-(N-Methylanilino)-3-methylpyrazine (1), Interaction of 2-Anilino-3-methylpyrazine (1) with Methyl Iodide. Employing the "Pyridine Solvent" Method above, 37.0 g. (0.2 mole) of 2-anilino-3-methylpyrazine, m.p. 92-94°C (1), was interacted with 0.2 mole of sodium amide and 14.2 g. (0.1 mole) of methyl iodide. Distillation of the ether extracts afforded the following three fractions: (1) 13.1 g., b.p. 104-144°C at 0.33 mm., n_D^{25} 1.6181; (2) 13.0 g., b.p. 114-127°C at 0.33 mm., which partially solidified upon standing; (3) 5.0 g., b.p. 127-133°C at 0.33 mm., which solidified completely, m.p. 92-93°C. Fraction 2 was filtered, the filtrate

Approved for Public Release

Contrails

was combined with fraction 1 and redistilled to give 16.1 g. (81%) of 2-(N-methylanilino)-3-methylpyrazine, b.p. 98°C at 0.4 mm. to 114°C at 0.35 mm., n_D^{25} 1.6132-1.6154, identified by elemental analysis, infrared and ultraviolet comparison with an authentic sample (1). Further distillation gave 3.1 g. of material, b.p. 114-124°C at 0.35 mm., which

Anal. Calc'd. for $C_{12}H_{13}N_3$: C, 72.33; H, 6.57; N, 21.09.
Found: C, 72.44; H, 6.67; N, 20.91.

solidified upon standing, m.p. 92-93°C. This solid was combined with fraction 3 and the solid product obtained from fraction 2, and identified as the starting 2-anilino-3-methylpyrazine (15.5 g., 42%), m.p. 92-93°C, and showed no depression when admixed with an authentic sample.

N-Butylaniline. This compound was prepared following the method of Alder et al. (17). A mixture of 274 g. (2.0 moles) of 1-bromobutane and 558 g. (6.0 moles) of aniline was heated on a steam bath. The temperature of the mixture rose from room temperature to 180°C in 15 minutes and gradually fell back to about 80°C. The mixture was heated for a total of 6 hours and then cooled. To this was added 600 ml. of 20% sodium hydroxide solution. The organic layer was separated and the aqueous fraction extracted twice with ether. Distillation of the combined organic fractions gave 418 g. (75%) of recovered aniline and 225.5 g. (76%) of the desired N-butylaniline, b.p. 236-238°C, n_D^{25} 1.5315.

2-(N-Butylanilino)-3-methylpyrazine, Interaction of N-Butylaniline and 2-Chloro-3-methylpyrazine. The following runs were performed under the conditions described under the "Direct"Method (p. 117).

(1) A mixture of 174.9 g. (1.1 moles) of N-butylaniline as prepared above and 70.4 g. (0.55 mole) of 2-chloro-3-methylpyrazine was refluxed for 5 hours during which time the temperature of the reaction mixture reached 210°C. Workup of the reaction product mixture and distillation of the chloroform extract gave 60 g. (85%) of recovered crude 2-chloro-3-methylpyrazine, b.p. 55-84°C at 10 mm., and 158 g. (91%) of recovered N-butylaniline, b.p. 233-238°C, n_D^{25} 1.5314. There was also 9 g. of intractable tar remaining in the distillation pot.

(2) The above procedure was modified by using a longer reaction time. A mixture of 149 g. (1.0 mole) of N-butylaniline and 64 g. (0.5 mole) of 2-chloro-3-methylpyrazine was refluxed for 23 hours and the temperature rose to 250°C. Upon cooling, the mixture solidified into an intractable tar which was not worked up further.

(3) Identical amounts of reactants as described in (2) were employed and the mixture was refluxed for 9 hours while the temperature rose gradually to 210°C. Upon distillation of the reaction product mixture after the usual workup, the following were obtained: 45 g. (70.3%) of recovered 2-chloro-3-methylpyrazine, 138 g. (92.7%) of N-butylaniline, and 11.5 g. (8.6%) of the desired product, 2-(N-butylanilino-3-methylpyrazine, b.p. 136-139°C at 1.5 mm., n_D^{25} 1.6060.

Approved for Public Release

Contrails

Anal. Calc'd. for $C_{15}H_{19}N_3$: C, 74.65; H, 7.93; N, 17.41.
Found: C, 74.37; H, 7.61; N, 17.92.

(4) Identical amounts of reactants as described in (2) were employed and the mixture was heated for 13.5 hours during which time the temperature reached 225°C. Obtained from this reaction were 15.5 g. (24.2%) of recovered 2-chloro-3-methylpyrazine, 68 g. (45.5%) of recovered N-butylaniline, and 54 g. of a higher-boiling fraction, b.p. 142-148°C at 1.5 mm., n_D^{25} 1.5905. This fraction was purified by redistillation, b.p. 103-120°C at 0.2 mm., n_D^{25} 1.5820, part of which solidified upon standing. The solid was filtered to give 15.1 g. (16%) of 2-anilino-3-methylpyrazine, m.p. 78-85°C, which was further purified by recrystallization from an ether-petroleum ether mixture, m.p. 91-93°C, and identified by a mixture-melting point determination and infrared comparison. The filtrate (24.2 g.) was shown to be crude product, 2-(N-butylanilino)-3-methylpyrazine (18%), by infrared comparison with an authentic sample. In addition, there was also 51 g. of tar remaining in the distillation pot.

Attempted Preparation of 2-(N-Butylanilino)-3-methylpyrazine, Interaction of 2-Anilino-3-methylpyrazine with 1-Bromobutane. Employing the conditions described under the "Direct" Method (p. 117), the following two attempts were made.

(1) 2-Anilino-3-methylpyrazine (1), 18.6 g. (0.1 mole) and 41.1 g. (0.3 mole) of 1-bromobutane were heated gradually from room temperature to 105°C over a 5-hour and 35-minute period. The distillation of product mixture afforded a quantitative recovery of the starting 2-anilino-3-methylpyrazine, b.p. 134-138°C at 0.8 mm.

(2) The above reaction was repeated employing an identical procedure, except that 2-anilino-3-methylpyrazine (1) (37.2 g., 0.2 mole) and 1-bromobutane (13.7 g., 0.1 mole) were in different molar ratio (2:1). Upon distillation, crude 2-anilino-3-methylpyrazine was recovered (24.5 g., 66%) b.p. 115-118°C at 0.1 mm. while 11.4 g. of intractable tar remained in the distillation pot.

2-(N-Butylanilino)-3-methylpyrazine, Interaction of 2-Anilino-3-methylpyrazine (1) with Sodium Amide and 1-Bromobutane in Pyridine. Using the "Pyridine Solvent" Method (p. 118), 37.0 g. (0.2 mole) of 2-anilino-3-methylpyrazine (1) was interacted with 0.2 mole of sodium amide and 13.7 g. (0.1 mole) of 1-bromobutane. Distillation of the product mixture afforded first a fraction, 26.2 g., b.p. 120-124°C at 0.25 mm., which solidified partially. Further distillation gave 10.4 g. of recovered 2-anilino-3-methylpyrazine, b.p. 124-127°C at 0.25 mm., which solidified upon standing, m.p. 92-93°C. The solid from the low-boiling fraction was filtered to give an additional 8 g. of 2-anilino-3-methylpyrazine, m.p. 92-93°C. The filtrate was redistilled to furnish 15.6 g. (65%) of desired pure 2-(N-butylanilino)-3-methylpyrazine, b.p. 120-121°C at 0.18 mm., n_D^{25} 1.5915.

Anal. Calc'd. for $C_{15}H_{19}N_3$: C, 74.65; H, 7.94; N, 17.41.
Found: C, 74.42; H, 8.22; N, 17.36.

Approved for Public Release

Contrails

From this reaction a total of 18.4 g. (49.6%) of starting 2-anilino-3-methylpyrazine was recovered and 15.6 g. (65%) of the desired 2-(N-butylanilino)-3-methylpyrazine was obtained.

2-(p-Pentylanilino)-3-methylpyrazine. The "Direct" Method (p. 117) was used in the preparation of this compound. A mixture of 142.8 g. (0.9 mole) of p-pentylaniline* and 25.6 g. (0.2 mole) of 2-chloro-3-methylpyrazine was refluxed for a 55-minute period during which time the temperature of the reaction mixture rose to 235°C. Distillation of the reaction product mixture furnished 113 g. (79.5%) of starting p-pentylaniline, b.p. 51-65°C at 0.15 mm., n_D^{25} 1.5350, and 42.5 g. (86%) of 2-(p-pentylanilino)-3-methylpyrazine, b.p. 140-143°C at 0.1 mm. The product was further purified by redistillation, b.p. 134-136°C at 0.12 mm.; it solidified upon cooling into a glassy solid.

Anal. Calc'd. for $C_{16}H_{21}N_3$: C, 75.04; H, 8.05; N, 16.67.
Found: C, 75.25; H, 8.29; N, 16.46.

2-(p-Dodecylanilino)-3-methylpyrazine. This compound was prepared by the "Direct" Method (p. 117). (1) A 156.6 g. (0.6 mole) quantity of p-dodecylaniline** was heated with 25.6 g. (0.2 mole) of 2-chloro-3-methylpyrazine for a 50-minute period during which time the temperature of the reaction mixture reached 268°C. Obtained from distillation after workup were 89.5 g. (58%) of recovered crude p-dodecylaniline, b.p. 128-130°C at 0.6 mm., n_D^{25} 1.5120; and 48.5 g. (63.3%) of the desired 2-(p-dodecylanilino)-3-methylpyrazine, b.p. 168-190°C at 0.05 mm., as a very viscous liquid. The desired product was purified by redistillation, b.p. 173-175°C at 0.10 mm.

Anal. Calc'd. for $C_{23}H_{35}N_3$: C, 78.13; H, 9.98; N, 11.89.
Found: C, 78.31; H, 9.88; N, 11.86.

(2) When the above reaction was repeated under identical conditions on a two-fold scale, 195.1 g. (62.1%) of crude p-dodecylaniline was recovered, b.p. 133°C at 0.3 mm. to 170°C at 0.17 mm., n_D^{25} 1.5133; and 107.5 g. (76.8%) of the crude desired product, b.p. 170-205°C at 0.17 mm., n_D^{25} 1.5300, was obtained. On redistillation of the product fraction, 85 g. (60.7%) of pure 2-(p-dodecylanilino)-3-methylpyrazine was obtained, b.p. 181-185°C at 0.1 mm.

---

* This compound was supplied as a courtesy sample by Monsanto Chemical Company under the name "Alkylaniline C-5". The alkyl group in this compound is a mixture ranging from C_3H_7 to C_9H_{19} with an average of C_5H_{11}.

** This compound was also supplied by Monsanto. The dodecyl substituent is present in a number of isomeric forms and about 90-95% of alkyl substitution is in the para position on the ring.

Approved for Public Release

Contrails

Attempted Preparation of 2-(N-Ethyl-p-pentylanilino)-3-methylpyrazine, Interaction of 2-(p-Pentylanilino)-3-methylpyrazine with Ethyl Bromide. The conditions and workup for this reaction were identical to that described in the general procedure under the "Pyridine Solvent" Method (p. 118). Thus, 51.0 g. (0.2 mole) of 2-(p-pentylanilino)-3-methylpyrazine (see p. 121) in 50 ml. of pyridine was interacted with 0.2 mole of sodium amide and 10.9 g. (0.1 mole) of ethyl bromide. Distillation of the reaction product mixture gave two broad-boiling fractions: (1) 23.8 g., b.p. 124-149°C at 0.2 mm., n_D^{25} 1.5692-1.5805; (2) 21.5 g., b.p. 149-175°C at 0.20 mm., n_D^{25} 1.5927. The infrared spectra of both fractions showed N-H absorption and were very similar, although not identical, to that of the starting 2-(p-pentylanilino)-3-methylpyrazine. It was concluded that from this reaction only starting 2-(p-pentylanilino)-3-methylpyrazine, which was contaminated with small amounts of alkylated product, was recovered.

N-Ethyl-p-pentylaniline. This compound was prepared in 76.4% yield (73 g.) by heating a mixture of 55 g. (0.5 mole) of ethyl bromide and 244 g. (1.5 moles) of p-pentylaniline to 110°C and by distilling the reaction product mixture after the usual workup, b.p. 78-80°C at 0.10 mm., n_D^{25} 1.5255.

Anal. Calc'd. for $C_{13}H_{21}N$: C, 81.61; H, 11.06; N, 7.32.
Found: C, 81.47; H, 10.82; N, 7.52.

Attempted Preparation of 2-(N-Ethyl-p-pentylanilino)-3-methylpyrazine, Interaction of 2-Chloro-3-methylpyrazine with N-Ethyl-p-pentylaniline. N-Ethyl-p-pentylaniline (71.9 g., 0.376 mole), as prepared above, was interacted with 24.2 g. (0.188 mole) of 2-chloro-3-methylpyrazine under the conditions described for the "Direct" Method (p. 117). The mixture was heated to 242°C during a period of 78 minutes. Following the usual workup, distillation of the ether extracts gave 34.3 g. (47.7%) of crude starting N-ethyl-p-pentylaniline, b.p. 80°C at 0.20 mm. to 80°C at 0.02 mm., n_D^{25} 1.5283, and 17.0 g. (36.7%) of the cleaved product, 2-(p-pentylanilino)-3-methylpyrazine, b.p. 173°C at 0.15 mm. to 170°C at 0.10 mm., n_D^{25} 1.6047-1.6037. This cleavage product was identified by infrared comparison with that of 2-(p-pentylanilino)-3-methylpyrazine prepared earlier (see p. 121). In addition, there was obtained considerable amounts of tar (25 g.) from this reaction.

Attempted Preparation of N,N-Di-[2-(3-methylpyrazyl)]aniline, Interaction of 2-(N-Methylanilino)-3-methylpyrazine (1) with 2-Chloro-3-methylpyrazine ("Direct" Method). A mixture of 41.8 g. (0.2 mole) of 2-(N-methylanilino)-3-methylpyrazine (1) and 25.7 g. (0.2 mole) of 2-chloro-3-methylpyrazine was heated for 14 hours during which time the temperature of the mixture reached 209°C. Distillation of the reaction product mixture resulted in the recovery of 10.5 g. (41%) of 2-chloro-3-methylpyrazine, b.p. 60-72°C at 20 mm., n_D^{25} 1.5309, and 24.5 g. (58.6%) of 2-(N-methylanilino)-3-methylpyrazine, b.p. 127-135°C at 0.20 mm., n_D^{25} 1.6132.

Approved for Public Release

Contrails

Attempted Preparation of N,N-Di-[2-(3-methylpyrazyl)]aniline, Interaction of 2-Anilino-3-methylpyrazine (1) with 2-Chloro-3-methylpyrazine ("Pyridine Solvent" Method). A quantity of 37.0 g. (0.20 mole) of 2-anilino-3-methylpyrazine (1) was interacted with 0.2 mole of sodium amide and 12.9 g. (0.10 mole) of 2-chloro-3-methylpyrazine. Following the usual workup, distillation of the ether extracts first recovered 4.6 g. (35.7%) of starting 2-chloro-3-methylpyrazine, b.p. 45-47°C at 12 mm. Further distillation furnished 32.6 g. (88%) of recovered 2-anilino-3-methylpyrazine, b.p. 145-148°C at 0.4 mm., which solidified upon standing, m.p. 92-93°C, and identified by a mixture-melting point determination with an authentic sample.

Attempted Preparation of N,N'-Diphenyl-N,N'-di-[2-(3-methylpyrazyl)]-1,2-diaminoethane, Interaction of 2-Anilino-3-methylpyrazine (1) with 1,2-Dibromoethane ("Pyridine Solvent" Method). 2-Anilino-3-methylpyrazine (1), 37.0 g. (0.2 mole), was interacted with 0.2 mole of sodium amide and 18.8 g. (0.1 mole) of 1,2-dibromoethane. Following the usual workup the ether extracts were evaporated to recover 33.5 g. (90.5 g.) of starting 2-anilino-3-methylpyrazine, m.p. 83-85°C.

N,N'-Diphenyl-N,N'-di-[2-(3-methylpyrazyl)]-1,2-diaminoethane. Sodium amide (0.2 mole) in 300 ml. of liquid ammonia was interacted with 39.8 g. (0.2 mole) of 2-(N-methylanilino)-3-methylpyrazine (1) over a 30-minute period. To this was added 18.8 g. (0.1 mole) of 1,2-dibromoethane during a 20-minute period and the resulting mixture was stirred for an additional 1 hour. The reaction was then quenched with the addition of 30 g. of ammonium chloride, followed by 300 ml. of ether. Upon removal of ammonia, the mixture was poured into water. The ether was separated from the aqueous fraction and the aqueous fraction was extracted with chloroform. Upon concentration, the ether extract precipitated 7.09 g. of yellow solid, m.p. 153-156°C. The mother liquid from the ether solution was combined with the chloroform extracts and distilled to give 23.0 g. (58%) of starting 2-(N-methylanilino)-3-methylpyrazine, b.p. 94-105°C at 0.17 mm., n_D^{25} 1.6131, and 6.2 g. of a very viscous, higher-boiling fraction, b.p. 228-235°C at 0.17 mm. This high-boiling fraction was recrystallized from ether to give 4.5 g. of yellow crystals, m.p. 151-155°C. These yellow crystals and the solid obtained earlier from the ether extracts were combined (a total of 11.5 g., 29%), recrystallized twice from an ether-chloroform mixture, m.p. 152-152.5°C, and identified as N,N'-diphenyl-N,N'-di-[2-(3-methylpyrazyl)]-1,2-diaminoethane by elemental analysis and molecular weight determination.

Anal. Calc'd. for $C_{24}H_{24}N_3$: C, 72.70; H, 6.10; N, 21.20.
Found: C, 72.63; H, 5.94; N, 21.30.
Molecular Wt.: 396.5
Found: 422

2-(N-Methylanilino)-3,6-dimethylpyrazine and 2-Anilino-3,6-dimethylpyrazine. In the following four runs, the conditions and workup described in the "Direct" Method (p. 117) under the general procedure were employed. (1) N-Methylaniline, 107 g. (1.0 mole) and 71.3 g. (0.5 mole) of 2-chloro-3,6-dimethylpyrazine were

Approved for Public Release

Contrails

heated gradually from room temperature to 215°C over a 9-hour period. Distillation of the product mixture afforded 64.5 g. (60%) of recovered N-methylaniline, b.p. 77-78°C at 9 mm., n_D^{25} 1.5551, and a high-boiling fraction, 60.5 g., b.p. 95-115°C at 0.2 mm., n_D^{25} 1.6215. This high-boiling fraction was redistilled to furnish 36.1 g. (30%) of 2-(N-methylanilino)-3,6-dimethylpyrazine, b.p. 97°C at 0.08 mm. to 100°C at 0.07 mm., n_D^{25} 1.6020-1.6072. The fraction, b.p. 99-100°C at 0.07 mm., n_D^{25} 1.6072, was analyzed.

Anal. Calc'd. for $C_{13}H_{15}N_3$: C, 73.21; H, 7.09; N, 19.70.
Found: C, 73.04; H, 7.00; N, 19.69.

Further distillation gave 8.1 g. (8.1% calculated as the demethylated material, 2-anilino-3,6-dimethylpyrazine), b.p. 116-117°C at 0.08 mm., n_D^{25} 1.6481, which solidified on standing, m.p. 79-80°C. The infrared spectrum of this material indicated the presence of N-H group in the molecule.

(2) The above experiment was repeated employing a slightly higher reaction temperature. A mixture of 428 g. (4.0 moles) of N-methylaniline and 285 g. (2.0 moles) of 2-chloro-3,6-dimethylpyrazine were heated to 225°C during a 9.4-hour period. Distillation of the reaction product mixture afforded 217 g. (52%) of recovered N-methylaniline, b.p. 81°C at 10 mm. to 78°C at 8 mm. Further distillation gave 140.5 g. (33%) of the desired 2-(N-methylanilino)-3,6-dimethylpyrazine, b.p. 99°C at 0.15 mm. to 106°C at 0.08 mm., n_D^{25} 1.6033-1.6083, and 170 g. (43.5%) of the cleavage product, 2-anilino-3,6-dimethylpyrazine, b.p. 106-125°C at 0.08 mm., which solidified on standing, m.p. 78-80°C. The crude 2-anilino-3,6-dimethylpyrazine was purified by recrystallization from an ether-petroleum ether mixture, m.p. 79-80°C.

Anal. Calc'd. for $C_{12}H_{13}N_3$: C, 72.33; H, 6.57; N, 21.09.
Found: C, 72.19; H, 6.38; N, 21.05.

A repeat melting point determination of 2-anilino-3,6-dimethylpyrazine after the material has been standing for three months showed that it melted over the range of 89-91°C.

(3) The above experiment was repeated employing similar reaction conditions and identical ratio of reactants as in (1). A mixture of 160.5 g. (1.5moles) of N-methylaniline and 106.9 g. (0.75 mole) of 2-chloro-3,6-dimethylpyrazine was heated for 9.75 hours during which time the temperature reached 223°C. The mixture was cooled and worked up as usual. Distillation of the product mixture furnished 73.7 g. (46%) of starting N-methylaniline, b.p. 32-33°C at 0.40 mm., n_D^{25} 1.5630; 77.2 g. (48.3%) of 2-(N-methylanilino)-3,6-dimethylpyrazine, b.p. 95-114°C at 0.20 mm., n_D^{25} 1.6020-1.6190; and 32.5 g. (21.7%) of 2-anilino-3,6-dimethylpyrazine, b.p. 114-118°C at 0.20 mm., n_D^{25} 1.6295.

(4) The above experiment was repeated employing a different ratio of reactants. N-Methylaniline, 642 g. (6.0 moles), and 285 g. (2.0 moles) of 2-chloro-3,6-dimethylpyrazine was heated to 212°C during a 12.25-hour period. Following

Approved for Public Release

Contrails

the usual workup the reaction product mixture was distilled to furnish the following: 337 g. (52.5%) of N-methylaniline; 146.7 g. (34.4%) of 2-(N-methylanilino)-3,6-dimethylpyrazine, b.p. 91-115°C at 0.1 mm., n_D^{25} 1.6174; and 161.6 g. (40.6%) of 2-anilino-3,6-dimethylpyrazine, b.p. 115-124°C at 0.1 mm., which solidified on standing, m.p. 75-79°C.

2-Anilino-3,6-dimethylpyrazine. This compound was prepared employing the "Direct" Method, (p. 117). A mixture of 186 g. (2.0 moles) of aniline and 142.5 g. (1.0 mole) of 2-chloro-3,6-dimethylpyrazine was heated to 222°C during a 50-minute period. Distillation of the ether extract after the usual workup yielded 83.5 g. (45%) of recovered aniline, b.p. 37°C at 1.0 mm. to 40°C at 0.8 mm., n_D^{25} 1.5821. Upon further distillation, a fraction, b.p. 128-135°C at 0.4 mm., was obtained. This fraction (172 g.) solidified upon standing, m.p. 84-93°C, and was recrystallized once from an ether-petroleum ether mixture, m.p. 88-89°C. The yield of 2-anilino-3,6-dimethylpyrazine based on the 172 g. of product was 86.4%. The melting point of this 88-89°C melting compound was not depressed when admixed with the 89-91°C melting 2-anilino-3,6-dimethylpyrazine obtained by the interaction of 2-chloro-3,6-dimethylpyrazine with N-methylaniline described above (see p. 124).

2-(p-Pentylanilino)-3,6-dimethylpyrazine. Employing the "Direct" Method (p. 117), the interaction of 489 g. (3.0 moles) of p-pentylaniline (see p. 121) and 214 g. (1.5 moles) of 2-chloro-3,6-dimethylpyrazine at 240°C during a 66-minute period afforded 355 g. (88%) of crude 2-(p-pentylanilino)-3,6-dimethylpyrazine, b.p. 151°C at 0.30 mm. to 181°C at 0.35 mm., n_D^{25} 1.576-1.595. This product, a highly viscous liquid, was purified by redistillation, b.p. 171°C at 0.25 mm. to 172°C at 0.20 mm.

Anal. Calc'd. for $C_{17}H_{23}N_3$: C, 75.80; H, 8.61; N, 15.60.
Found: C, 76.47; H, 8.69; N, 14.99.

D. 2-Alkylamino-3-methylpyrazines and 2-Alkylamino-3,6-dimethylpyrazines

General Procedure. The "Direct" Method and "Pyridine Solvent" Method described for the preparation of 2-anilino-3-methylpyrazines and 2-anilino-3,6-dimethylpyrazines (p. 117) were also employed here with the exception that an alkylamine was employed in place of the aniline.

2-(N-n-Hexylamino)-3-methylpyrazine. The "Direct" Method (p. 117) was used for the preparation of this compound. A 90.9 g. (0.9 mole) quantity of n-hexylamine was heated with 38.4 g. (0.3 mole) of 2-chloro-3-methylpyrazine for an 8-hour period during which time the temperature reached 165°C. Distillation of the product mixture after the usual workup gave 59.5 g. (65%) of crude recovered n-hexylamine, b.p. 95-130°C, n_D^{25} 1.4185, along with 45.5 g. (80%) of 2-n-hexylamino-3-methylpyrazine, b.p. 115-117°C at 1 mm., n_D^{25} 1.5307. The desired product was purified by redistillation, b.p. 90°C at 0.05 mm., n_D^{25} 1.5308.

Anal. Calc'd. for $C_{11}H_{19}N_3$: C, 68.35; H, 9.91; N, 21.74.
Found: C, 68.48; H, 9.78; N, 22.11.

Approved for Public Release

Contrails

2-(2-Ethylhexylamino)-3-methylpyrazine. Employing the "Direct" Method (p. 117), heating a mixture of 116.1 g. (0.9 mole) of 2-ethylhexylamine and 38.4 g. (0.3 mole) of 2-chloro-3-methylpyrazine to 218°C during a 24-hour period gave 69 g. (59.4%) of crude recovered 2-ethylhexylamine, b.p. 163-165°C, n_D^{25} 1.4285, along with 51.7 g. (78%) of the desired 2-(2-ethylhexylamino)-3-methylpyrazine, b.p. 165-169°C at 10 mm., n_D^{25} 1.5154. The desired product was purified by redistillation, b.p. 98-99°C at 0.05 mm., n_D^{25} 1.5212.

Anal. Calc'd. for $C_{13}H_{23}N_3$: C, 70.54; H, 10.47; N, 18.99.
Found: C, 69.84; H, 10.66; N, 18.60.
70.46 10.91 18.70.

Attempted Preparation of N,N-Di-[2-(3-methylpyrazyl)]hexylamine. Using the conditions described in the "Direct" Method (p. 117), a 30.3 g. (0.3 mole) quantity of n-hexylamine was heated with 76.8 g. (0.6 mole) of 2-chloro-3-methylpyrazine for a period of 4 hours and 55 minutes during which time the temperature reached 195°C. The usual workup procedure was followed and upon distillation of the ether extract, 48 g. (62.5%) of crude 2-chloro-3-methylpyrazine, b.p. 60-63°C at 20 mm., and 17.8 g. (30.6%) of 2-(n-hexylamino)-3-methylpyrazine, b.p. 93-97°C at 0.05 mm., n_D^{25} 1.5288, were obtained. A 21.5 g. quantity of intractable tar was left in the distillation pot.

2-(N,N-Di-n-butylamino)-3-methylpyrazine. The two following runs were performed under the conditions described in the "Direct" Method (p. 117). (1) Di-n-butylamine, 103.2 g. (0.8 mole), and 51.4 g. (0.4 mole) of 2-chloro-3-methylpyrazine were heated to 168°C during a 33-hour and 40-minute period. Following the usual workup the reaction mixture was distilled to afford 98.5 g. of presumably a mixture of starting di-n-butylamine and 2-chloro-3-methylpyrazine, b.p. 60°C at 25-20 mm., n_D^{25} 1.4363. No effort was made to separate this mixture. Upon further distillation, 34.5 g. (39.0%) of the crude 2-(N,N-di-n-butylamino)-3-methylpyrazine was obtained, b.p. 83°C at 0.20 mm. to 88°C at 0.10 mm., n_D^{25} 1.5072-1.5131. This crude product was purified by redistillation, b.p. 75°C at 0.07 mm. to 76°C at 0.08 mm., n_D^{25} 1.5063.

Anal. Calc'd. for $C_{13}H_{23}N_3$: C, 70.54; H, 10.47; N, 18.99.
Found: C, 70.56; H, 10.58; N, 18.78.

(2) The above reaction was repeated using a different ratio of reactants and a shorter reaction period. When a quantity of 116.1 g. (0.9 mole) of di-n-butylamine was heated with 38.6 g. (0.3 mole) of 2-chloro-3-methylpyrazine for an 8-hour and 20-minute period to 161°C, the desired 2-(N,N-di-n-butylamino)-3-methylpyrazine was obtained in only 9.5% crude yield, b.p. 99°C at 0.30 mm. to 104°C at 0.25 mm., n_D^{25} 1.4895.

2-(N,N-Di-n-pentylamino)-3-methylpyrazine. The following two runs were performed using the "Direct" Method (p. 117). (1) Di-n-pentylamine, 125.6 g. (0.80 mole), and 51.4 g. (0.4 mole) of 2-chloro-3-methylpyrazine was heated to 193°C during a 24-hour and 55-minute period. The mixture was cooled and worked up in

Approved for Public Release

Contrails

the usual manner. Distillation of the product mixture gave 82.7 g. (65.8%) of recovered di-n-pentylamine, b.p. 73°C at 19 mm. to 82°C at 17 mm., n_D^{25} 1.4300, and 40.0 g. (40.2%) of crude 2-(N,N-di-n-pentylamino)-3-methylpyrazine, b.p. 90°C at 0.10 mm. to 104°C at 0.13 mm., n_D^{25} 1.4981. The product fraction was purified by redistillation, b.p. 90-94°C at 0.04 mm., n_D^{25} 1.5017.

Anal. Calc'd. for $C_{15}H_{27}N_3$: C, 72.24; H, 10.91; N, 16.85.
Found: C, 72.44; H, 10.92; N, 16.72.

(2) The above reaction was repeated using a different ratio of reactants and milder reaction conditions. The interaction of di-n-pentylamine (141.3 g., 0.9 mole) with 2-chloro-3-methylpyrazine (38.6 g., 0.3 mole) was attempted with a shorter reaction time (5.5 hours) and lower temperature of reaction (up to 183°C). The desired 2-(N,N-di-n-pentylamino)-3-methylpyrazine was obtained in 13.4% yield, b.p. 87-97°C at 0.03 mm., n_D^{25} 1.4902.

2-(N,N-Di-n-hexylamino)-3-methylpyrazine. The following two runs were performed using the "Direct" Method (p. 117). (1) A quantity of 185 g. (1.0 mole) of di-n-hexylamine was heated with 64.3 g. (0.5 mole) of 2-chloro-3-methylpyrazine during a 4-hour and 20-minute period during which time the temperature of the mixture reached 247°C. The mixture was then cooled and worked up in the usual manner. Upon distillation, the following fractions were obtained: 118.5 g., b.p. 65-122°C at 10 mm., n_D^{25} 1.4362, identified as the crude starting di-n-hexylamine (64%); and 97.7 g. (70.6%) of the desired product, 2-(N,N-di-n-hexylamino)-3-methylpyrazine, b.p. 105-118°C at 0.1 mm., n_D^{25} 1.4948. The product was purified by redistillation, b.p. 118-121°C at 0.08 mm., n_D^{25} 1.4942.

Anal. Calc'd. for $C_{17}H_{31}N_3$: C, 73.59; H, 11.26; N, 15.15.
Found: C, 73.33; H, 11.05; N, 14.92.

(2) In a similar run, where the mole ratio of di-n-hexylamine (166.5 g., 0.9 mole) and 2-chloro-3- methylpyrazine (38.4 g., 0.3 mole) was 3 to 1 and the mixture was heated to 245°C during a 4-hour and 50-minute period, the desired 2-(N,N-di-n-hexylamino)-3-methylpyrazine was obtained in 74% yield, b.p. 128-134°C at 1.0 mm., n_D^{25} 1.4839. In addition, there was also recovered 99.7 g. (60%) of starting di-n-hexylamine, b.p. 120-121°C at 20 mm., n_D^{25} 1.4324.

2-(N-n-Hexyl-N-n-octylamino)-3-methylpyrazine. Employing the "Pyridine Solvent" Method (p. 118), 77.6 g. (0.4 mole) of 2-(N-n-hexylamino)-3-methylpyrazine (p. 125) was interacted with 0.4 mole of sodium amide and 38.6 g. (0.2 mole) of 1-bromooctane. From this reaction were isolated 40 g. (51.4%) of starting 2-(N-n-hexylamino)-3-methylpyrazine, b.p. 110-113°C at 0.8 mm., n_D^{25} 1.5290, and 45 g. (73.7%) of desired 2-(N-n-hexyl-N-n-octylamino)-3-methylpyrazine, b.p. 125-130°C at 0.08 mm., n_D^{25} 1.4940. The product was purified by redistillation, b.p. 128-129°C at 0.03 mm., n_D^{25} 1.4938.

Anal. Calc'd. for $C_{19}H_{35}N_3$: C, 74.70; H, 11.55; N, 13.76.
Found: C, 74.57; H, 11.40; N, 13.86.

Approved for Public Release

Contrails

2-(n-Hexylamino)-3,6-dimethylpyrazine. A quantity of 404 g. (4.0 moles) of n-hexylamine was interacted with 285 g. (2.0 moles) of 2-chloro-3,6-dimethylpyrazine under the conditions described in the "Direct" Method (p. 117). The mixture reached a maximum temperature of 195°C during a 12.5-hour reaction period. Distillation of the product mixture afforded 191 g. (46.1%) of 2-(n-hexylamino)-3,6-dimethylpyrazine, b.p. 112-118°C at 0.9 mm. This product was purified by redistillation, b.p. 90-91.5°C at 0.02 mm., n_D^{25} 1.5273.

Anal. Calc'd. for $C_{12}H_{21}N_3$: C, 69.52; H, 10.21; N, 20.27.
Found: C, 69.38; H, 10.16; N, 20.44.

2-(N,N-Di-n-butylamino)-3,6-dimethylpyrazine. The following four runs were performed under the conditions described in the "Direct" Method (p. 117). Modifications are indicated under each separate run. (1) A quantity of 90.3 g. (0.7 mole) of di-n-butylamine was refluxed with 49.9 g. (0.35 mole) of 2-chloro-3,6-dimethylpyrazine during a 42-hour and 15-minute period at atmospheric pressure during which time the temperature of the mixture reached 171°C. Distillation after the usual workup gave 74 g. (82%) of recovered di-n-butylamine, b.p. 54-58°C at 10 mm., n_D^{25} 1.4414, and 28.2 g. (34.3%) of 2-(N,N-di-n-butylamino)-3,6-dimethylpyrazine, b.p. 90°C at 0.50 mm. to 89°C at 0.30 mm., n_D^{25} 1.4926. The product fraction was purified by redistillation, b.p. 83°C at 0.12 mm. to 84°C at 0.10 mm., n_D^{25} 1.5022.

Anal. Calc'd. for $C_{14}H_{25}N_3$: C, 71.43; H, 10.71; N, 17.85.
Found: C, 71.46; H, 10.55; N, 17.71.

(2) A mixture of 57 g. (0.4 mole) of 2-chloro-3,6-dimethylpyrazine and 103.2 g. (0.8 mole) of di-n-butylamine was heated in a sealed steel bomb for a 2.25-hour period during which time the temperature rose to 200°C. The line joining the pressure gauge to the steel bomb was plugged due to formation of solid amine hydrochloride. No reliable pressure reading could be obtained in this run. The mixture was then cooled and worked up as usual. Distillation of the product mixture gave 75.5 g. (73.2%) of recovered di-n-butylamine, b.p. 52-57°C at 13 mm., n_D^{25} 1.4235, and 18.2 g. (19.3%) of desired 2-(N,N-di-n-butylamino)-3,6-dimethylpyrazine, b.p. 89-93°C at 0.3 mm., n_D^{25} 1.4980.

(3) Identical quantities of reactants described in (2) were employed and the reaction was performed in a bomb. The mixture was heated to 250°C during a 4-hour period. As in the case of (2), no pressure reading could be obtained. From this run, 42 g. (40.7%) of starting di-n-butylamine, b.p. 64-70°C at 18 mm., n_D^{25} 1.4120-1.4125, was recovered; and 67 g. (71.3%) of the desired 2-(N,N-di-n-butylamino)-3,6-dimethylpyrazine, b.p. 88-92°C at 0.3 mm., n_D^{25} 1.5040, was obtained.

(4) Identical quantities of reactants described in (2) were employed and the reaction was performed in a bomb. The mixture was heated to 260°C during a 4-hour period and the maximum pressure was 95 lb./in.^{2}. The mixture was cooled and worked up as usual. From this experiment, 38.3 g. (37.1%) of starting di-

Approved for Public Release

Contrails

n-butylamine was recovered, and 62.2 g. (66%) of the product, 2-(N,N-di-n-butylamino)-3,6-dimethylpyrazine, b.p. 100°C at 0.9 mm. to 103°C at 0.8 mm., n_D^{25} 1.5066, was obtained.

Attempted Preparation of 2-(N,N-Di-n-butylamino)-3,6-dimethylpyrazine, Interaction of Di-n-butylamine with Sodium Hydride and 2-Chloro-3,6-dimethylpyrazine. (1) A quantity of 25.8 g. (0.2 mole) of di-n-butylamine was added to a suspension of 9.2 g. (0.2 mole) of sodium hydride in 75 ml. of tetrahydrofuran. No evolution of hydrogen was noted. The mixture was heated under reflux and still no gaseous evolution could be observed. This mixture was not worked up further.

(2) A mixture of 51.6 g. (0.4 mole) of di-n-butylamine and 9.2 g. (0.2 mole) of sodium hydride was heated to reflux (160°C) during a 17-minute period. The heating was continued for two additional hours until the evolution of gas had stopped. At this point the temperature of the mixture has risen to 173°C. Excess di-n-butylamine was removed at reduced pressure. The mixture was cooled to 0°C and to it was added 57.0 g. (0.4 mole) of 2-chloro-3,6-dimethylpyrazine. Since no apparent reaction had taken place, the mixture was heated to 190°C for a 15-minute period. Upon cooling, 200 ml. of ether was added and the mixture was filtered. Distillation of the filtrate gave 46.3 g. (81.2%) of starting 2-chloro-3,6-dimethylpyrazine, b.p. 30°C at 0.5 mm. to 33°C at 0.2 mm., n_D^{25} 1.5211. No product was isolated from this experiment.

(3) The above experiment (run 2) was repeated with identical quantities of reactants but modified reaction conditions. The 2-chloro-3,6-dimethylpyrazine was added to the presumed sodium salt of di-n-butylamine at 40°C and the resulting mixture was stirred overnight at room temperature. The workup gave mostly tar and no desired product was obtained.

2-(N,N-Di-i-butylamino)-3,6-dimethylpyrazine. A modified "Direct" Method (p. 117) was employed for the preparation of this material. A mixture of 103.2 g. (0.8 mole) of di-i-butylamine and 57.0 g. (0.4 mole) of 2-chloro-3,6-dimethylpyrazine was heated to 240°C during a 4-hour period in a sealed steel bomb. The pressure reading was 150-160 lb./in.^{2} at the end of this period. Upon cooling, the mixture was worked up as usual to give the following: 60.7 g. (59.3%) of starting di-i-butylamine, b.p. 55-57°C at 30 mm., n_D^{25} 1.4083-1.410; 26 g. (45.6%) of starting 2-chloro-3,6-dimethylpyrazine, b.p. 60°C at 0.30 mm. to 67°C at 0.25 mm., n_D^{25} 1.5100; and 32.7 g. (34.8%) of desired 2-(N,N-di-i-butylamino)-3,6-dimethylpyrazine, b.p. 67°C at 0.25 mm. to 74°C at 0.20 mm., n_D^{25} 1.5000. The desired product was purified by redistillation, b.p. 66°C at 0.08 mm. to 67°C at 0.10 mm., n_D^{25} 1.5015.

Anal. Calc'd. for $C_{14}H_{25}N_3$: C, 71.43; H, 10.71; N, 17.85.
Found: C, 71.11; H, 10.53; N, 17.90.

2-(N,N-Di-n-pentylamino)-3,6-dimethylpyrazine. The "Direct" Method (p. 117) was employed in the two following runs. (1) Di-n-pentylamine (109.9 g., 0.70 mole)

Approved for Public Release

Contrails

was heated with 2-chloro-3,6-dimethylpyrazine (49.9 g., 0.35 mole) to 201°C during a 25-hour and 45-minute period at atmospheric pressure. The materials isolated were 78.9 g. (71.7%) of starting di-n-pentylamine, b.p. 77°C at 15 mm. to 82°C at 12 mm., n_D^{25} 1.4439, and 38.0 g. (41.3%) of the desired 2-(N,N-di-n-pentylamino)-3,6-dimethylpyrazine, b.p. 85-105°C at 0.15 mm., n_D^{25} 1.4802. The product was purified by redistillation, b.p. 95°C at 0.06 mm., n_D^{25} 1.4963.

Anal. Calc'd. for $C_{18}H_{29}N_3$: C, 72.95; H, 11.10; N, 15.95.
Found: C, 73.04; H, 10.90; N, 15.81.

(2) Identical quantities of materials described in (1) were employed and the reactants were mixed in a steel bomb, sealed, and heated to a temperature of 260°C during a 3.5-hour period. Due to plugging of the pressure line leading to the pressure gauge by the formation of solid amine hydrochloride, no pressure reading could be taken during this run. The reaction product mixture was cooled and worked up in the usual manner. The desired 2-(N,N-di-n-pentylamino)-3,6-dimethylpyrazine (50.6 g.) was obtained in 54.9% yield, b.p. 97°C at 0.55 mm. to 110°C at 0.40 mm., n_D^{25} 1.4935.

2-(N,N-Di-n-hexylamino)-3,6-dimethylpyrazine. Employing the conditions described under the "Direct" Method (p. 117), 129.5 g. (0.7 mole) of di-n-hexylamine was heated with 2-chloro-3,6-dimethylpyrazine (49.9 g., 0.35 mole) to 252°C during a 7-hour and 20-minute period at atmospheric pressure. Obtained from this reaction were 59.5 g. (46%) of starting di-n-hexylamine, b.p. 120-130°C at 15 mm., n_D^{25} 1.4341, and 67.8 g. (58.6%) of 2-(N,N-di-n-hexylamino)-3,6-dimethylpyrazine, b.p. 102°C at 0.12 mm. to 115°C at 0.10 mm., n_D^{25} 1.4890. The product fraction was purified by redistillation, b.p. 108-109°C at 0.05 mm., n_D^{25} 1.4935.

Anal. Calc'd. for $C_{18}H_{33}N_3$: C, 74.17; H, 11.41; N, 14.42.
Found: C, 74.35; H, 11.24; N, 14.61.

E. x-Alkyl-x'-methylpyrazines

General Procedure. The procedure described below is applicable to the preparation of all the members of this class. Modifications, if any, are indicated under each individual compound. To a suspension of sodium amide, prepared from 4.6 g. (0.2 g. atom) of sodium in 300 ml. of liquid ammonia and a few crystals of ferric nitrate, was added 0.2 mole of the dimethyl- or tetramethylpyrazine over a 15 to 30-minute period. The mixture was stirred for an additional 30 minutes and to this was added 0.1 mole of an alkyl halide (or a solution of the alkyl halide in ether) over a 20-minute period. The resulting mixture was stirred for one hour, then the reaction was quenched with the addition of 30 g. of ammonium chloride, followed by 200 ml. of ether. The ammonia was evaporated and the mixture was poured into water. The organic layer was evaporated and the aqueous fraction was made alkaline by sodium hydroxide, salted out with sodium chloride and extracted further with ether. The ether fractions were combined, dried over sodium sulfate and the solvent was evaporated on the

Approved for Public Release

Contrails

steam bath. The remaining liquid was distilled at reduced pressure to obtain the desired product.

2-n-Heptyl-5-methylpyrazine. (1) A quantity of 21.6 g. (0.2 mole) of 2,5-dimethylpyrazine was reacted with 0.2 mole of sodium amide and 16.5 g. (0.1 mole) of 1-bromohexane in 300 ml. of liquid ammonia. Distillation of the reaction product mixture gave 8.6 g. (40%) of crude starting 2,5-dimethylpyrazine, b.p. 140-148°C, n_D^{25} 1.4938; 16.9 g. (88.5%) of desired 2-n-heptyl-5-methylpyrazine, b.p. 113-116°C at 5.0 mm., n_D^{25} 1.4840; and 3 g. of a higher boiling fraction, b.p. 133-135°C at 0.60 mm., n_D^{25} 1.4940. The desired product was purified by redistillation, b.p. 82-84°C at 0.75 mm., n_D^{25} 1.4835.

Anal. Calc'd. for $C_{12}H_{20}N_2$: C, 74.95; H, 10.48; N, 14.47.
Found: C, 74.79; H, 10.32; N, 14.66.

The higher boiling fraction was also purified by redistillation, b.p. 116-118°C at 0.05 mm., n_D^{25} 1.4878. Based on results of elemental analysis, this material is a mixture of 2-n-heptyl-5-methylpyrazine and 2,5-di-n-heptylpyrazine.

Anal. Calc'd. for 2,5-di-n-heptylpyrazine $C_{18}H_{32}N_2$: C, 78.20; H, 11.67; N, 10.13.

Found: C, 76.50; H, 10.78; N, 12.38.

(2) The above reaction was repeated on a larger scale. Thus, 1296 g. (12.0 moles) of 2,5-dimethylpyrazine was interacted with 12.0 moles of sodium amide and 990 g. (6.0 moles) of 1-bromohexane in 4 l. of liquid ammonia. From this experiment the desired product, 2-n-heptyl-5-methylpyrazine, b.p. 98°C at 2.0 mm. to 106°C at 1.6 mm., n_D^{25} 1.4836-1.4841, was obtained in 69.3% yield (798 g.). In addition, a higher boiling fraction, 72.5 g., b.p. 85°C at 0.5 mm. to 140°C at 0.4 mm., was isolated. This fraction was redistilled to furnish first, a small amount of a solid, m.p. 106-107°C after recrystallization from petroleum ether, tentatively identified as 2,5-dimethyl-3-[5-(2-methylpyrazylmethyl)] pyrazine.

Anal. Calc'd. for $C_{12}H_{14}N_4$: C, 67.26; H, 6.59; N, 26.15.
Found: C, 67.30; H, 6.35; N, 25.82.

Further distillation of this higher boiling fraction gave 19.3 g. of sharp boiling material, b.p. 121-123°C at 0.10 mm., n_D^{25} 1.4813, tentatively identified as 2,5-di-n-heptylpyrazine (1.7%).

Anal. Calc'd. for $C_{18}H_{32}N_2$: C, 78.20; H, 11.67; N, 10.14.
Found: C, 77.94; H, 11.35; N, 10.08.

(3) The above reaction was repeated employing a different ratio of reactants. When 21.6 g. (0.2 mole) of 2,5-dimethylpyrazine was interacted with a 0.4 mole of sodium amide and 16.5 g. (0.1 mole) of 1-bromohexane in 20 ml. of ether,

Approved for Public Release

Contrails

the desired 2-n-heptyl-5-methylpyrazine was obtained in 40% yield (7.8 g.) b.p. 230-235°C, n_D^{25} 1.4835.

2-n-Heptyl-6-methylpyrazine. (1) A quantity of 0.4 mole of sodium amide was allowed to interact with 43.2 g. (0.4 mole) of 2,6-dimethylpyrazine in 75 ml. of ether and 31.0 g. (0.2 mole) of 1-bromohexane in 20 ml. of ether. Distillation of the product mixture gave 20.5 g. (47.4%) of crude recovered 2,6-dimethylpyrazine, b.p. 68-72°C at 32 mm. along with 30.8 g. (80%) of 2-n-heptyl-6-methylpyrazine, b.p. 106-108°C at 3.0 mm., n_D^{25} 1.4838. The desired product was purified by redistillation, b.p. 67-67.5°C at 0.07 mm., n_D^{25} 1.4839.

Anal. Calc'd. for $C_{12}H_{20}N_2$: C, 74.95; H, 10.48; N, 14.47.
Found: C, 75.03; H, 10.45; N, 14.39.

(2) The above reaction was repeated on a larger scale. Thus, 1296 g. (12.0 moles) of 2,6-dimethylpyrazine was interacted with 12 moles of sodium amide and 990 g. (6.0 moles) of 1-bromohexane. A total of 423.5 g. (32.6%) of starting 2,6-dimethylpyrazine was recovered, b.p. 80°C at 60 mm. to 60°C at 10 mm., and 1017 g. (88.3%) of desired 2-n-heptyl-6-methylpyrazine, b.p. 91°C at 0.6 mm. to 87°C at 0.4 mm., n_D^{25} 1.4847-1.4843, was obtained.

2-n-Nonyl-5-methylpyrazine. The reaction of 216 g. (2.0 moles) of 2,5-dimethylpyrazine with 2.0 moles of sodium amide and 193 g. (1.0 mole) of 1-bromoöctane in 1 l. of liquid ammonia gave 67 g. (31.1%) of starting 2,5-dimethylpyrazine, b.p. 40°C at 5.0 mm. to 54°C at 3.0 mm., n_D^{25} 1.4970-1.4992; and 198 g. (90%) of desired 2-n-nonyl-5-methylpyrazine, b.p. 120°C at 0.46 mm. to 129°C at 0.50 mm., n_D^{25} 1.4820. The product was purified by redistillation, b.p. 99°C at 0.12 mm., n_D^{25} 1.4820.

Anal. Calc'd. for $C_{14}H_{24}N_2$: C, 76.31; H, 10.98; N, 12.72.
Found: C, 76.44; H, 11.03; N, 12.60.

2-n-Nonyl-6-methylpyrazine. This compound was prepared from 216 g. (2.0 moles) of 2,6-dimethylpyrazine, 2.0 moles of sodium amide and 193 g. (1.0 mole) of 1-bromoöctane in 94.8% yield (208.9 g.), b.p. 105°C at 0.30 mm. to 110°C at 0.20 mm., n_D^{25} 1.4826-1.4829. The fraction, b.p. 103°C at 0.22 mm. to 102°C at 0.20 mm., n_D^{25} 1.4827, was shown to be pure by elemental analysis.

Anal. Calc'd. for $C_{14}H_{24}N_2$: C, 76.31; H, 10.98; N, 12.72.
Found: C, 76.34; H, 11.02; N, 12.88.

2-n-Heptyl-3,5,6-trimethylpyrazine and 2,5-Di-n-heptyl-3,6-dimethylpyrazine. A 27.2 g. (0.2 mole) quantity of tetramethylpyrazine was treated of 0.4 mole of sodium amide in 300 ml. of liquid ammonia and 66.0 g. (0.4 mole) of 1-bromohexane. Distillation of the reaction product mixture gave two fractions: (1) 18.6 g., b.p. 168-172°C at 35 mm., and (2) 18.5 g., 130-140°C at 0.1 mm. Fraction (1) was redistilled to give 18.5 g. (42.2%) of 2-n-heptyl-3,5,6-trimethylpyrazine, b.p. 85-87°C at 0.15 mm., n_D^{25} 1.4895.

Approved for Public Release

Contrails

Anal. Calc'd. for $C_{14}H_{24}N_2$: C, 76.31; H, 10.98; N, 12.71.
Found: C, 75.90; H, 10.74; N, 12.70.

Fraction (2) was tentatively assigned to be 2,5-di-n-heptyl-3,6-dimethylpyrazine (25.5% yield), based on analysis of a redistilled sample, b.p. 128-129°C at 0.03 mm., n_D^{25} 1.4861.

Anal. Calc'd. for $C_{20}H_{36}N_2$: C, 78.88; H, 11.92; N, 9.20.
Found: C, 78.17; H, 11.27; N, 9.74.

II. ADVANCED INTERMEDIATES

This category consisted of the 2,6-disubstituted-3-methylpyrazines. Depending on the nature of the 6-substituent (namely, aralkyl or alkyl), one of the two following general procedures was employed for the preparation of this type of material. The "arylation" method was applied to the preparation of 2-substituted-3-methyl-6-benzylpyrazines. When the 6-substituent was alkyl, the "alkylation" method was used. Modifications of procedure, if any, are given under the preparation of each compound.

1. "Arylation" Method. In a typical run, sodium amide, prepared by dissolving sodium in liquid ammonia to which a few crystals of ferric nitrate have been added, was allowed to interact with a solution of a 2-substituted-3,6-dimethylpyrazine in ether during a 60 to 70-minute period. To this was then added, over a 15-minute period, an aryl halide and the reaction mixture was stirred for an additional 10-minute period. The reaction was then quenched with the addition of excess ammonium chloride, followed by ether. The ammonia was evaporated and the remaining reaction product mixture was poured into cold water. The ether fraction was separated and the aqueous layer was made basic with sodium hydroxide, saturated with sodium chloride, and extracted with ether. All of the ether fractions were combined, dried over sodium sulfate and the solvent was removed by evaporation on the steam bath. The remaining liquid was then distilled to obtain the desired product.

2. "Alkylation" Method. To a suspension of sodium amide in liquid ammonia was added the 2-substituted-3,6-dimethylpyrazine over a 10-minute period. The mixture was stirred for an additional 30-45 minutes. To this red mixture was then introduced the corresponding alkyl halide during 45 minutes and the mixture was stirred for 1 to 2 hours. The reaction was quenched with the addition of ammonium chloride and ether. The workup described above in the "arylation" method was then followed.

Approved for Public Release

Contrails

A. 2-Phenoxy-3-methyl-6-substitutedpyrazines

2-Phenoxy-3-methyl-6-benzylpyrazine. Employing the "arylation" method (p. 133), a quantity of 100 g. (0.5 mole) of 2-phenoxy-3,6-dimethylpyrazine (1) in 100 ml. of ether was interacted with 2.0 moles of sodium amide in 800 ml. of liquid ammonia and 39.3 g. (0.25 mole) of bromobenzene. From this reaction 29.5 g. (29.5%) of 2-phenoxy-3,6-dimethylpyrazine, b.p. 80-100°C at 0.3 mm., n_D^{25} 1.5696-1.5682 was recovered, and 28.1 g. (41%) of crude 2-phenoxy-3-methyl-6-benzylpyrazine, b.p. 161-167°C at 0.25 mm., n_D^{25} 1.5962, was obtained. The crude product was then redistilled to obtain a purified sample, b.p. 158-160°C at 0.17 mm., n_D^{25} 1.5977.

Anal. Calc'd. for $C_{18}H_{16}N_2O$: C, 78.23; H, 5.84; N, 10.14.
Found: C, 78.14; H, 5.94; N, 10.28.

2-(p-Nonylphenoxy)-3-methyl-6-benzylpyrazine. Identical quantities of reactants described above for the preparation of 2-phenoxy-3-methyl-6-benzylpyrazine were employed except that 163 g. (0.5 mole) of 2-(p-nonylphenoxy)-3,6-dimethylpyrazine (1) was used in place of the 2-phenoxy-3,6-dimethylpyrazine. From this reaction the following fractions were isolated by distillation of the reaction product mixture: 89.6 g. (54.5%) of starting 2-(p-nonylphenoxy)-3,6-dimethylpyrazine, b.p. 160-180°C at 0.3 mm., n_D^{25} 1.5256, and 58.2 g. (58.4%) of crude product, b.p. 216°C at 0.30 mm. to 246°C at 0.50 mm., n_D^{25} 1.5584-1.5620, which was purified by redistillation, b.p. 221-226°C at 0.05 mm., n_D^{25} 1.5610.

Anal. Calc'd. for $C_{27}H_{34}N_2O$: C, 80.55; H, 8.51; N, 6.96.
Found: C, 80.40; H, 8.57; N, 6.91.

2-(p-Nonylphenoxy)-3-methyl-6-(p-phenoxybenzyl)pyrazine (1). The procedure for the preparation of 2-phenoxy-3-methyl-6-benzylpyrazine described above was employed except 163 g. (0.5 mole) of 2-(p-nonylphenoxy)-3,6-dimethylpyrazine (1) and 62.5 g. (0.25 mole) of p-bromophenyl phenyl ether were used in place of 2-phenoxy-3,6-dimethylpyrazine and bromobenzene, respectively. Distillation of the reaction product mixture gave 25.3 g. (23%) of p-nonylphenol, b.p. 123°C at 0.45 mm. to 156°C at 0.37 mm., n_D^{25} 1.5503, identified by infrared comparison; 66.2 g. (40.5%) of starting 2-(p-nonylphenoxy)-3,6-dimethylpyrazine, b.p. 156-165°C at 0.37 mm., n_D^{25} 1.5320; and 61.1 g. (49%) of the desired 2-(p-nonylphenoxy)-3-methyl-6-(p-phenoxybenzyl)pyrazine, b.p. 246°C at 0.38 mm. to 267°C at 0.50 mm., n_D^{25} 1.5589. The crude product was then purified by redistillation, b.p. 232 to 240°C at 0.04 mm., n_D^{25} 1.5831.

Attempted Preparation of 2-(p-Nonylphenoxy)-3-methyl-6-[p-(p'-phenyldimethylsilylphenoxy)benzyl]pyrazine. The "arylation" method (p. 133) was employed using 18.4 g. (0.8 g. atom) of sodium in 500 ml. of liquid ammonia, 65.2 g. (0.2 mole) of 2-(p-nonylphenoxy)-3,6-dimethylpyrazine (1) in 50 ml. of ether and 38.3 g. (0.1 mole) of p-phenyldimethylsilylphenyl p-bromophenyl ether (1). After the customary workup, distillation of the reaction product mixture furnished 36.5 g. (56%) of starting 2-(p-nonylphenoxy)-3,6-dimethylpyrazine and

Approved for Public Release

Contrails

25.9 g. of a high-boiling fraction, b.p. 240-250°C at 0.22-0.30 mm., which was purified by redistillation, b.p. 220-233°C at 0.02-0.03 mm., n_D^{25} 1.5748.

The infrared spectrum of this high-boiling material was identical to that of the known 2-(p-nonylphenoxy)-3-methyl-6-(p-phenoxybenzyl)pyrazine (see p. 134), although results from elemental analysis indicated it was probably a mixture of starting 2-(p-nonylphenoxy)-3,6-dimethylpyrazine, the cleavage product of 2-(p-nonylphenoxy)-3-methyl-6-(p-phenoxybenzyl)pyrazine, and a small amount of the desired 2-(p-nonylphenoxy)-3-methyl-6-[p-(p'-phenyldimethylsilylphenoxy)-benzyl]-pyrazine.

Anal. Calc'd. for $C_{21}H_{30}N_2O$: C, 77.25; H, 9.26; N, 8.58.
$C_{33}H_{38}N_2O_2$: C, 80.12; H, 7.74; N, 5.67.
$C_{41}H_{48}N_2O_2Si$: C, 78.30; H, 7.68; N, 4.46; Si, 4.47.
Found: C, 76.72; H, 7.56; N, 5.72; Si, 1.66.

2-(p-Nonylphenoxy)-3-methyl-6-(2-trimethylsilylethyl)pyrazine. The following two runs were performed under the conditions described in the "alkylation" procedure (p. 133) with modifications. (1) A suspension of 0.2 mole of sodium amide in 300 ml. of liquid ammonia was allowed to interact with 65.2 g. (0.2 mole) of 2-(p-nonylphenoxy)-3,6-dimethylpyrazine (1) in 75 ml. of ether over an 1-hour period. To this was then added 12.3 g. (0.1 mole) of chloromethyltrimethylsilane over a 30-minute period and the mixture was stirred for an additional 2 hours. Following the usual workup the reaction product mixture was distilled to give 11.7 g. (28.3%) of crude 2-(p-nonylphenoxy)-3-methyl-6-(2-trimethylsilylethyl)pyrazine, b.p. 157-177°C at 0.04 mm., n_D^{25} 1.5278, which was purified by redistillation, b.p. 156-160°C at 0.03 mm., n_D^{25} 1.5214.

Anal. Calc'd. for $C_{25}H_{40}N_2Si$: C, 72.76; H, 9.77; N, 6.79; Si, 6.81.
Found: C, 72.97; H, 9.67; N, 6.94; Si, 6.99.

Further distillation afforded a higher boiling fraction, 21.7 g. (50%), calculated as 2-(p-nonylphenoxy)-3-methyl-6-[2-(3,6-dimethylpyrazylmethyl)]pyrazine, b.p. 199-210°C at 0.04 mm., n_D^{25} 1.5470, which was purified by redistillation, b.p. 202-203°C at 0.03 mm., n_D^{25} 1.5548.

Anal. Calc'd. for $C_{27}H_{35}N_4O$: C, 75.13; H, 8.17; N, 12.98.
Found: C, 74.90; H, 8.45; N, 13.11.

(2) the above reaction was repeated by using a different ratio of reactants and employing a shorter reaction time. A suspension of sodium amide was prepared by dissolving 4.6 g. (0.2 g. atom) of sodium in 350 ml. of liquid ammonia to which had been added a few crystals of ferric nitrate. To this was added a solution of 65.2 g. (0.2 mole) of 2-(p-nonylphenoxy)-3,6-dimethylpyrazine (1) in 50 ml. of ether over a 20-minute period. After the reaction mixture was stirred for 60 minutes to insure the complete formation of the pyrazylmethyl anion, a quantity of 24.5 g. (0.2 mole) of chloromethyltrimethylsilane was added over a 10-minute period and stirring was allowed to continue for an additional

Approved for Public Release

Contrails

50 minutes. The reaction was then quenched by the addition of 11.5 g. ammonium chloride, followed by 250 ml. of ether. Following the usual workup, distillation afforded 29 g. (44.5%) of starting 2-(p-nonylphenoxy)-3,6-dimethylpyrazine, b.p. 156°C at 0.04 mm. to 166°C at 0.03 mm., n_D^{25} 1.5260-1.5224, and 33.4 g. (43.5%) of crude 2-(p-nonylphenoxy)-3-methyl-6-(2-trimethylsilylethyl)pyrazine, b.p. 166°C at 0.03 mm. to 187°C at 0.04 mm., n_D^{25} 1.5190-1.5198. The crude product was then purified by redistillation, b.p. 173-180°C at 0.07 mm., n_D^{25} 1.5192.

2-(p-Nonylphenoxy)-3-methyl-6-(5-nonyl)pyrazine. (1) Employing the "alkylation" method (p. 133), 32.7 g. (0.1 mole) of 2-(p-nonylphenoxy)-3,6-dimethylpyrazine (1) in 50 ml. of ether was interacted with 0.3 mole of sodium amide in 400 ml. of liquid ammonia and 41.1 g. (0.3 mole) of 1-bromobutane. Distillation of the ether extracts furnished 26.1 g. (58%) of the desired 2-(p-nonylphenoxy)-3-methyl-6-(5-nonyl)pyrazine, b.p. 193°C at 0.16 mm. to 202°C at 0.14 mm., n_D^{25} 1.5089.

Anal. Calc'd. for $C_{29}H_{47}N_2O$: C, 79.40; H, 10.57; N, 6.39.
Found: C, 79.45; H, 10.49; N, 6.41.

(2) When the above reaction was repeated on a three-fold larger scale and employing identical reaction conditions and workup, the desired 2-(p-nonylphenoxy)-3-methyl-6-(5-nonyl)pyrazine, b.p. 214°C at 0.30 mm. to 215°C at 0.25 mm., n_D^{25} 1.5089-1.5076, was obtained in 80% yield.

2-(p-Nonylphenoxy)-3-methyl-6-(2-phenylethyl)pyrazine. Using the "alkylation" procedure (p. 133), a quantity of 0.25 mole of sodium amide, prepared from 5.8 g. (0.25 g. atom) of sodium and 300 ml. of liquid ammonia, was allowed to interact with a solution of 81.5 g. (0.25 mole) of 2-(p-nonylphenoxy)-3,6-dimethylpyrazine (1) in 25 ml. of ether. To this mixture was then added 36.1 g. (0.25 mole) of benzyl chloride during a 1-hour period and the resulting reaction mixture was distilled to give 55.9 g. (53.6%) of the crude 2-(p-nonylphenoxy)-3-methyl-6-(2-phenylethyl)pyrazine, b.p. 196°C at 0.03 mm. to 217°C at 0.06 mm. This material was purified by redistillation, b.p. 208-211°C at 0.04 mm., n_D^{25} 1.5558.

Anal. Calc'd. for $C_{28}H_{36}N_2O$: C, 80.72; H, 8.71; N, 6.73.
Found: C, 80.58; H, 8.54; N, 7.08.

2-(p-Nonylphenoxy)-3-methyl-6-tridecylpyrazine. The "alkylation" method (p. 133) was modified for the preparation of this compound. A suspension of 0.161 mole of sodium amide in 300 ml. of liquid ammonia was allowed to interact with 52.5 g. (0.161) mole of 2-(p-nonylphenoxy)-3,6-dimethylpyrazine (1) in 25 ml. of ether and 40.2 g. (0.161 mole) of n-dodecyl bromide. Identical reaction conditions and workup as described above for the preparation of 2-(p-nonylphenoxy)-3-methyl-6-(2-phenylethyl)pyrazine were employed, with the exception that the addition time for the n-dodecyl bromide was 10 minutes, followed by a 50-minute reaction period before quenching. Distillation of the reaction product mixture afforded 52.3 g. (65.6%) of 2-(p-nonylphenoxy)-3-methyl-6-tridecylpyrazine, b.p. 230-237°C at 0.10 mm., n_D^{25} 1.5107-1.5098. This material was further purified by

Approved for Public Release

Contrails

redistillation, b.p. 235-237°C at 0.05 mm., n_D^{25} 1.5090.

Anal. Calc'd. for $C_{33}H_{54}N_2O$: C, 80.10; H, 11.00; N, 5.66.
C, 79.94; H, 10.89; N, 5.86.

B. 2-Alkoxy-3-methyl-6-substitutedpyrazines

2-(2,2-Dimethylpentoxy)-3-methyl-6-(n-heptyl)pyrazine. (1) The "alkylation" method (p. 133) described in the general procedure was employed. Thus, 49.4 g. (0.22 mole) of 2-(2,2-dimethylpentoxy)-3,6-dimethylpyrazine (see p. 116) was reacted with 0.22 mole of sodium amide in 400 ml. of liquid ammonia and 18 g. (0.11 mole) of 1-bromohexane. Isolated from the reaction product mixture were 25.5 g. (51.6%) of starting 2-(2,2-dimethylpentoxy)-3,6-dimethylpyrazine, b.p. 61°C at 1.0 mm. to 71°C at 0.07 mm., n_D^{25} 1.4828-1.4850; and 24.6 g. (73%) of crude product, 2-(2,2-dimethylpentoxy)-3-methyl-6-(n-heptyl)pyrazine, b.p. 108-122°C at 0.07 mm., n_D^{25} 1.4809. The product was purified by redistillation, b.p. 111-112°C at 0.09 mm., n_D^{25} 1.4802.

Anal. Calc'd. for $C_{19}H_{34}N_2O$: C, 74.46; H, 11.18; N, 9.14.
Found: C, 74.32; H, 11.17; N, 9.22.

(2) The above reaction was repeated on a larger scale. Thus, the interaction of 222 g. (1.0 mole) of 2-(2,2-dimethylpentoxy)-3,6-dimethylpyrazine with 1.0 mole of sodium amide in 1400 ml. of liquid ammonia, and 82.5 g. (0.5 mole) of 1-bromohexane furnished 126 g. (82%) of 2-(2,2-dimethylpentoxy)-3-methyl-6-(n-heptyl)pyrazine, b.p. 122°C at 0.28 mm. to 125°C at 0.26 mm., n_D^{25} 1.4796. In addition, 92 g. (41%) of starting 2-(2,2-dimethylpentoxy)-3,6-dimethylpyrazine, b.p. 82°C at 0.60 mm. to 90°C at 0.70 mm., n_D^{25} 1.4825, was recovered.

2-(2,2-Dimethylpentoxy)-3-methyl-6-(n-pentyl)pyrazine and 2-(2,2-Dimethylpentoxy)-3-methyl-6-(5-nonyl)pyrazine. Using the "alkylation" procedure (p. 133), 222 g. (1.0 mole) of 2-(2,2-dimethylpentoxy)-3,6-dimethylpyrazine (see p. 116) was interacted with 3.0 moles of sodium amide in 1400 ml. of liquid ammonia and 411 g. (3.0 moles) of 1-bromobutane. Distillation of the reaction product mixture gave two fractions: (1) 64 g., b.p. 112°C at 0.30 mm. to 120°C at 0.20 mm., n_D^{25} 1.4806, and (2) 204.5 g., b.p. 120-132°C at 0.20 mm., n_D^{25} 1.4793. Fraction (2) was redistilled and the lower boiling fraction, 51.3 g., b.p. 105-122°C at 0.18 mm., was combined with fraction (1) to obtain a total of 115.3 g. (41.3%) of crude 2-(2,2-dimethylpentoxy)-3-methyl-6-(n-pentyl)pyrazine. This product was purified by redistillation, b.p. 105-110°C at 0.09 mm., n_D^{25} 1.4804.

Anal. Calc'd. for $C_{17}H_{30}N_2O$: C, 73.33; H, 10.86; N, 10.06.
Found: C, 73.38; H, 10.76; N, 10.01.

The higher boiling fraction from the redistillation of fraction (2) was 152.7 g. (45.7%) of 2-(2,2-dimethylpentoxy)-3-methyl-6-(5-nonyl)pyrazine, b.p. 131-137°C at 0.18 mm., n_D^{25} 1.4794. The fraction, b.p. 135-136°C at 0.18 mm.,

Approved for Public Release

Contrails

n_D^{25} 1.4794, was shown to be pure product by elemental analysis.

Anal. Calc'd. for $C_{21}H_{38}N_2O$: C, 75.39; H, 11.45; N, 8.38.
Found: C, 75.43; H, 11.52; N, 8.44.

C. 2-Anilino-3-methyl-6-substitutedpyrazines

2-(N-Methylanilino)-3-methyl-6-(5-nonyl)pyrazine. (1) The "alkylation" method described on p. 133 was employed for the preparation of this compound. A quantity of 21.3 g. (0.1 mole) of 2-(N-methylanilino)-3,6-dimethylpyrazine (1) was interacted with 0.3 mole of sodium amide in 400 ml. of liquid ammonia and 41.1 g. (0.3 mole) of 1-bromobutane. Distillation of the product mixture furnished 19.6 g. (60.1%) of 2-(N-methylanilino)-3-methyl-6-(5-nonyl)pyrazine, b.p. 142-158°C at 0.15 mm., n_D^{25} 1.5457-1.5390. The fraction, b.p. 157-158°C at 0.15 mm., n_D^{25} 1.5390, was shown to be pure by analysis.

Anal. Calc'd. for $C_{12}H_{31}N_3$: C, 77.49; H, 9.60; N, 12.91.
Found: C, 77.67; H, 9.57; N, 12.63.

(2) When the above preparation was repeated in a larger scale employing 31.0 g. (1.35 g. atoms) of sodium, 800 ml. of liquid ammonia, 95.0 g. (0.45 mole) of 2-(N-methylanilino)-3,6-dimethylpyrazine (1) and 185 g. (1.35 moles) of 1-bromobutane, 106 g. (72.5%) of the desired 2-(N-methylanilino)-3-methyl-6-(5-nonyl)pyrazine was obtained, b.p. 147-160°C at 0.15 mm., n_D^{25} 1.5407-1.5316.

2-(N-Methylanilino)-3-methyl-6-(n-heptyl)pyrazine. (1) Employing identical reaction conditions as that described in the "alkylation" method (p. 133), 0.1 mole of sodium amide was interacted with 21.3 g. (0.1 mole) of 2-(N-methylanilino)-3,6-dimethylpyrazine (1) and 16.5 g. (0.1 mole) of 1-bromohexane. After the usual workup, distillation of the ether extracts furnished 12.9 g. (43.4%) of 2-(N-methylanilino)-3-methyl-6-(n-heptyl)pyrazine, b.p. 138°C at 0.09 mm. to 145°C at 0.08 mm., n_D^{25} 1.5568-1.5553, which was purified by redistillation, b.p. 132-136°C at 0.08 mm., n_D^{25} 1.5578.

Anal. Calc'd. for $C_{19}H_{27}N_3$: C, 76.72; H, 9.15; N, 14.13.
Found: C, 76.47; H, 9.02; N, 14.25.

(2) The above experiment was repeated employing identical reaction conditions and workup but a different ratio of reactants. A quantity of 0.2 mole of sodium amide was interacted with 42.6 g. (0.2 mole) of 2-(N-methylanilino)-3,6-dimethylpyrazine (1) and 16.5 g. (0.1 mole) of 1-bromohexane. Distillation of the reaction product mixture afforded 10.1 g. (23.7%) of crude starting 2-(N-methylanilino)-3,6-dimethylpyrazine, b.p. 86-120°C at 0.05 mm., n_D^{25} 1.6035, and 17.2 g. (57.8%) of 2-(N-methylanilino)-3-methyl-6-(n-heptyl)pyrazine, b.p. 135-140°C at 0.05 mm., n_D^{25} 1.5575.

Approved for Public Release

Contrails

D. 2-Alkylamino-3-methyl-6-substitutedpyrazines

2-(N,N-Di-n-pentylamino)-3-methyl-6-(n-heptyl)pyrazine. The conditions described in the "alkylation" method (p. 133) were employed. 2-(N,N-Di-n-pentylamino)-3,6-dimethylpyrazine (27.2 g., 0.103 mole) (see p. 129), was treated with 0.103 mole of sodium amide in 300 ml. of liquid ammonia and 8.6 g. (0.052 mole) of 1-bromohexane. Distillation of the reaction product mixture yielded 12.0 g. (44%) of crude, recovered 2-(N,N-di-n-pentylamino)-3,6-dimethylpyrazine, b.p. 93-105°C at 0.03 mm., n_D^{25} 1.4963-1.4953; and 15.2 g. (84%) of desired 2-(N,N-di-n-pentylamino)-3-methyl-6-(n-heptyl)pyrazine, b.p. 137-141°C at 0.03 mm., n_D^{25} 1.4896. This product was purified by redistillation, b.p. 137-140°C at 0.02 mm., n_D^{25} 1.4884.

Anal. Calc'd. for $C_{22}H_{41}N_3$: C, 76.02; H, 11.89; N, 12.09.
Found: C, 76.00; H, 11.97; N, 12.21.

2-(N,N-Di-n-hexylamino)-3-methyl-6-(n-heptyl)pyrazine. (1) Using the "alkylation" method (p. 133), the treatment of 29.2 g. (0.1 mole) of 2-(N,N-di-n-hexylamino)-3,6-dimethylpyrazine (see p. 130) with 0.1 mole of sodium amide and 8.3 g. (0.05 mole) of 1-bromohexane in 300 ml. of liquid ammonia gave 67 g. (35.6%) of pure 2-(N,N-di-n-hexylamino)-3-methyl-6-(n-heptyl)pyrazine, b.p. 161-163°C at 0.20 mm., n_D^{25} 1.4878.

Anal. Calc'd. for $C_{24}H_{45}N_3$: C, 76.74; H, 12.08; N, 11.19.
Found: C, 76.64; H, 12.04; N, 11.41.

In addition, a quantity of 16.5 g. (56.5%) of starting 2-(N,N-di-n-hexylamino)-3,6-dimethylpyrazine was recovered, b.p. 121°C at 0.18 mm. to 129°C at 0.20 mm., n_D^{25} 1.4924.

(2) The above experiment was repeated employing a different reaction condition. The "pyridine solvent" method, which has been described in detail under the general procedure for the preparation of 2-anilino-3-methylpyrazines (p. 118), was used. Thus, 116.8 g. (0.4 mole) of 2-(N,N-di-n-hexylamino)-3,6-dimethylpyrazine was treated first with 0.4 mole of sodium amide in 400 ml. of liquid ammonia, followed by the addition of 250 ml. of pyridine. Upon removal of liquid ammonia, 33.2 g. (0.2 mole) of 1-bromohexane was added to the mixture in the usual manner. Following the customary workup, distillation of the product mixture gave 56.7 g. (48.5%) of starting 2-(N,N-di-n-hexylamino)-3,6-dimethylpyrazine, b.p. 129°C at 0.4-0.15 mm., n_D^{25} 1.4944-1.4938; and 50.6 g. (66.5%) of the product, 2-(N,N-di-n-hexylamino)-3-methyl-6-(n-heptyl)pyrazine, b.p. 155-163°C at 0.13 mm., n_D^{25} 1.4875.

III. CANDIDATE PRODUCTS

A. 2-Phenoxy-3-substitutedpyrazines and 2-Phenoxy-3,6-disubstitutedpyrazines

General Procedure. The two general procedures, namely, the "arylation" method and the "alkylation" method, described earlier on page 133 for the preparation of

Approved for Public Release

Contrails

advance intermediates, were also applicable here for the preparation of these groups of compounds. For the sake of simplicity, only the name of the general procedure, the quantities of reactants, the yield and physical properties of the products are given under each individual compound.

2-Phenoxy-3-(p-phenylbenzyl)pyrazine. This compound was prepared by the "arylation" method (p. 133) from 0.4 mole of sodium amide in 300 ml. of liquid ammonia, a solution of 37.2 g. (0.2 mole) of 2-phenoxy-3-methylpyrazine (1) in 50 ml. of ether, and a solution of 23.3 g. (0.1 mole) of 4-bromobiphenyl in 200 ml. of ether. The product (17.1 g., 51%), b.p. 214-232°C at 0.04 mm., was purified by redistillation, b.p. 216-219°C at 0.04 mm., n_D^{25} 1.6522.

Anal. Calc'd. for $C_{23}H_{18}N_2O$: C, 81.63; H, 5.36; N, 8.28.
Found: C, 81.81; H, 5.63; N, 8.42.

In addition, 18.1 g. (49%) of starting 2-phenoxy-3-methylpyrazine, b.p. 77-94°C at 0.05 mm., was recovered.

2-(p-Nonylphenoxy)-3-benzylpyrazine. This compound was prepared by the "arylation" method (p. 133) from 0.4 mole of sodium amide in 300 ml. of liquid ammonia, 62.4 g. (0.2 mole) of 2-(p-nonylphenoxy)-3-methylpyrazine (1) in 50 ml. of ether and 15.8 g. (0.1 mole) of bromobenzene. The product (18.9 g., 49%), b.p. 174-208°C at 0.2 mm., n_D^{25} 1.5565-1.5669, was purified by redistillation, b.p. 197-200°C at 0.04 mm., n_D^{25} 1.5645.

Anal. Calc'd. for $C_{26}H_{32}N_2O$: C, 80.37; H, 8.30; N, 7.21.
Found: C, 80.42; H, 8.22; N, 7.08.

In addition, 28.6 g. (46%) of starting 2-(p-nonylphenoxy)-3-methylpyrazine contaminated with a small amount of p-nonylphenol, b.p. 122°C at 0.4 mm. to 158°C at 0.25 mm., n_D^{25} 1.5306, was recovered.

2-(p-Nonylphenoxy)-3-(p-phenoxybenzyl)pyrazine. This compound was prepared by the "arylation" method (p. 133) from 0.38 mole of sodium amide in 300 ml. of liquid ammonia, 56.6 g. (0.19 mole) of 2-(p-nonylphenoxy)-3-methylpyrazine (1) in 50 ml. of ether, and 23.9 g. (0.096 mole) of p-bromophenyl phenyl ether. The product (10.9 g., 24%), b.p. 265°C at 0.15-0.10 mm., n_D^{25} 1.5898, was purified by redistillation, b.p. 237-238°C at 0.03 mm., n_D^{25} 1.5898.

Anal. Calc'd. for $C_{32}H_{36}N_2O_2$: C, 79.96; H, 7.55; N, 5.83.
Found: C, 80.07; H, 7.46; N, 6.05.

In addition, 41.3 g. (68.5%) of starting 2-(p-nonylphenoxy)-3-methylpyrazine was recovered.

p-Phenyldimethylsilylchlorobenzene. An 8.99 g. (1.28 g. atom) quantity of finely cut lithium wire was added to 250 ml. of anhydrous ether. The mixture was swept with dry nitrogen and the temperature was reduced to -10°C. To this

Approved for Public Release

Contrails

mixture, 58.6 g. (0.43 mole) of 1-bromobutane in 100 ml. of ether was added over a period of one hour. The butyllithium solution thus prepared was siphoned rapidly into a solution of 82 g. (0.43 mole) of p-bromochlorobenzene in 900 ml. of anhydrous ether at -50°C. The temperature was raised to -35°C and 65.9 g. (0.39 mole) of phenyldimethylchlorosilane in 50 ml. of ether was added, keeping the temperature at -35°C. The mixture was allowed to warm up to room temperature and was stirred for an additional 3 hours at room temperature and then refluxed overnight. The reaction product mixture was poured into water and extracted with ether. The ether extracts were combined, dried, and distilled to give 68.8 g. (72%) of p-phenyldimethylsilylchlorobenzene, b.p. 98-99°C at 0.1 mm., n_D^{25} 1.5672.

Anal. Calc'd. for $C_{14}H_{15}ClSi$: C, 68.11; H, 6.13; Cl, 14.38.
Found: C, 67.94; H, 6.02; Cl, 14.19.

p-Phenyldimethylsilylbromobenzene. This compound was prepared employing identical reaction conditions and method of workup described above for the preparation of p-phenyldimethylsilylchlorobenzene with the exception that a two-fold scale of reactants was employed and 203 g. (0.86 mole) 1,4-dibromobenzene was used in place of p-bromochlorobenzene. The product, b.p. 114°C at 0.1 mm. to 118°C at 0.07 mm., n_D^{25} 1.5859-1.5863, was obtained in 84% yield (191 g.).

Anal. Calc'd. for $C_{14}H_{15}BrSi$: C, 57.72; H, 5.19; Br, 27.32.
Found: C, 57.28; H, 5.09; Br, 28.71.

Attempted Preparation of 2-Phenoxy-3-(p-phenyldimethylsilylbenzyl)pyrazine, 2-Phenoxy-3-benzylpyrazine. (1) This reaction was attempted under the conditions described in the "arylation" method. Thus, 0.5 mole of sodium amide in 500 ml. of liquid ammonia was interacted with 37.2 g. (0.2 mole) of 2-phenoxy-3-methylpyrazine (1) in 30 ml. of ether and 24.6 g. (0.1 mole) of p-phenyldimethylsilylchlorobenzene (see above) in 20 ml. of ether. On distillation of the reaction product mixture the following materials were isolated: 28.5 g. (77%) of recovered 2-phenoxy-3-methylpyrazine, b.p. 92-95°C at 0.6 mm., n_D^{25} 1.5564, and 15.1 g. (57.6%) of 2-phenoxy-3-benzylpyrazine (1), b.p. 137-138°C at 0.02 mm., n_D^{25} 1.6049. The latter compound was identified by infrared comparison and elemental analysis.

Anal. Calc'd. for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.37; N, 10.68.
Found: C, 76.49; H, 5.70; N, 10.48.

(2) The above experiment was repeated using p-phenyldimethylsilylbromobenzene (see above) in place of p-phenyldimethylsilylchlorobenzene. Distillation of the product mixture gave 9.1 g. (60%) of impure 1,3-diphenyltetramethyldisiloxane, b.p. 66-87°C at 0.35 mm., n_D^{25} 1.5183; 17.2 g. (46%) of recovered 2-phenoxy-3-methylpyrazine, b.p. 87-90°C at 0.35 mm., n_D^{25} 1.5557; and 13.2 g. (50%) of 2-phenoxy-3-benzylpyrazine (1), b.p. 145-150°C at 0.30 mm., which was purified by redistillation, b.p. 125-127°C at 0.02 mm., n_D^{25} 1.6040.

Approved for Public Release

Contrails

Anal. Calc'd. for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.37; N, 10.68.
Found: C, 77.93; H, 5.75; N, 10.89.

Attempted Preparation of 2-(p-Nonylphenoxy)-3-(p-phenyldimethylsilylbenzyl)-pyrazine, 2-(p-Nonylphenoxy)-3-benzylpyrazine. This reaction was attempted under the conditions described in the "arylation" method using 0.5 mole of sodium amide in 500 ml. of liquid ammonia, a solution of 62.4 g. (0.2 mole) of 2-(p-nonylphenoxy)-3-methylpyrazine (1) in 10 ml. of ether, and 29.1 g. (0.1 mole) of p-phenyldimethylsilylbromobenzene in 20 ml. of ether. From this reaction the following fractions were obtained by distillation of the product mixture: 35.5 g. (57%) of 2-(p-nonylphenoxy)-3-methylpyrazine, b.p. 135-140°C at 0.03 mm., n_D^{25} 1.5345, and 12 g. (30%) of 2-(p-nonylphenoxy)-3-benzylpyrazine (see p. 140), b.p. 185-187°C at 0.03 mm., n_D^{25} 1.5615, which was identified by infrared comparison.

Attempted Preparation of 2-Phenoxy-3-(p-trimethylsilylmethylbenzyl)pyrazine. This reaction was attempted under the conditions described in the "arylation" method using 0.4 mole of sodium amide in 300 ml. of liquid ammonia, 37.2 g. (0.2 mole) of 2-phenoxy-3-methylpyrazine (1) in 50 ml. of ether, and 19.9 g. (0.1 mole) of (p-chlorobenzyl)trimethylsilane (21). Distillation of the reaction product mixture gave 27.8 g. (75%) of recovered 2-phenoxy-3-methylpyrazine, b.p. 81°C at 0.18 mm. to 85°C at 0.15 mm., n_D^{25} 1.5738-1.5760. Further distillation gave 2.4 g. of a higher boiling liquid, b.p. 154°C at 0.20 mm. to 156°C at 0.17 mm., n_D^{25} 1.5900. This high-boiling fraction, based on results of elemental analysis, was presumed to be a mixture of 2-phenoxy-3-methylpyrazine and 2-phenoxy-3-(p-methylbenzyl)pyrazine.

Anal. Calc'd. for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.05.
$C_{18}H_{18}N_2O$: C, 78.23; H, 5.84; N, 10.10.
Found: C, 72.73; H, 5.56; N, 12.86.
72.56 5.61 12.89

(2) From a repeated run, employing identical reaction conditions and work-up, the starting 2-phenoxy-3-methylpyrazine was recovered in 81% yield.

2-Phenoxy-3-tridecylpyrazine. This compound was prepared by the "alkylation" procedure (p. 133) from 0.1 mole of sodium amide in 250 ml. of liquid ammonia, 18.6 g. (0.1 mole) of 2-phenoxy-3-methylpyrazine (1) in 50 ml. of ether, and 24.9 g. (0.1 mole) of n-dodecyl bromide. The product (21.4 g., 59.1%), b.p. 155°C at 0.15 mm. to 185°C at 0.10 mm., was purified by redistillation, b.p. 173-174°C at 0.10 mm., and it partially solidified on standing.

Anal. Calc'd. for $C_{23}H_{34}N_2O$: C, 77.92; H, 9.67; N, 7.90.
Found: C, 77.69; H, 9.41; N, 8.04.

2-Phenoxy-3-(5-nonyl)pyrazine. (1) This compound was prepared by the "alkylation" procedure (p. 133) from 0.3 mole of sodium amide in 300 ml. of liquid ammonia, 18.6 g. (0.1 mole) of 2-phenoxy-3-methylpyrazine (1) in 30 ml.

Approved for Public Release

Contrails

of ether, and 41.1 g. (0.3 mole) of 1-bromobutane. The product (22.1 g., 74%), b.p. 131-136°C at 0.13 mm., n_D^{25} 1.5204, was purified by redistillation, b.p. 133-136°C at 0.05 mm., n_D^{25} 1.5222.

Anal. Calc'd. for $C_{19}H_{26}N_2O$: C, 76.47; H, 8.78; N, 9.39.
Found: C, 76.15; H, 8.93; N, 9.90.
9.86.

(2) The above experiment was repeated under similar conditions except 0.6 mole of sodium amide, 0.6 mole of 1-bromobutane, and 0.1 mole of 2-phenoxy-3-methylpyrazine were employed. Distillation of the reaction product mixture gave 22.4 g. (75%) of the desired crude 2-phenoxy-3-(5-nonyl)pyrazine, b.p. 135°C at 0.5 mm. to 150°C at 0.4 mm., n_D^{25} 1.5156-1.5188, which was redistilled for elemental analysis, b.p. 122-124°C at 0.07 mm., n_D^{25} 1.5185.

Anal. Calc'd. for $C_{19}H_{26}N_2O$: C, 76.47; H, 8.78; N, 9.39.
Found: C, 76.23; H, 9.01; N, 9.52.

Only 1.7 g. of a higher boiling fraction, b.p. 150°C at 0.04 mm. to 173°C at 0.3 mm., was obtained upon continuation of distillation. This fraction was not worked up further.

Attempted Preparation of 2-Phenoxy-3-(tributylmethyl)pyrazine. This reaction was attempted under the conditions described in the "alkylation" method (p. 133) using 0.06 mole of sodium amide in 300 ml. of liquid ammonia, 14.9 g. (0.05 mole) of 2-phenoxy-3-(5-nonyl)pyrazine (see above) in 50 ml. of ether, and 8.2 g. (0.06 mole) of 1-bromobutane. Following the usual workup, the distillation of the reaction product mixture gave 14.1 g. (95%) of recovered 2-phenoxy-3-(5-nonyl)pyrazine, b.p. 124-140°C at 0.10 mm., n_D^{25} 1.5166, identified by infrared comparison with an authentic sample.

2-(p-Phenylphenoxy)-3-(5-nonyl)pyrazine. This compound was prepared by the "alkylation" method (p. 133) from 0.3 mole of sodium amide in 300 ml. of liquid ammonia, 26.2 g. (0.1 mole) of 2-(p-phenylphenoxy)-3-methylpyrazine (m.p. 112-114°C, see p. 108) in 50 ml. of ether and 41.1 g. (0.3 mole) of 1-bromobutane. The product (26.4 g., 70.5%), b.p. 198-213°C at 0.18 mm., n_D^{25} 1.5725-1.5722, was purified by redistillation, b.p. 203°C at 0.13 mm. to 213°C at 0.18 mm., n_D^{25} 1.5722.

Anal. Calc'd. for $C_{25}H_{30}N_2O$: C, 80.17; H, 8.07; N, 7.48.
Found: C, 80.02; H, 7.98; N, 7.60.

2-(m-Phenoxyphenoxy)-3-(5-nonyl)pyrazine. This compound was prepared by the "alkylation" method (p. 133) from 0.3 mole of sodium amide in 300 ml. of liquid ammonia, 27.8 g. (0.1 mole) of 2-(m-phenoxyphenoxy)-3-methylpyrazine (1) in 100 ml. of ether, and 41.1 g. (0.3 mole) of 1-bromobutane. The product (23 g., 59%), b.p. 183-193°C at 0.18 mm., n_D^{25} 1.5515, was purified by redistillation, b.p. 191-192°C at 0.02 mm., n_D^{25} 1.5535.

Approved for Public Release

Contrails

Anal. Calc'd. for $C_{25}H_{30}N_2O_2$: C, 76.87; H, 7.74; N, 7.18.
Found: C, 76.80; H, 7.77; N, 7.24.

2-(2-Methyl-6-ethylphenoxy)-3-(5-nonyl)pyrazine. This compound was prepared by the "alkylation" method (p. 133) from 0.3 mole of sodium amide in 300 ml. of liquid ammonia, 22.8 g. (0.1 mole) of 2-(2-methyl-6-ethylphenoxy)-3-methylpyrazine (see p. 112) in 20 ml. of ether, and 41.1 g. (0.3 mole) of 1-bromobutane. The product (31.1 g., 91.4%), b.p. 142-147°C at 0.15 mm., was purified by redistillation, b.p. 142-146°C at 0.08 mm., n_D^{25} 1.5185.

Anal. Calc'd. for $C_{22}H_{32}N_2O$: C, 77.60; H, 9.47; N, 8.23.
Found: C, 77.36; H, 9.54; N, 8.40.

2-(p-Nonylphenoxy)-3-pentylpyrazine. This compound was prepared by the "alkylation" method (p. 133) from 0.3 mole of sodium amide in 300 ml. of liquid ammonia, 31.2 g. (0.1 mole) of 2-(p-nonylphenoxy)-3-methylpyrazine (1) in 100 ml. of ether and 41.1 g. (0.3 mole) of 1-bromobutane. The product (21 g., 50%), b.p. 181-185°C at 0.18 mm., n_D^{25} 1.5185, was purified by redistillation, b.p. 181-185°C at 0.15 mm., n_D^{25} 1.5206.

Anal. Calc'd. for $C_{24}H_{36}N_2O$: C, 78.21; H, 9.85; N, 7.60.
Found: C, 78.08; H, 9.75; N, 7.46.

2-(p-t-Butylphenoxy)-3-(5-nonyl)pyrazine. This compound was prepared by the "alkylation" method (p. 133) from 0.3 mole of sodium amide in 300 ml. of liquid ammonia, 24.2 g. (0.1 mole) of 2-(p-t-butylphenoxy)-3-methylpyrazine (1) in 100 ml. of ether, and 41.1 g. (0.3 mole) of 1-bromobutane. The product (30.6 g., 86%), b.p. 186-198°C at 0.20 mm., n_D^{25} 1.5197-1.5189, was purified by redistillation, b.p. 183-185°C at 0.02 mm., n_D^{25} 1.5193.

Anal. Calc'd. for $C_{23}H_{34}N_2O$: C, 77.92; H, 9.67; N, 7.90.
Found: C, 78.04; H, 9.78; N, 8.06.

2-(p-Nonylphenoxy)-3-tridecylpyrazine. This compound was prepared by the "alkylation" procedure (p. 133) from 0.4 mole of sodium amide in 300 ml. of liquid ammonia, 124.8 g. (0.4 mole) of 2-(p-nonylphenoxy)-3-methylpyrazine (1) in 50 ml. of ether, and 99.6 g. (0.4 mole) of n-dodecyl bromide. The product (164.2 g., 85.5%), b.p. 224°C at 0.1 mm. to 233°C at 0.05 mm., n_D^{25} 1.5103-1.5102, was purified by redistillation, b.p. 232-233°C at 0.06 mm., n_D^{25} 1.5105.

Anal. Calc'd. for $C_{32}H_{52}N_2O$: C, 79.94; H, 10.90; N, 5.83.
Found: C, 79.74; H, 10.71; N, 5.90.

2-(p-Nonylphenoxy)-3-(2-phenylethyl)pyrazine. This compound was prepared by the "alkylation" method (p. 133) from 0.4 mole of sodium amide in 300 ml. of liquid ammonia, 124.8 g. (0.4 mole) of 2-(p-nonylphenoxy)-3-methylpyrazine (1) in 50 ml. of ether, and 50.6 g. (0.4 mole) of benzyl chloride. The product (58.1 g., 36.3%), b.p. 201°C at 0.08 mm. to 207°C at 0.15 mm., n_D^{25} 1.5553-1.5568,

Approved for Public Release

Contrails

was purified by redistillation, b.p. 205-209°C at 0.02 mm., n_D^{25} 1.5560.

Anal. Calc'd. for $C_{27}H_{34}N_2O$: C, 80.55; H, 8.51; N, 6.96.
Found: C, 80.66; H, 8.54; N, 7.14.

In addition, 23 g. (26%) of crude p-nonylphenol, b.p. 110°C at 0.13 mm. to 146°C at 0.08 mm., n_D^{25} 1.5150; and 12.7 g. (10.2%) of starting 2-(p-nonylphenoxy)-3-methylpyrazine, b.p. 146-155°C at 0.08 mm., n_D^{25} 1.5280, were isolated by distillation.

2-(m-Phenoxyphenoxy)-3-(2-trimethylsilylethyl)pyrazine. This compound was prepared by the "alkylation" method (p. 133) from 0.111 mole of sodium amide in 300 ml. of liquid ammonia, 30.9 g. (0.111 mole) of 2-(m-phenoxyphenoxy)-3-methylpyrazine (1) in 50 ml. of ether, and 13.6 g. (0.111 mole) of chloromethyltrimethylsilane. The product (24.7 g., 61.3%), b.p. 161-168°C at 0.07 mm., n_D^{25} 1.5743-1.5670, was purified by redistillation, b.p. 177°C at 0.06 mm., n_D^{25} 1.5656.

Anal. Calc'd. for $C_{21}H_{24}N_2O_2Si$: C, 69.18; H, 6.63; N, 7.69; Si, 7.70.
Found: C, 69.25; H, 6.70; N, 7.70; Si, 7.52.

2-(p-t-Butylphenoxy)-3-(2-trimethylsilylethyl)pyrazine. This compound was prepared by the "alkylation" method (p. 133) from 0.114 mole of sodium amide in 300 ml. of liquid ammonia, 29.7 g. (0.114 mole) of 2-(p-t-butylphenoxy)-3-methylpyrazine (1) in 50 ml. of ether, and 14 g. (0.114 mole) of chloromethyltrimethylsilane. The product (20 g., 53.4%), b.p. 119°C at 0.06 mm. to 129°C at 0.07 mm., solidified on standing and was recrystallized from an ethanol-water mixture, m.p. 61-62°C.

Anal. Calc'd. for $C_{19}H_{28}N_2OSi$: C, 69.46; H, 8.59; N, 8.52; Si, 8.55.
Found: C, 69.38; H, 8.64; N, 8.72; Si, 8.66.

2-(p-t-Butylphenoxy)-3-(2-phenylethyl)pyrazine. This compound was prepared by the "alkylation" method (p. 133) from 0.2 mole of sodium amide in 200 ml. of liquid ammonia, 48.4 g. (0.2 mole) of 2-(p-t-butylphenoxy)-3-methylpyrazine (1), and 25.3 g. (0.2 mole) of benzyl chloride. The product (29 g., 46.7%) was obtained as a solid upon removal of solvent, m.p. 102-103.5°C, and was purified by recrystallization two times from ether, m.p. 105-105.5°C.

Anal. Calc'd. for $C_{22}H_{24}N_2O$: C, 79.48; H, 7.28; N, 8.43.
Found: C, 79.31; H, 7.21; N, 8.50.

2-Phenoxy-3-pyrazinoic Acid Monohydrate (1). A mixture of 18.6 g. (0.1 mole) of 2-phenoxy-3-methylpyrazine (1), 11.1 g. (0.1 mole) of selenium dioxide, 100 ml. of pyridine and 5 ml. of distilled water was heated under reflux. Reduced selenium was removed by filtration at the end of each consecutive 1-hour period. At the end of 5 hours' refluxing a total of 63% of reduced selenium was recovered and an additional one hour of refluxing failed to produce additional reduced selenium. The pyridine was then removed by evaporation in vacuo and the residue treated with

Approved for Public Release

Contrails

60 ml. of 10% sodium hydroxide solution. The basic solution was extracted with ether thoroughly. Distillation of the ether extracts gave 7.6 g. (41%) of, presumably, a mixture of starting 2-phenoxy-3-methylpyrazine and the decarboxylated product, phenoxypyrazine, b.p. 76-81°C at 0.15 mm., n_D^{25} 1.5773. Careful acidification of the basic solution furnished 4.0 g. (20%) of 2-phenoxy-3-pyrazinoic acid monohydrate, m.p. 130-132°C, identified by infrared comparison, with an authentic sample.

Phenylhydrazone of 2-Phenoxy-3-benzoylpyrazine and 1,3-Diphenylpyrazolo[2,3-b]pyrazine. A quantity of 0.5 g. of 2-phenoxy-3-benzoylpyrazine (1) was dissolved in 10 ml. of ethanol and to it was added a solution of phenylhydrazine hydrochloride in 95% ethanol. The mixture was heated on the steam bath for 1 hour. Upon cooling, about 1 ml. of water was added and the pale yellow crystals which separated out on standing were filtered, m.p. 122-124°C. The product was recrystallized from an ethanol-water mixture, m.p. 124.5-125°C. Based on the absence of N-H absorption band (5) in the infrared spectrum of this material and the results from elemental analysis, it was concluded that this material possesses the structure of 1,3-diphenylpyrazolo[2,3-b]pyrazine.

Anal. Calc'd. for $C_{17}H_{12}N_4$: C, 74.98; H, 4.41; N, 20.58.
Found: C, 74.69; H, 4.50; N, 20.80.

The mother liquor from which the 1,3-diphenylpyrazolo[2,3-b]pyrazine was isolated was further concentrated on the steam bath. Upon cooling, the desired phenylhydrazone of 2-phenoxy-3-benzoylpyrazine separated out as bright yellow crystals, m.p. 135-139°C. Recrystallization of this solid from an ethanol-water mixture gave the pure hydrazone, m.p. 136-137.5°C.

Anal. Calc'd. for $C_{23}H_{18}N_4O$: C, 75.39; H, 4.95; N, 15.29.
Found: C, 75.44; H, 4.91; N, 15.40.

2-(p-Nonylphenoxy)-3-pentyl-6-(5-nonyl)pyrazine. This compound was prepared by the "alkylation" method (p. 133) from 0.3 mole of sodium amide in 300 ml. of liquid ammonia, 43.9 g. (0.1 mole) of 2-(p-nonylphenoxy)-3-methyl-6-(5-nonyl)-pyrazine (see p. 136), and 41.1 g. (0.3 mole) of 1-bromobutane. The product (29.7 g., 60%), b.p. 212°C at 0.14 mm. to 214°C at 0.12 mm., n_D^{25} 1.5078-1.5066, was purified by redistillation, b.p. 208-209°C at 0.08 mm., n_D^{25} 1.5076.

Anal. Calc'd. for $C_{33}H_{54}N_2O$: C, 80.10; H, 11.00; N, 5.66.
Found: C, 79.99; H, 10.84; N, 5.75.

In addition, 9.4 g. (21%) of starting 2-(p-nonylphenoxy)-3-methyl-6-(5-nonyl)-pyrazine, b.p. 201°C at 0.16 mm. to 212°C at 0.14 mm., n_D^{25} 1.5086, was recovered.

Approved for Public Release

Contrails

B. 2-Phenoxy-6-substitutedpyrazines

General Procedure. This class of compounds was prepared by the oxidation of the corresponding 2-phenoxy-3-methyl-6-substitutedpyrazines with selenium dioxide. In a typical run, a mixture of an equimolar quantity of a 2-phenoxy-3-methyl-6-substitutedpyrazine and selenium dioxide, 5 ml. of distilled water and about 100 ml. of pyridine was heated under reflux for 22 hours. The reaction mixture was filtered while hot to remove reduced selenium. The filtrate was distilled in vacuo to remove pyridine. The residue was treated with approximately 100 ml. of 10% sodium hydroxide and extracted with ether. The ether extracts were combined, washed three times with water, and dried over sodium sulfate. The dried ether solution was then distilled under reduced pressure to obtain the desired product. Modifications in reaction conditions are given under each individual compound.

2-Phenoxy-6-benzylpyrazine. Following the general procedure (p. 147), the interaction of 12.8 g. (0.0463 mole) of 2-phenoxy-3-methyl-6-benzylpyrazine (see p. 134) with 5.14 g. (0.0463 mole) of selenium dioxide gave 2.77 g. (76%) of reduced seleniim and 6.4 g. (52.7%) of crude 2-phenoxy-6-benzylpyrazine, b.p. 144-152°C at 0.15 mm., n_D^{25} 1.5998-1.6008. This crude product was purified by redistillation, b.p. 147-148°C at 0.05 mm., n_D^{25} 1.5997. The infrared spectrum of this material showed distinct differences as compared to that of 2-phenoxy-3-benzylpyrazine (b.p. 138-139°C at 0.04 mm., n_D^{25} 1.6108) (1).

Anal. Calc'd. for $C_{17}H_{14}N_2O$: C, 77.84; H, 5.38; N, 10.68.
Found: C, 77.85; H, 5.21; N, 10.36.
77.67 5.21 10.27.

2-Phenoxy-6-benzoylpyrazine. The general procedure (p. 147) was modified for the preparation of this compound. Thus, a mixture of 6.3 g. (0.023 mole) of 2-phenoxy-3-methyl-6-benzylpyrazine (see p. 134), 12.8 g. (0.115 mole) of selenium dioxide, 100 ml. of pyridine and 5 ml. of distilled water was heated under reflux for 114 hours. A quantity of 6.4 g. of brown solid (assumed to be partially reduced selenium dioxide) was filtered off and pyridine was removed in vacuo. The residue was treated with 100 ml. of 10% sodium hydroxide and extracted with chloroform. The chloroform extracts were washed with water until the washing was neutral and dried over sodium sulfate. Distillation of the chloroform solution gave 1.5 g. (23.6%) of 2-phenoxy-6-benzoylpyrazine, b.p. 164-168°C at 0.18 mm., n_D^{25} 1.6197. The infrared spectrum of this material showed distinct differences when compared to that of the 2-phenoxy-3-benzoylpyrazine (1).

Anal. Calc'd. for $C_{17}H_{12}N_2O_2$: C, 73.90; H, 4.38; N, 10.14.
Found: C, 73.85; H, 4.38; N, 10.31.

Phenylhydrazone of 2-Phenoxy-6-benzoylpyrazine. A quantity of 0.5 g. of 2-phenoxy-6-benzoylpyrazine as prepared above was dissolved in 10 ml. of ethanol and to it was added a solution of phenylhydrazine hydrochloride in 95% ethanol. The mixture was heated on the steam bath for 1 hour. Upon cooling, about 1 ml. of

Approved for Public Release

Contrails

water was added and the bright yellow crystals which separated out on standing were filtered. After one recrystallization from an ethanol-water mixture, the product melted at 129-130.5°C. Only the desired phenylhydrazone was isolated in this instance.

Anal. Calc'd. for $C_{23}H_{18}N_4O$: C, 75.39; H, 4.95; N, 15.29.
Found: C, 75.25; H, 5.02; N, 15.29.

2-(p-Nonylphenoxy)-6-benzylpyrazine. Following the general procedure (p. 147), the interaction of 30 g. (0.0745 mole) of 2-(p-nonylphenoxy)-3-methyl-6-benzylpyrazine (see p. 134) with 8.3 g. (0.0745 mole) of selenium dioxide gave a quantitative amount of reduced selenium and 8.6 g. (30%) of crude 2-(p-nonylphenoxy)-6-benzylpyrazine, b.p. 238°C at 0.5 mm. to 263°C at 0.6 mm., n_D^{25} 1.5535-1.5485. The product was purified by redistillation, b.p. 199-202°C at 0.04 mm., n_D^{25} 1.5590. The infrared spectrum of the redistilled material, although different from that of 2-(p-nonylphenoxy)-3-benzylpyrazine (see p. 140), was quite similar to that of the starting 2-(p-nonylphenoxy)-3-methyl-6-benzylpyrazine.

Anal. Calc'd. for $C_{26}H_{32}N_2O$: C, 80.37; H, 8.30; N, 7.21.
Found: C, 80.32; H, 8.29; N, 7.07.

2-(p-Nonylphenoxy)-6-(p-phenoxybenzyl)pyrazine. Following the general procedure (p. 147), the interaction of 28 g. (0.0566 mole) of 2-(p-nonylphenoxy)-3-methyl-6-(p-phenoxybenzyl)pyrazine (see p. 134) with 6.6 g. (0.0566 mole) of selenium dioxide gave 3.52 g. (78.8%) of reduced selenium and 9.0 g. (33%) of crude 2-(p-nonylphenoxy)-6-(p-phenoxybenzyl)pyrazine, b.p. 255-273°C at 0.15 mm., n_D^{25} 1.5786. This crude product was then purified by redistillation, b.p. 240-246°C at 0.12 mm., n_D^{25} 1.5828. As in the case of 2-(p-nonylphenoxy)-6-benzylpyrazine described above, the infrared spectrum of 2-(p-nonylphenoxy)-6-(p-phenoxybenzyl)pyrazine was very similar to that of the starting 2,3,6-trisubstituted pyrazine, although different from that of the 2,3-isomer (see p. 140).

Anal. Calc'd. for $C_{32}H_{36}N_2O_2$: C, 79.96; H, 7.55; N, 5.83.
Found: C, 80.06; H, 7.62; N, 5.69.

2-(p-Nonylphenoxy)-6-(5-nonyl)pyrazine. The reaction conditions described in the general procedure (p. 147) were followed with the exception that excess selenium dioxide and a longer reaction time were employed. Thus, a mixture of 15 g. (0.034 mole) of 2-(p-nonylphenoxy)-3-methyl-6-(5-nonyl)pyrazine (see p. 136), 23.8 g. (0.214 mole) of selenium dioxide, 100 ml. of pyridine and 5 ml. of distilled water was heated under reflux over a 42-hour period. From this reaction, a quantitative amount of reduced selenium was recovered and 6.3 g. (43.5%) of the crude 2-(p-nonylphenoxy)-6-(5-nonyl)pyrazine, b.p. 193°C at 0.10 mm. to 221°C at 0.50 mm., was obtained. This crude material was then purified by redistillation, b.p. 194-201°C at 0.10 mm., n_D^{25} 1.5145. The infrared spectrum of this material showed distinct differences as compared to that of the starting 2-(p-nonylphenoxy)-3-methyl-6-(5-nonyl)pyrazine.

Approved for Public Release

Contrails

Anal. Calc'd. for $C_{28}H_{45}N_2O$: C, 79.00; H, 10.66; N, 6.58.
Found: C, 78.85; H, 10.59; N, 6.37.

2-(p-Nonylphenoxy)-6-(2-phenylethyl)pyrazine. The conditions described in the general procedure (p. 147) were followed with the exception that a longer reaction time was employed. Thus, 14.9 g. (0.036 mole) of 2-(p-nonylphenoxy)-3-methyl-6-(2-phenylethyl)pyrazine (see p. 136) was interacted with 4.0 g. (0.036 mole) of selenium dioxide over a 92-hour period. From this reaction, 2.2 g. (78%) of reduced selenium was recovered, and 10.8 g. (75%) of the crude 2-(p-nonylphenoxy)-6-(2-phenylethyl)pyrazine, b.p. 213-232°C at 0.16 mm., n_D^{25} 1.5616-1.5700, was obtained. This crude product was purified by redistillation, b.p. 206-207°C at 0.06 mm., n_D^{25} 1.5589.

Anal. Calc'd. for $C_{27}H_{34}N_2O$: C, 80.55; H, 8.51; N, 6.96.
Found: C, 80.62; H, 8.44; N, 7.16.

2-(p-Nonylphenoxy)-6-tridecylpyrazine. The conditions described in the general procedure (p. 147) were followed with the exception that a longer reaction time was employed. Thus, 21.4 g. (0.043 mole) of 2-(p-nonylphenoxy)-3-methyl-6-tridecylpyrazine (see p. 136) was interacted with 4.8 g. (0.043 mole) of selenium dioxide over a 36-hour period. From this reaction, 2.8 g. (81%) of reduced selenium was recovered, and 14.0 g. (68%) of 2-(p-nonylphenoxy)-6-tridecylpyrazine, b.p. 236-248°C at 0.3 mm., n_D^{25} 1.5094-1.5097, was obtained. This material was further purified by redistillation, b.p. 232-234°C at 0.10 mm., n_D^{25} 1.5094.

Anal. Calc'd. for $C_{32}H_{52}N_2O$: C, 79.94; H, 10.90; N, 5.83.
Found: C, 79.77; H, 10.78; N, 5.89.

Attempted Interaction of Pyrazine with Selenium Dioxide in Pyridine. A mixture of 8.0 g. (0.1 mole) of pyrazine, 11.1 g. (0.1 mole) of selenium dioxide, 100 ml. of pyridine and 5 ml. of water was refluxed for 96 hours. No reduced selenium was recovered and the reaction was not worked up further.

C. 2-Alkoxy-3-substitutedpyrazines and 2-Alkoxy-3,6-disubstitutedpyrazines

General Procedure. The "alkylation" method described under the general procedure for the preparation of Advanced Intermediates (p. 133) was also employed for the preparation of these groups of material. Modifications in reaction conditions and workup, if any, were described under each individual compound. Otherwise, only the quantities of reactants, the yield and physical properties of the products are given.

2-(2,2-Dimethylpentoxy)-3-(n-pentyl)pyrazine and 2-(2,2-Dimethylpentoxy)-3-(5-nonyl)pyrazine. Following the "alkylation" method (p. 133), 20.8 g. (0.1 mole) of 2-(2,2-dimethylpentoxy)-3-methylpyrazine (see p. 114) was alkylated with 0.3 mole of sodium amide and 41.1 g. (0.3 mole) of 1-bromobutane in 400 ml. of liquid ammonia. Distillation of the product mixture gave 21.5 g. of a broad boiling

Approved for Public Release

Contrails

fraction, b.p. 94°C at 0.04 mm. to 126°C at 0.07 mm., n_D^{25} 1.4790-1.4780. This fraction was redistilled to give an initial cut of 11.6 g. (44%) of 2-(2,2-dimethylpentoxy)-3-(n-pentyl)pyrazine, b.p. 95-99°C at 0.02 mm., n_D^{25} 1.4786.

Anal. Calc'd. for $C_{16}H_{28}N_2O$: C, 72.68; H, 10.67; N, 10.60.
Found: C, 72.88; H, 10.88; N, 10.74.

Further distillation afforded 4.3 g. (13%) of 2-(2,2-dimethylpentoxy)-3-(5-nonyl)pyrazine, b.p. 105-107°C at 0.02 mm., n_D^{25} 1.4775.

Anal. Calc'd. for $C_{20}H_{36}N_2O$: C, 74.94; H, 11.32; N, 8.74.
Found: C, 74.88; H, 11.34; N, 8.69.

2-(2,2,4-Trimethylpentoxy)-3-(n-pentyl)pyrazine and 2-(2,2,4-Trimethylpentoxy)-3-(5-nonyl)pyrazine. Following the "alkylation" method (p. 133), 22.2 g. (0.1 mole) of 2-(2,2,4-trimethylpentoxy)-3-methylpyrazine (see p. 115) was alkylated with 0.3 mole of sodium amide and 41.1 g. (0.3 mole) of 1-bromobutane in 400 ml. of liquid ammonia. Distillation of the product mixture gave 17.1 g. (61.5%) of 2-(2,2,4-trimethylpentoxy)-3-(n-pentyl)pyrazine, b.p. 96-100°C at 0.10 mm., n_D^{25} 1.4787.

Anal. Calc'd. for $C_{17}H_{30}N_2O$: C, 73.33; H, 10.86; N, 10.06.
Found: C, 73.23; H, 10.90; N, 9.84.

Upon further distillation, 7.3 g. of a relatively broad boiling fraction, b.p. 100-118°C at 0.08 mm., n_D^{25} 1.4783-1.4729, was obtained. This fraction was redistilled to afford 5.1 g. (15%) of 2-(2,2,4-trimethylpentoxy)-3-(5-nonyl)-pyrazine, b.p. 108-114°C at 0.06 mm., n_D^{25} 1.4774.

Anal. Calc'd. for $C_{21}H_{38}N_2O$: C, 75.39; H, 11.72; N, 8.35.
Found: C, 75.24; H, 11.91; N, 8.54.

2-(2,2-Dimethylpentoxy)-3,6-di(n-heptyl)pyrazine. Following the "alkylation" method (p. 133), 61.5 g. (0.2 mole) of 2-(2,2-dimethylpentoxy)-3-methyl-6-(n-heptyl)pyrazine (see p. 137) in 50 ml. of ether was interacted with 0.2 mole of sodium amide and 33.0 g. (0.2 mole) of 1-bromohexane in 400 ml. of liquid ammonia. Distillation of the reaction product mixture gave 33.7 g. (54.8%) of starting 2-(2,2-dimethylpentoxy)-3-methyl-6-(n-heptyl)pyrazine, b.p. 130°C at 0.4 mm. to 150°C at 0.35 mm., n_D^{25} 1.4796-1.4795; and 24.0 g. (30.7%) of the desired 2-(2,2-dimethylpentoxy)-3,6-di(n-heptyl)pyrazine, b.p. 164-175°C at 0.35 mm., n_D^{25} 1.4784. This product was then purified by redistillation, b.p. 167-170°C at 0.20 mm., n_D^{25} 1.4782.

Anal. Calc'd. for $C_{25}H_{46}N_2O$: C, 76.86; H, 11.87; N, 7.17.
Found: C, 77.06; H, 11.93; N, 7.07.

Approved for Public Release

Contrails

2-(2,2-Dimethylpentoxy)-3-(n-pentyl)-6-(n-heptyl)pyrazine. Following the "alkylation" method (p. 133), 61.2 g. (0.2 mole) of 2-(2,2-dimethylpentoxy)-3-methyl-6-(n-heptyl)pyrazine (see p. 137) in 50 ml. of ether was interacted with 0.6 mole of sodium amide and 82.2 g. (0.6 mole) of 1-bromobutane in 400 ml. of liquid ammonia. The reaction time after the addition of 1-bromobutane to the reaction mixture was extended to 3 hours as compared to the usual 1- to 2-hour period as indicated in the "alkylation" method. Distillation of the reaction product mixture gave 24.1 g. (39.4%) of crude starting 2-(2,2-dimethylpentoxy)-3-methyl-6-(n-heptyl)pyrazine, b.p. 131°C at 0.33 mm. to 149°C at 0.30 mm., n_D^{25} 1.4792; and 34.3 g. (47.3%) of desired 2-(2,2-dimethylpentoxy)-3-(n-pentyl)-6-(n-heptyl)pyrazine, b.p. 149-157°C at 0.30 mm., n_D^{25} 1.4787. This product was then purified by redistillation, b.p. 143-146°C at 0.09 mm., n_D^{25} 1.4786.

Anal. Calc'd. for $C_{23}H_{42}N_2O$: C, 76.18; H, 11.68; N, 7.73.
Found: C, 76.26; H, 11.64; N, 7.90.

D. 2-Anilino-3-substitutedpyrazines and 2-Anilino-3,6-disubstitutedpyrazines

General Procedure. Three general methods were employed for the preparation of these groups of materials and they are described as follows.

1. The "Arylation" Method.

   This method has been described in detail under the preparation of Advanced Intermediates, page 133.

2. The "Alkylation" Method.

   This method has also been described in detail under the preparation of Advanced Intermediates, page 133.

3. The "Pyridine Solvent" Method.

   This method has been described in detail under the preparation of 2-anilino-3-methylpyrazines and 2-anilino-3,6-dimethylpyrazines, page 118. However, the molar ratio of reactants used in this method have been modified and are indicated under the individual preparations.

2-(N-Methylanilino)-3-benzylpyrazine. Employing the "arylation" method (p. 133), 20 g. (0.1 mole) of 2-(N-methylanilino)-3-methylpyrazine (1) in 20 ml. of ether was treated with 0.2 mole of sodium amide and 7.9 g. (0.05 mole) of bromobenzene in 200 ml. of liquid ammonia. Distillation of the reaction product mixture afforded 6.7 g. (49%) of crude 2-(N-methylanilino)-3-benzylpyrazine, b.p. 142-151°C at 0.09 mm., n_D^{25} 1.6401, along with 8.5 g. (42%) of recovered 2-(N-methylanilino)-3-methylpyrazine, b.p. 85°C at 0.10 mm. to 86°C at 0.09 mm., n_D^{25} 1.6135. The crude product was purified by redistillation, b.p. 135°C at 0.08 mm. to 133°C at 0.07 mm., n_D^{25} 1.6386.

Approved for Public Release

Contrails

Anal. Calc'd. for $C_{18}H_{17}N_3$: C, 78.51; H, 6.23; N, 15.26.
Found: C, 78.58; H, 6.09; N, 15.36.

2-(N-Methylanilino)-3-(p-phenoxybenzyl)pyrazine. Employing the "arylation" method (p. 133), 40 g. (0.2 mole) of 2-(N-methylanilino)-3-methylpyrazine (1) in 40 ml. of ether was treated with 0.4 mole of sodium amide and 25 g. (0.1 mole) of p-bromophenyl phenyl ether in 400 ml. of liquid ammonia. Distillation of the reaction product mixture gave 23.3 g. (58%) of recovered 2-(N-methylanilino)-3-methylpyrazine, b.p. 95-110°C at 0.28 mm., n_D^{25} 1.6092; and 17.4 g. (47.5%) of 2-(N-methylanilino)-3-(p-phenoxybenzyl)pyrazine, b.p. 229°C at 0.19 mm. to 245°C at 0.22 mm., which was purified by redistillation, b.p. 230-232°C at 0.08 mm., n_D^{25} 1.6530.

Anal. Calc'd. for $C_{24}H_{21}N_3O$: C, 78.45; H, 5.76; N, 11.44.
Found: C, 78.51; H, 5.81; N, 11.58.

2-(N-Methylanilino)-3-(2-trimethylsilylethyl)pyrazine. Following the "alkylation" method (p. 133), 0.3 mole of sodium amide in 300 ml. of liquid ammonia was interacted with 59.7 g. (0.3 mole) of 2-(N-methylanilino)-3-methylpyrazine (1) in 25 ml. of ether and 36.8 g. (0.3 mole) of chloromethyltrimethylsilane. A total of 41.4 g. (48.3%) of the desired 2-(N-methylanilino)-3-(2-trimethylsilylethyl)-pyrazine, b.p. 107-113°C at 0.05 mm., n_D^{25} 1.5597 was obtained from distillation of the product mixture. The crude product was then purified by redistillation; b.p. 104-106°C at 0.07 mm., n_D^{25} 1.5594.

Anal. Calc'd. for $C_{16}H_{23}N_3Si$: C, 67.32; H, 8.12; N, 14.72; Si, 9.84.
C, 67.48; H, 7.95; N, 14.66; Si, 9.91.

2-(N-Methylanilino)-3-tridecylpyrazine. Following the "alkylation" method (p. 133), 0.123 mole of sodium amide in 300 ml. of liquid ammonia was interacted with 24.5 g. (0.123 mole) of 2-(N-methylanilino)-3-methylpyrazine (1) in 25 ml. of ether and 30.6 g. (0.123 mole) of n-dodecyl bromide. A total of 23.4 g. (51.8%) of the desired 2-(N-methylanilino)-3-tridecylpyrazine, b.p. 191-194°C at 0.3 mm., n_D^{25} 1.5361, was obtained from distillation. This material was then purified by redistillation, b.p. 194-197°C at 0.14 mm., n_D^{25} 1.5352.

Anal. Calc'd. for $C_{24}H_{37}N_2$: C, 78.42; H, 10.15; N, 11.43.
Found: C, 78.70; H, 10.21; N, 11.48.

2-(N-Butylanilino)-3-pentylpyrazine and 2-(N-Methylanilino)-3-(5-nonyl)-pyrazine, Interaction of 2-(N-Methylanilino)-3-methylpyrazine with Excess Sodium Amide and 1-Bromobutane. (1) Employing the "alkylation" method (p. 133), a quantity of 0.48 mole of sodium amide in liquid ammonia was treated with 32.5 g. (0.16 mole) of 2-(N-methylanilino)-3-methylpyrazine (1) in 50 ml. of ether and 65.8 g. (0.48 mole) of 1-bromobutane. Distillation of the reaction product mixture afforded as the first fraction, 21.5 g. (53%) of 2-(N-butylanilino)-3-pentylpyrazine, b.p. 134-139°C at 0.25 mm., n_D^{25} 1.5519-1.5508, which was purified by redistillation, b.p. 131-134°C at 0.15 mm., n_D^{25} 1.5513.

Approved for Public Release

Contrails

Anal. Calc'd. for $C_{19}H_{27}N_3$: C, 76.72; H, 9.15; N, 14.13.
Found: C, 76.91; H, 9.28; N, 14.20.
77.03 9.01 13.72

Further distillation of the reaction product mixture gave 14 g. (28%) of the pure dialkylated product, 2-(N-methylanilino)-3-(5-nonyl)pyrazine, b.p. 149-152°C at 0.25 mm., n_D^{25} 1.5508.

Anal. Calc'd. for $C_{20}H_{29}N_3$: C, 77.12; H, 9.39; N, 13.49.
Found: C, 77.21; H, 9.29; N, 13.40.

(2) The above reaction was repeated on a larger scale. Thus, 7.53 mole of sodium amide in 2500 ml. of liquid ammonia was interacted with 500 g. (2.51 mole) of 2-(N-methylanilino)-3-methylpyrazine (1) in 100 ml. of ether, and 1032 g. (7.53 mole) of 1-bromobutane. The desired 2-(N-butylanilino)-3-pentylpyrazine was obtained exclusively in 94% yield (700 g.), b.p. 135-140°C at 0.30 mm., n_D^{25} 1.5478. This product was further purified by redistillation, b.p. 128°C at 0.12 mm. to 131°C at 0.09 mm., n_D^{25} 1.5476.

Anal. Calc'd. for $C_{19}H_{27}N_3$: C, 76.72; H, 9.15; N, 14.13.
Found: C, 76.71; H, 9.28; N, 14.02.

2-(N-Butylanilino)-3-(n-pentyl)pyrazine, Interaction of 2-Anilino-3-methylpyrazine with Sodium Amide and 1-Bromobutane in Pyridine. Employing the "Pyridine Solvent" method (p. 118), 0.3 mole of sodium amide in 300 ml. of liquid ammonia was interacted with 18.5 g. (0.1 mole) of 2-anilino-3-methylpyrazine (m.p. 92-94°C) (1), and later with 250 ml. of pyridine and 41.1 g. (0.3 mole) of 1-bromobutane. Distillation of the reaction product mixture gave 20.2 g. (68%) of crude 2-(N-butylanilino)-3-(n-pentyl)pyrazine, b.p. 132:C at 0.17 mm. to 145°C at 0.11 mm., n_D^{25} 1.5638-1.5571. This crude product was purified by redistillation, b.p. 135-138°C at 0.06 mm., n_D^{25} 1.5559. The infrared spectrum of this material possesses no N-H absorption band.

Anal. Calc'd. for $C_{19}H_{27}N_3$: C, 76.72; H, 9.15; N, 14.13.
Found: C, 76.62; H, 9.10; N, 13.98.

2-(N-Methylanilino)-3-(2-phenylethyl)pyrazine. Following the "alkylation" method (p. 133), 0.2 mole of sodium amide in 200 ml. of liquid ammonia was interacted with 39.8 g. (0.2 mole) of 2-(N-methylanilino)-3-methylpyrazine (1) and 25.3 g. (0.2 mole) of benzyl chloride. A total of 42.2 g. (73%) of crude 2-(N-methylanilino)-3-(2-phenylethyl)pyrazine, b.p. 145-177°C at 0.05 mm., n_D^{25} 1.6230-1.6299, was obtained. The product was then purified by redistillation, b.p. 157-158°C at 0.08 mm., n_D^{25} 1.6211.

Anal. Calc'd. for $C_{19}H_{19}N_3$: C, 78.86; H, 6.62; N, 14.52.
Found: C, 78.97; H, 6.72; N, 14.52.
78.99 6.62

Approved for Public Release

Contrails

2-Anilino-3-(n-pentyl)pyrazine. Following the "alkylation" method (p. 133), 0.6 mole of sodium amide in 400 ml. of liquid ammonia was interacted with 37.0 g. (0.2 mole) of 2-anilino-3-methylpyrazine (m.p. 92-94°C) (1), and followed by 40 ml. of ether. The mixture was stirred for 1.5 hours but the usual red anion color due to the formation of pyrazylmethylsodium in liquid ammonia did not appear. Thus, an additional 50 ml. of ether was added and the light yellowish-green mixture was stirred for 30 minutes more. To this was added 82.2 g. (0.6 mole) of 1-bromobutane during a 45-minute period and the mixture was stirred for 2.5 hours. Following the usual workup and distillation of the reaction product mixture, 30.2 g. (81.6%) of the starting 2-anilino-3-methylpyrazine, b.p. 120°C at 0.25 mm. to 135°C at 0.20 mm., was recovered. This material solidified upon standing, m.p. 77-91°C. Upon further distillation 6.8 g. (14.7%) of 2-anilino-3-(n-pentyl)pyrazine, b.p. 135-142°C at 0.20 mm., n_D^{25} 1.6037, was obtained. This compound was purified by redistillation, b.p. 139-141°C at 0.13 mm., which solidified upon standing, m.p. 45-47°C. The structure of this product was confirmed by the presence of N-H absorption in its infrared spectrum and elemental analysis.

Anal. Calc'd. for $C_{15}H_{19}N_3$: C, 74.65; H, 7.94; N, 17.41.
Found: C, 74.48; H, 7.78; N, 17.50.

2-(N-Butyl-p-pentylanilino)-3-(n-pentyl)pyrazine. Following the "Pyridine Solvent" method (p. 118), 0.3 mole of sodium amide in 300 ml. of liquid ammonia was interacted with 25.5 g. (0.1 mole) of 2-(p-pentylanilino)-3-methylpyrazine in 100 ml. of ether and 41.1 g. (0.3 mole) of 1-bromobutane. Distillation of the product mixture gave 29.9 g. of a broad boiling fraction, b.p. 141°C at 0.04 mm. to 175°C at 0.08 mm., n_D^{25} 1.5470-1.5447. This fraction was fractionated to give 26.0 g. (71%) of crude 2-(N-butyl-p-pentylanilino)-3-(n-pentyl)pyrazine, b.p. 143-155°C at 0.03 mm., n_D^{25} 1.5450-1.5421. A pure sample of this product was obtained after two redistillations, b.p. 140-142°C at 0.02 mm., n_D^{25} 1.5450.

Anal. Calc'd. for $C_{24}H_{37}N_3$: C, 78.42; H, 10.15; N, 11.43.
Found: C, 78.14; H, 10.01; N, 11.33.

2-(N-Methylanilino)-3-(n-hexyl)pyrazine. Employing the "alkylation" method (p. 133), 0.3 mole of sodium amide in 300 ml. of liquid ammonia was interacted with 19.9 g. (0.1 mole) of 2-(N-methylanilino)-3-methylpyrazine (1) in 25 ml. of ether during a 2-hour period. This anion formation time was longer than the general method indicated. To this was then introduced 48.3 g. (0.3 mole) of 1-bromopentane and the mixture was stirred for an additional 2 hours. Distillation of the reaction product mixture gave first 4.8 g. (25.1%) of 2-anilino-3-methylpyrazine, b.p. 90°C at 0.1 mm. to 142°C at 0.6 mm., which solidified on standing, m.p. 87-94°C and showed no depression when admixed with an authentic sample. Further distillation gave 14.6 g. (54.3%) of the desired 2-(N-methylanilino)-3-(n-hexyl)pyrazine, b.p. 142°C at 0.06 mm. to 146°C at 0.04 mm., n_D^{25} 1.5468. This product was purified by redistillation, b.p. 140-145°C at 0.01 mm., n_D^{25} 1.5519.

Approved for Public Release

Contrails

Anal. Calc'd. for $C_{17}H_{23}N_3$: C, 75.80; H, 8.61; N, 15.60.
Found: C, 75.81; H, 8.75; N, 15.44.

2-(N-Methylanilino)-3-(9-heptadecyl)pyrazine. A modified "alkylation" procedure identical to the above was employed except that 57.6 g. (0.3 mole) of 1-bromooctane was used in place of the 1-bromopentane. Distillation of the reaction product mixture gave 29.4 g. (69.3%) of 2-(N-methylanilino)-3-(9-heptadecyl)pyrazine, b.p. 178°C at 0.12 mm. to 205°C at 0.15 mm., as the only product. This material was redistilled twice, b.p. 185-189°C at 0.01 mm., n_D^{25} 1.5242, to obtain a pure sample.

Anal. Calc'd. for $C_{28}H_{45}N_3$: C, 79.37; H, 10.71; N, 9.92.
Found: C, 79.04; H, 10.42; N, 10.69.

2-(N-n-Hexylanilino)-3-(n-heptyl)pyrazine. Employing the "Pyridine Solvent" method (p. 118), 0.3 mole of sodium amide in 300 ml. of liquid ammonia was interacted with 18.5 g. (0.1 mole) of 2-anilino-3-methylpyrazine (1) and 49.5 g. (0.3 mole) of 1-bromohexane. Distillation of the product mixture afforded 18.7 g. (53%) of desired 2-(N-n-hexylanilino)-3-(n-heptyl)pyrazine, b.p. 151-163°C at 0.04 mm., n_D^{25} 1.5382-1.5366. This product was purified by redistillation, b.p. 151°C at 0.01 mm., n_D^{25} 1.5382.

Anal. Calc'd. for $C_{23}H_{35}N_3$: C, 78.13; H, 9.98; N, 11.89.
C, 78.36; H, 10.01; N, 12.01.

2-(N-Methylanilino)-3-(n-pentyl)-6-(5-nonyl)pyrazine. Employing a modified "alkylation" procedure (p. 133), 2-(N-methylanilino)-3-methyl-6-(5-nonyl)pyrazine (see p. 138) (32.5 g., 0.1 mole), was alkylated with 41.1 g. (0.3 mole) of 1-bromobutane and 0.3 mole of sodium amide in 400 ml. of liquid ammonia. The alkylation reaction time was 3 hours instead of the usual 1 to 2-hour period. Distillation of the product mixture gave 15.8 g. (41%) of pure 2-(N-methylanilino)-3-(n-pentyl)-6-(5-nonyl)pyrazine, b.p. 155-158°C at 0.03 mm., n_D^{25} 1.5278.

Anal. Calc'd. for $C_{25}H_{39}N_3$: C, 78.69; H, 10.30; N, 11.01.
Found: C, 78.49; H, 9.97; N, 11.27.

2-(N-Methylanilino)-3-(n-pentyl)-6-(n-heptyl)pyrazine. Employing the "alkylation" procedure (p. 133), 0.072 mole of sodium amide in 300 ml. of liquid ammonia was interacted with 21.5 g. (0.072 mole) of 2-(N-methylanilino)-3-methyl-6-(n-heptyl)pyrazine (see p. 138) and 9.8 g. (0.072 mole) of 1-bromobutane. The desired 2-(N-methylanilino)-3-(n-pentyl)-6-(n-heptyl)pyrazine was obtained in 27% yield (11.3 g.), b.p. 158-161.5°C at 0.01 mm., n_D^{25} 1.5392.

Anal. Calc'd. for $C_{23}H_{35}N_3$: C, 78.13; H, 9.98; N, 11.89.
Found: C, 77.93; H, 10.00; N, 12.20.

Approved for Public Release

Contrails

E. 2-Anilino-6-substitutedpyrazines

2-(N-Methylanilino)-6-(5-nonyl)pyrazine. A mixture of 32.5 g. (0.1 mole) of 2-(N-methylanilino)-3-methyl-6-(5-nonyl)pyrazine (see p. 138), 11.1 g. (0.1 mole) of selenium dioxide, 100 ml. of pyridine and 5 ml. of water was refluxed for a 72-hour period. The mixture was then filtered while hot to give 7.2 g. (91%) of reduced selenium. Pyridine was then removed from the filtrate in vacuo, the residue treated with 200 ml. of a 10% sodium hydroxide solution and extracted with ether. Distillation of the ether extracts gave 22.1 g. (71.1%) of 2-(N-methylanilino)-6-(5-nonyl)pyrazine, b.p. 159-172°C at 0.27 mm., n_D^{25} 1.5459-1.5433. The fraction, b.p. 163-167°C at 0.27 mm., n_D^{25} 1.5447, was analyzed.

Anal. Calc'd. for $C_{20}H_{29}N_3$: C, 77.12; H, 9.39; H, 13.49.
Found: C, 76.86; H, 9.54; H, 13.38.

F. 2-Alkylamino-3-substitutedpyrazines and 2-Alkylamino-3,6-disubstituted-pyrazines

General Procedure. Two general methods were followed for the preparation of these groups of materials and they are described as follows.

1. The "Alkylation" Method.

This method has been described in detail under the preparation of Advanced Intermediates, page 133.

2. The "Pyridine Solvent" Method.

This method has been described in detail under the preparation of 2-anilino-3-methylpyrazines and 2-anilino-3,6-dimethylpyrazines, page 118. However, the molar ratio of reactants have been modified in this method and are given under each individual preparation.

2-(N,N-Di-n-butylamino)-3-(n-pentyl)pyrazine and 2-(N,N-Di-n-butylamino)-3-(5-nonyl)pyrazine. Employing the "alkylation" method (p. 133), 22.1 g. (0.1 mole) of 2-(N,N-di-n-butylamino)-3-methylpyrazine (see p. 126), was interacted with 0.3 mole of sodium amide in 400 ml. of liquid ammonia and 41.1 g. (0.3 mole) of 1-bromobutane. Distillation of the product mixture gave first 10.6 g. (38%) of 2-(N,N-di-n-butylamino)-3-(n-pentyl)pyrazine, b.p. 100-104°C at 0.08 mm., n_D^{25} 1.4945.

Anal. Calc'd. for $C_{17}H_{31}N_3$: C, 73.59; H, 11.26; N, 15.15.
Found: C, 73.64; H, 11.20; N, 15.11.

Further distillation gave 5.3 g. (16%) of the crude dialkylated product, 2-(N,N-di-n-butylamino)-3-(5-nonyl)pyrazine, b.p. 113-116°C at 0.08 mm., n_D^{25} 1.4943.

Approved for Public Release

Contrails

Anal. Calc'd. for $C_{21}H_{39}N_3$: C, 75.62; H, 11.79; N, 12.60.
Found: C, 74.87; H, 11.56; N, 13.39.

2-(N,N-Di-n-pentylamino)-3-(n-pentyl)pyrazine. Employing the "alkylation" procedure (p. 133), 24.9 g. (0.1 mole) of 2-(N,N-di-n-pentylamino)-3-methylpyrazine (see p. 126) was treated with 0.3 mole of sodium amide in 400 ml. of liquid ammonia and 41.1 g. (0.3 mole) of 1-bromobutane. Distillation of the product mixture gave 25.3 g. (83%) of 2-(N,N-di-n-pentylamino)-3-(n-pentyl)-pyrazine, b.p. 121-141°C at 0.27 mm., n_D^{25} 1.4927-1.4946. This product was purified by redistillation, b.p. 115-117°C at 0.01 mm., n_D^{25} 1.4949.

Anal. Calc'd. for $C_{19}H_{35}N_3$: C, 74.70; H, 11.55; N, 13.75.
Found: C, 74.80; H, 11.38; N, 13.38.

2-(N-n-Butyl-N-n-hexylamino)-3-(5-nonyl)pyrazine. (1) Employing the "alkylation" procedure (p. 133), 27.7 g. (0.1 mole) of 2-(N,N-di-n-hexylamino)-3-methylpyrazine was treated with 0.3 mole of sodium amide in 400 ml. of liquid ammonia and 41.1 g. (0.3 mole) of 1-bromobutane. Distillation of the product mixture gave 24.4 g. (67.5%) of 2-(N-n-butyl-N-n-hexylamino)-3-(5-nonyl)pyrazine, b.p. 140°C at 0.03 mm. to 147°C at 0.04 mm., n_D^{25} 1.4890-1.4895. This product was purified by redistillation, b.p. 135-137°C at 0.02 mm., n_D^{25} 1.4895. The assignment of structure was based on elemental analysis.

Anal. Calc'd. for $C_{23}H_{43}N_3$: C, 76.39; H, 11.99; N, 11.62.
Found: C, 76.32; H, 11.83; N, 11.91.

(2) When the above reaction was repeated in a 2.18-mole scale run with respect to the starting 2-(N,N-di-n-hexylamino)-3-methylpyrazine, the desired product, 2-(N-n-butyl-N-n-hexylamino)-3-(5-nonyl)pyrazine was obtained in 77% yield, b.p. 144°C at 0.04 mm. to 155°C at 0.02 mm., n_D^{25} 1.4893-1.4902. The fraction, b.p. 144°C at 0.04 mm. to 146°C at 0.03 mm., n_D^{25} 1.4893, was shown by elemental analysis to be pure product.

Anal. Calc'd. for $C_{23}H_{43}N_3$: C, 76.39; H, 11.99; N, 11.62.
Found: C, 76.40; H, 11.77; N, 11.55.

2-(N,N-Di-n-hexylamino)-3-(n-heptyl)pyrazine. This compound was prepared by the "Pyridine Solvent" method (p. 118) from 0.3 mole of sodium amide in 300 ml. of liquid ammonia, 19.3 g. (0.1 mole) of 2-(N-n-hexylamino)-3-methylpyrazine (see p. 125), and 49.5 g. (0.3 mole) of 1-bromohexane. The product (24.0 g., 66.3%), b.p. 144°C at 0.03 mm. to 157°C at 0.06 mm., n_D^{25} 1.4884-1.4864, was purified by redistillation, b.p. 147-148°C at 0.05 mm., n_D^{25} 1.4877.

Anal. Calc'd. for $C_{23}H_{43}N_3$: C, 76.39; H, 11.99; N, 11.62.
Found: C, 76.69; H, 12.09; N, 11.55.

2-(N-n-Hexyl-N-n-octylamino)-3-(n-nonyl)pyrazine. This compound was prepared by the "Pyridine Solvent" method (p. 118) from 0.3 mole of sodium amide

Approved for Public Release

Contrails

in 300 ml. of liquid ammonia, 19.4 g. (0.1 mole) of 2-(N-n-hexylamino)-3-methylpyrazine, and 57.9 g. (0.3 mole) of 1-bromooctane. The crude product (32.2 g., 76.8%), b.p. 165-210°C at 0.08 mm., n_D^{25} 1.4860-1.4855, was redistilled to obtain 77% (31.8 g.) of pure material, b.p. 175-176°C at 0.025 mm., n_D^{25} 1.4880.

Anal. Calc'd. for $C_{27}H_{51}N_3$: C, 77.45; H, 12.28; N, 10.04.
Found: C, 77.33; H, 12.06; N, 10.24.

2-(N,N-Di-n-hexylamino)-3-(n-pentyl)-6-(n-heptyl)pyrazine. This compound was prepared by the "Pyridine Solvent" method (p. 118) from 0.15 mole of sodium amide in 200 ml. of liquid ammonia, 18.8 g. (0.05 mole) of 2-(N,N-di-n-hexylamino)-3-methyl-6-(n-heptyl)pyrazine (see p. 139), and 20.6 g. (0.15 mole) of 1-bromobutane. The crude product (9.0 g., 36.9%), b.p. 166-190°C at 0.09 mm., n_D^{25} 1.4864, was purified by redistillation, b.p. 199-201°C at 0.4 mm., n_D^{25} 1.4860.

Anal. Calc'd. for $C_{28}H_{53}N_3$: C, 77.89; H, 12.37; N, 9.73.
Found: C, 77.97; H, 12.18; N, 9.68.

Attempted Preparation of 2-(N,N-Di-n-pentylamino)-3-(n-pentyl)-6-(n-heptyl)-pyrazine. Employing the "alkylation" procedure (p. 133), 13.5 g. (0.039 mole) of 2-(N,N-di-n-pentylamino)-3-methyl-6-(n-heptyl)pyrazine (see p. 139) was treated with 0.039 mole of sodium amide in 200 ml. of liquid ammonia and 5.3 g. (0.039 mole) of 1-bromobutane. Distillation of reaction product mixture gave 11.3 g. (83.6%) of starting 2-(N,N-di-n-pentylamino)-3-methyl-6-(n-heptyl)pyrazine, b.p. 139-148°C at 0.03 mm., n_D^{25} 1.4892-1.4887. No other material could be isolated from this reaction.

G. Alkylpyrazines

General Procedure. The general procedure, described on page 130 for the preparation of alkylpyrazine, was employed. Initial intermediates were also applicable for the preparation of alkylpyrazine candidate products indicated here.

2-n-Heptyl-5-n-pentylpyrazine. Following the general procedure (p. 130), this compound was prepared by the interaction of 0.15 mole of sodium amide in 300 ml. of liquid ammonia, 28.8 g. (0.15 mole) of 2-n-heptyl-5-methylpyrazine (see p. 131) and a solution of 10.3 g. (0.075 mole) of 1-bromobutane. The product (16 g., 86%), b.p. 132-136°C at 0.9 mm., n_D^{25} 1.4815, was purified by redistillation, b.p. 108-110°C at 0.04 mm., n_D^{25} 1.4796.

Anal. Calc'd. for $C_{16}H_{28}N_2$: C, 77.36; H, 11.36; N, 11.28.
Found: C, 77.29; H, 11.21; N, 11.37.

In addition, a quantity of 16.5 g. (57%) of crude starting 2-n-heptyl-3-methylpyrazine, b.p. 92-98°C at 0.7 mm., n_D^{25} 1.4830, was recovered.

Approved for Public Release

Contrails

2-n-Heptyl-5-n-nonylpyrazine. (1) Employing the general procedure, 0.13 mole of sodium amide in 300 ml. of liquid ammonia was allowed to react with 24.5 g. (0.13 mole) of 2-n-heptyl-5-methylpyrazine (see p. 131) and a solution of 14.47 g. (0.075 mole) of 1-bromooctane in 20 ml. of ether. Distillation of the reaction mixture gave 7.8 g. (32%) of crude recovered 2-n-heptyl-3-methylpyrazine, b.p. 75-76°C at 0.25 mm., n_D^{25} 1.4825; and 21.1 g. (92.5%) of 2-n-heptyl-5-n-nonylpyrazine, b.p. 134°C at 0.07 mm. to 151°C at 0.05 mm., n_D^{25} 1.4790. An 18.7 g. (82.4%) quantity of the desired product was obtained on redistillation, b.p. 147-149°C at 0.2 mm., n_D^{25} 1.4792.

Anal. Calc'd. for $C_{20}H_{36}N_2$: C, 78.88; H, 11.92; N, 9.20.
Found: C, 79.00; H, 11.88; N, 9.16.

(2) The above preparation was repeated under identical conditions in a 4.16-mole scale with respect to the starting 2-n-heptyl-5-methylpyrazine. The desired product, 2-n-heptyl-5-n-nonylpyrazine was obtained in 85.1% yield (539 g.) b.p. 147°C at 0.1 mm. to 153°C at 0.15 mm., n_D^{25} 1.4794-1.4793. This material was then purified by redistillation, b.p. 142-143°C at 0.13 mm., n_D^{25} 1.4794.

Anal. Calc'd. for $C_{20}H_{36}N_2$: C, 78.88; H, 11.92; N, 9.20.
Found: C, 78.91; H, 11.72; N, 9.22.

2-n-Heptyl-6-n-pentylpyrazine. Employing the general procedure (p. 130), 0.2 mole of sodium amide in 400 ml. of liquid ammonia was reacted with 38.4 g. (0.2 mole) of 2-n-heptyl-6-methylpyrazine (see p. 132), and 13.7 g. (0.1 mole) 1-bromobutane. Distillation of the reaction product mixture gave 18.6 g. (48.5%) of starting 2-n-heptyl-6-methylpyrazine, b.p. 68°C at 0.12 mm. to 91°C at 0.10 mm., n_D^{25} 1.4835-1.4830, and 22.6 g. (91.1%) of 2-n-heptyl-6-n-pentylpyrazine, b.p. 91-108°C at 0.10 mm., n_D^{25} 1.4797-1.4793. This product was then purified by redistillation, b.p. 101-104°C at 0.08 mm., n_D^{25} 1.4794.

Anal. Calc'd. for $C_{16}H_{28}N_2$: C, 77.36; H, 11.36; N, 11.28.
Found: C, 77.17; H, 11.47; N, 11.09.

2-n-Heptyl-6-n-nonylpyrazine. Following the general procedure (p. 130), 0.2 mole of sodium amide in 300 ml. of liquid ammonia was interacted with 38.4 g. (0.2 mole) of 2-n-heptyl-6-methylpyrazine (see p. 132) and 19.3 g. (0.1 mole) of 1-bromooctane. Distillation of the product mixture gave 18 g. (47%) of starting 2-n-heptyl-6-methylpyrazine, b.p. 63-70°C at 0.03 mm., n_D^{25} 1.4840; and 26.7 g. (87.8%) of desired 2-n-heptyl-6-n-nonylpyrazine, b.p. 130-143°C at 0.02 mm., n_D^{25} 1.4781. This product was purified by redistillation, b.p. 132-134°C at 0.02 mm., n_D^{25} 1.4780.

Anal. Calc'd. for $C_{20}H_{36}N_2$: C, 78.88; H, 11.92; N, 9.20.
Found: C, 78.48; H, 11.89; N, 9.70.

2,5-Di-n-nonylpyrazine. Employing the general procedure (p. 130), 0.39 mole of sodium amide in 500 ml. of liquid ammonia was interacted with 86 g.

Approved for Public Release

Contrails

(0.39 mole) of 2-n-nonyl-5-methylpyrazine (see p.132) and 37.6 g. (0.195 mole) of 1-bromooctane. Distillation of the product mixture gave 28.9 g. (33.6%) of starting 2-n-nonyl-5-methylpyrazine, b.p. 110-123°C at 0.40 mm., n_D^{25} 1.4817; and 53.3 g. (82.1%) of desired 2,5-di-n-nonylpyrazine, b.p. 168-188°C at 0.40 mm., n_D^{25} 1.4786. This product was purified by redistillation, b.p. 165-168°C at 0.2 mm., which solidified upon standing, m.p. 33-34°C.

Anal. Calc'd. for $C_{22}H_{40}N_2$: C, 79.45; H, 12.12; N, 8.43.
Found: C, 79.60; H, 12.04; N, 8.50.

2,6-Di-n-nonylpyrazine. Employing the general procedure (p. 130), 0.48 mole of sodium amide in 1000 ml. of liquid ammonia was interacted with 100 g. (0.48 mole) of 2-n-nonyl-6-methylpyrazine (see p. 132) and 46.3 g. (0.24 mole) of 1-bromooctane. Distillation of the product mixture gave 44 g. (44%) of starting 2-n-nonyl-6-methylpyrazine, b.p. 100°C at 0.5 mm. to 115°C at 0.20 mm., n_D^{25} 1.4829, and 69.2 g. (86.7%) of desired 2,6-di-n-nonylpyrazine, b.p. 163-170°C at 0.20 mm., n_D^{25} 1.4776. The product was then purified by redistillation, b.p. 155-156°C at 0.20 mm., n_D^{25} 1.4773.

Anal. Calc'd. for $C_{22}H_{40}N_2$: C, 79.45; H, 12.12; N, 8.43.
Found: C, 79.33; H, 12.11; N, 8.35.

2,5-Di-(5-nonyl)pyrazine. Employing the conditions described in the general procedure (p. 130) and a different molar ratio of reactants, 1.0 mole of sodium amide was allowed to interact with 10.8 g. (0.1 mole) of 2,5-dimethylpyrazine in 50 ml. of ether and 137 g. (1.0 mole) of 1-bromobutane. Distillation after the usual workup, gave a fraction, b.p. 144-155°C, which solidified on standing, m.p. 40-42°C. This fraction (21.3 g., 64%) was identified as 2,5-di-(5-nonyl)pyrazine, based on results from elemental analysis.

Anal. Calc'd. for $C_{22}H_{40}N_2$: C, 79.45; H, 12.12; N, 8.43.
Found: C, 79.60; H, 12.20; N, 8.62.

2-n-Pentyl-6-(5-nonyl)pyrazine and 2,6-Di-(5-nonyl)pyrazine. The general procedure (p. 130) was modified by employing a different molar ratio of reactants. Thus, 1.0 mole of sodium amide was interacted with 10.8 g. (0.1 mole) of 2,6-dimethylpyrazine and 137.0 g. (1.0 mole) 1-bromobutane. Distillation of the product mixture gave 8.4 g. (30.5%) of 2-n-pentyl-6-(5-nonyl)pyrazine, b.p. 117°C at 0.32 mm. to 136°C at 0.35 mm., n_D^{25} 1.4750. The fraction, b.p. 125-126°C at 0.33 mm., n_D^{25} 1.4755 was analyzed.

Anal. Calc'd. for $C_{18}H_{32}N_2$: C, 78.20; H, 11.67; N, 10.13.
Found: C, 77.94; H, 11.54; N, 10.41.

Further distillation furnished 4.4 g. (10.2%) of 2,6-di-(5-nonyl)pyrazine, b.p. 136°C at 0.35 mm. to 144°C at 0.45 mm., n_D^{25} 1.4716. This tetralkylated product was purified by redistillation, b.p. 140-142°C at 0.50 mm., n_D^{25} 1.4716.

Approved for Public Release

Contrails

Anal. Calc'd. for $C_{22}H_{40}N_2$: C, 79.45; H, 12.12; N, 8.43.
Found: C, 79.45; H, 11.96; N, 8.54.

1,4-Bis[2-(5-n-heptylpyrazyl)]butane. Employing the general procedure (p. 130), 0.2 mole of sodium amide in 300 ml. of liquid ammonia was interacted with 38.4 g. (0.2 mole) of 2-n-heptyl-5-methylpyrazine (see p. 131) and 16.8 g. (0.1 mole) of 1,2-dibromoethane in 20 ml. of ether. Distillation of the reaction mixture gave 13 g. (34%) of crude recovered 2-n-heptyl-5-methylpyrazine, b.p. 70-73°C at 0.07 mm., n_D^{25} 1.4835 and 19 g. (61.6%) of the desired 1,4-bis[2-(5-n-heptylpyrazyl)]butane, b.p. 190-195°C at 0.05-0.03 mm., which solidified on standing. This solid on two recrystallizations from an ethanol-water mixture gave colorless fine needles, m.p. 72-74°C.

Anal. Calc'd. for $C_{26}H_{42}N_4$: C, 76.04; H, 10.31; N, 13.65.
Found: C, 74.91; H, 9.59; N, 14.79.

1,4-Bis[2-(6-n-heptylpyrazyl)]butane. (1) The general procedure (p. 130) was employed to prepare this compound. A 0.15 mole quantity of sodium amide in 300 ml. of liquid ammonia was allowed to interact with 28.8 g. (0.15 mole) of 2-n-heptyl-6-methylpyrazine (see p. 132) and 12.6 g. (0.075 mole) of 1,2-dibromoethane in 20 ml. of ether. Distillation of the reaction mixture gave 9.5 g. (33%) of crude recovered 2-n-heptyl-6-methylpyrazine, b.p. 67-70°C at 0.15 mm., n_D^{25} 1.4834 and 16.3 g. (52.9%) of the desired 1,4-bis[2-(6-n-heptylpyrazyl)]butane, b.p. 190-205°C at 0.02-0.05 mm., n_D^{25} 1.5106, which was purified by redistillation, b.p. 188-190°C at 0.03 mm., n_D^{25} 1.5110.

Anal. Calc'd. for $C_{26}H_{42}N_4$: C, 76.04; H, 10.31; N, 13.65.
Found: C, 75.92; H, 10.21; N, 13.74.

(2) The above reaction was repeated on a 2.34-mole scale with respect to the starting 2-n-heptyl-6-methylpyrazine. The desired 1,4-bis[2-(6-n-heptylpyrazyl)]-butane, b.p. 192°C at 0.1 mm. to 205°C at 0.08 mm., n_D^{25} 1.5110-1.5112, was obtained in 57.3% yield (275 g.). In addition, a quantity of 104 g. (23.1%) of starting 2-n-heptyl-6-methylpyrazine, b.p. 70-80°C at 0.1 mm., was recovered.

1,4-Bis[2-(5-n-nonylpyrazyl)]butane. The general procedure (p. 130) was employed to prepare this compound. A 0.39 mole quantity of sodium amide in 400 ml. of liquid ammonia was interacted with 86 g. (0.39 mole) of 2-n-nonyl-5-methylpyrazine and 36.7 g. (0.195 mole) of 1,2-dibromoethane. Upon removal of solvent from the product mixture the remaining material solidified. A total of 40 g. (44%) of crude product, 1,4-bis[2-(5-n-nonylpyrazyl)]butane, was isolated, m.p. 69-79°C. A pure sample was obtained by recrystallization of the crude product from an ether-petroleum ether mixture, m.p. 78-79°C.

Anal. Calc'd. for $C_{30}H_{50}N_4$: C, 77.20; H, 10.80; N, 12.00.
Found: C, 77.21; H, 10.95; N, 11.87.

Approved for Public Release

Contrails

1,4-Bis[2-(6-n-nonylpyrazyl)]butane. The general procedure (p. 130) was employed to prepare this compound. A 0.48 mole quantity of sodium amide was interacted with 100 g. (0.48 mole) of 2-n-nonyl-6-methylpyrazine and 45.1 g. (0.24 mole) of 1,2-dibromoethane. Distillation of the reaction product mixture gave 24.7 g. (24.7%) of unreacted 2-n-nonyl-6-methylpyrazine, b.p. 100°C at 0.6-0.4 mm., n_D^{25} 1.4820; and 63.2 g. (56.4%) of desired 1,4-bis[2-(6-n-nonylpyrazyl)]butane, b.p. 220-235°C at 0.25 mm., n_D^{25} 1.5040. The product was then purified by redistillation, b.p. 231-232°C at 0.20 mm., n_D^{25} 1.5053, which solidified upon standing, m.p. 40-42°C.

Anal. Calc'd. for $C_{30}H_{50}N_4$: C, 77.20; H, 10.80; N, 12.00.
Found: C, 76.89; H, 10.53; N, 12.38.

IV. MODEL REACTIONS

Attempted Preparation of (Phenyldimethylsilylmethyl)pyrazine, Treatment of Pyrazylmethylsodium with Phenyldimethylsilane. To a suspension of sodium amide, prepared from 13.8 g. (0.6 g. atom) of sodium, approximately 400 ml. of liquid ammonia, and a few crystals of ferric nitrate, was added 56.4 g. (0.6 mole) of methylpyrazine over a 20-minute period. The mixture was stirred for an additional 15 minutes and to it was added 13.6 g. (0.1 mole) of phenyldimethylsilane (22) over a 10-minute period. After the mixture was stirred for one hour the reaction was quenched by the addition of 100 g. of ammonium chloride, followed by 400 ml. of ether. The ammonia was allowed to evaporate and the mixture was poured into cold water. The aqueous fraction was made strongly basic with sodium hydroxide, salted out with sodium chloride, and extracted thoroughly with ether. All the ether fractions were combined, dried over sodium sulfate, and evaporated. The remaining liquid was distilled to give the following fractions: 48.8 g. (86.5%) of recovered methylpyrazine, b.p. 125-132°C, n_D^{25} 1.4992-1.5004; 9.2 g. (65%) of 1,3-diphenyltetramethyldisiloxane, b.p. 89-92°C at 0.2 mm., n_D^{25} 1.5178.

(Phenyldimethylsilylmethyl)pyrazine. Pyrazylmethylsodium was prepared from 0.4 mole of sodium amide and 41.4 g. (0.44 mole) of methylpyrazine in 250 ml. of liquid ammonia. The liquid ammonia was then displaced by 200 ml. of freshly distilled pyridine. To this mixture was added a solution of 34.1 g. (0.2 mole) of phenyldimethylchlorosilane in 75 ml. of pyridine over a 45-minute period while the temperature of the mixture during addition was maintained between 28-30°C. After the completion of addition, the resulting mixture was stirred for 15 hours at room temperature. The reaction was then quenched by the addition of 50 ml. of methanol over a 20-minute period, stirred for an additional 30 minutes and then filtered. A quantity of 20 ml. of water was added to the filtrate and solvent was removed in vacuo below room temperature. The remaining liquid was dissolved in 10% sodium hydroxide solution and extracted with ether. Distillation of the ether extracts gave 5.7 g. (18.8%) of crude phenyldimethylsilanol, b.p. 68-69°C at 0.3 mm., n_D^{25} 1.5127, and 18.4 g. (40.4%) of the desired (phenyldimethylsilylmethyl)pyrazine, b.p. 97°C at 0.3 mm. to 100°C at 0.33 mm., n_D^{25} 1.5324. The product was then purified by redistillation, b.p. 83-84°C at 0.09 mm., n_D^{25} 1.5348.

Approved for Public Release

Contrails

Anal. Calc'd. for $C_{13}H_{16}N_2Si$: C, 68.37; H, 7.06; N, 12.27; Si, 12.30.
Found: C, 68.22; H, 7.14; N, 12.12; Si, 12.50.
68.30 7.09

Attempted Interaction of Pyrazylmethylsodium with Dimethyldichlorosilane. (1) To a suspension of 0.4 mole of sodium amide in 300 ml. of liquid ammonia was added 41.4 g. (0.44 mole) of methylpyrazine over a 15-minute period. The mixture was stirred for 10 minutes and then to it was introduced 200 ml. of pyridine. The liquid ammonia was removed by evaporation of the reaction mixture under a stream of nitrogen. To this was added a solution of 25.8 g. (0.2 mole) of dimethyldichlorosilane in 50 ml. of pyridine over a 40-minute period, while maintaining the temperature of the mixture between 20-25°C with an ice bath. The resulting mixture appeared to be quite viscous and to it was added an additional 100 ml. of pyridine. The mixture was stirred for 19 hours at room temperature. The reaction was quenched by the addition of 50 ml. of water. Pyridine was removed *in vacuo* below room temperature. The remaining material was poured into water, made basic with sodium hydroxide, salted out with sodium chloride and extracted with ether. Distillation of the ether extracts did not furnish any sharp boiling material.

(2) The above attempt was repeated employing identical amounts of reactants but modified reaction conditions. The pyridine solution of dimethyldichlorosilane was added to the reaction mixture which was cooled to -10°C and maintained at -10°C during addition. The resulting mixture was stirred for 2 hours while gradually warming to room temperature. The reaction was quenched and worked up in the usual manner. Distillation again did not give any sharp boiling material.

(3) The above attempt was repeated employing identical amounts of reactants but the addition of the dimethyldichlorosilane in pyridine was performed at -15°C. The resulting mixture was allowed to warm up to room temperature during a 1-hour period and stirred for an additional 16 hours at room temperature. Following the usual workup, only tarry material remained.

Attempted Reaction of Methylpyrazine with 1,2-Diphenyltetramethyldisilane and Lithium. To a mixture of 13.5 g. (0.05 mole) of 1,2-diphenyltetramethyldisilane (23) and 0.9 g. (0.13 g. atom) of finely cut lithium wire was added about 1 ml. of methylpyrazine and the resulting paste-like mixture was stirred for one hour. There was no great extent of reaction observed. The remaining methylpyrazine (total: 50 g.) was added and the mixture was first stirred for 19 hours at room temperature and then heated under reflux for 24 hours. The mixture was cooled and cautiously poured into 500 ml. of water in small portions with stirring. When all the unreacted lithium was decomposed, the aqueous solution was made strongly basic with sodium hydroxide, salted out with sodium chloride, and extracted with ether. The ether extracts were combined, dried over sodium sulfate, and solvent removed with the aid of a steam bath. The remaining liquid was distilled to recover 31 g. (62%) of methylpyrazine, b.p. 50°C at 30 mm. to 48°C at 28 mm., n_D^{25} 1.5020, and 10.0 g. (74%) of 1,2-diphenyltetramethyldisilane, b.p. 86-94°C at 0.13 mm.

Approved for Public Release

Contrails

Attempted Preparation of p-Phenyldimethylsilylbenzylpyrazine, Benzylpyrazine and Benzhydrylpyrazine. Sodium amide, prepared from 11.5 g. (0.5 g. atom) of sodium, 400 ml. of liquid ammonia and a catalytic quantity of ferric nitrate, was allowed to interact with 19.8 g. (0.2 mole) of methylpyrazine in 20 ml. of ether over a 90-minute period. To this was then added a solution of 24.6 g. (0.1 mole) of p-phenyldimethylsilylchlorobenzene (see p. 140) in 20 ml. of ether over a 20-minute period. The mixture was stirred for an additional 10 minutes. The reaction was quenched by the addition of 40 g. of ammonium chloride, followed by 250 ml. of ether. Following the evaporation of ammonia, the reaction mixture was poured into 200 ml. of water, made basic with sodium hydroxide, salted out with sodium chloride, and extracted with ether. Distillation of the ether extracts furnished the following fractions: 9.1 g. (50%) of recovered methylpyrazine, b.p. 123-130°C, n_D^{25} 1.4581, and 8.3 g. (48%) of crude 2-benzylpyrazine, b.p. 76-78°C at 0.08 mm., n_D^{25} 1.5803, identified by elementary analysis and infrared spectrum.

Anal. Calc'd. for $C_{11}H_{10}N_2$: C, 77.62; H, 5.92; N, 16.46.
Found: C, 76.26; H, 5.86; N, 15.39.

A small quantity (0.3 g.) of a higher boiling material, b.p. 98-127°C at 0.12 mm., was also obtained. This material solidified on standing and was purified by recrystallization from an ether-petroleum ether mixture, m.p. 109-110°C. It was tentatively identified as benzhydrylpyrazine based on the results of elemental analysis.

Anal. Calc'd. for $C_{17}H_{14}N_2$: C, 82.90; H, 5.71; N, 11.38.
Found: C, 83.01; H, 5.90; N, 10.85.

Attempted Amination of (p-Chlorobenzyl)trimethylsilane. To a suspension of 0.4 mole of sodium amide in 300 ml. of liquid ammonia was added a solution of 19.9 g. (0.1 mole) of (p-chlorobenzyl)trimethylsilane (21) in 20 ml. of ether over a 25-minute period and the mixture was stirred for an additional 2 hours. To this was then added 40 g. of ammonium chloride, followed by 300 ml. of ether. After the removal of liquid ammonia, the residue was poured into cold water, made strongly basic with sodium hydroxide, salted out with sodium chloride, and extracted thoroughly with ether. Distillation of the ether extracts gave as the first fraction, 3.9 g. (36.4%) of crude p-toluidine, b.p. 54°C at 1.2 mm. to 43°C at 0.5 mm., n_D^{25} 1.5604. This product showed two NH bands (5) in its infrared spectrum.

Anal. Calc'd. for C_7H_9N: C, 78.46; H, 8.47; N, 13.07.
Found: C, 77.32; H, 8.65; N, 12.81.

Further distillation gave a higher boiling fraction, 2.7 g. (27.6% calculated as di-(p-tolyl)amine), b.p. 123-130°C at 0.4 mm., n_D^{25} 1.6004. The infrared spectrum of this material indicated the presence of one N-H band at 2.9μ.

Approved for Public Release

Contrails

Anal. Calc'd. for $C_{14}H_{15}N$: C, 85.23; H, 7.67; N, 7.10.
Found: C, 82.10; H, 7.60; N, 7.04.

(5-Nonyl)pyrazine and (Tributyl)methylpyrazine. Employing the "alkylation" procedure (p. 130), 1.2 moles of sodium amide was treated with 18.8 g. (0.2 mole) of methylpyrazine and 164.4 g. (1.2 moles) of 1-bromobutane. Distillation of the product mixture furnished three broad boiling fractions: (1) 17.8 g., b.p. 92°C at 0.6 mm. to 100°C at 0.4 mm., (2) 14.6 g., b.p. 100-135°C at 0.4 mm., (3) 8.0 g., b.p. 135-183°C at 0.4 mm. Fractions 1 and 2 were combined and redistilled to give 18.6 g. (45%) of (5-nonyl)pyrazine, b.p. 74°C at 0.12 mm. to 76°C at 0.10 mm., n_D^{25} 1.4800. This material was again distilled for elemental analysis, b.p. 69°C at 0.03 mm., n_D^{25} 1.4802.

Anal. Calc'd. for $C_{13}H_{22}N_2$: C, 75.67; H, 10.75; N, 13.58.
Found: C, 75.81; H, 10.75; N, 13.62.

Fraction 3 obtained from the first distillation was redistilled to give 2.7 g. (5%) of (tributyl)methylpyrazine, b.p. 137-147°C at 0.08 mm., n_D^{25} 1.4850. This material was further purified by a third distillation, b.p. 134-139°C at 0.02 mm., n_D^{25} 1.4871.

Anal. Calc'd. for $C_{17}H_{30}N_2$: C, 77.80; H, 11.52; N, 10.68.
Found: C, 77.66; H, 11.68; N, 10.72.

(2-Phenylethyl)pyrazine (4). To a suspension of sodium amide, prepared from 4.6 g. (0.2 g.-atom) of sodium, 300 ml. of liquid ammonia and a few crystals of ferric nitrate, was added 18.8 g. (0.2 mole) of methylpyrazine over a 10-minute period and the resulting red mixture was stirred for an additional 30 minutes. To this was then added 300 ml. of xylene during a 30-minute period. The liquid ammonia was evaporated under a stream of nitrogen and by warming the mixture with a hot water bath. A quantity of 25.3 g. (0.2 mole) of benzyl chloride was added. The resulting mixture was stirred for 1 hour and then heated under reflux for 15 hours. The mixture was cooled, filtered to remove 7.8 g. of precipitated salt, and solvent was stripped from the filtrate at 46°C under 25 mm. pressure. The remaining liquid was distilled to give 7.7 g. (21%) of (2-phenylethyl)pyrazine, b.p. 153-157°C at 8 mm., n_D^{25} 1.5630, which was purified by redistillation, b.p. 131-132°C at 2.5 mm., n_D^{25} 1.5672 (lit. reported (4) a boiling point of 116.5 at 2 mm., n_D^{25} 1.5673, for the compound). Further distillation gave 7.8 g. of a higher boiling material, b.p. 213-220°C at 8 mm., presumably a mixture of di- (and tri-)alkylated materials.

n-Pentylpyrazine (4). (1) A quantity of pyrazylmethylsodium was prepared from the interaction of 0.4 mole of sodium amide and 0.4 mole of methylpyrazine in 300 ml. of liquid ammonia in the same manner as described in the previous experiment. To this was added 300 ml. of pyridine over a 15-minute period and the liquid ammonia was removed by a hot water bath under a stream of nitrogen. 1-Bromobutane, 27.4 g. (0.2 mole), was added during a 15-minute period while the temperature of the mixture rose from room temperature to about 75°C. This

Approved for Public Release

Contrails

resulting mixture was refluxed for 18 hours. After cooling, 50 ml. of methanol was added to decompose the excess pyrazylmethylsodium. Insoluble material was filtered and the filtrate was distilled between 30-35°C at 50-40 mm. to remove pyridine. The remaining viscous liquid was dissolved in 300 ml. of 10% sodium hydroxide, saturated with sodium chloride and extracted with ether. Distillation of the ether extracts gave 10.1 g. (33.4%) of n-pentylpyrazine, b.p. 93°C at 12 mm. to 94°C at 11 mm., n_D^{25} 1.4869, identified by infrared comparison with an authentic sample (4).

(2) The above reaction was repeated using a slight excess of methylpyrazine with respect to sodium amide and modified reaction conditions. Pyrazylmethylsodium was prepared from 4.6 g. (0.2 mole) of sodium amide and 20.8 g. (0.22 mole) of methylpyrazine in liquid ammonia. After the liquid ammonia was displaced by 300 ml. of pyridine, 13.7 g. (0.1 mole) of 1-bromobutane was added and the resulting mixture was stirred for 20 hours at room temperature. Following the same workup as described in the previous experiment and distillation of the reaction product mixture gave 7.5 g. (50%) of n-pentylpyrazine, b.p. 91-104°C at 15 mm., n_D^{25} 1.4865.

Phenacylpyrazine (25). (1) Pyrazylmethylsodium was prepared from 0.4 mole of sodium amide and 41.4 g. (0.44 mole) of methylpyrazine in 300 ml. of liquid ammonia. The ammonia was then displaced by 200 ml. of pyridine and to it was added 27.2 g. (0.2 mole) of methyl benzoate in 100 ml. of pyridine over a 50-minute period. A quantity of 100 ml. of ethanol was added to quench the excess pyrazylmethylsodium. The mixture was filtered and pyridine removed in vacuo below room temperature. To the residue was added 100 ml. of chloroform. A sudden exothermic reaction occurred, and the heat generated from the addition was sufficient to boil the chloroform solution. The mixture was then poured into cold water and extracted with chloroform thoroughly. Attempted distillation of the chloroform extracts resulted in decomposition of the material into a tarry mess.

(2) The above reaction was repeated employing a modified workup procedure. This reaction was performed using identical quantities of starting materials and reaction conditions as described above. When the methyl benzoate had been interacted with pyrazylmethylsodium overnight at room temperature, the reaction was quenched by the addition of 100 ml. of methanol, followed by 20 ml. of water. The mixture was then poured into 4 liters of water, made strongly acidic (pH 2) with concentrated hydrochloric acid, and extracted with chloroform. Evaporation of the chloroform extracts left a dark brown solid (36 g.) which was extracted with petroleum ether thoroughly using a Soxhlet extractor. Concentration of the petroleum ether solution and filtration gave a total of 29 g. (73%) of the desired phenacylpyrazine, m.p. 81-89°C, identified by infrared comparison with an authentic sample (25).

Approved for Public Release

Contrails

SUMMARY AND CONCLUSIONS

The synthesis and evaluation of a number of new pyrazine derivatives have been described in the first Summary Report (1). This included the preparation of a variety of 2-substituted-3-methylpyrazine initial intermediates and their subsequent conversion to unsymmetrical 2,3-disubstitutedpyrazine candidate products. Initial thermal stability (9 hours at 500°F) and oxidative stability (6 hours at 400°F) screening tests conducted with the 2-substituted-3-methylpyrazine intermediates showed these materials to possess generally good stability. During the current reporting period, work was continued employing the same general approach, which included the preparation of additional representatives of various established classes as well as members of some new classes. The determination of thermal and oxidative stabilities of these materials under more severe conditions (higher temperatures) was also initiated to gain further understanding of the effect of various linkages upon the physical properties of the molecule as a whole.

In particular, additional initial intermediates of the 2-phenoxy-3-methylpyrazine class were obtained in good yield employing the sodium alkoxide method to prepare the intermediate sodium phenoxides. The condensation of the sodium salts of two diprotic phenols, namely, disodium salts of resorcinol and hydroquinone, with 2-chloro-3-methylpyrazine afforded the desired dicoupling products in good yield only after extended reaction time periods were employed. Isomeric substances were encountered in the products obtained by the interaction of 2-chloro-3-methylpyrazine with sodium p-phenylphenoxide and with the disodium salt of hydroquinone. In the case of sodium p-phenylphenoxide, the desired 2-(p-phenylphenoxy)-3-methylpyrazine was obtained as the major product, the structure of which was established *via* selenium dioxide oxidative demethylation to the corresponding p-phenylphenoxypyrazine. Other initial intermediates containing the 2-phenoxy moiety were extended to include an ester substituent as well as silyl substituents on the phenoxy nucleus. A di-o-substituted phenoxy product was also prepared to study the influence of such a structure upon thermal stability.

A number of 2-alkoxy-3-methylpyrazines which contained no β-hydrogen with respect to the oxygen function were synthesized in good yield. These compounds were prepared by the interaction of an excess of the alcohol reagent with metallic sodium, followed by the condensation of the resulting sodium alkoxide with 2-chloro-3-methyl(and 3,6-dimethyl)pyrazine. A silicon-containing initial intermediate of the alkoxypyrazine class, namely, bis-{3-[2-(3-methylpyrazoxy]-2,2,4,4-tetramethyl-1-cyclobutoxy}dimethylsilane, was also prepared in 69% yield by the treatment of 2-[1-(3-hydroxy-2,2,4,4-tetramethylcyclobutoxy)]-3-methylpyrazine with dimethyldichlorosilane in the presence of pyridine.

Two general methods were employed in the preparation of 2-(N-alkylanilino)-3-methylpyrazines. One method, designated the "Direct" method, consisted of the coupling of 2-chloro-3-methylpyrazine with an N-alkylaniline. This procedure afforded the desired 2-(N-alkylanilino)-3-methylpyrazine in up to 50% yield, together with a considerable amount of a dealkylated product, 2-anilino-3-methylpyrazine. The

Approved for Public Release

Contrails

use of an acid catalyst, zinc chloride, did not improve the yield to any extent. The second method involved the alkylation of 2-anilino-3-methylpyrazine with an alkyl halide in pyridine (the "Pyridine Solvent" method). This method gave better yields of the desired compounds as the exclusive products. Thus, the second method should be the method of choice. Attempts to prepare the known N,N-di[2-(3-methylpyrazyl)]-aniline in good yield by both the "Direct" and "Pyridine Solvent" procedures were unsuccessful. The preparation of an alkyl bridged bis(anilinopyrazine), namely, N,N'-diphenyl-N,N'-di[2-(3-methylpyrazyl)]-1,2-diaminoethane, was also unsuccessful by using the "Pyridine Solvent" method. However, this product was obtained unexpectedly by the reaction of 2-(N-methylanilino)-3-methylpyrazine with 1,2-dibromoethane and sodium amide in liquid ammonia.

With respect to the preparation of 2-alkylamino-3-methyl(and 3,6-dimethyl)-pyrazines employing the "Direct" method, it was found that the yield of product is directly proportional to the maximum temperature achieved during the reaction and the total reaction time. Monoalkylamine appeared to couple more readily with 2-chloro-3-methylpyrazine at lower temperatures than dialkylamine of comparable molecular weight. For the preparation of several 2-alkylamino-3,6-dimethylpyrazines, the standard "Direct" method gave only low yields over extended reaction time periods at atmospheric pressure. A modified procedure involving a sealed bomb reaction under increased pressure was adopted and afforded significantly improved yields of the desired product with shorter reaction times.

A number of initial intermediates of the x-alkyl-x'-methylpyrazine class were prepared by monoalkylating 2,5-(and 2,6-)dimethylpyrazines with alkyl halides in the presence of sodium amide and liquid ammonia in excellent yields. The treatment of tetramethylpyrazine with 1-bromohexane under similar conditions gave a mixture of mono- and dialkylated products.

In the area of preparing 2,6-disubstituted-3-methylpyrazine advanced intermediates, two general methods were devised. The "Monoarylation" procedure afforded 2-substituted-3-methyl-6-benzylpyrazines and the "Monoalkylation" procedure led to the 2-substituted-3-methyl-6-alkylpyrazines. The structures of these products were indicated by a selenium dioxide oxidation of these compounds to the demethylated 2,6-disubstitutedpyrazines, which possess different infrared spectra as well as other physical properties when compared to the corresponding 2,3-disubstitutedpyrazines. In one case, conclusive evidence was obtained for the monophenylation of 2-phenoxy-3,6-dimethylpyrazine to yield 2-phenoxy-3-methyl-6-benzylpyrazine. Proof for the 6-substitution instead of 3-substitution was shown by a one-step oxidation of the phenylated product to 2-phenoxy-6-benzoylpyrazine. The phenylhydrazone derivative of this ketone was different from the phenylhydrazone of previously prepared 2-phenoxy-3-benzoylpyrazine. Thus, the feasibility of preparing 2-phenoxy-6-substitutedpyrazines via a preferential substitution at the 6-methyl site of 2-phenoxy-3,6-dimethylpyrazine and followed by a selenium dioxide oxidation of the product was clearly demonstrated. A number of other 2,6-disubstitutedpyrazines were prepared by similar routes. The assignment of their structure was based on analogy with the above case as well as infrared spectra and other evidence.

Approved for Public Release

Contrails

Starting from the 2-substituted(and 2,6-disubstituted)-3-methylpyrazine intermediates mentioned above, three general methods were developed for the preparation of 2,3-disubstituted(and 2,3,6-trisubstituted)pyrazine candidate products, namely, the "Arylation", the "Alkylation", and the "Pyridine Solvent" procedures. Employing the "Arylation" method, a number of 2-substituted-3-benzylpyrazines were prepared in moderate to good yields. Attempts to introduce silyl-substituted aryl groups on the methyl site of either 2-phenoxy-3-methylpyrazine or the simpler compound methylpyrazine by the "Arylation" method have resulted in a cleavage of the aryl-silicon bond to give 2-phenoxy-3-benzylpyrazine and benzylpyrazine, respectively, as the major products. Likewise, attempts to phenylate 2-phenoxy-3-methylpyrazine with (p-chlorobenzyl)trimethylsilane were not successful. That the sodium amide-liquid ammonia conditions alone could cause the cleavage side reaction was demonstrated by an attempted amination of (p-chlorobenzyl)trimethylsilane with sodium amide which resulted in the cleavage of the silyl radical to give p-toluidine.

The alkylation of variety of 2-substituted(and 2,6-disubstituted)-3-methylpyrazines with different alkyl halides using the "Alkylation" procedure resulted in a number of candidate products in excellent yields. Conditions for preferential mono- or dialkylation on the methyl site have been developed. At times, when the methyl site was adjacent to bulky substituent, the monoalkylated product was obtained as the major product even under dialkylation conditions. Trialkylation with 1-bromobutane on the methyl site of these derivatives could not be realized under various conditions.

Two unexpected displacement reactions were observed. The interaction of 2-(N-methylanilino)-3-methylpyrazine with excess 1-bromobutane and sodium amide in liquid ammonia gave a product which appeared to be 2-(N-butylanilino)-3-pentylpyrazine. Similarly, a compound presumed to be 2-(N-n-butyl-N-n-hexylamino)-3-(5-nonyl)-pyrazine was obtained from the treatment of 2-(N,N-di-n-hexylamino)-3-methylpyrazine with excess 1-bromobutane. The former case involved the displacement of the methyl group on the amino site by a butyl group and the latter a similar displacement of a hexyl group by a butyl group. At this point, the mechanism of this unusual type of displacement is not known.

The "Pyridine Solvent" method, which has been applied successfully for the N-alkylation of 2-anilino-3-methylpyrazines, was also adopted for alkylation of intermediates having poor solubility in liquid ammonia. The versatility of this method was further demonstrated by its application to the simultaneous alkylation of the amine functions and 3-methyl sites of 2-anilino-3-methylpyrazines and of 2-(N-alkylamino)-3-methylpyrazines. This procedure required the use of excess of both alkyl halide and sodium amide and afforded the desired candidate products in excellent yields.

Thirteen members of the purely alkylsubstituted pyrazine class of candidate products were prepared either by one-step polyalkylation of 2,5-(and 2,6)-dimethylpyrazine or by alkylation of a previously obtained x-alkyl-x'-methylpyrazine in excellent yields. The alkylating reagents employed included long chain alkyl halides as well as alkyl dihalides. Candidate products of moderately high molecular weight were thus prepared.

Approved for Public Release

Contrails

In the area of model compounds, efforts to prepare silicon-containing pyrazine derivatives in good yield were continued. The interaction of pyrazylmethylsodium with phenyldimethylsilane in the presence of liquid ammonia did not furnish the desired (phenyldimethylsilylmethyl)pyrazine; rather, the side product, 1,3-diphenyltetramethyldisiloxane, was obtained. However, the desired compound was synthesized (40% yield) by the treatment of pyrazylmethylsodium with phenyldimethylchlorosilane using the "Pyridine Solvent" procedure. This reaction represented the first successful placement of a silyl group on the methyl site of methylpyrazine. When the above described reaction was attempted with dimethyldichlorosilane as the silylating reagent in an effort to prepare bis(pyrazylmethyl)silane, only tarry materials were obtained. Similarly, the treatment of methyl pyrazine with phenyldimethylsilyllithium under the "azomethine" addition conditions did not yield the desired x-phenyldimethylsilyl-x'-methylpyrazine.

The "Pyridine Solvent" method, which has been applied to the preparation of various types of pyrazine derivatives and has been cited in numerous places earlier, was also successfully employed in acylating and alkylating methyl pyrazine. These results are believed to be significant, inasmuch as all the previous reactions involved on the methyl site were performed in liquid ammonia. Thus, the development of this method allowed the use of reagents which were not compatible with liquid ammonia (such as chlorosilane) for reactions on the methyl site.

Concurrent with the synthesis portion of this program an examination of the physical properties of intermediates as well as candidate products which were prepared was conducted. The purpose of this examination was to establish the influence of the different types of linkages and the effects of the various substituents attached to the pyrazine nucleus by these linkages upon the physical properties. The properties considered to be of major importance to the attainment of this program's objectives were fluidity, thermal stability, oxidative stability and lubricity.

The fluidity (as measured by viscosity) of a variety of pyrazine derivatives was observed. As far as the effect of the various linkages, the alkylpyrazines appeared to offer the best fluid properties followed by the alkoxy, dialkylamino and N-alkyl-N-arylamino pyrazines in that order. The remaining phenoxy, thiophenoxy and anilino pyrazines appeared to offer little hope of providing materials having the required fluidity. The di- and tri-substituted pyrazine candidate products which contained one of the aforementioned hetero-atom linkages also contained alkyl or aralkyl substituents at other sites on the pyrazine nucleus. It was found that the alkyl substituents provided better fluidity properties than the aralkyl groups in any of the different classes. Thus, at this stage the simple polyalkyl pyrazines appear to offer the best possibility of achieving the fluidity properties to meet this program's target requirements.

The importance of good thermal stability demanded that representatives of all classes of pyrazine derivatives prepared in this program be screened for this property. Since relatively higher molecular weight materials were prepared during this report period, it was possible to examine the stability of some compounds at

Approved for Public Release

Contrails

higher temperatures than previously (up to 700°F). The original proposition for the attainment of pyrazine derivatives with high thermal stability by the introduction of highly aromatic substituents (linked by hetero-atoms or short alkyl radicals) on the pyrazine nucleus has now been found to be untenable. The most highly aromatic substituted pyrazines proved to be the least stable candidate products. Phenoxy substituted pyrazines which had previously exhibited good stability at 500°F were found to be unstable without exception at 600°F. An apparent molecular rearrangement is believed to occur at the higher temperature which results in significant changes in fluid properties. The N-alkyl-N-arylaminopyrazines, N,N-dialkylaminopyrazines and alkoxypyrazines were increasingly more stable in approximately that order. Compounds with these structural features appeared to have their thermal stability limit somewhere between 600° and 700°F. The most thermally stable family of pyrazine derivatives found so far in this program have been the nuclear alkyl substituted pyrazines. These materials were generally highly stable at the 700°F temperature test conditions. It is a fortunate coincidence that the same structural features which so far afford the best fluidity properties also provide the best thermal stability characteristics.

The examples of pyrazine derivatives tested for oxidative stability were not as extensive as that examined for thermal stability, and so no detailed correlation of oxidative stability with structure was made. Only limited representatives of some classes which exhibited promising fluidity and thermal stability were examined for their oxidative stability. Measurements were also made on the reference materials Mil-L-9236 Base Stock and Mil-L-9236 Formulation fluids for a comparison with the pyrazine derivatives. Tests were conducted at 400°F, as previously, as well as at the higher temperature of 500°F during the current report period. Most of the substituted pyrazines exhibited oxidative stability superior to that of the Mil-L-9236 Base Stock fluid and comparable or better than the Mil-L-9236 Formulation fluid. This observed high order of natural oxidative stability is very encouraging since it is conceivable that appropriate additives might provide even higher stability.

Only one pyrazine derivative was examined for its lubricity properties during this report period. This compound displayed lubricity comparable to Mil-L-9236 Formulation fluid at elevated temperatures (400°F). This result coupled with results of previous preliminary studies suggest that pyrazine derivatives should be capable of meeting the desired lubricity requirements.

The synthesis aspect of this program has demonstrated the versatility of the system under investigation and the fruitfulness of the approaches taken in affording a wide variety of pyrazine derivatives. The simultaneous examination of the physical properties of the compounds prepared in this program has helped to guide the continued synthesis effort toward materials of increasing desirable properties. In this manner a stepwise progression of candidate products with improved characteristics has been realized. These results offer continued encouragement to the realistic possibility of achieving this program's objectives.

Approved for Public Release

Contrails

APPENDIX

INFRARED SPECTRA

Approved for Public Release

Contrails

INDEX OF INFRARED SPECTRA

	Page
2-(o-i-Propylphenoxy)-3-methylpyrazine	180
2-(p-i-Propylphenoxy)-3-methylpyrazine	180
2-(p-Phenylphenoxy)-3-methylpyrazine (m.p. 113-114.5°C)	180
2-(p-Phenylphenoxy)-3-methylpyrazine (m.p. 75-76°C)	181
2-(p-Phenylphenoxy)-3-methylpyrazine Monopicrate (m.p. 143-144°C)	181
2-(p-Phenylphenoxy)-3-methylpyrazine Monopicrate (m.p. 140-141°C)	181
p-Phenylphenoxypyrazine	182
p-Phenylene Bis-2-(3-methylpyrazyl) Ether (m.p. 185.5-186°C)	182
p-Phenylene Bis-2-(3-methylpyrazyl) Ether (m.p. 127-128°C)	182
p-Phenylene Bis-2-(3-methylpyrazyl) Ether (m.p. 150.5-152°C)	183
p-Phenylene Bis-2-(3-methylpyrazyl) Ether Dipicrate (m.p. 216-217°C)	183
p-Phenylene Bis-2-(3-methylpyrazyl) Ether Dipicrate (m.p. 154-160°C)	183
p-Phenylene Bis-2-(3-methylpyrazyl) Ether Dipicrate (m.p. 157-158°C)	184
m-Phenylene Bis-2-(3-methylpyrazyl) Ether	184
m-Carbomethoxyphenol	184
2-(m-Carbomethoxyphenoxy)-3-methylpyrazine	185
2-(2-Methyl-6-ethylphenoxy)-3-methylpyrazine	185
p-Trimethylsiloxybromobenzene	185
(m-Trimethylsiloxy)trimethylsilylbenzene	186
(p-Trimethylsiloxy)trimethylsilylbenzene	186
2-(m-Trimethylsilylphenoxy)-3-methylpyrazine	186
2-(p-Trimethylsilylphenoxy)-3-methylpyrazine	187

Approved for Public Release

Contrails

INDEX OF INFRARED SPECTRA (continued)

	Page
2-(p-t-Butylphenoxy)-3,6-dimethylpyrazine	187
2-(p-Phenylphenoxy)-3,6-dimethylpyrazine	187
2-(2,2-Dimethylpentoxy)-3-methylpyrazine	188
2-(2,2,4-Trimethylpentoxy)-3-methylpyrazine	188
2-[1-(3-Hydroxy-2,2,4,4-tetramethylcyclobutoxy)]-3-methylpyrazine	188
Bis-{3-[2-(3-methylpyrazoxy)]-2,2,4,4-tetramethyl-1-cyclobutoxy}-dimethylsilane	189
2-(2,2-Dimethylpentoxy)-3,6-dimethylpyrazine	189
2-(2,2,4-Trimethylpentoxy)-3,6-dimethylpyrazine	189
2-(N-Methylanilino)-3-methylpyrazine	190
2-(N-Butylanilino)-3-methylpyrazine	190
2-(p-Pentylanilino)-3-methylpyrazine	190
2-(p-Dodecylanilino)-3-methylpyrazine	191
N-Ethyl-p-pentylaniline	191
N,N'-Diphenyl-N,N'-di-[2-(3-methylpyrazyl)]-1,2-diaminoethane	191
2-(N-Methylanilino)-3,6-dimethylpyrazine	192
2-Anilino-3,6-dimethylpyrazine (m.p. 79-80°C)	192
2-Anilino-3,6-dimethylpyrazine (m.p. 89-91°C)	192
2-(p-Pentylanilino)-3,6-dimethylpyrazine	193
2-(N-n-Hexylamino)-3-methylpyrazine	193
2-(2-Ethylhexylamino)-3-methylpyrazine	193
2-(N,N-Di-n-butylamino)-3-methylpyrazine	194

Approved for Public Release

Contrails

INDEX OF INFRARED SPECTRA (continued)

	Page
2-(N,N-Di-n-pentylamino)-3-methylpyrazine	194
2-(N,N-Di-n-hexylamino)-3-methylpyrazine	194
2-(N-n-Hexyl-N-n-octylamino)-3-methylpyrazine	195
2-(N-n-Hexylamino)-3,6-dimethylpyrazine	195
2-(N,N-Di-n-butylamino)-3,6-dimethylpyrazine	195
2-(N,N-Di-i-butylamino)-3,6-dimethylpyrazine	196
2-(N,N-Di-n-pentylamino)-3,6-dimethylpyrazine	196
2-(N,N-Di-n-hexylamino)-3,6-dimethylpyrazine	196
2-n-Heptyl-5-methylpyrazine	197
2-n-Heptyl-6-methylpyrazine	197
2-n-Nonyl-5-methylpyrazine	197
2-n-Nonyl-6-methylpyrazine	198
2-n-Heptyl-3,5,6-trimethylpyrazine	198
2,5-Di-n-heptyl-3,6-dimethylpyrazine	198
2-Phenoxy-3-methyl-6-benzylpyrazine	199
2-(p-Nonylphenoxy)-3-methyl-6-benzylpyrazine	199
2-(p-Nonylphenoxy)-3-methyl-6-(p-phenoxybenzyl)pyrazine	199
2-(p-Nonylphenoxy)-3-methyl-6-(2-trimethylsilylethyl)pyrazine	200
2-(p-Nonylphenoxy)-3-methyl-6-(5-nonyl)pyrazine	200
2-(p-Nonylphenoxy)-3-methyl-6-(2-phenylethyl)pyrazine	200
2-(p-Nonylphenoxy)-3-methyl-6-tridecylpyrazine	201
2-(2,2-Dimethylpentoxy)-3-methyl-6-(n-heptyl)pyrazine	201

Approved for Public Release

Contrails

INDEX OF INFRARED SPECTRA (continued)

	Page
2-(2,2-Dimethylpentoxy)-3-methyl-6-(n-pentyl)pyrazine	201
2-(2,2-Dimethylpentoxy)-3-methyl-6-(5-nonyl)pyrazine	202
2-(N-Methylanilino)-3-methyl-6-(5-nonyl)pyrazine	202
2-(N-Methylanilino)-3-methyl-6-(n-heptyl)pyrazine	202
2-(N,N-Di-n-pentylamino)-3-methyl-6-(n-heptyl)pyrazine	203
2-(N,N-Di-n-hexylamino)-3-methyl-6-(n-heptyl)pyrazine	203
2-Phenoxy-3-(p-phenylbenzyl)pyrazine	203
2-(p-Nonylphenoxy)-3-benzylpyrazine	204
2-(p-Nonylphenoxy)-3-(p-phenoxybenzyl)pyrazine	204
2-Phenoxy-3-tridecylpyrazine	204
2-Phenoxy-3-(5-nonyl)pyrazine	205
2-(p-Phenylphenoxy)-3-(5-nonyl)pyrazine	205
2-(m-Phenoxyphenoxy)-3-(5-nonyl)pyrazine	205
2-(2-Methyl-6-ethylphenoxy)-3-(5-nonyl)pyrazine	206
2-(p-Nonylphenoxy)-3-pentylpyrazine	206
2-(p-t-Butylphenoxy)-3-(5-nonyl)pyrazine	206
2-(p-Nonylphenoxy)-3-tridecylpyrazine	207
2-(p-Nonylphenoxy)-3-(2-phenylethyl)pyrazine	207
2-(m-Phenoxyphenoxy)-3-(2-trimethylsilylethyl)pyrazine	207
2-(p-t-Butylphenoxy)-3-(2-trimethylsilylethyl)pyrazine	208
2-(p-t-Butylphenoxy)-3-(2-phenylethyl)pyrazine	208
2-Phenoxy-3-pyrazinoic acid Monohydrate	208

Approved for Public Release

Contrails

INDEX OF INFRARED SPECTRA (continued)

	Page
2-Phenoxy-3-benzoylpyrazine Phenylhydrazone	209
1,3-Diphenylpyrazolo[2,3-b]pyrazine	209
2-(p-Nonylphenoxy)-3-pentyl-6-(5-nonyl)pyrazine	209
2-Phenoxy-6-benzylpyrazine	210
2-Phenoxy-6-benzoylpyrazine	210
2-Phenoxy-6-benzoylpyrazine Phenylhydrazone	210
2-(p-Nonylphenoxy)-6-benzylpyrazine	211
2-(p-Nonylphenoxy)-6-(p-phenoxybenzyl)pyrazine	211
2-(p-Nonylphenoxy)-6-(5-nonyl)pyrazine	211
2-(p-Nonylphenoxy)-6-(2-phenylethyl)pyrazine	212
2-(p-Nonylphenoxy)-6-tridecylpyrazine	212
2-(2,2-Dimethylpentoxy)-3-(n-pentyl)pyrazine	212
2-(2,2-Dimethylpentoxy)-3-(5-nonyl)pyrazine	213
2-(2,2,4-Trimethylpentoxy)-3-(n-pentyl)pyrazine	213
2-(2,2,4-Trimethylpentoxy)-3-(5-nonyl)pyrazine	213
2-(2,2-Dimethylpentoxy)-3,6-di(n-heptyl)pyrazine	214
2-(2,2-Dimethylpentoxy)-3-(n-pentyl)-6-(n-heptyl)pyrazine	214
2-(N-Methylanilino)-3-benzylpyrazine	214
2-(N-Methylanilino)-3-(p-phenoxybenzyl)pyrazine	215
2-(N-Methylanilino)-3-(2-trimethylsilylethyl)pyrazine	215
2-(N-Methylanilino)-3-tridecylpyrazine	215

Approved for Public Release

Contrails

INDEX OF INFRARED SPECTRA (continued)

Page

2-(N-Butylanilino)-3-pentylpyrazine (from Interaction of 2-(N-Methylanilino)-3-methylpyrazine with 1-Bromobutane). 216

2-(N-Methylanilino)-3-(5-nonyl)pyrazine. 216

2-(N-Butylanilino)-3-(n-pentyl)pyrazine (from Interaction of 2-Anilino-3-methylpyrazine and 1-Bromobutane). 216

2-(N-Methylanilino)-3-(2-phenylethyl)pyrazine. 217

2-Anilino-3-(n-pentyl)pyrazine 217

2-(N-Butyl-p-pentylanilino)-3-(n-pentyl)pyrazine 217

2-(N-Methylanilino)-3-(n-hexyl)pyrazine. 218

2-(N-Methylanilino)-3-(9-heptadecyl)pyrazine 218

2-(N-n-Hexylanilino)-3-(n-heptyl)pyrazine. 218

2-(N-Methylanilino)-3-(n-pentyl)-6-(5-nonyl)pyrazine 219

2-(N-Methylanilino)-3-(n-pentyl)-6-(n-heptyl)pyrazine. 219

2-(N-Methylanilino)-6-(5-nonyl)pyrazine. 219

2-(N,N-Di-n-butylamino)-3-(n-pentyl)pyrazine 220

2-(N,N-Di-n-butylamino)-3-(5-nonyl)pyrazine. 220

2-(N,N-Di-n-pentylamino)-3-(n-pentyl)pyrazine. 220

2-(N-n-Butyl-N-n-hexylamino)-3-(5-nonyl)pyrazine 221

2-(N,N-Di-n-hexylamino)-3-(n-heptyl)pyrazine 221

2-(N-n-Hexyl-N-n-octylamino)-3-(n-nonyl)pyrazine 221

2-(N,N-Di-n-hexylamino)-3-(n-pentyl)-6-(n-heptyl)pyrazine. 222

2-n-Heptyl-5-n-pentylpyrazine. 222

Approved for Public Release

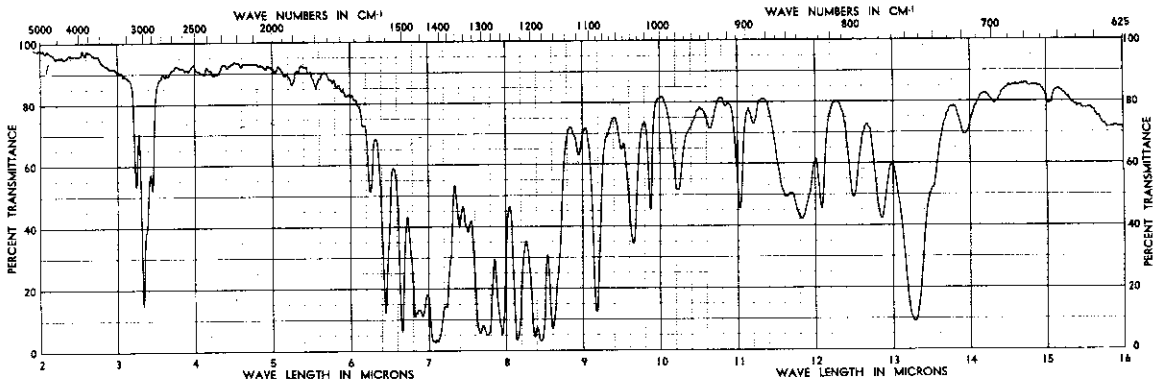
Contrails

INDEX OF INFRARED SPECTRA (continued)

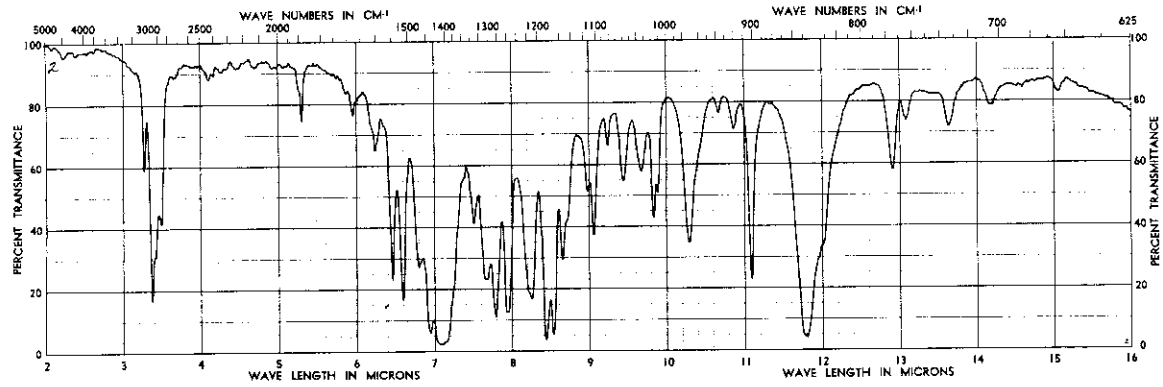
	Page
2-n-Heptyl-5-n-nonylpyrazine	222
2-n-Heptyl-6-n-pentylpyrazine	223
2-n-Heptyl-6-n-nonylpyrazine	223
2,5-Di-n-nonylpyrazine	223
2,6-Di-n-nonylpyrazine	224
2,5-Di-(5-nonyl)pyrazine	224
2-(n-Pentyl)-6-(5-nonyl)pyrazine	224
2,6-Di-(5-nonyl)pyrazine	225
1,4-Bis[2-(5-n-heptylpyrazyl)]butane	225
1,4-Bis-[2-(6-n-heptylpyrazyl)]butane	225
1,4-Bis-[2-(5-n-nonylpyrazyl)]butane	226
1,4-Bis-[2-(6-n-nonylpyrazyl)]butane	226
(Phenyldimethylsilyl)methylpyrazine	226
Benzylpyrazine	227
Benzhydrylpyrazine	227
(5-Nonyl)pyrazine	227
(Tributyl)methylpyrazine	228
(2-Phenylethyl)pyrazine	228
n-Pentylpyrazine	228
Phenacylpyrazine	229

Approved for Public Release

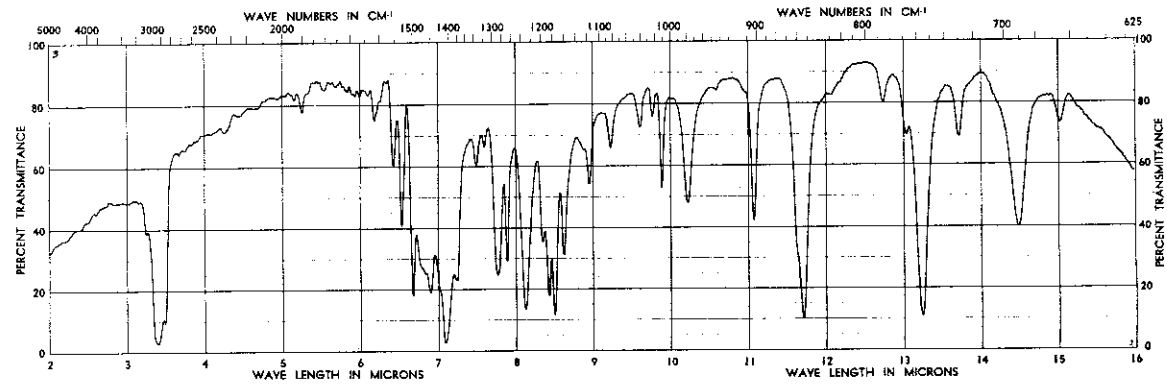
Contrails



2-(o-i-Propylphenoxy)-3-methylpyrazine



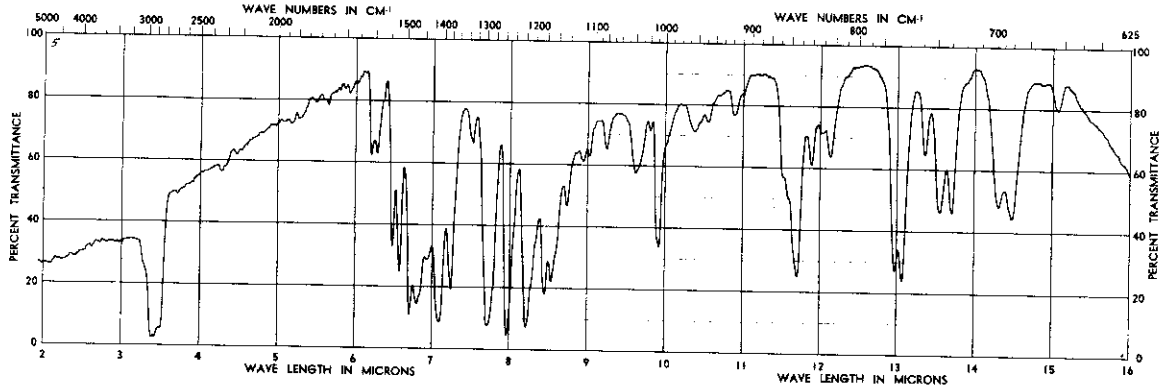
2-(p-i-Propylphenoxy)-3-methylpyrazine



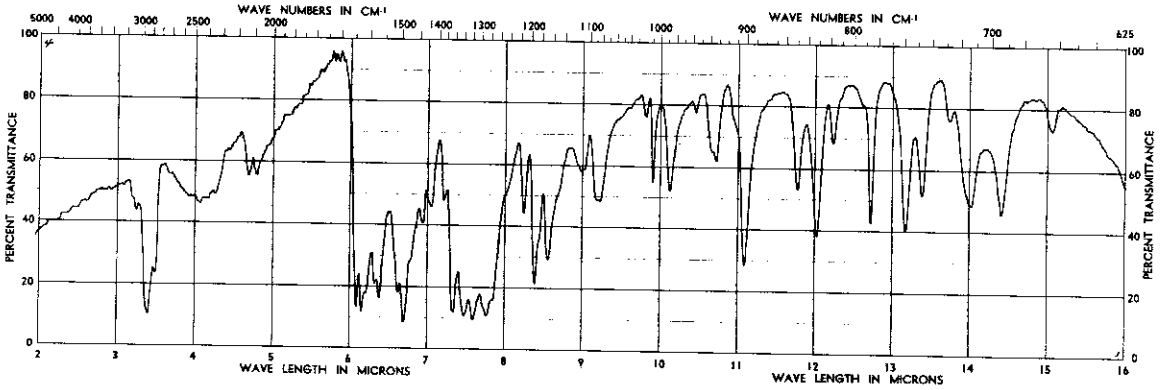
2-(p-Phenylphenoxy)-3-methylpyrazine (m.p. 113-114.5°C)

Approved for Public Release

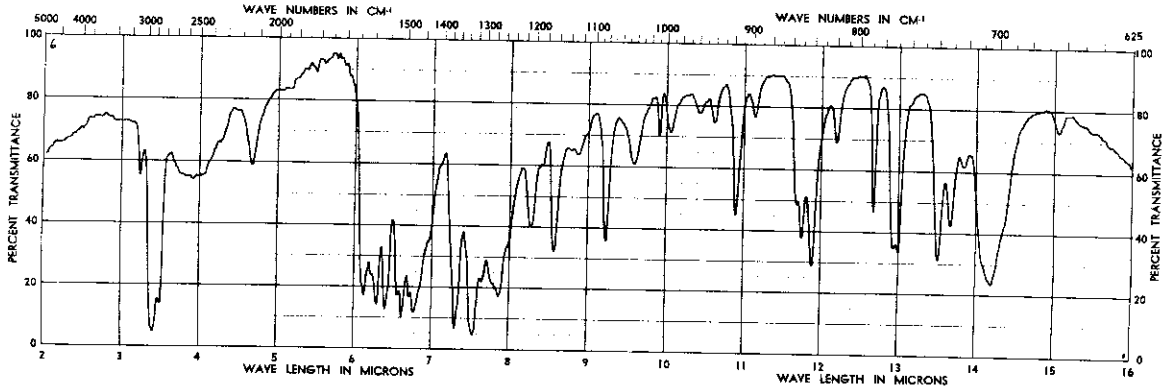
Contrails



2-(p-Phenylphenoxy)-3-methylpyrazine (m.p. 75-76°C)



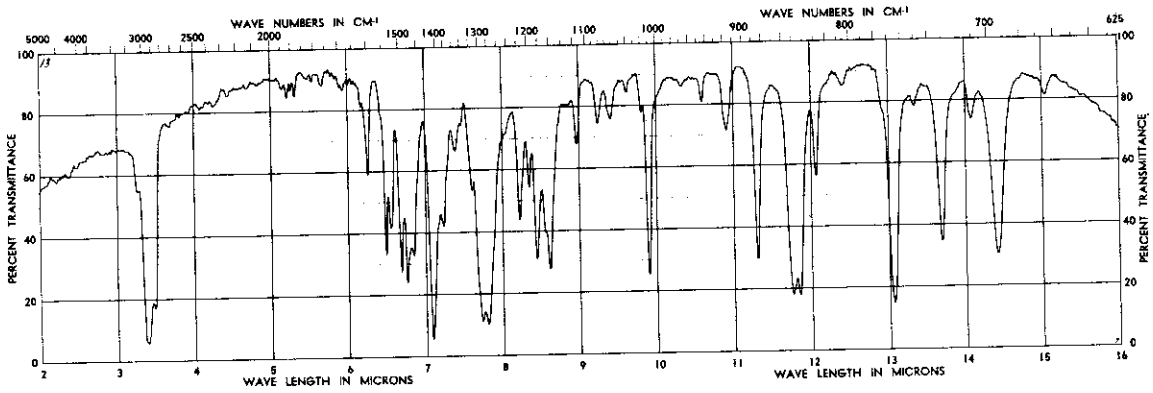
2-(p-Phenylphenoxy)-3-methylpyrazine Monopicrate (m.p. 143-144°C)



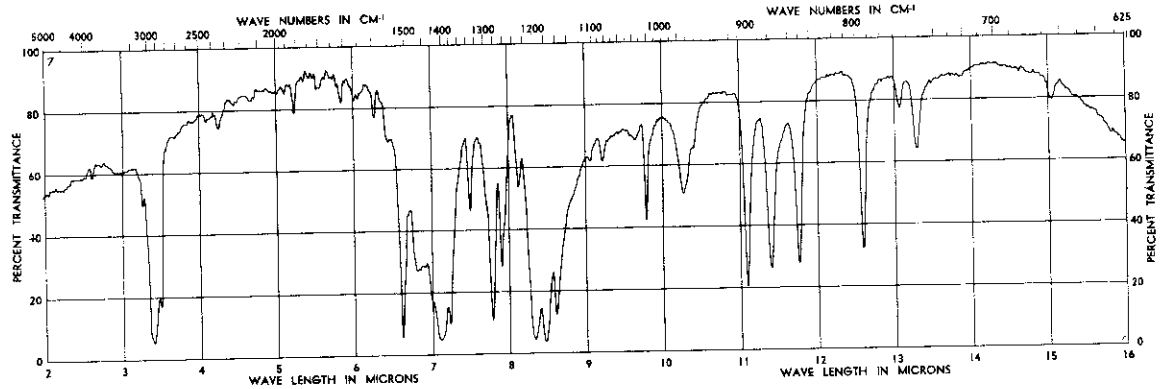
2-(p-Phenylphenoxy)-3-methylpyrazine Monopicrate (m.p. 140-141°C)

Approved for Public Release

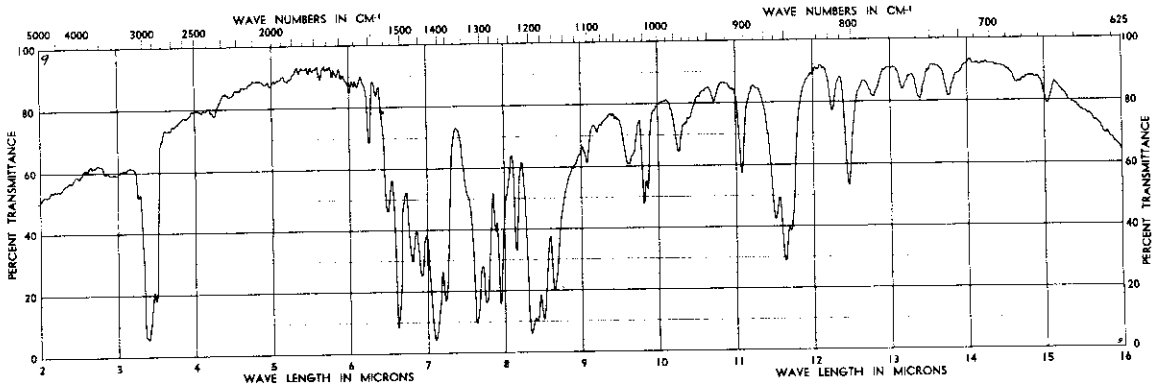
Contrails



p-Phenylphenoxypyrazine



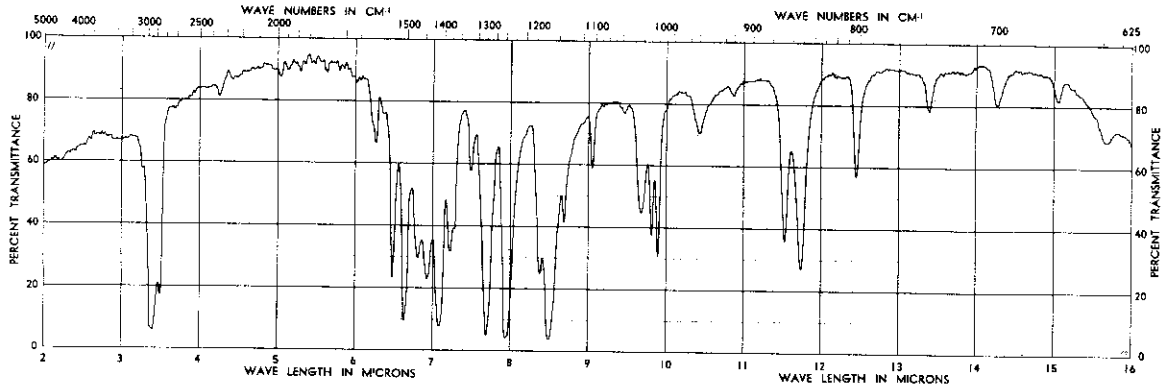
p-Phenylene Bis-2-(3-methylpyrazyl) Ether (m.p. 185.5-186°C)



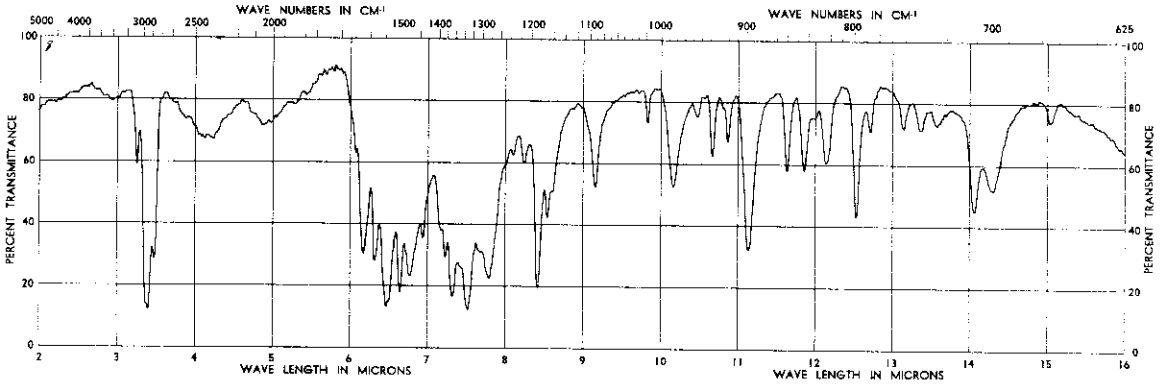
p-Phenylene Bis-2-(3-methylpyrazyl) Ether (m.p. 127-128°C)

Approved for Public Release

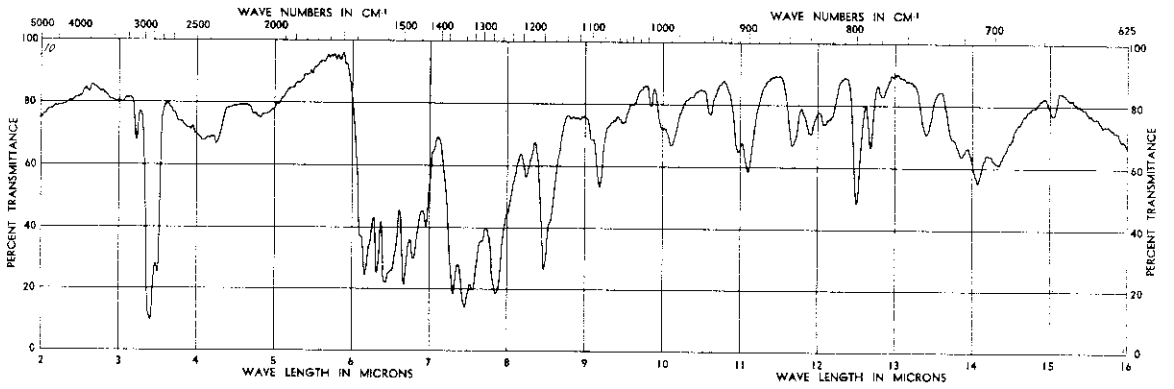
Contrails



p-Phenylene Bis-2-(3-methylpyrazyl) Ether (m.p. 150.5-152°C)



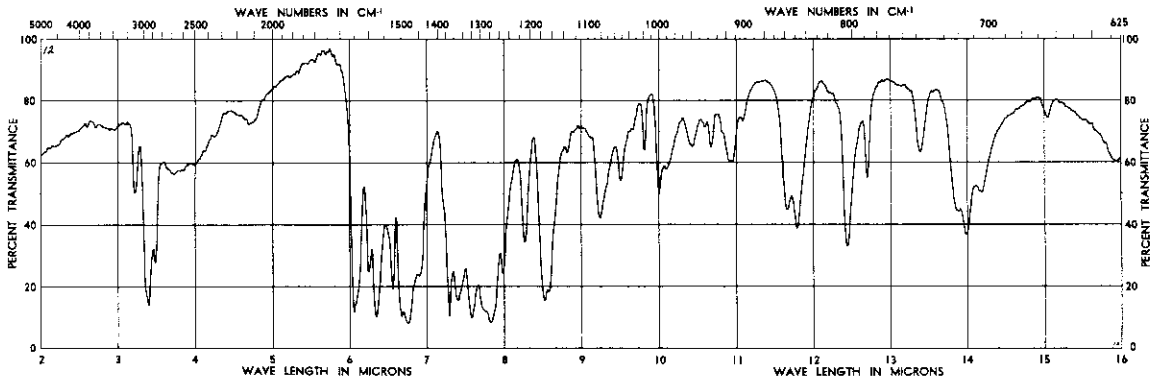
p-Phenylene Bis-2-(3-methylpyrazyl) Ether Dipicrate (m.p. 216-217°C)



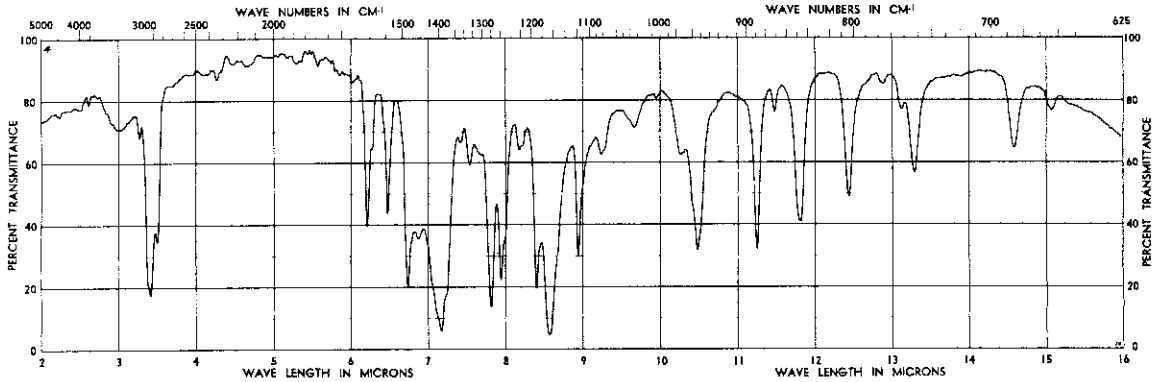
p-Phenylene Bis-2-(3-methylpyrazyl) Ether Dipicrate (m.p. 154-160°C)

Approved for Public Release

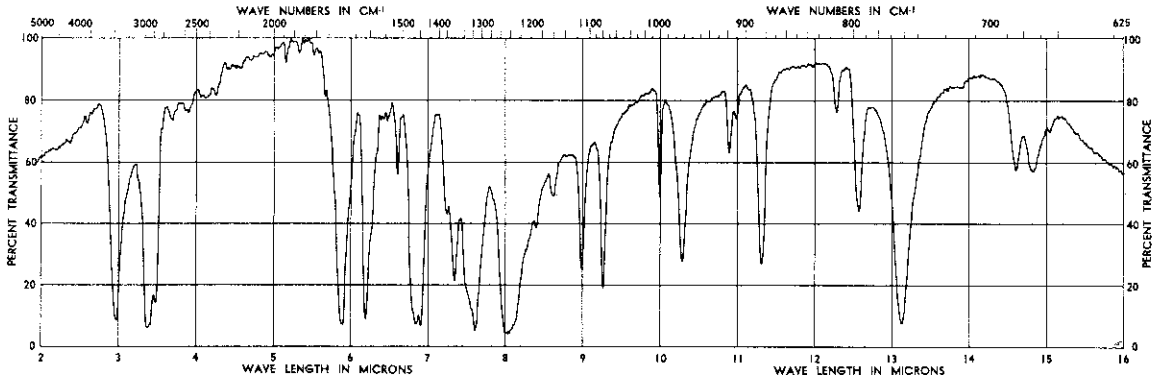
Contrails



p-Phenylene Bis-2-(3-methylpyrazyl) Ether Dipicrate (m.p. 157-158°C)



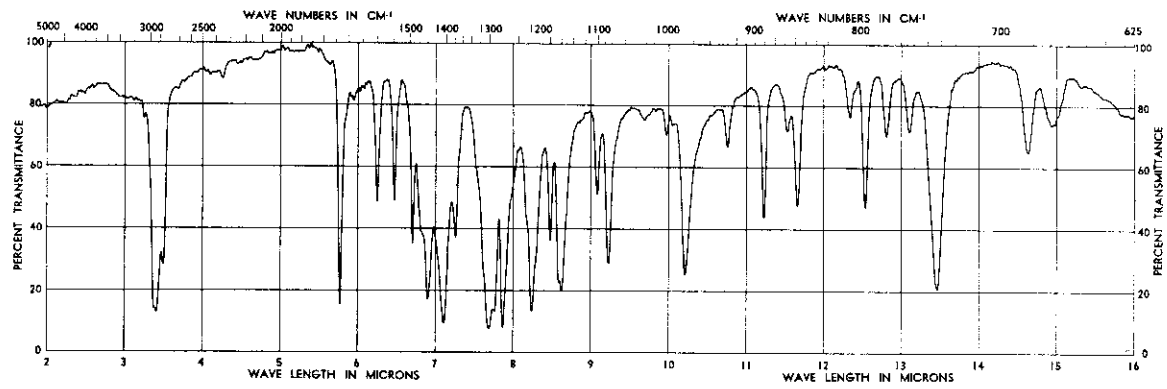
m-Phenylene Bis-2-(3-methylpyrazyl) Ether



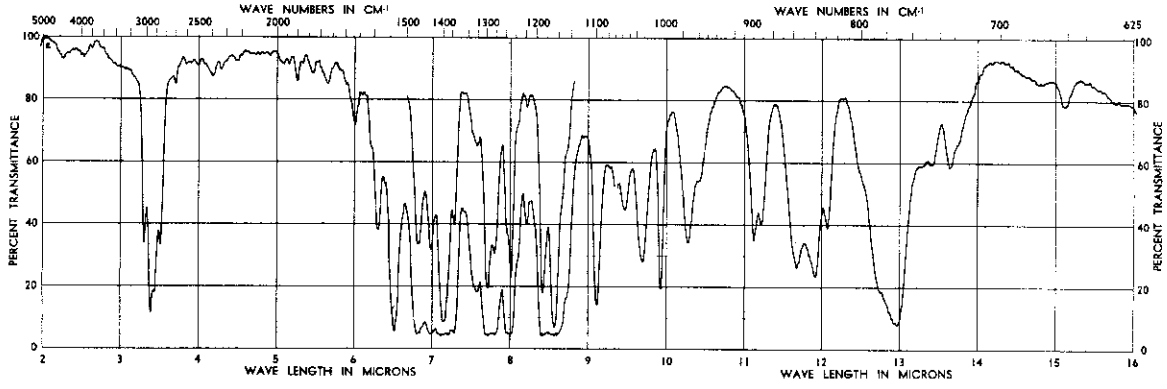
m-Carbomethoxyphenol

Approved for Public Release

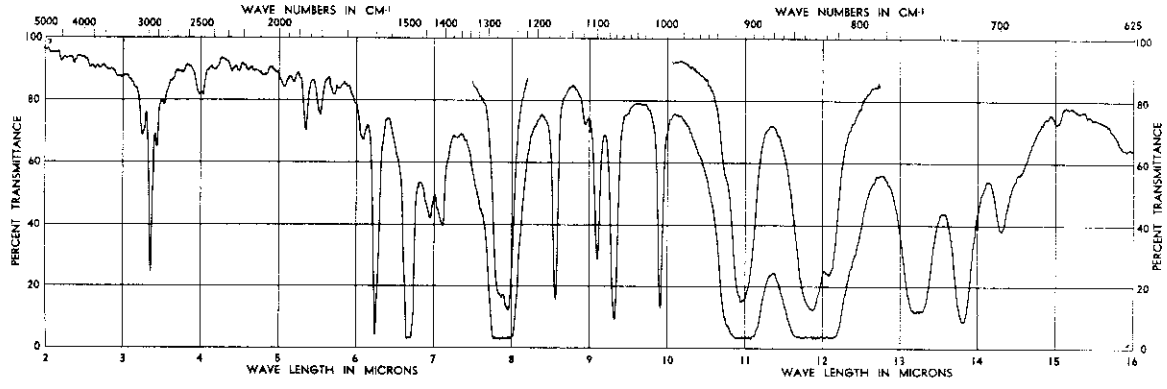
Contrails



2-(m-Carbomethoxyphenoxy)-3-methylpyrazine



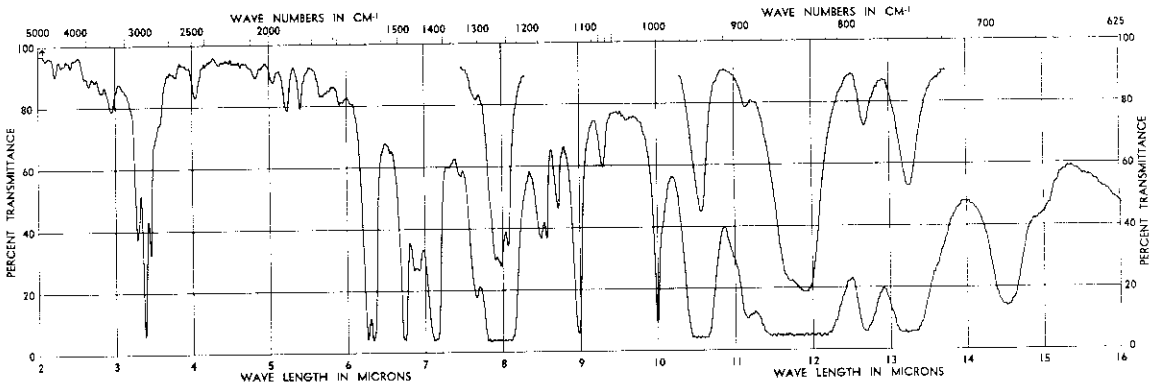
2-(2-Methyl-6-ethylphenoxy)-3-methylpyrazine



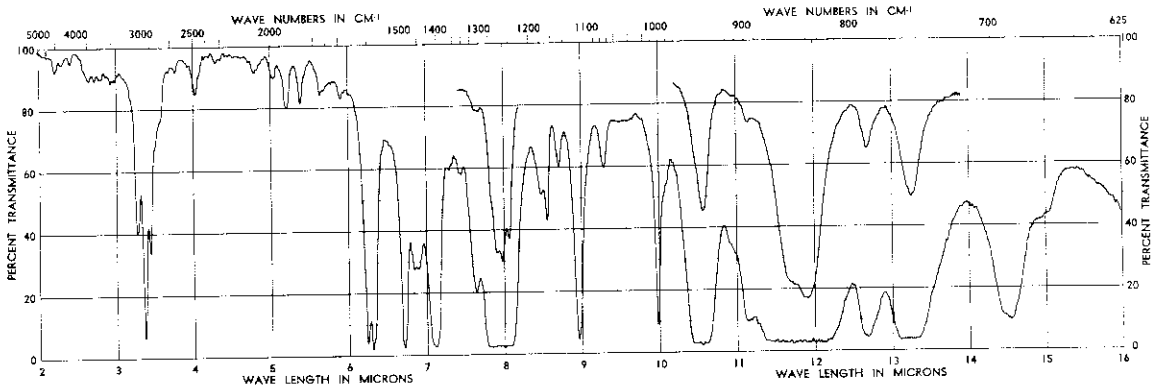
p-Trimethylsiloxybromobenzene

Approved for Public Release

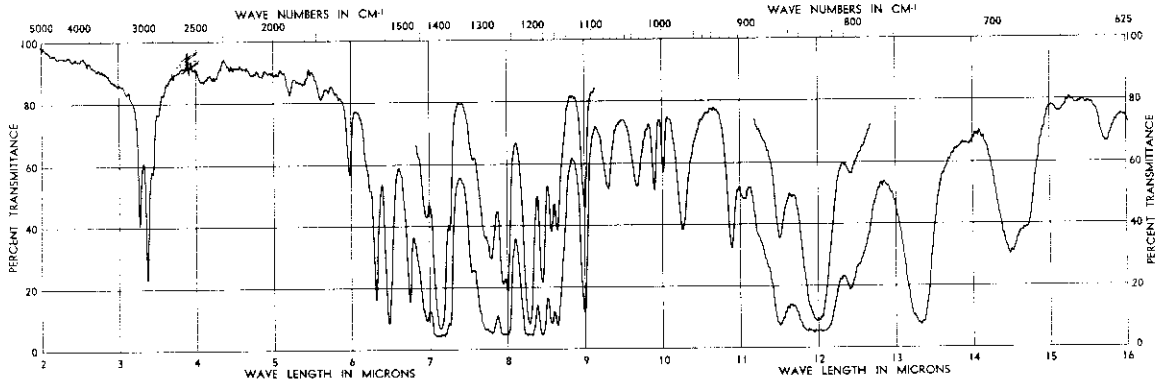
Contrails



(m-Trimethylsiloxy)trimethylsilylbenzene



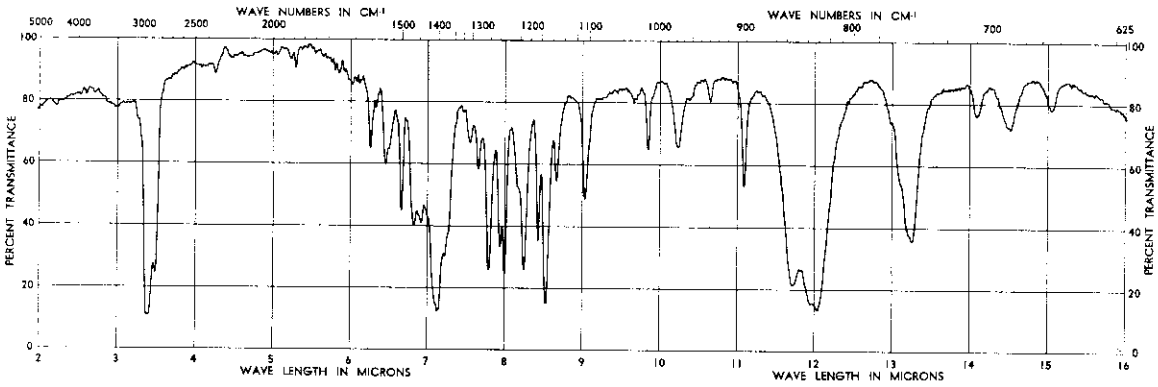
(p-Trimethylsiloxy)trimethylsilylbenzene



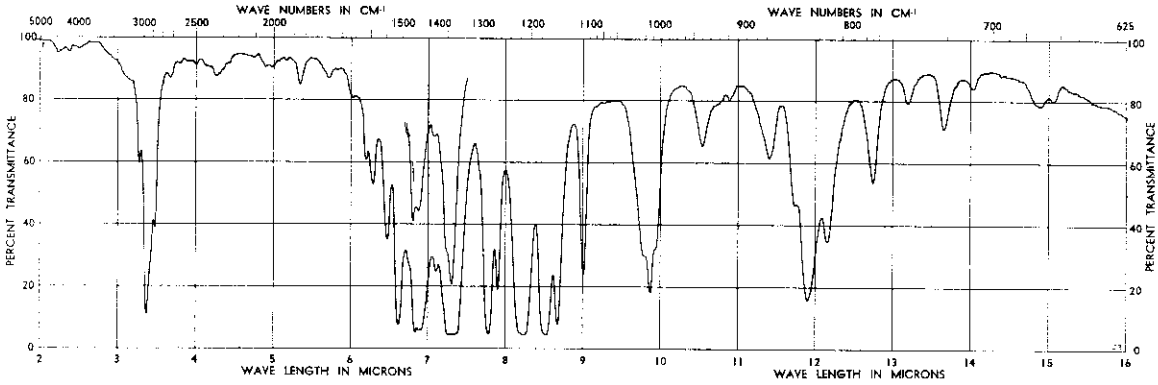
2-(m-Trimethylsilylphenoxy)-3-methylpyrazine

Approved for Public Release

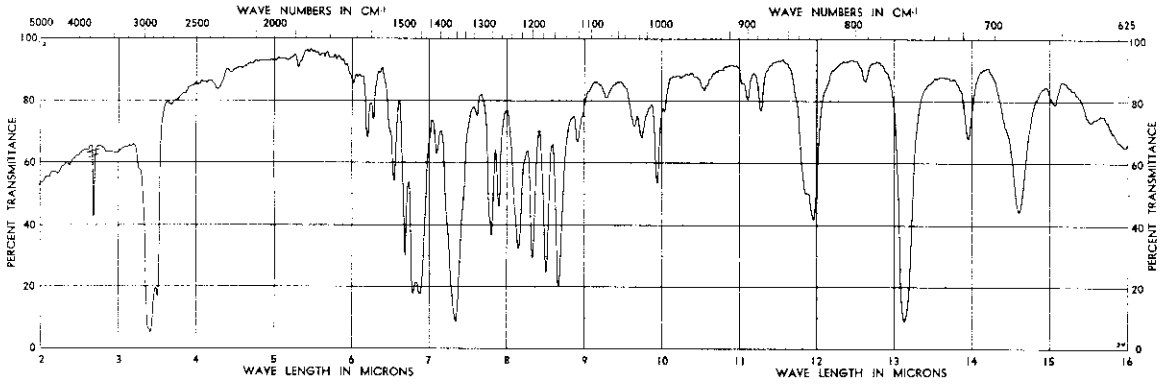
Contrails



2-(p-Trimethylsilylphenoxy)-3-methylpyrazine



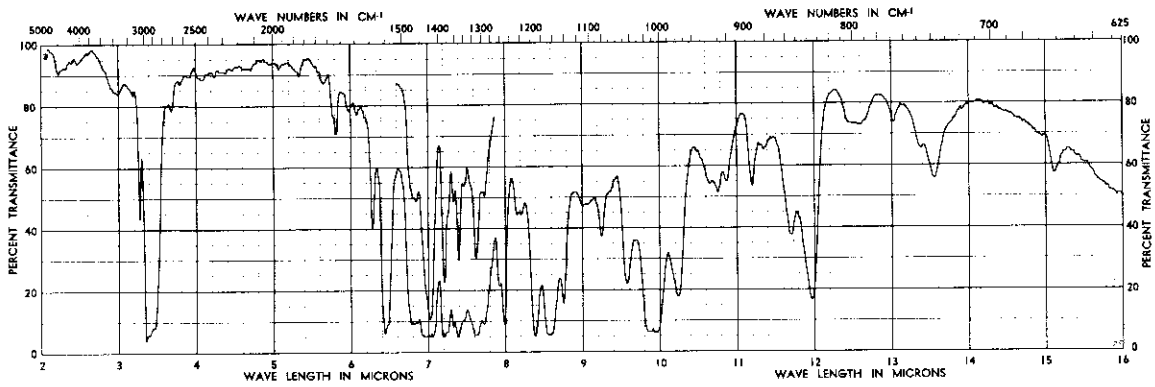
2-(p-t-Butylphenoxy)-3,6-dimethylpyrazine



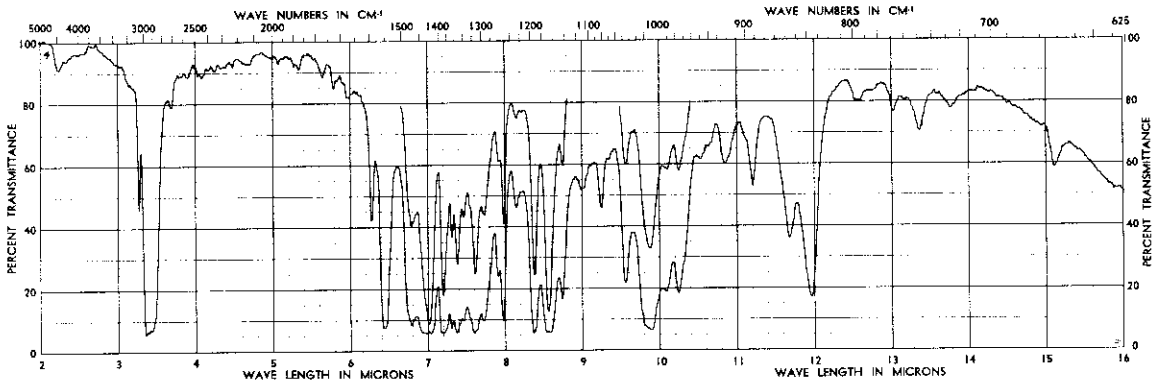
2-(p-Phenylphenoxy)-3,6-dimethylpyrazine

Approved for Public Release

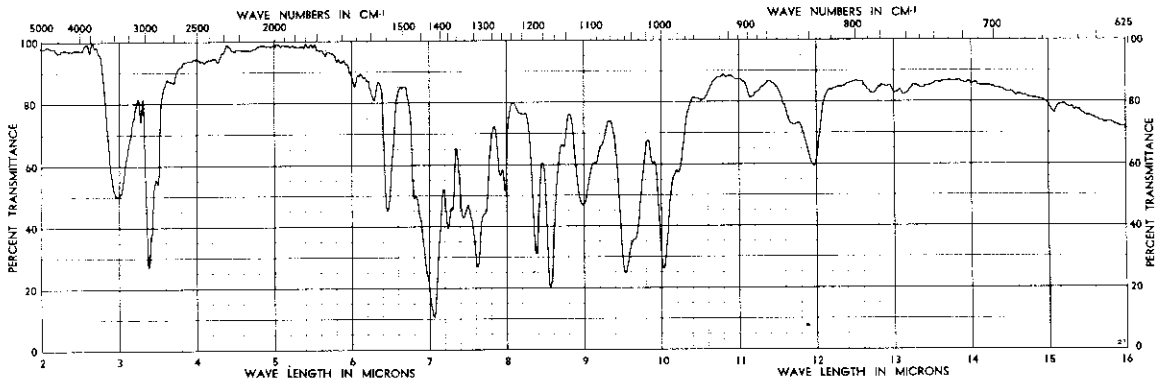
Contrails



2-(2,2-Dimethylpentoxy)-3-methylpyrazine



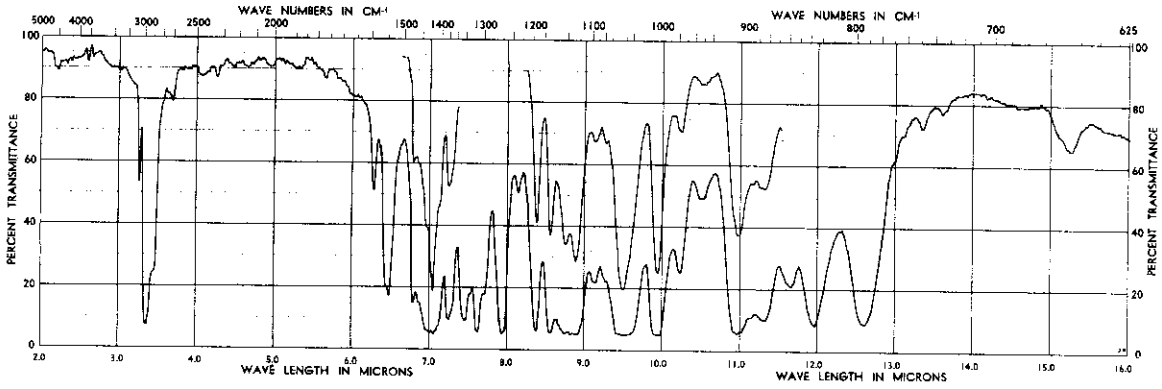
2-(2,2,4-Trimethylpentoxy)-3-methylpyrazine



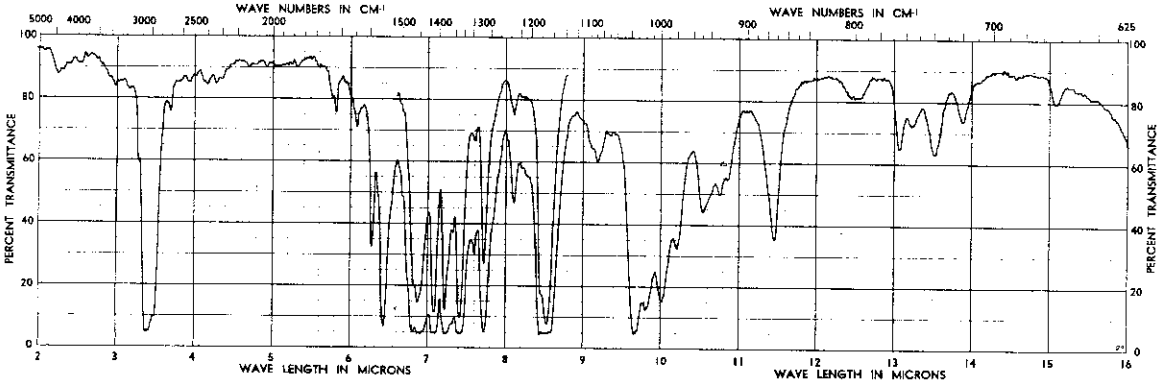
2-[1-(3-Hydroxy-2,2,4,4-tetramethylcyclobutoxy)] -3-methylpyrazine

Approved for Public Release

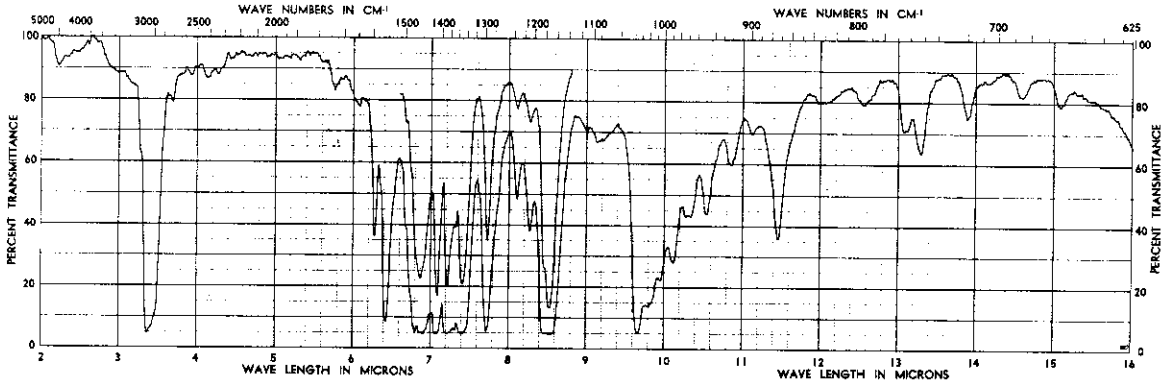
Contrails



Bis-{3-[2-(3-methylpyrazoxy)]-2,2,4,4-tetramethyl-1-cyclobutoxy}-dimethyl-silane



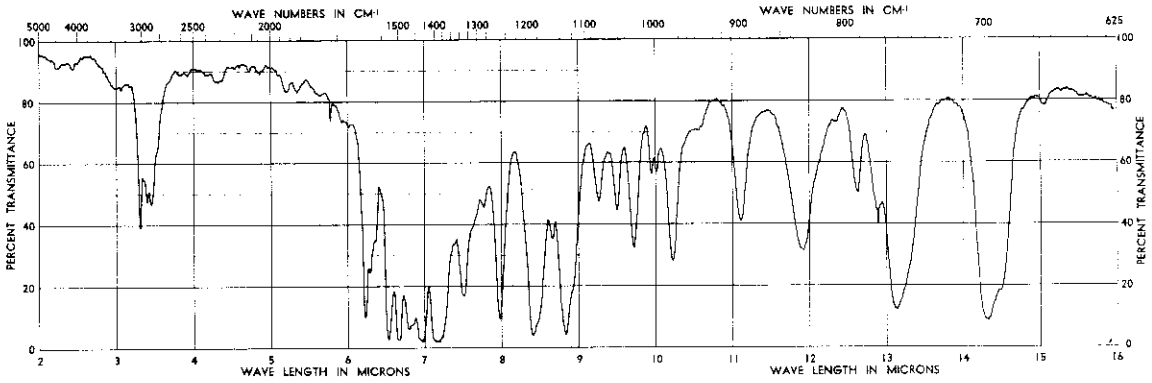
2-(2,2-Dimethylpentoxy)-3,6-dimethylpyrazine



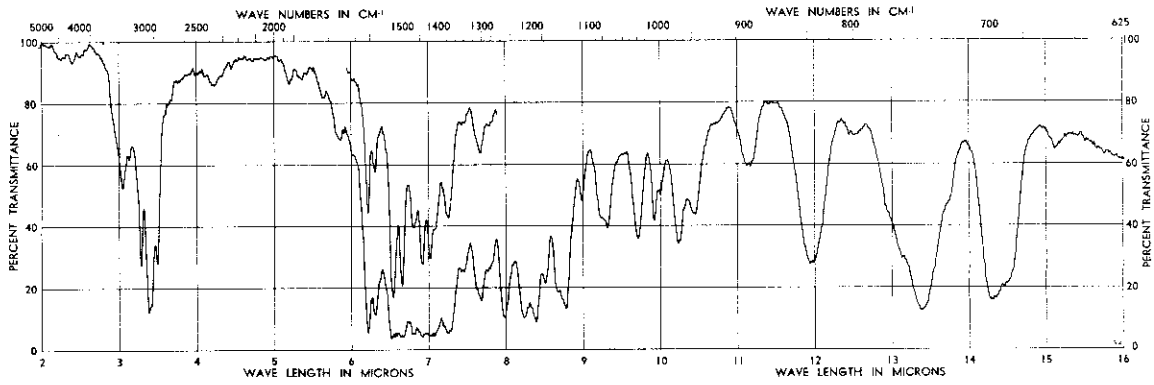
2-(2,2,4-Trimethylpentoxy)-3,6-dimethylpyrazine

Approved for Public Release

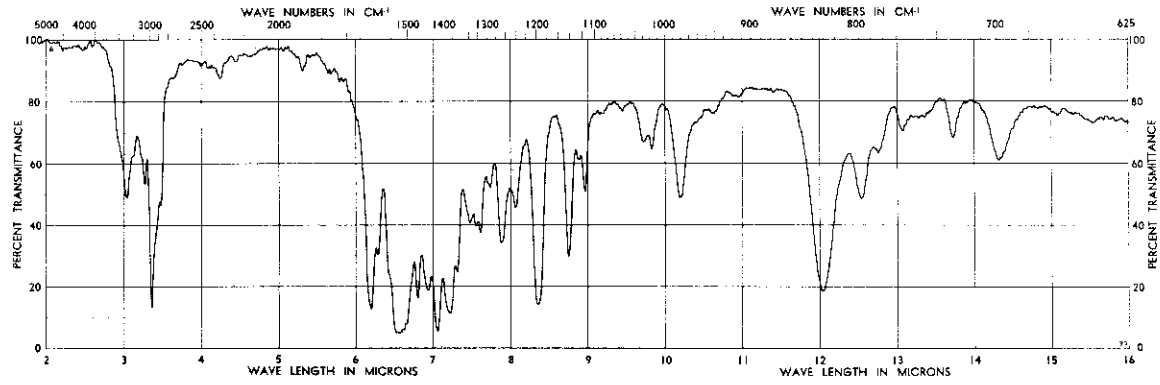
Contrails



2-(N-Methylanilino)-3-methylpyrazine



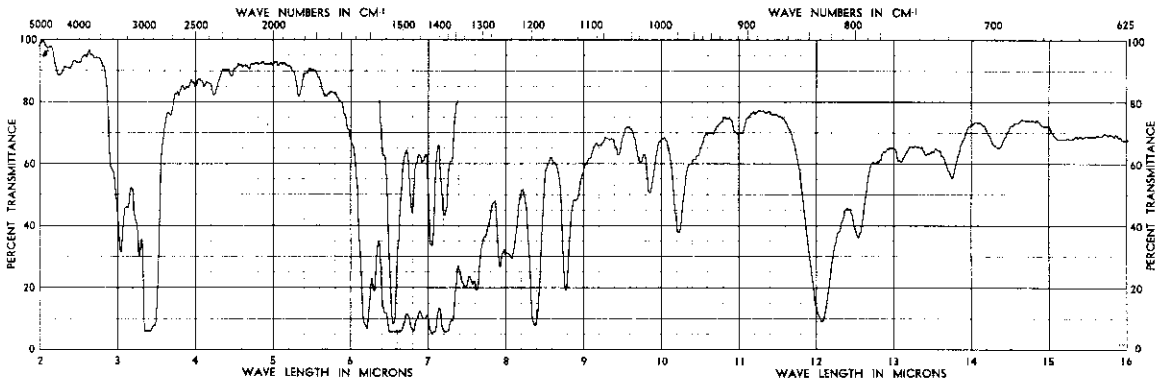
2-(N-Butylanilino)-3-methylpyrazine



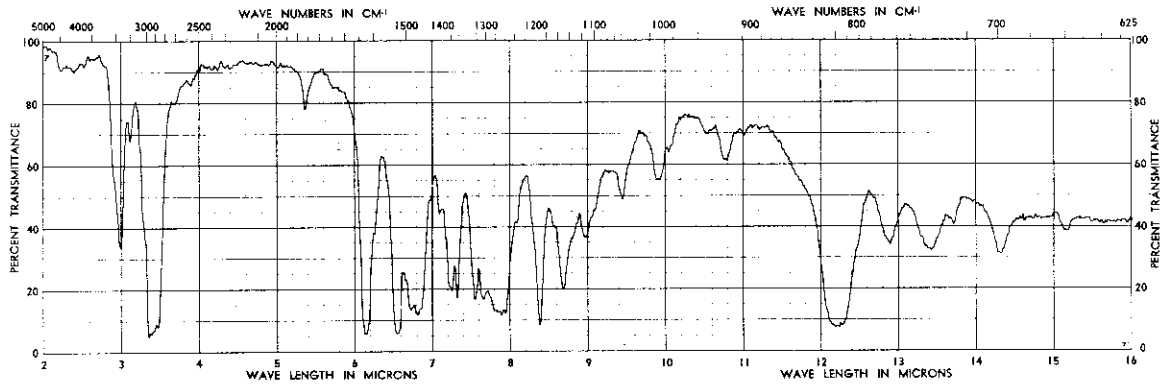
2-(p-Pentylanilino)-3-methylpyrazine

Approved for Public Release

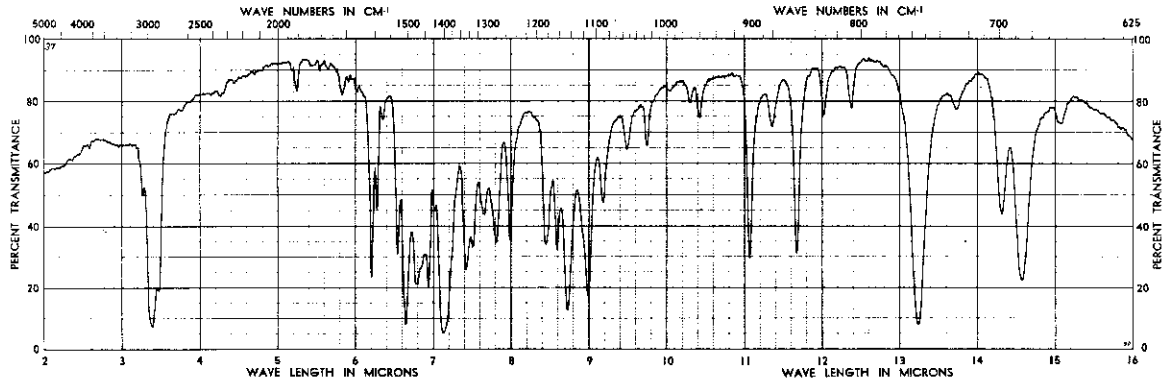
Contrails



2-(p-Dodecylanilino)-3-methylpyrazine



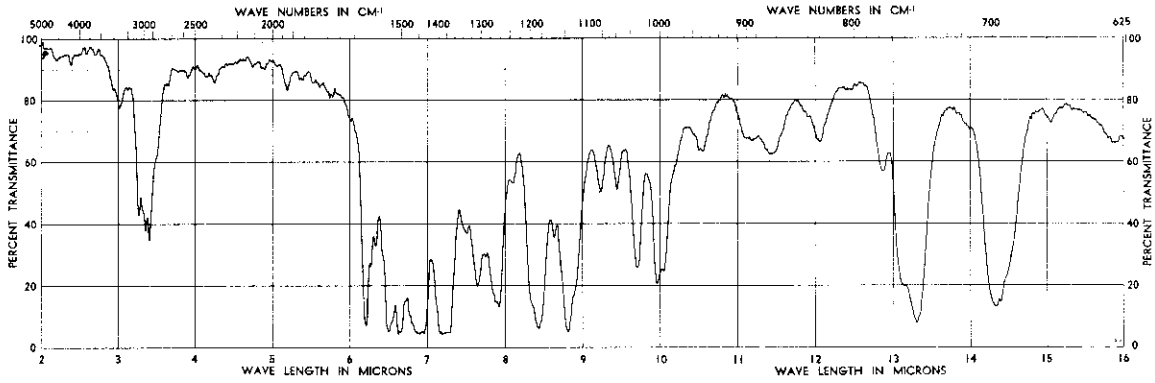
N-Ethyl-p-pentylaniline



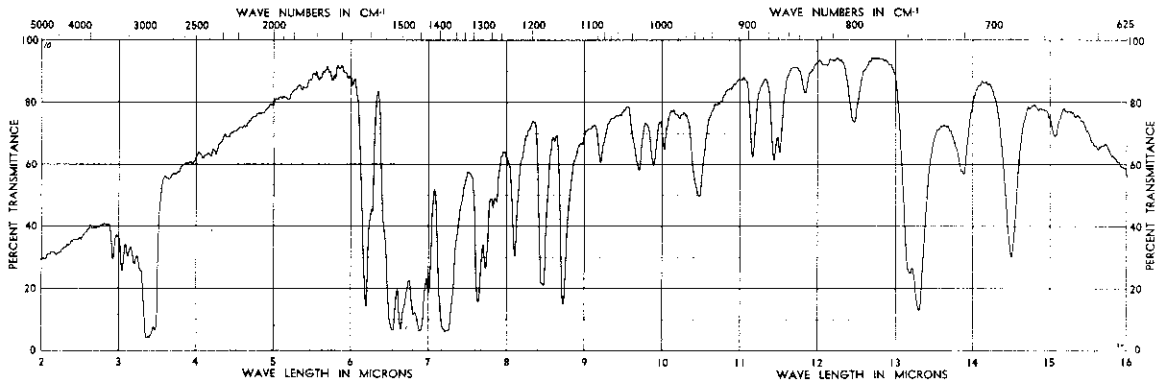
N,N'-Diphenyl-N,N'-di-[2-(3-methylpyrazyl)]-1,2-diaminoethane

Approved for Public Release

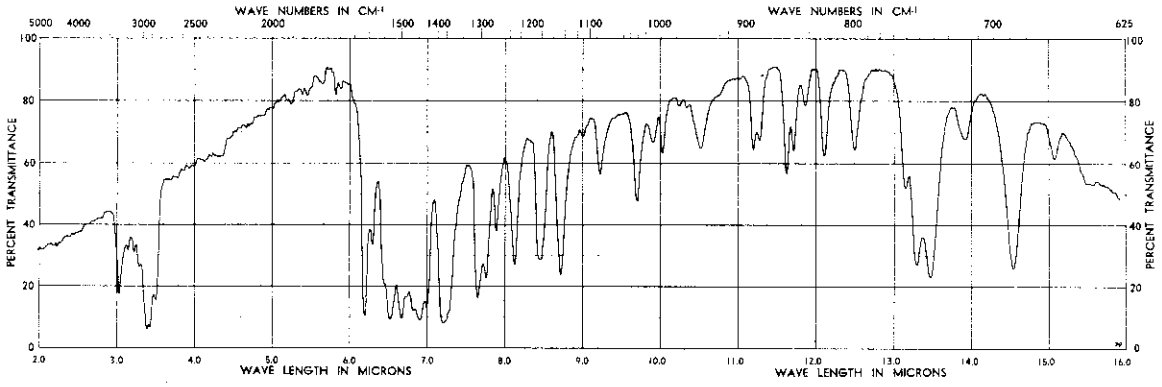
Contrails



2-(N-Methylanilino)-3,6-dimethylpyrazine



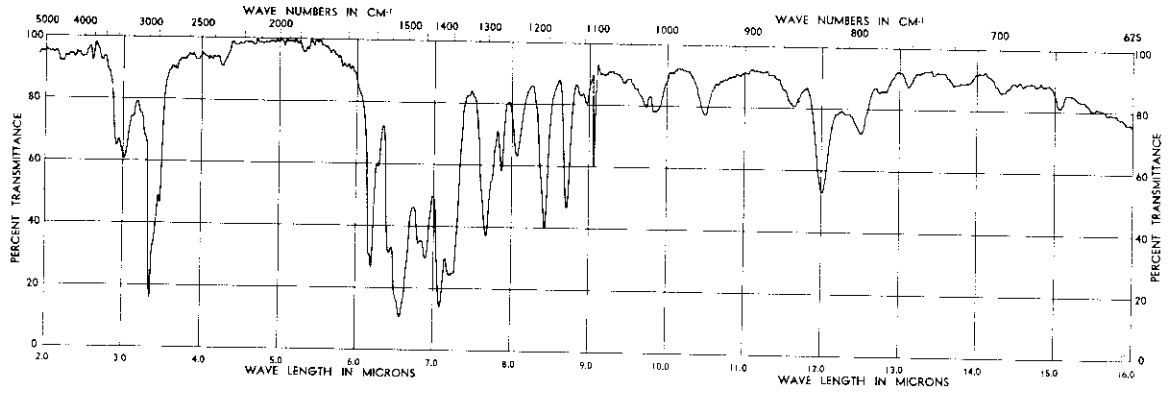
2-Anilino-3,6-dimethylpyrazine (m.p. 79-80°C)



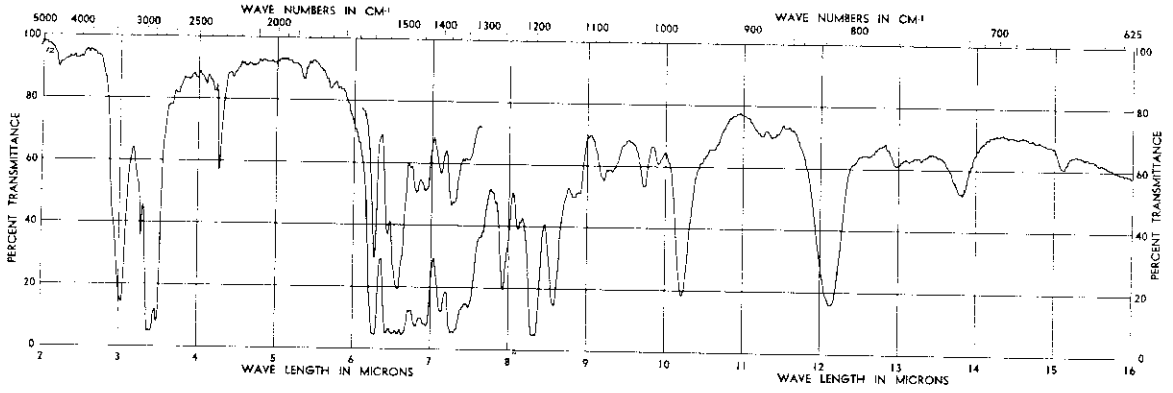
2-Anilino-3,6-dimethylpyrazine (m.p. 89-91°C)

Approved for Public Release

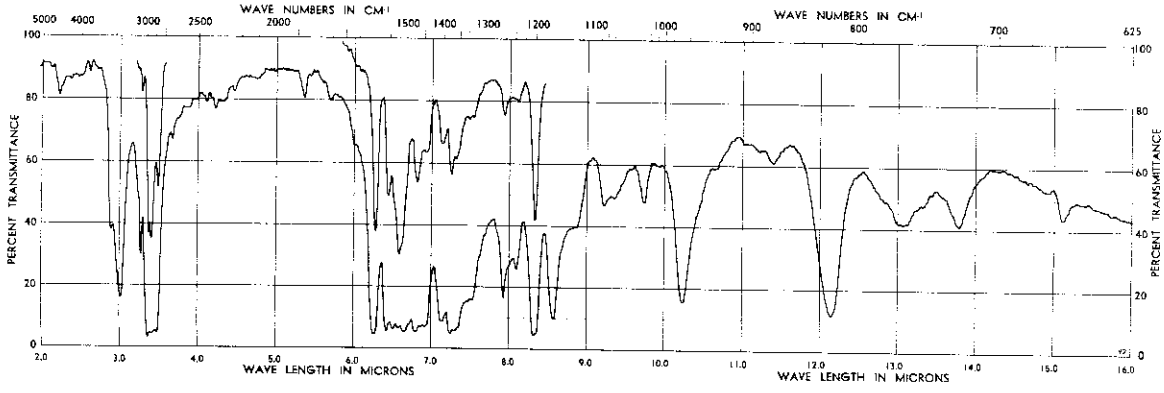
Contrails



2-(p-Pentylanilino)-3,6-dimethylpyrazine



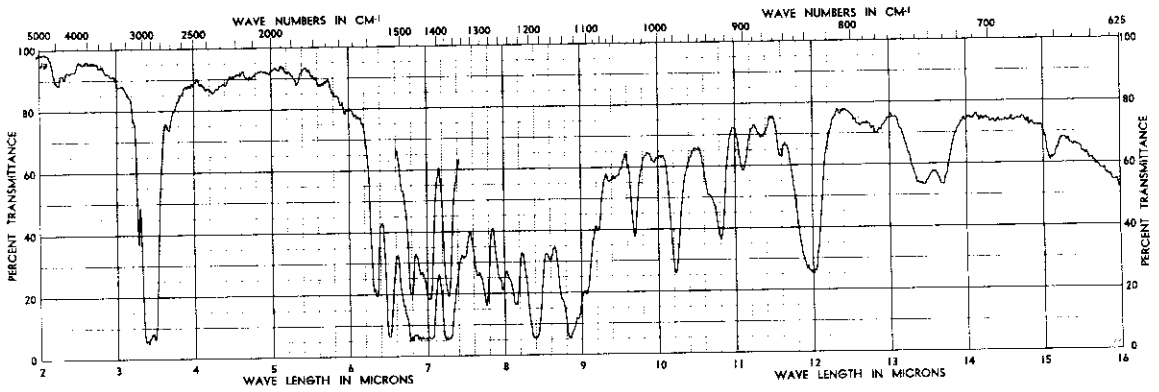
2-(N-n-Hexylamino)-3-methylpyrazine



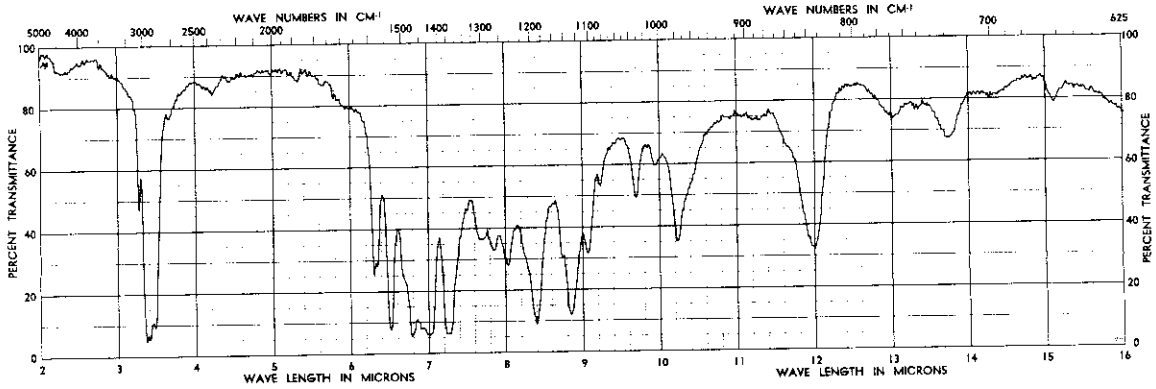
2-(2-Ethylhexylamino)-3-methylpyrazine

Approved for Public Release

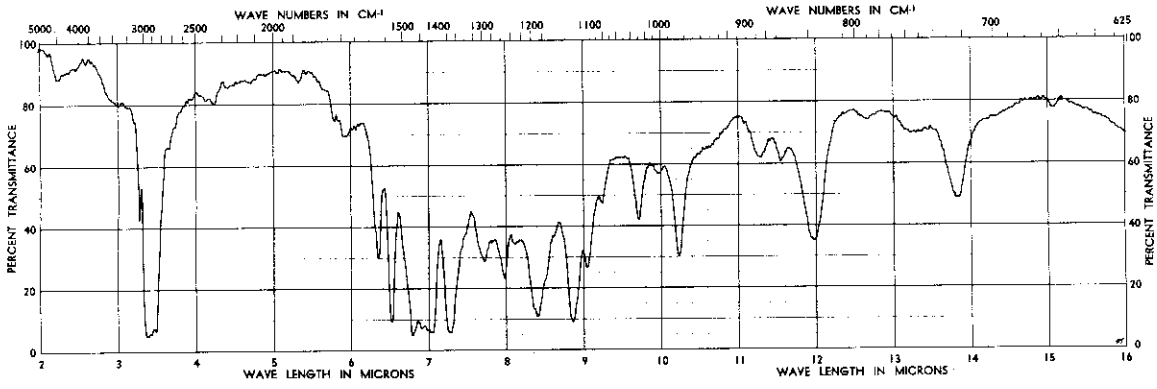
Contrails



2-(N,N-Di-n-butylamino)-3-methylpyrazine



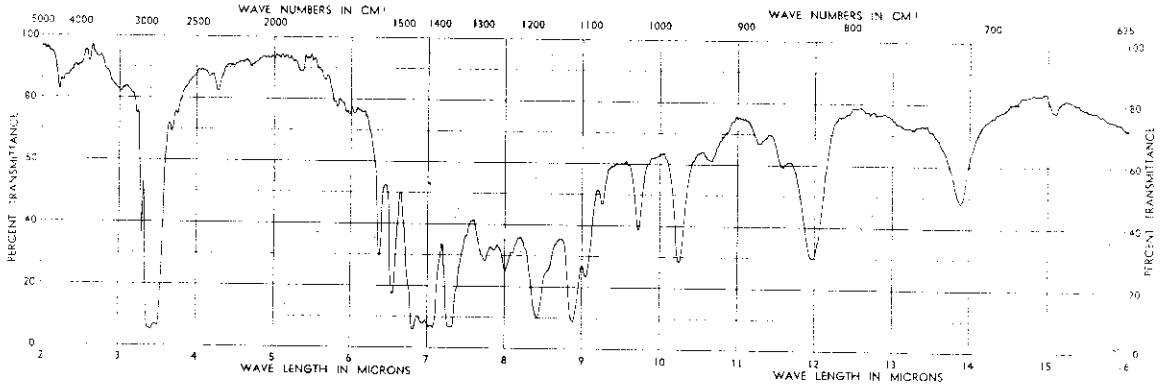
2-(N,N-Di-n-pentylamino)-3-methylpyrazine



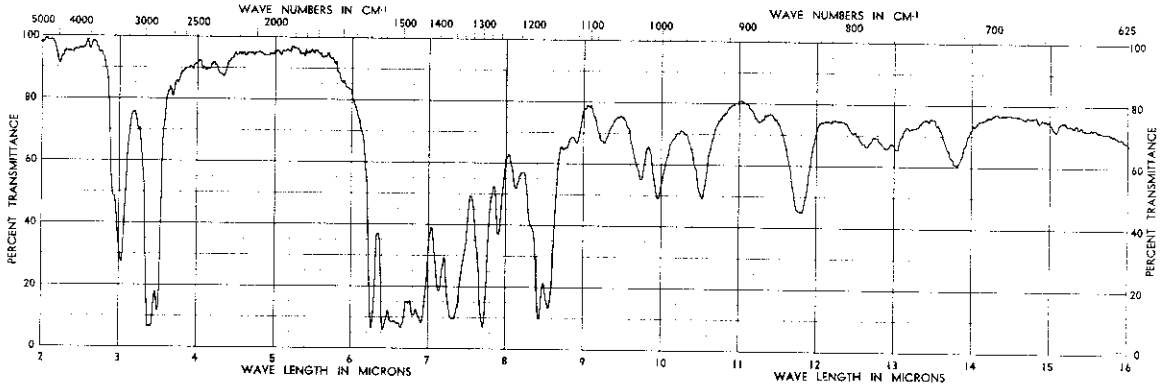
2-(N,N-Di-n-hexylamino)-3-methylpyrazine

Approved for Public Release

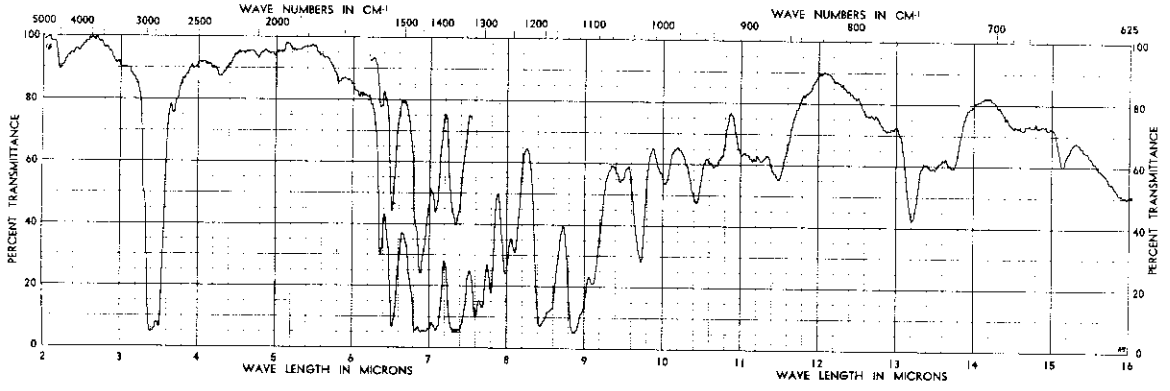
Contrails



2-(N-n-Hexyl-N-n-octylamino)-3-methylpyrazine



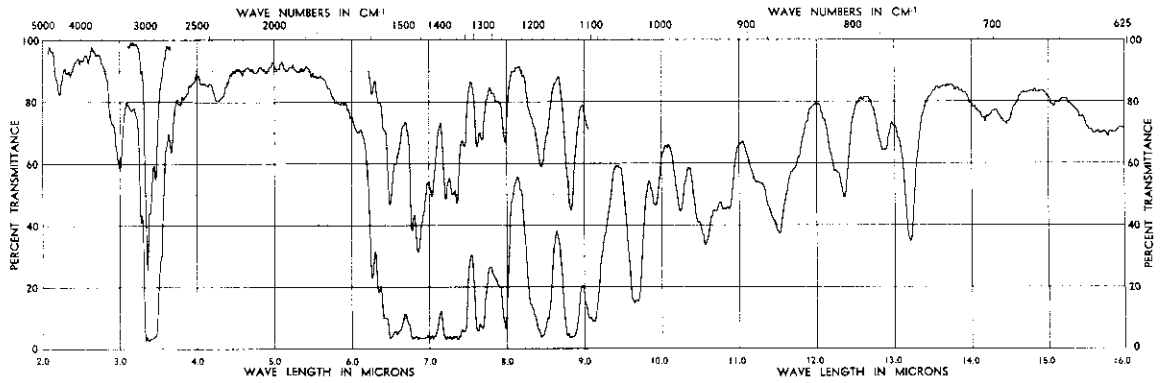
2-(N-n-Hexylamino)-3,6-dimethylpyrazine



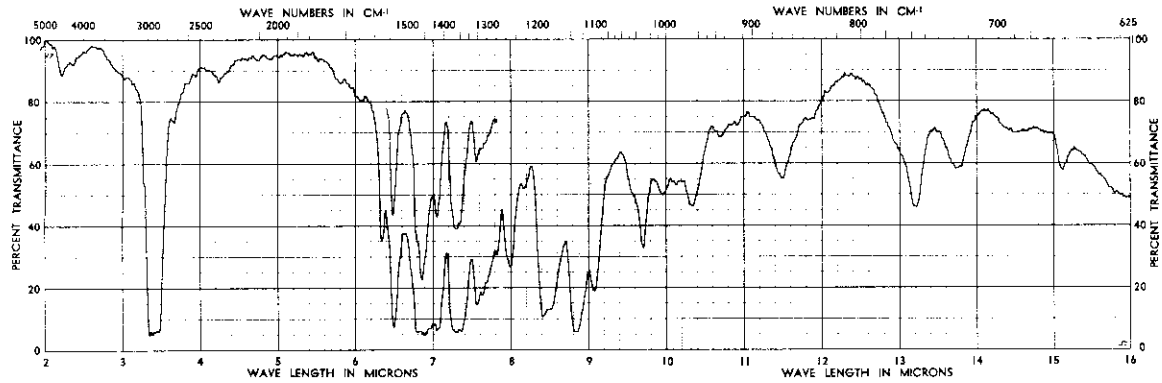
2-(N,N-Di-n-butylamino)-3,6-dimethylpyrazine

Approved for Public Release

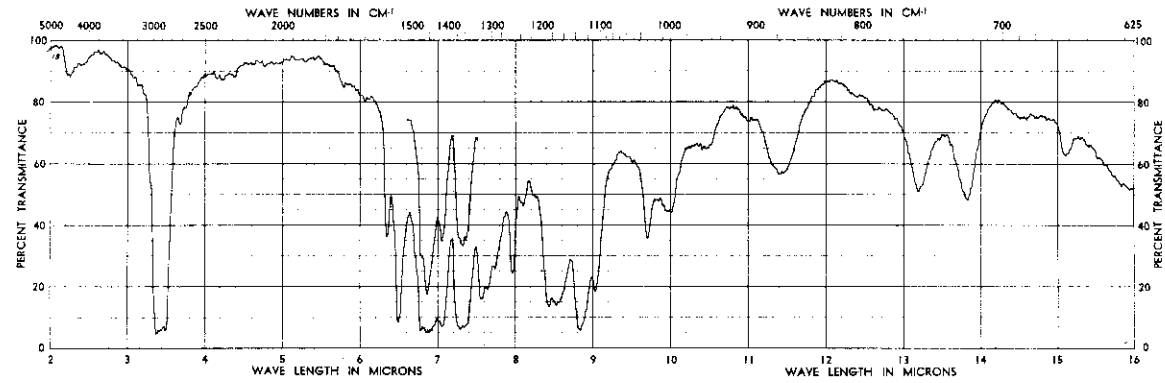
Contrails



2-(N,N-Di-i-butylamino)-3,6-dimethylpyrazine



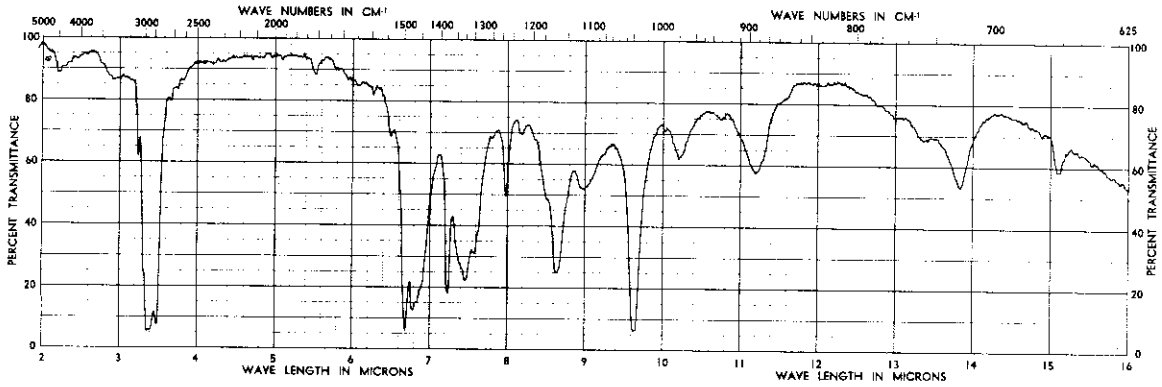
2-(N,N-Di-n-pentylamino)-3,6-dimethylpyrazine



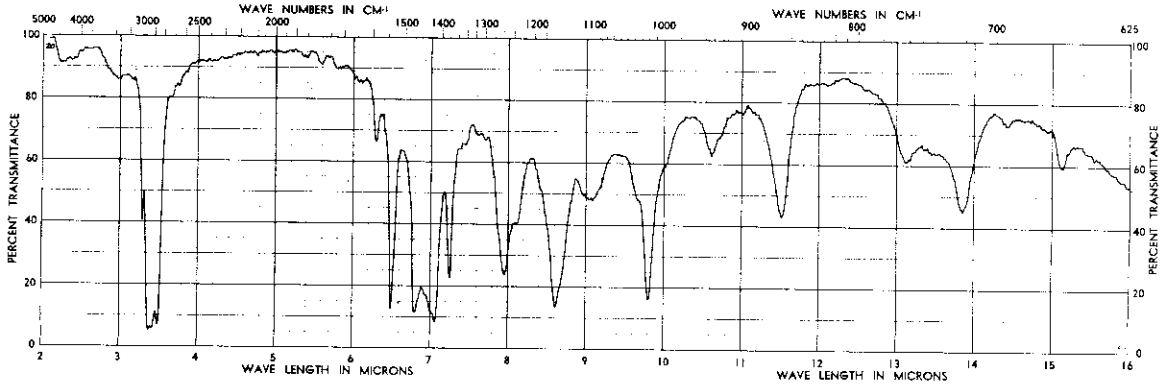
2-(N,N-Di-n-hexylamino)-3,6-dimethylpyrazine

Approved for Public Release

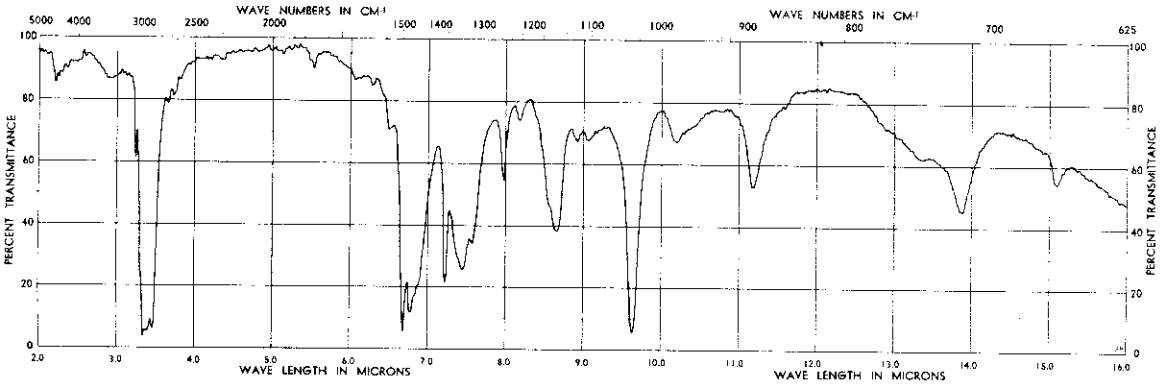
Contrails



2-n-Heptyl-5-methylpyrazine



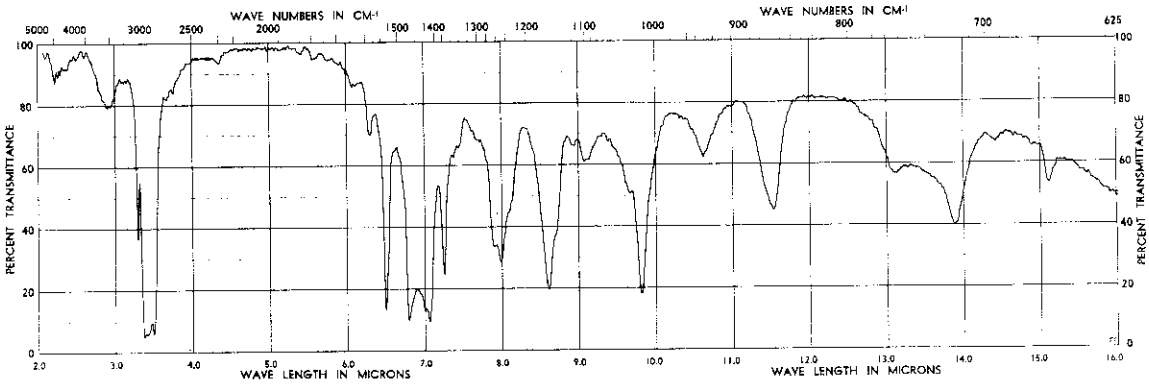
2-n-Heptyl-6-methylpyrazine



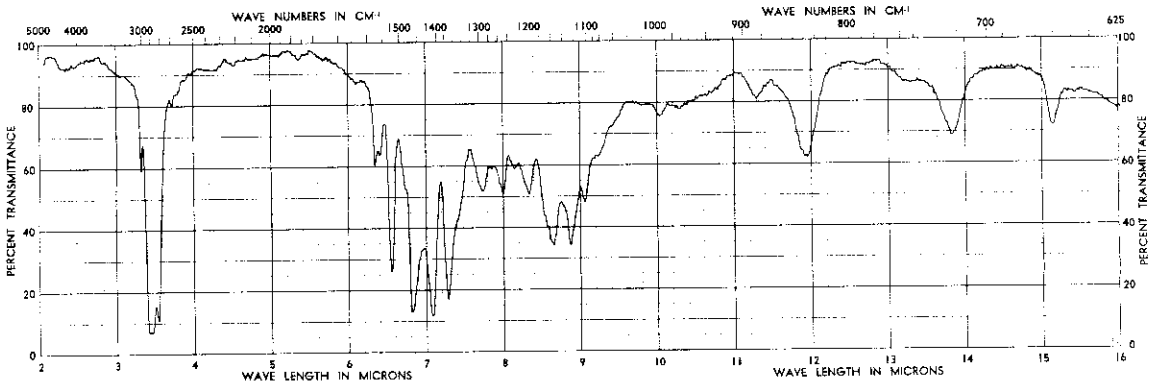
2-n-Nonyl-5-methylpyrazine

Approved for Public Release

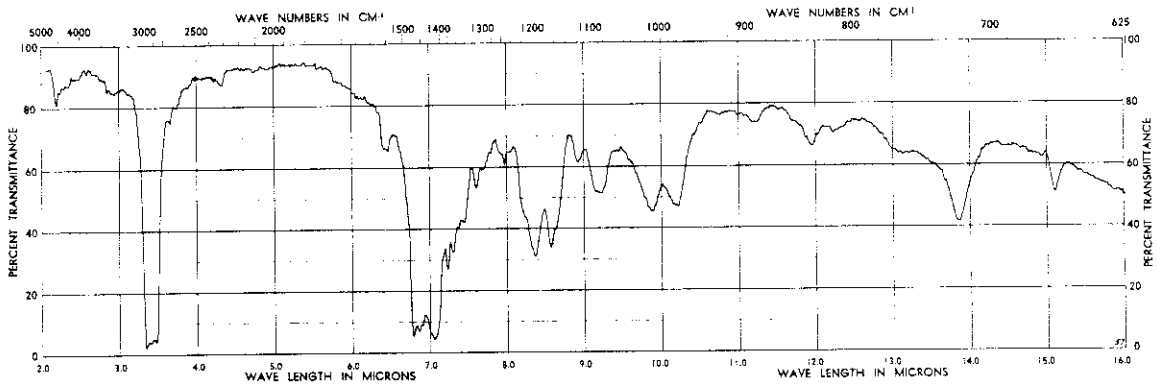
Contrails



2-n-Nonyl-6-methylpyrazine



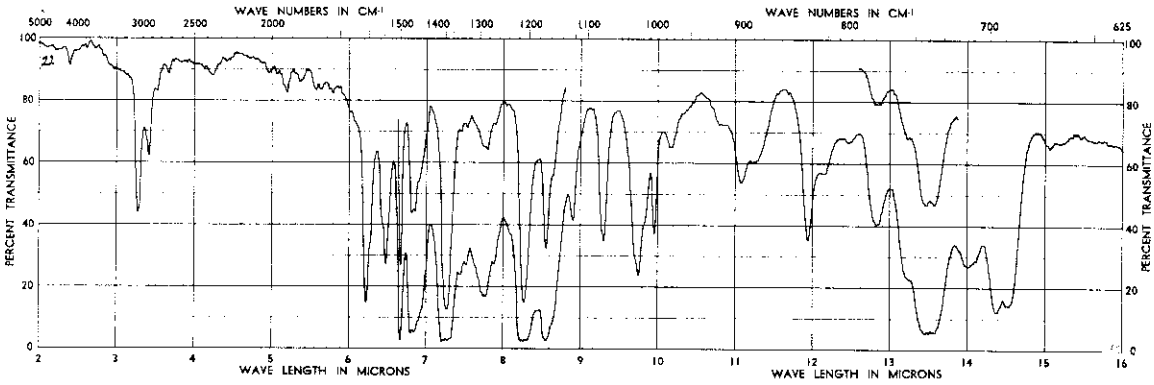
2-n-Heptyl-3,5,6-trimethylpyrazine



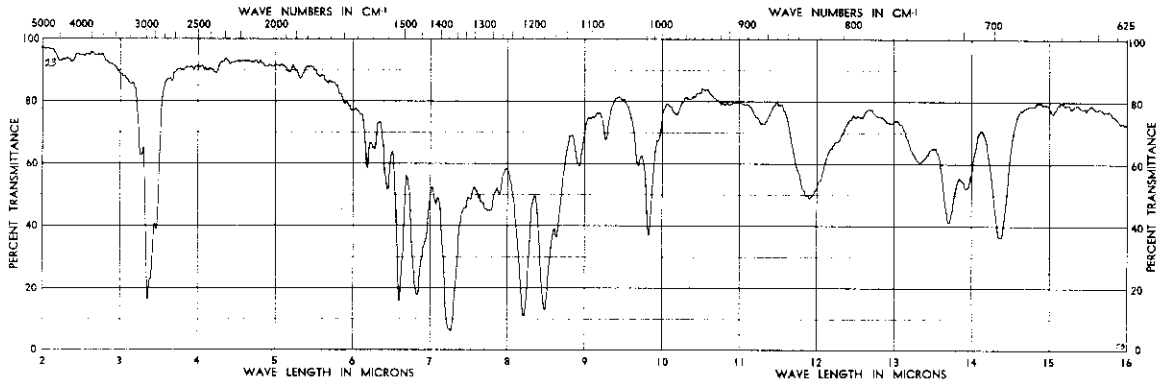
2,5-Di-n-heptyl-3,6-dimethylpyrazine

Approved for Public Release

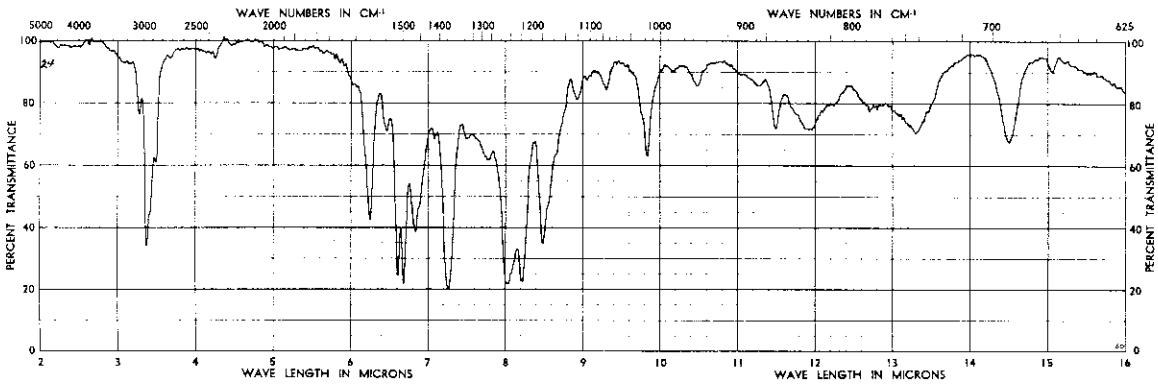
Contrails



2-Phenoxy-3-methyl-6-benzylpyrazine



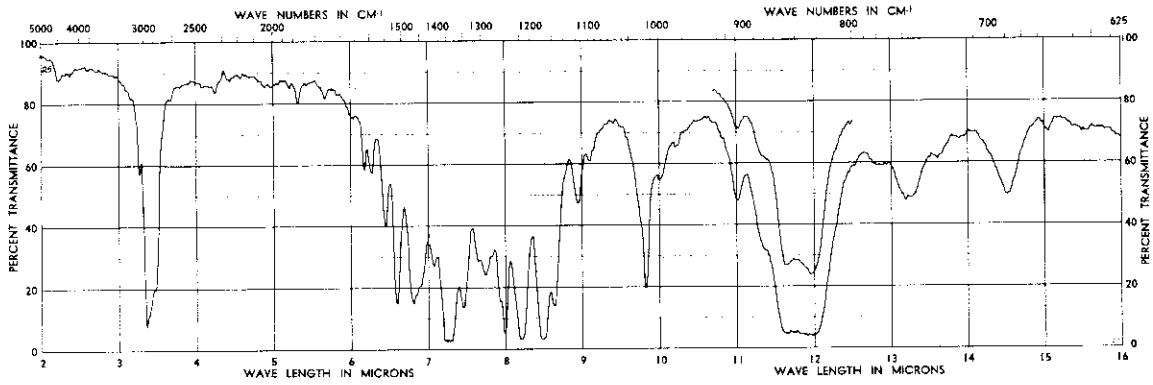
2-(p-Nonylphenoxy)-3-methyl-6-benzylpyrazine



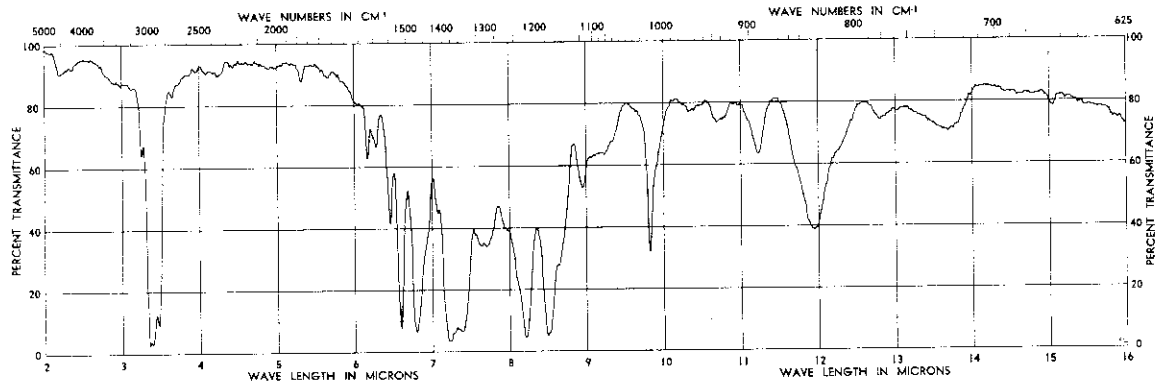
2-(p-Nonylphenoxy)-3-methyl-6-(p-phenoxybenzyl)pyrazine

Approved for Public Release

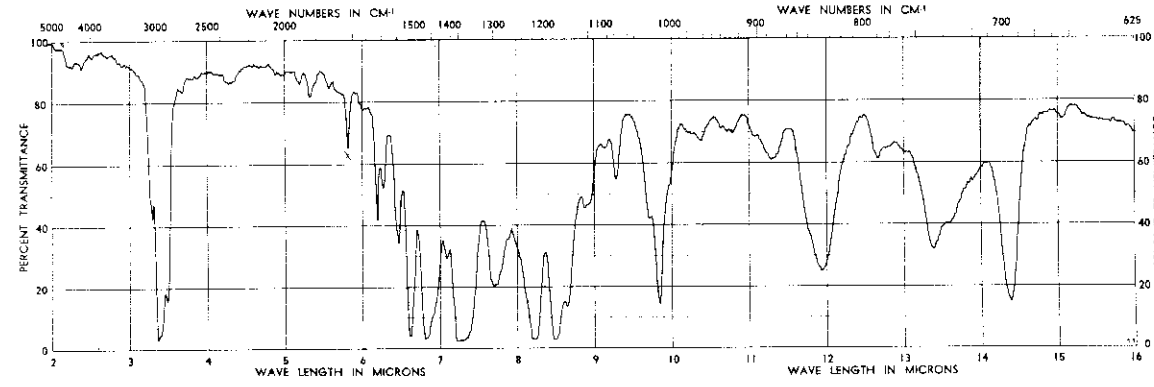
Contrails



2-(p-Nonylphenoxy)-3-methyl-6-(2-trimethylsilylethyl)pyrazine



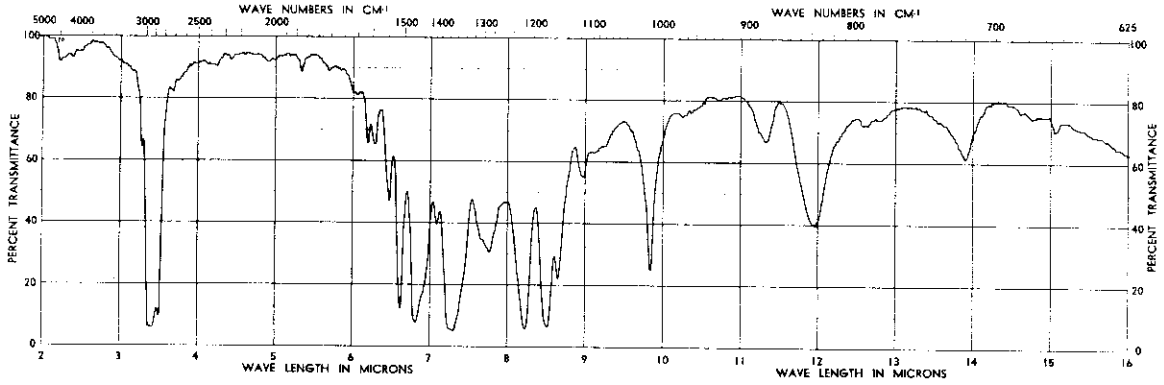
2-(p-Nonylphenoxy)-3-methyl-6-(5-nonyl)pyrazine



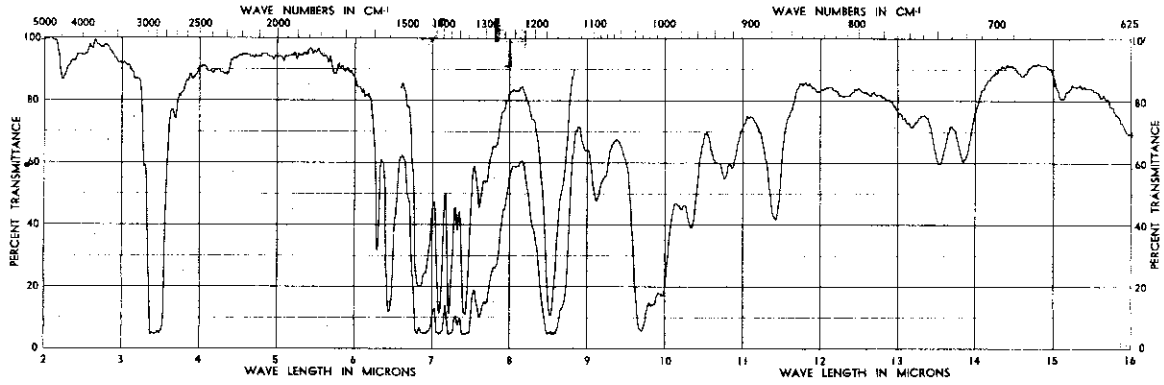
2-(p-Nonylphenoxy)-3-methyl-6-(2-phenylethyl)pyrazine

Approved for Public Release

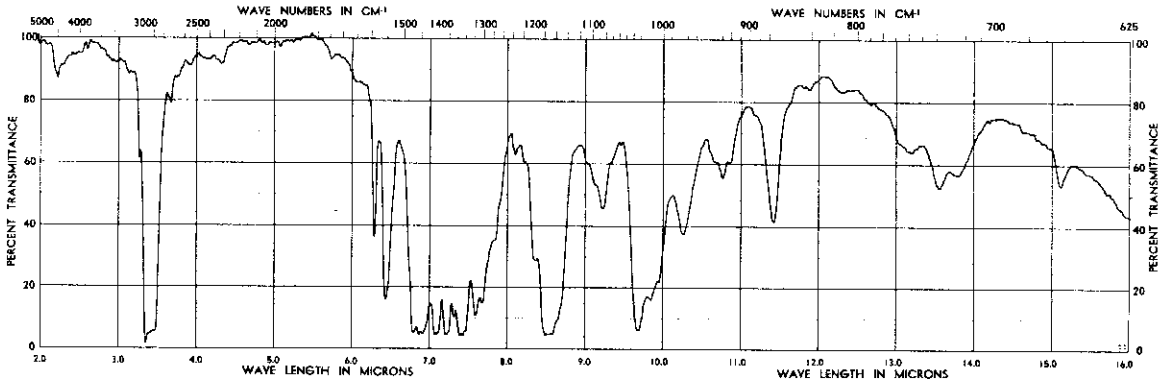
Contrails



2-(p-Nonylphenoxy)-3-methyl-6-tridecylpyrazine



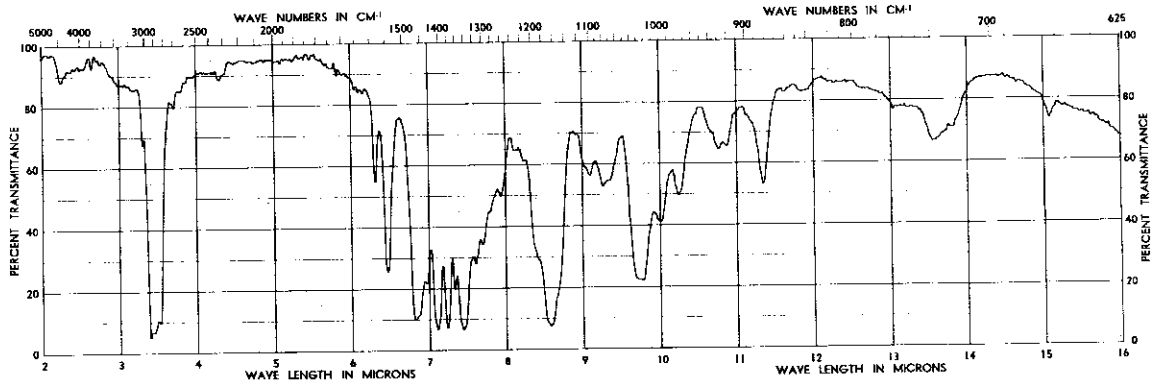
2-(2,2-Dimethylpentoxy)-3-methyl-6-(n-heptyl)pyrazine



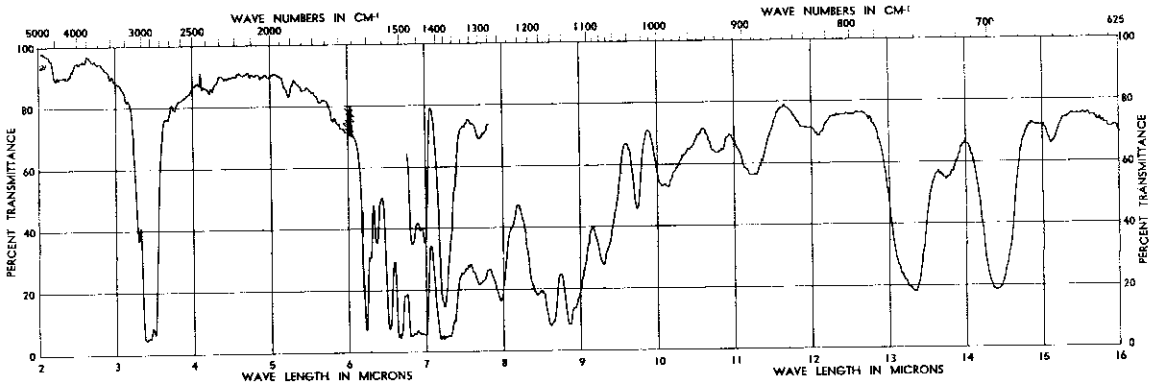
2-(2,2-Dimethylpentoxy)-3-methyl-6-(n-pentyl)pyrazine

Approved for Public Release

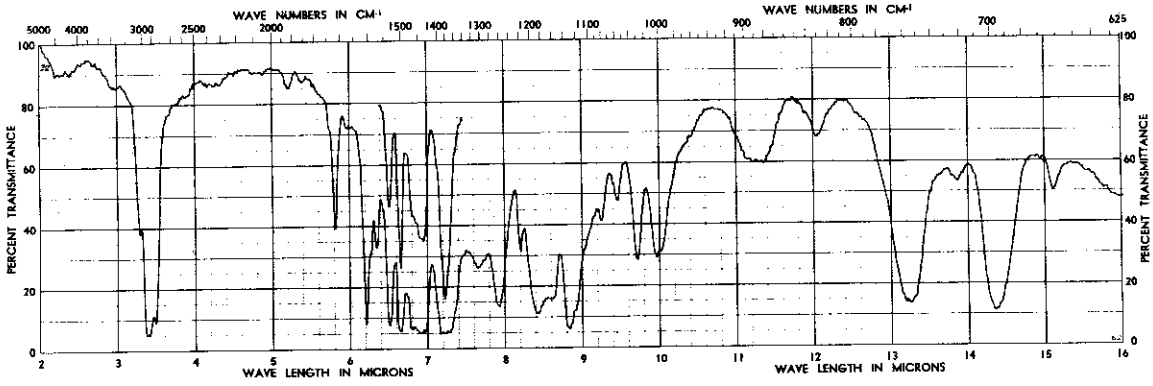
Contrails



2-(2,2-Dimethylpentoxy)-3-methyl-6-(5-nonyl)pyrazine



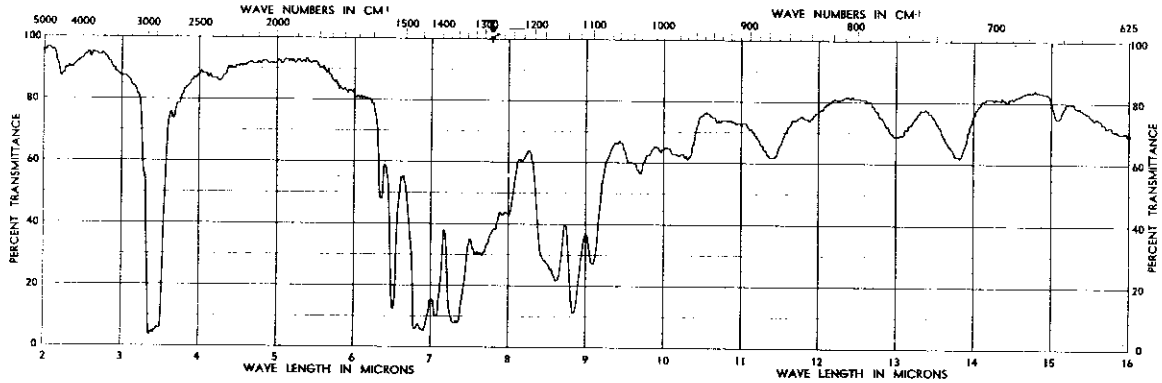
2-(N-Methylanilino)-3-methyl-6-(5-nonyl)pyrazine



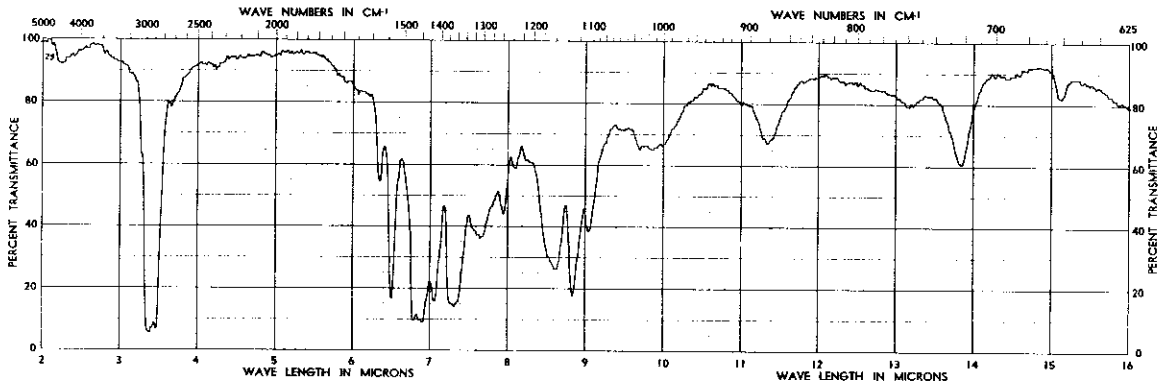
2-(N-Methylanilino)-3-methyl-6-(n-heptyl)pyrazine

Approved for Public Release

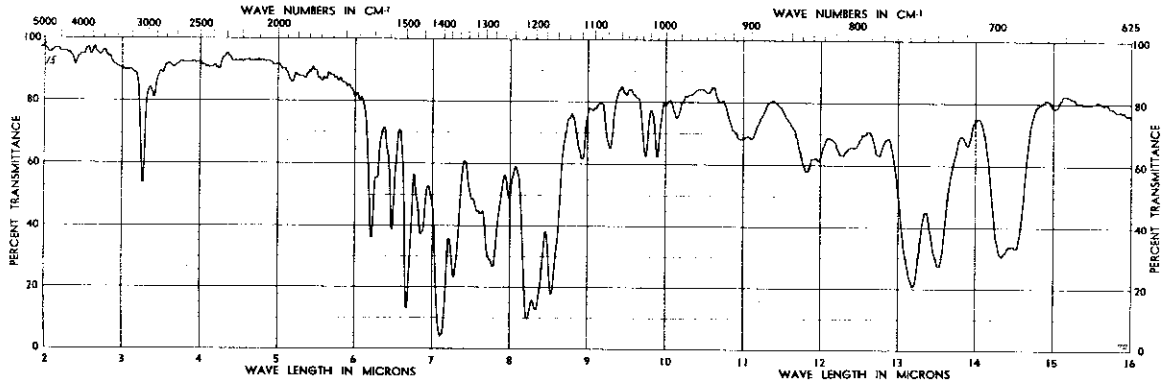
Contrails



2-(N,N-Di-n-pentylamino)-3-methyl-6-(n-heptyl)pyrazine



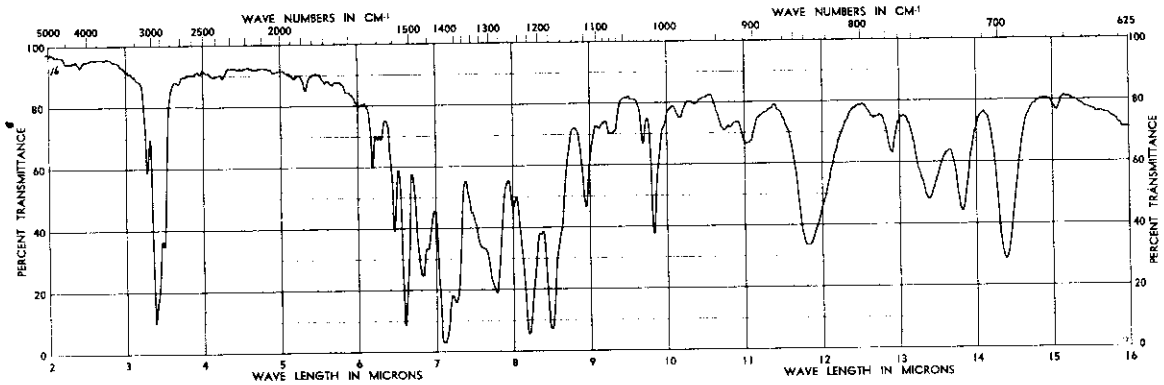
2-(N,N-Di-n-hexylamino)-3-methyl-6-(n-heptyl)pyrazine



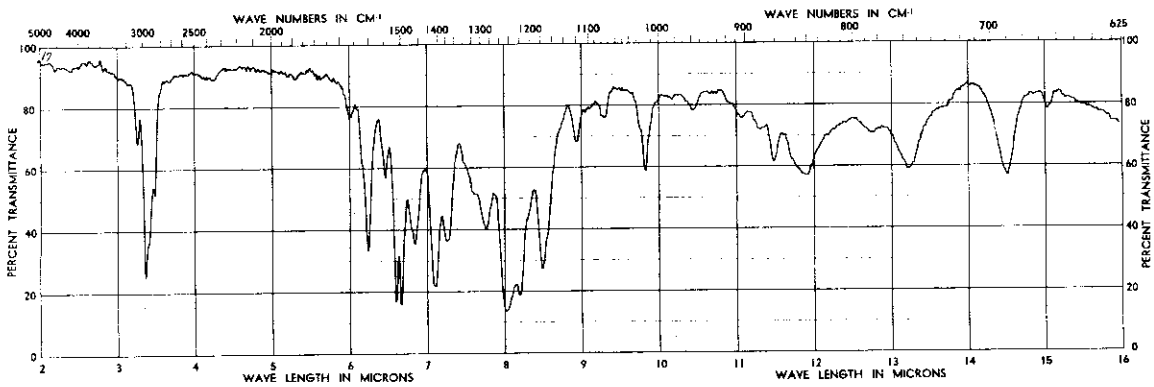
2-Phenoxy-3-(p-phenylbenzyl)pyrazine

Approved for Public Release

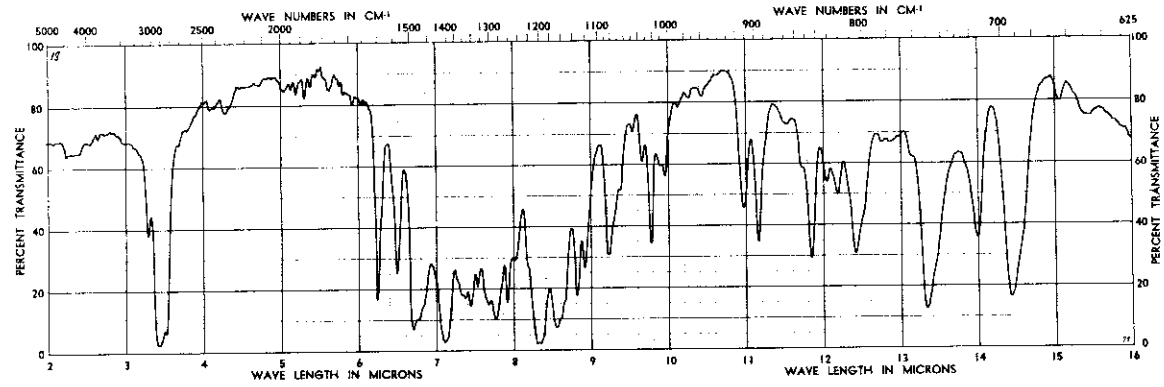
Contrails



2-(p-Nonylphenoxy)-3-benzylpyrazine



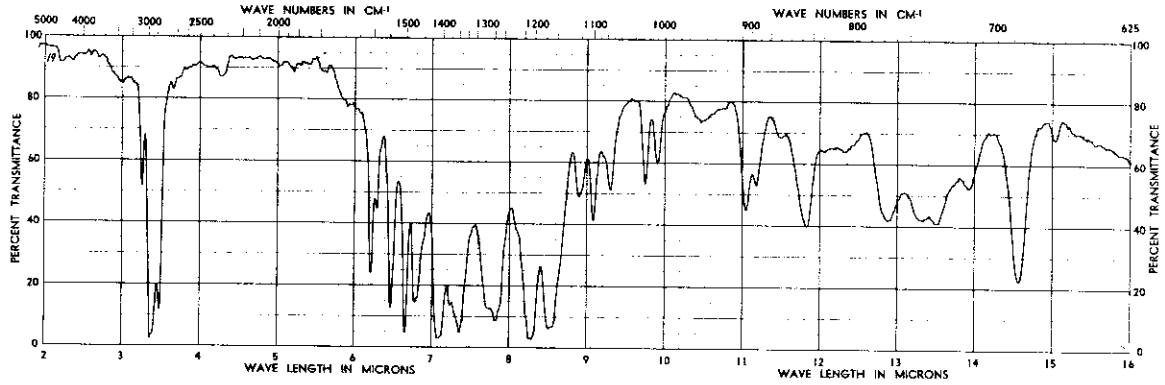
2-(p-Nonylphenoxy)-3-(p-phenoxybenzyl)pyrazine



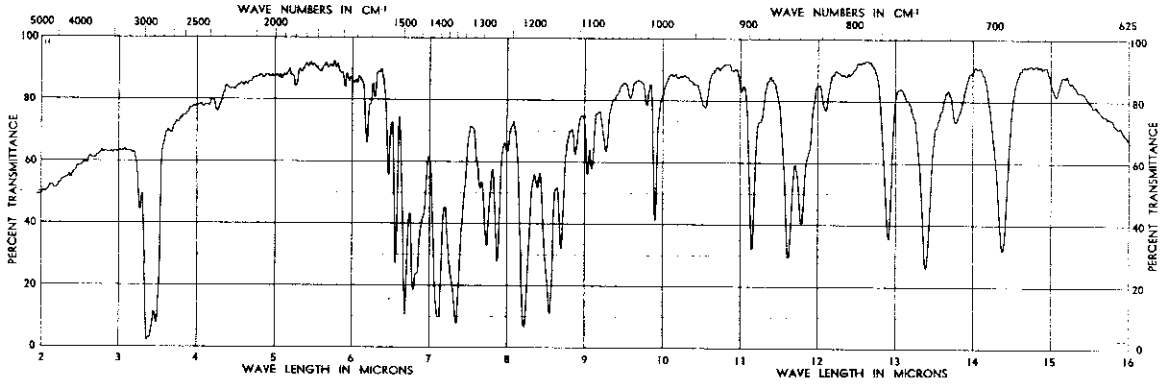
2-Phenoxy-3-tridecylpyrazine

Approved for Public Release

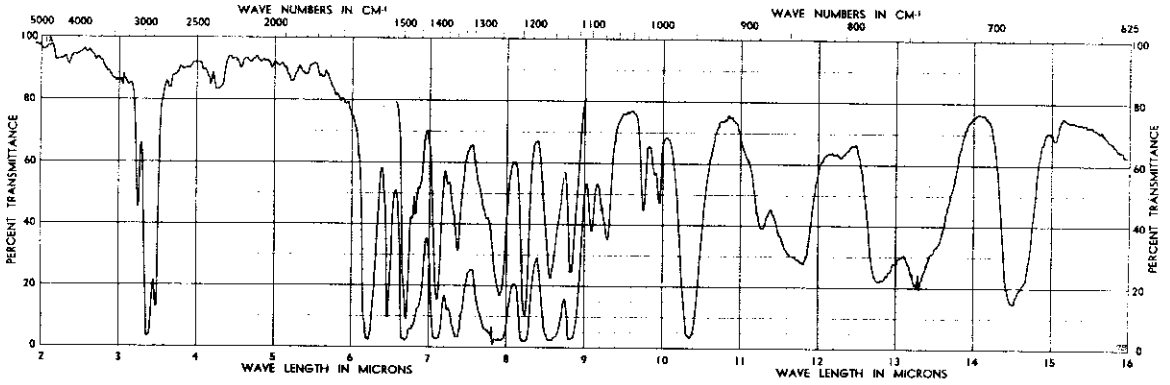
Contrails



2-Phenoxy-3-(5-nonyl)pyrazine



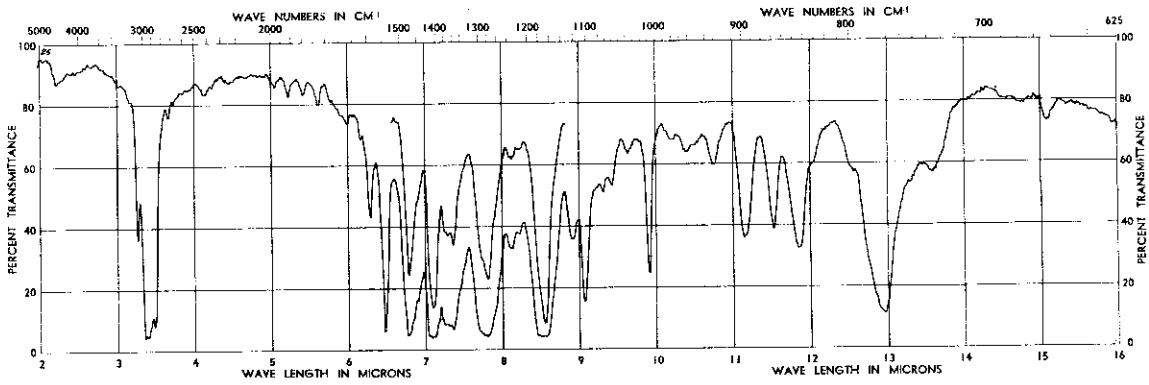
2-(p-Phenylphenoxy)-3-(5-nonyl)pyrazine



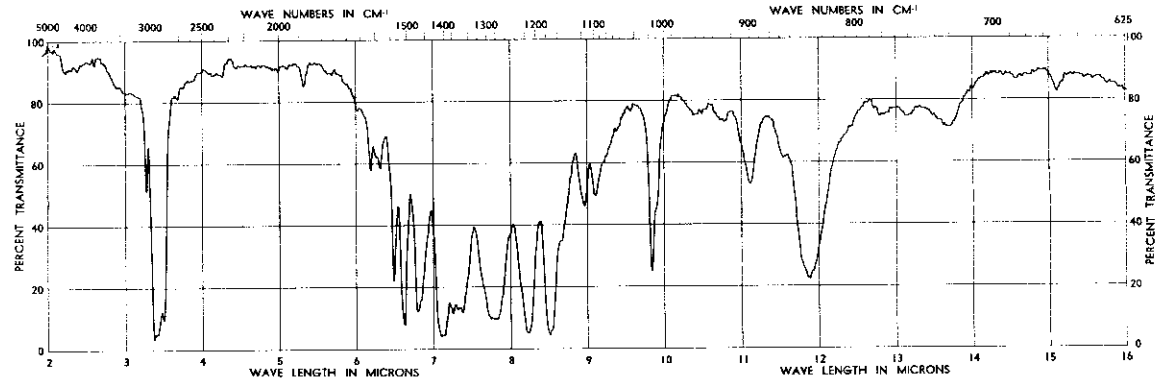
2-(m-Phenoxyphenoxy)-3-(5-nonyl)pyrazine

Approved for Public Release

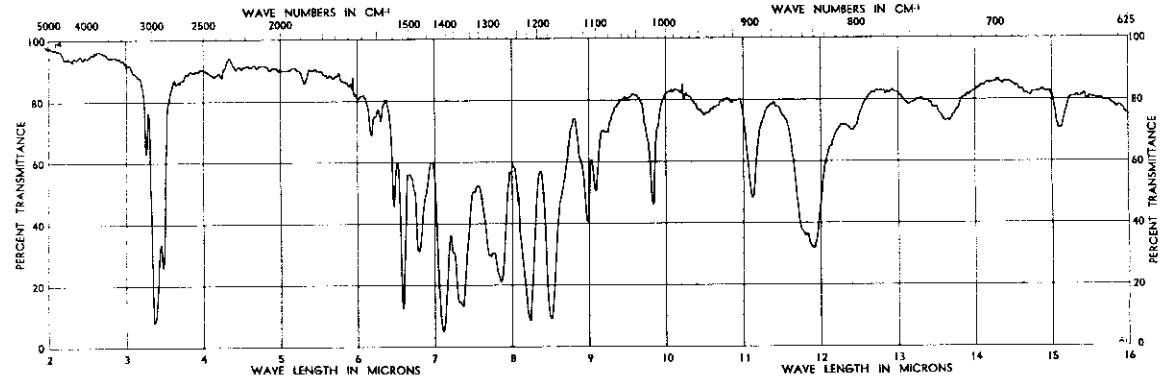
Contrails



2-(2-Methyl-6-ethylphenoxy)-3-(5-nonyl)pyrazine



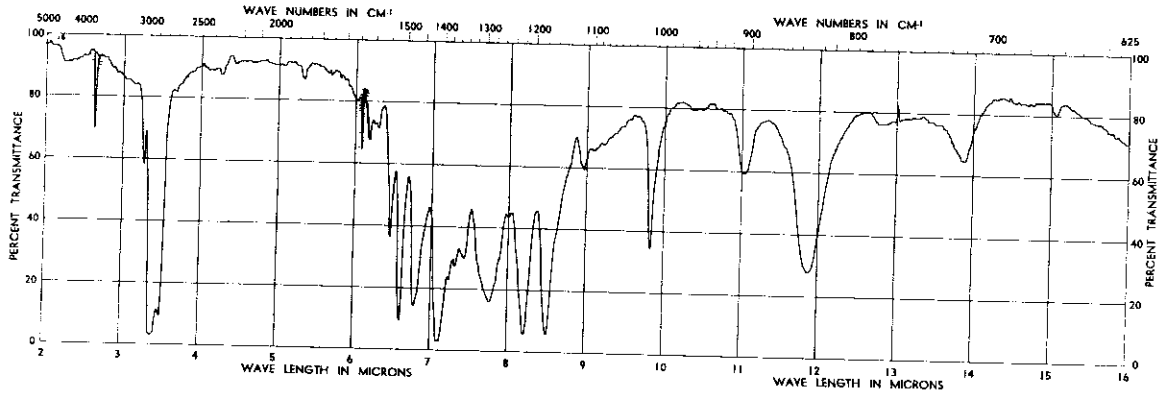
2-(p-Nonylphenoxy)-3-pentylpyrazine



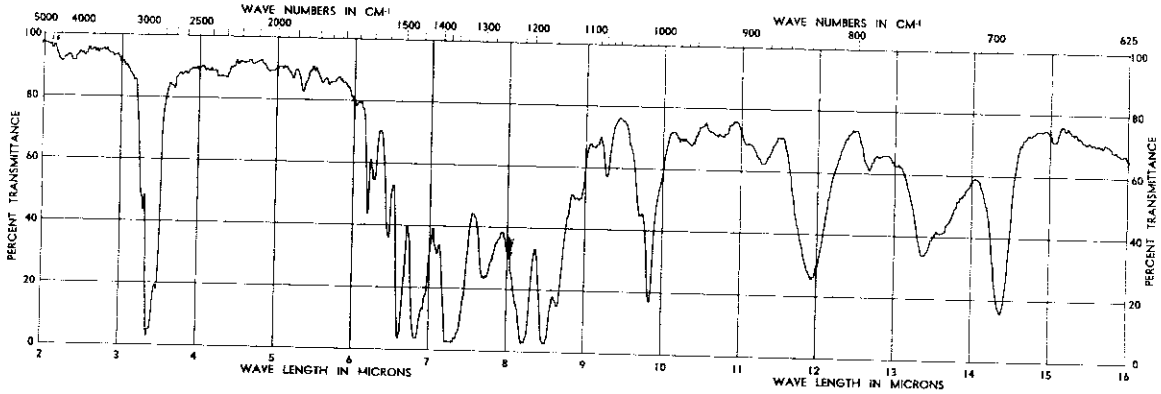
2-(p-t-Butylphenoxy)-3-(5-nonyl)pyrazine

Approved for Public Release

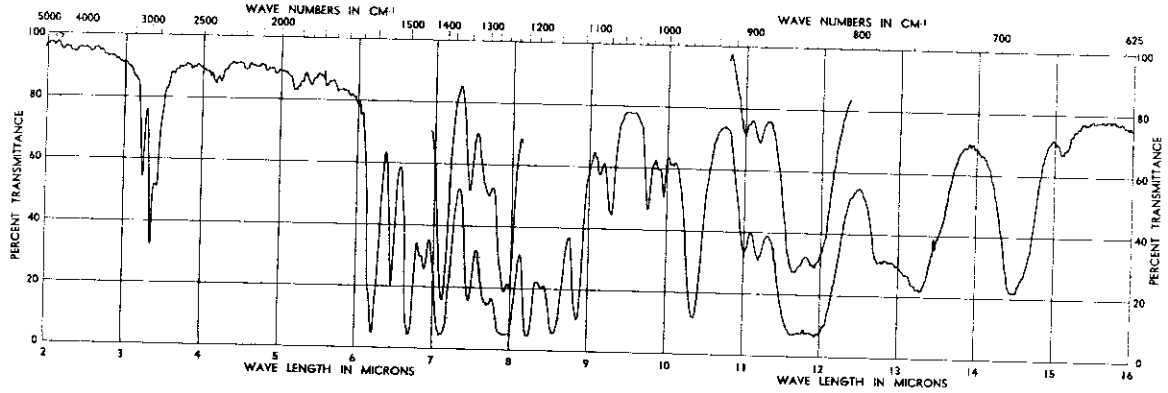
Contrails



2-(p-Nonylphenoxy)-3-tridecylpyrazine



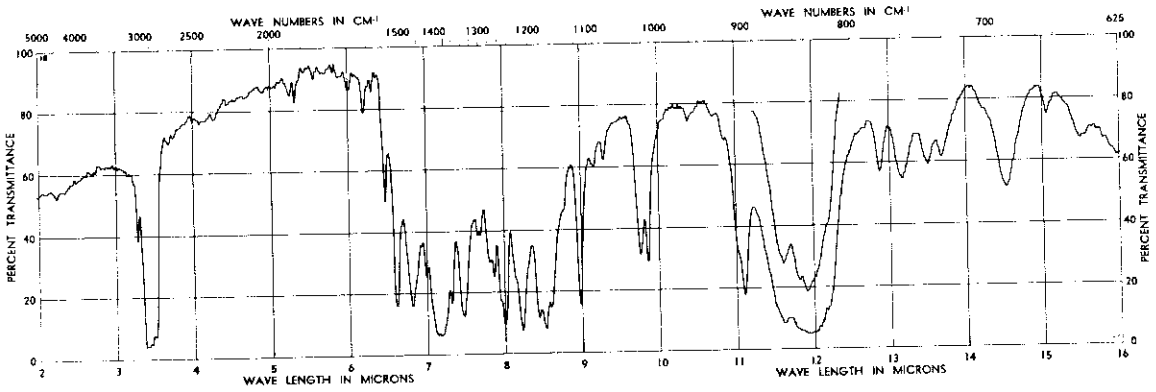
2-(p-Nonylphenoxy)-3-(2-phenylethyl)pyrazine



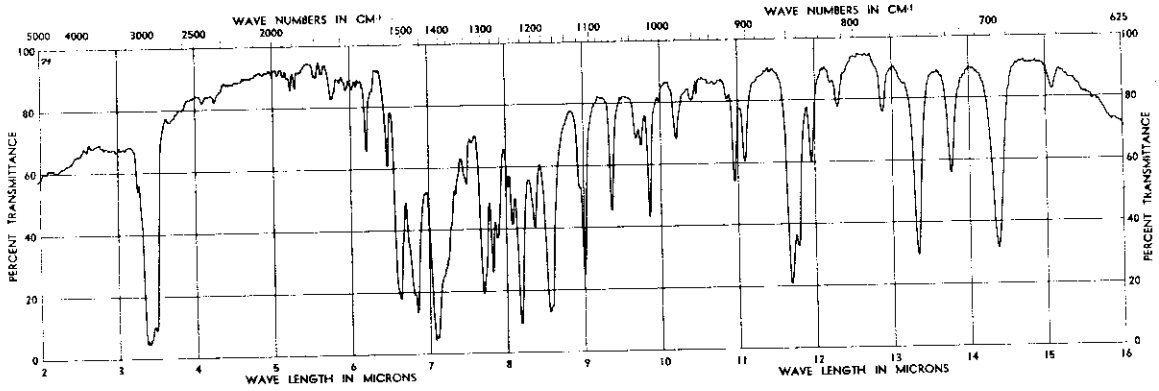
2-(m-Phenoxyphenoxy)-3-(2-trimethylsilylethyl)pyrazine

Approved for Public Release

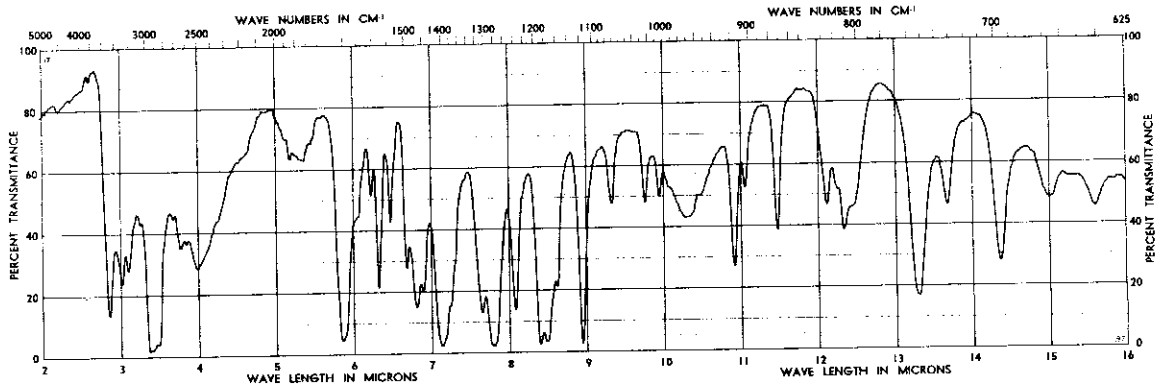
Contrails



2-(p-t-Butylphenoxy)-3-(2-trimethylsilylethyl)pyrazine



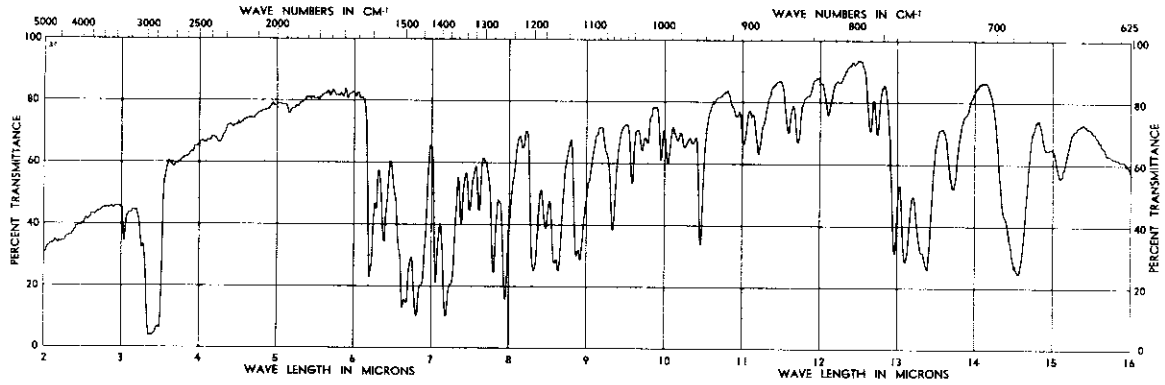
2-(p-t-Butylphenoxy)-3-(2-phenylethyl)pyrazine



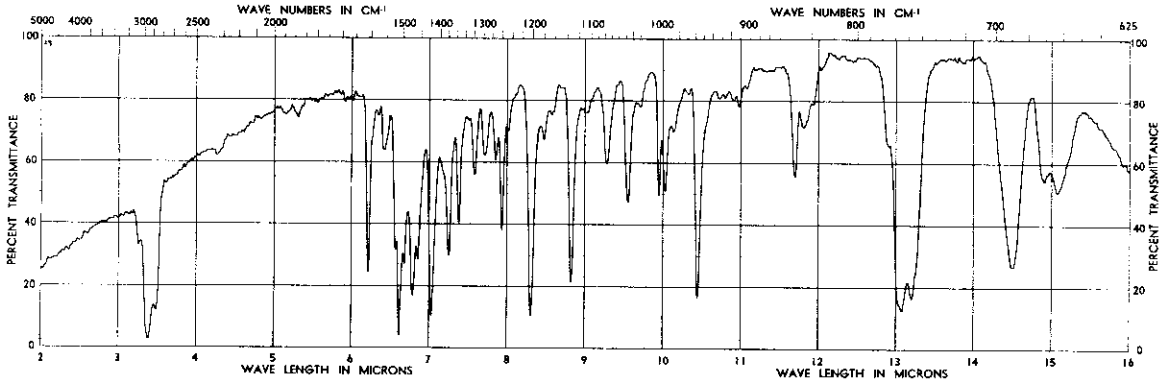
2-Phenoxy-3-pyrazinoic acid Monohydrate

Approved for Public Release

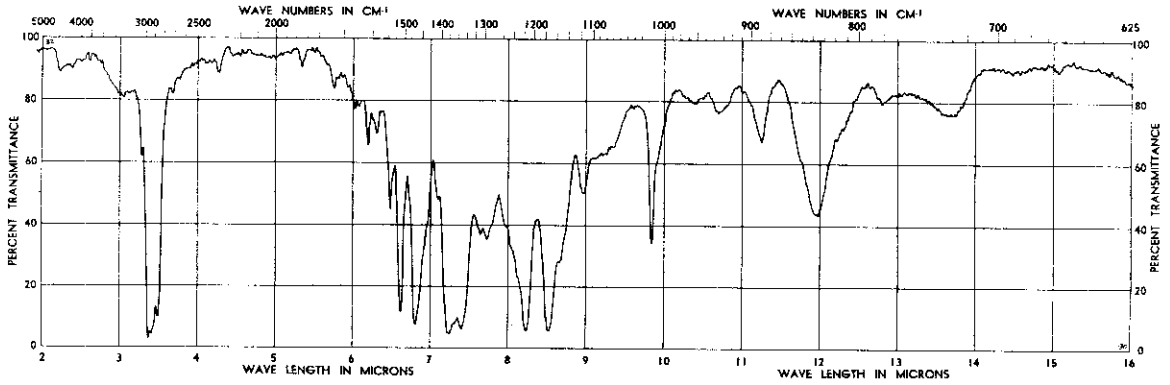
Contrails



2-Phenoxy-3-benzoylpyrazine Phenylhydrazone



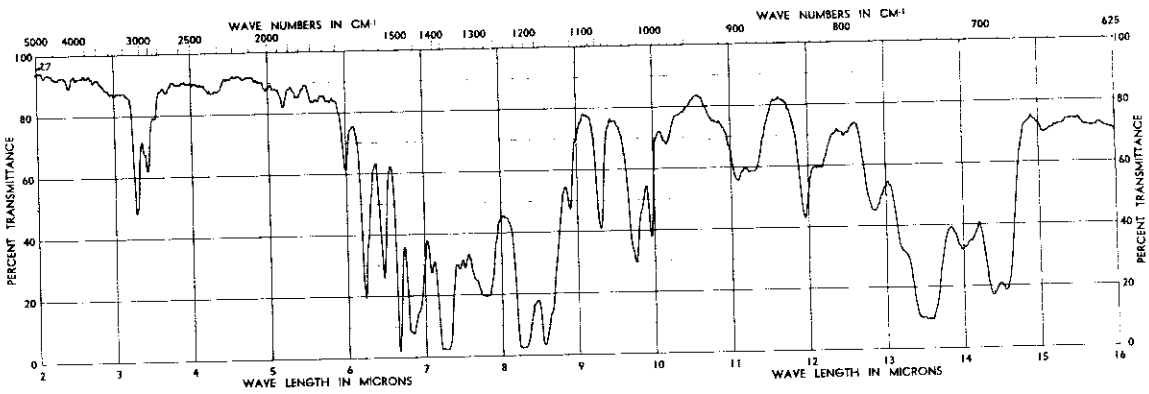
1,3-Diphenylpyrazolo[2,3-b]pyrazine



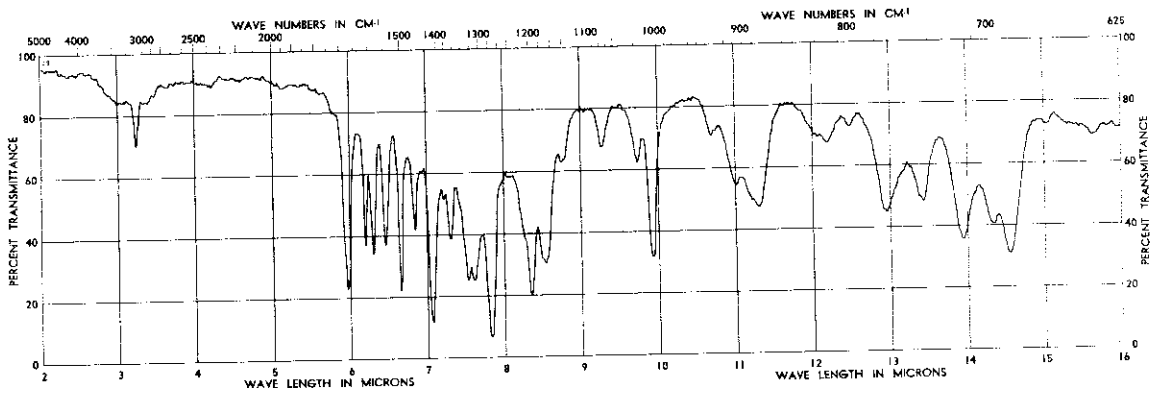
2-(p-Nonylphenoxy)-3-pentyl-6-(5-nonyl)pyrazine

Approved for Public Release

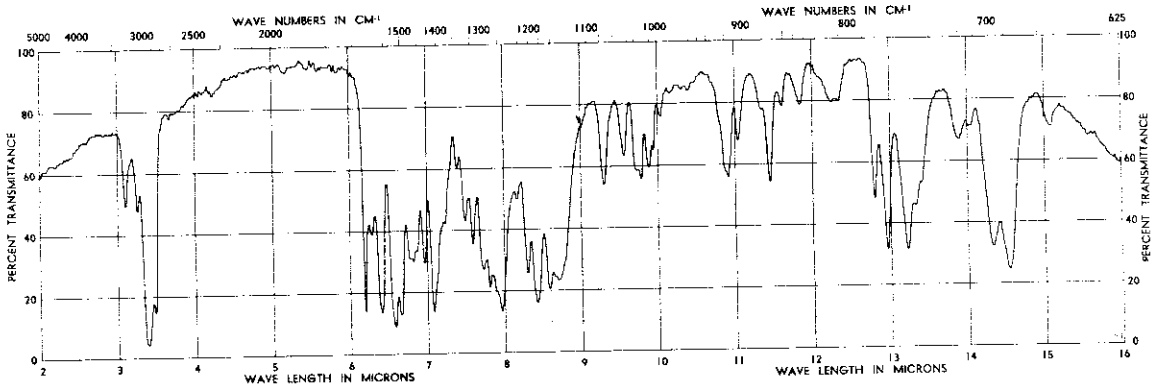
Contrails



2-Phenoxy-6-benzylpyrazine



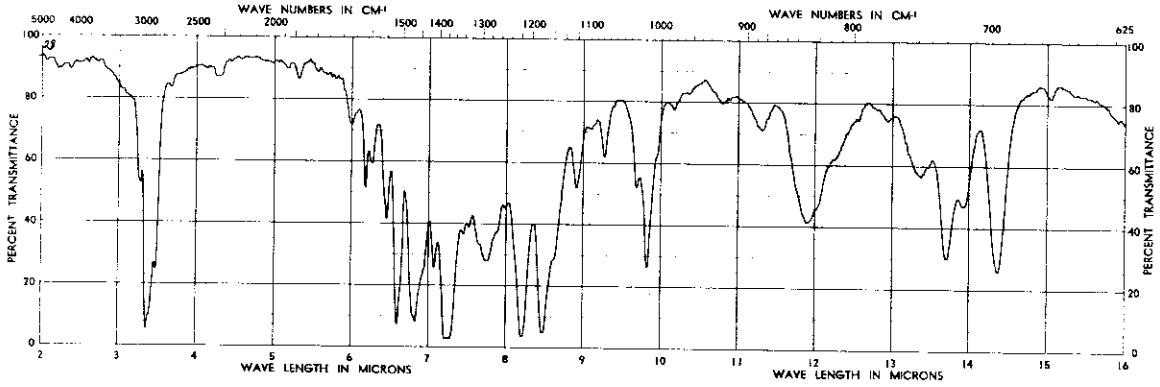
2-Phenoxy-6-benzoylpyrazine



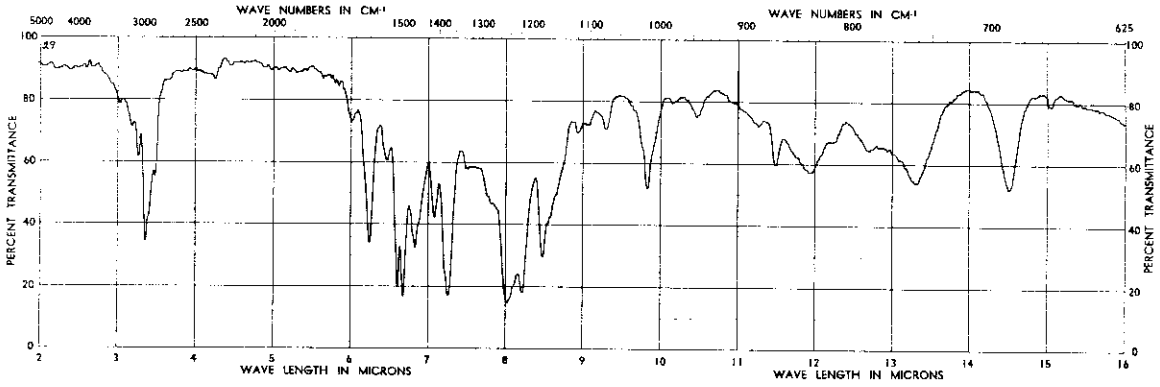
2-Phenoxy-6-benzoylpyrazine Phenylhydrazone

Approved for Public Release

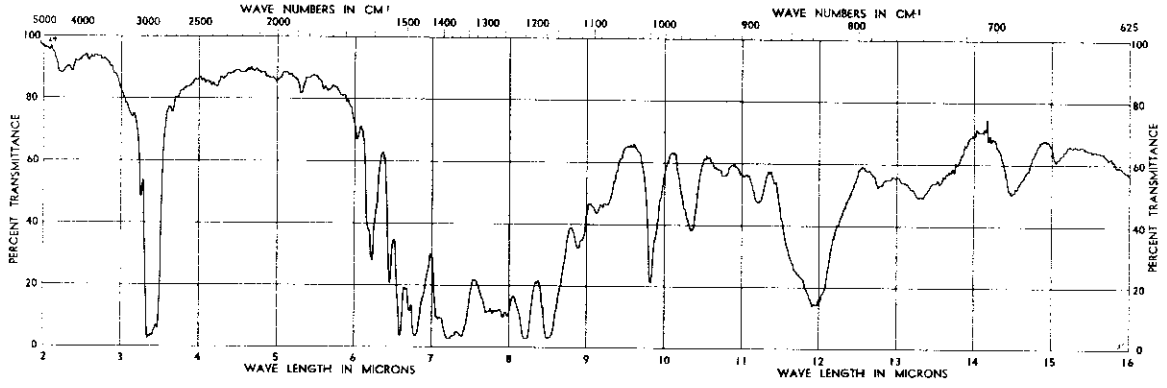
Contrails



2-(p-Nonylphenoxy)-6-benzylpyrazine



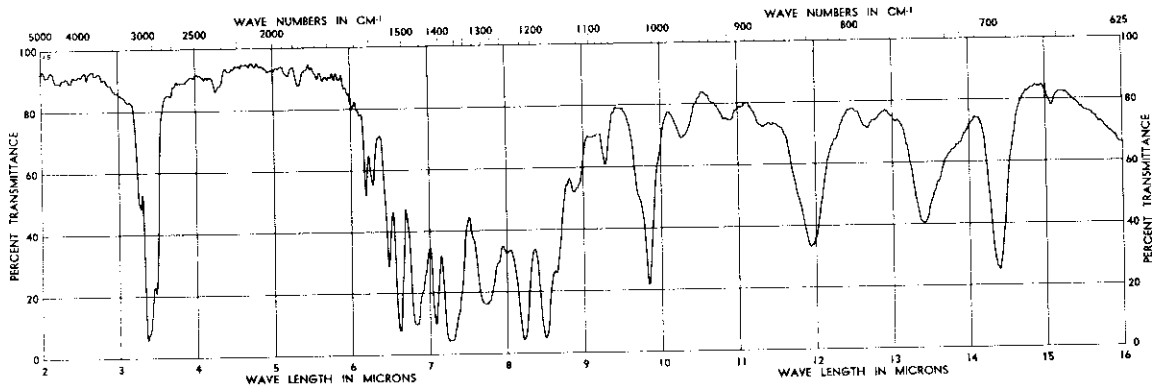
2-(p-Nonylphenoxy)-6-(p-phenoxybenzyl)pyrazine



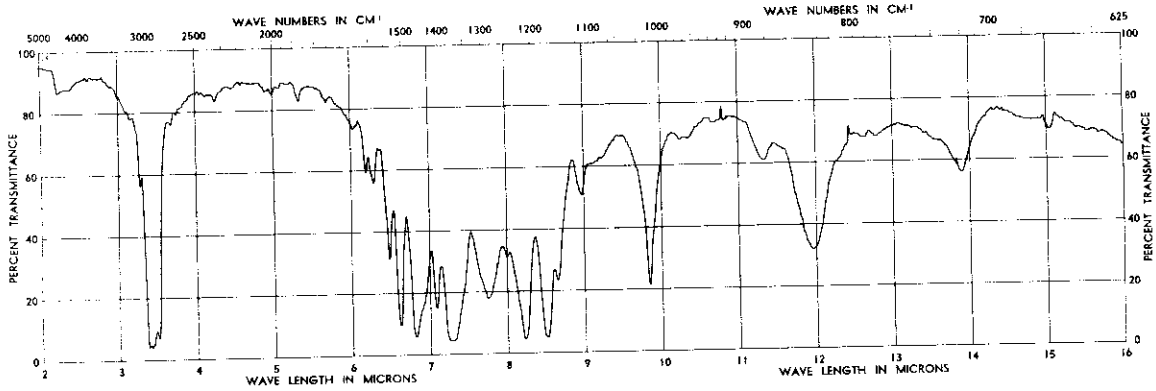
2-(p-Nonylphenoxy)-6-(5-nonyl)pyrazine

Approved for Public Release

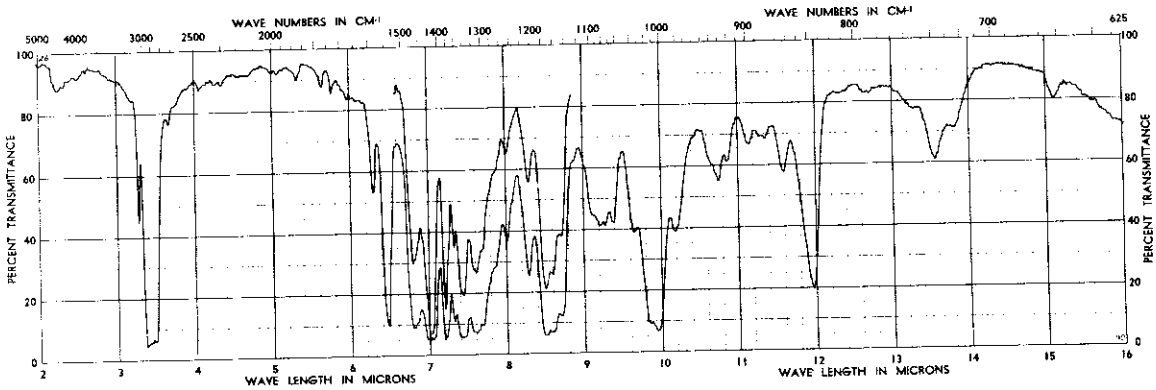
Contrails



2-(p-Nonylphenoxy)-6-(2-phenylethyl)pyrazine



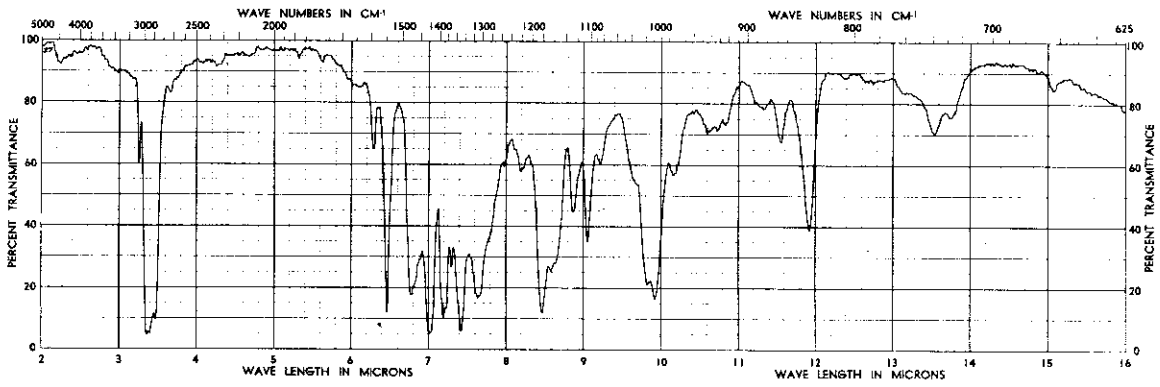
2-(p-Nonylphenoxy)-6-tridecylpyrazine



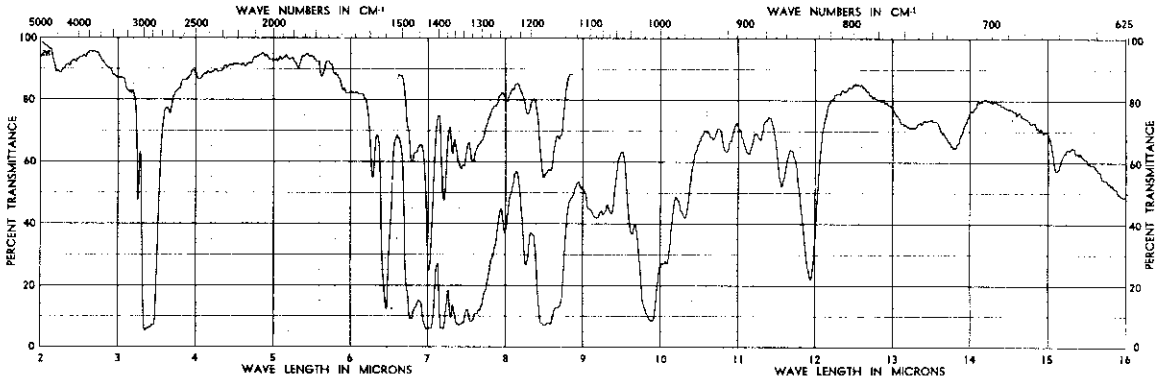
2-(2,2-Dimethylpentoxy)-3-(n-pentyl)pyrazine

Approved for Public Release

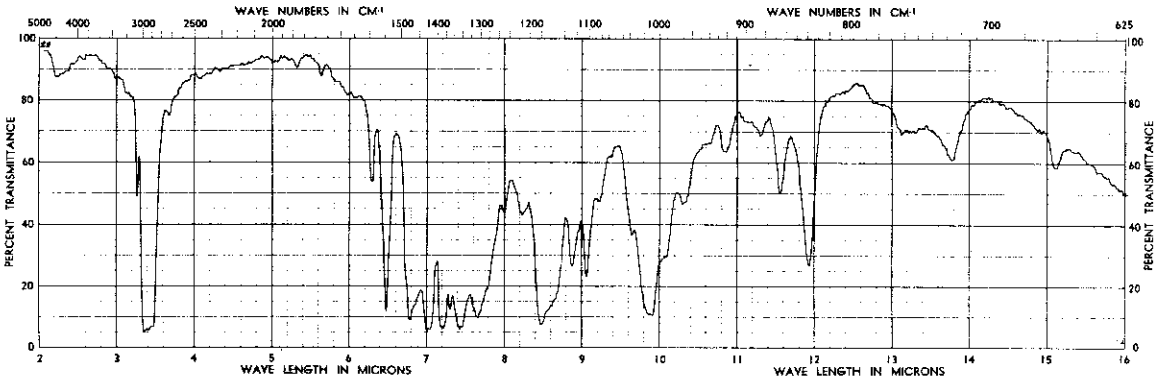
Contrails



2-(2,2-Dimethylpentoxy)-3-(5-nonyl)pyrazine



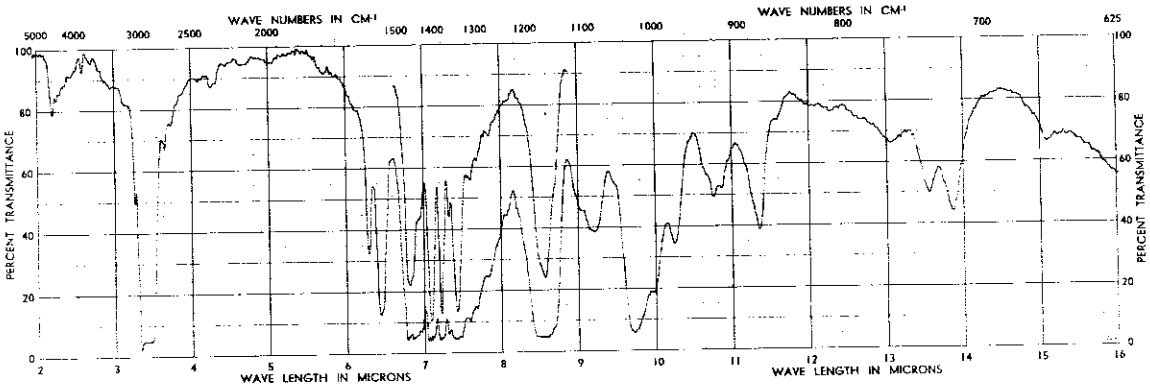
2-(2,2,4-Trimethylpentoxy)-3-(n-pentyl)pyrazine



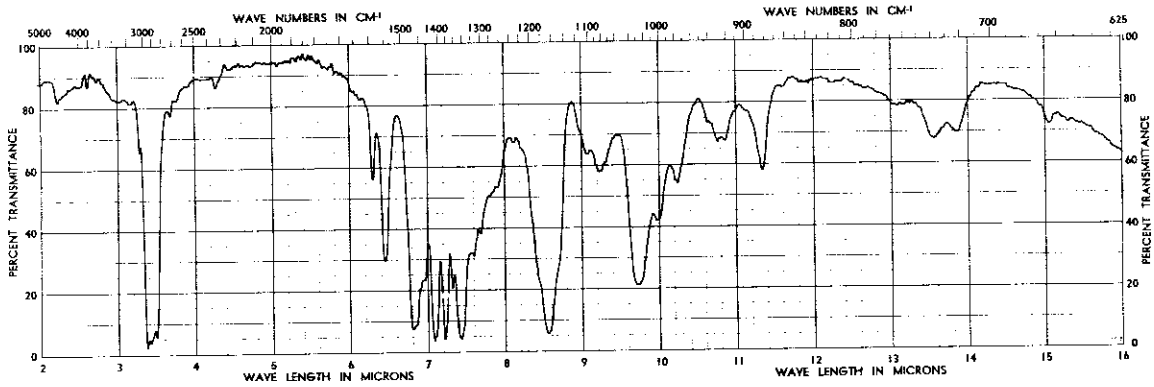
2-(2,2,4-Trimethylpentoxy)-3-(5-nonyl)pyrazine

Approved for Public Release

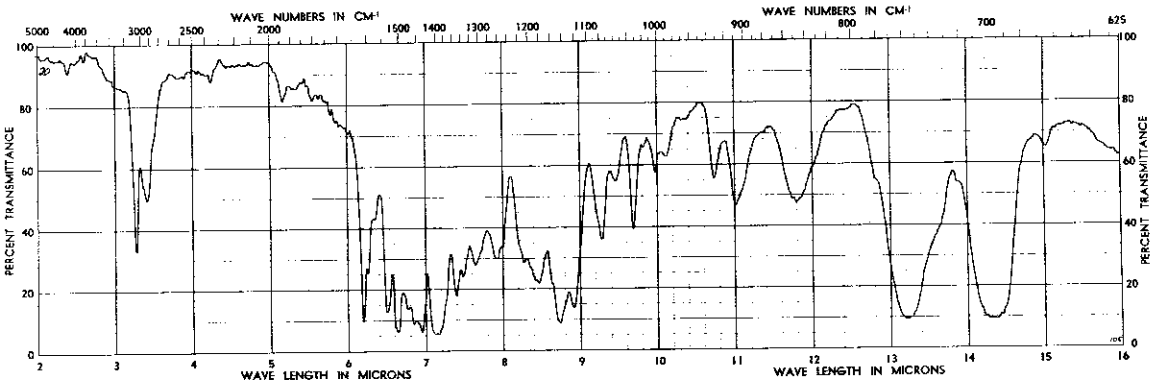
Contrails



2-(2,2-Dimethylpentoxy)-3,6-di(n-heptyl)pyrazine



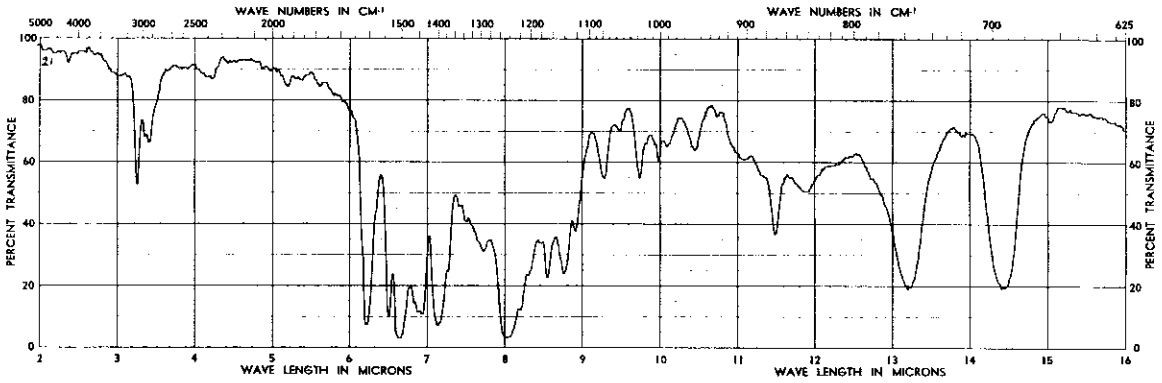
2-(2,2-Dimethylpentoxy)-3-(n-pentyl)-6-(n-heptyl)pyrazine



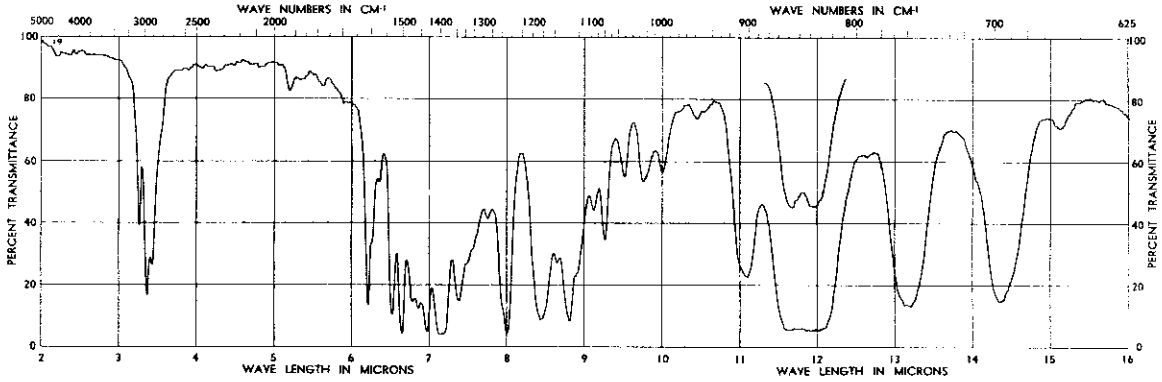
2-(N-Methylanilino)-3-benzylpyrazine

Approved for Public Release

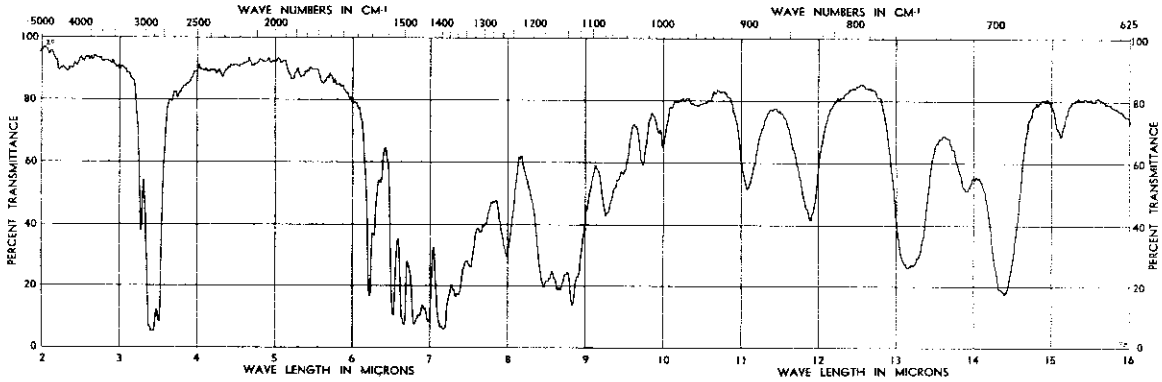
Contrails



2-(N-Methylanilino)-3-(p-phenoxybenzyl)pyrazine



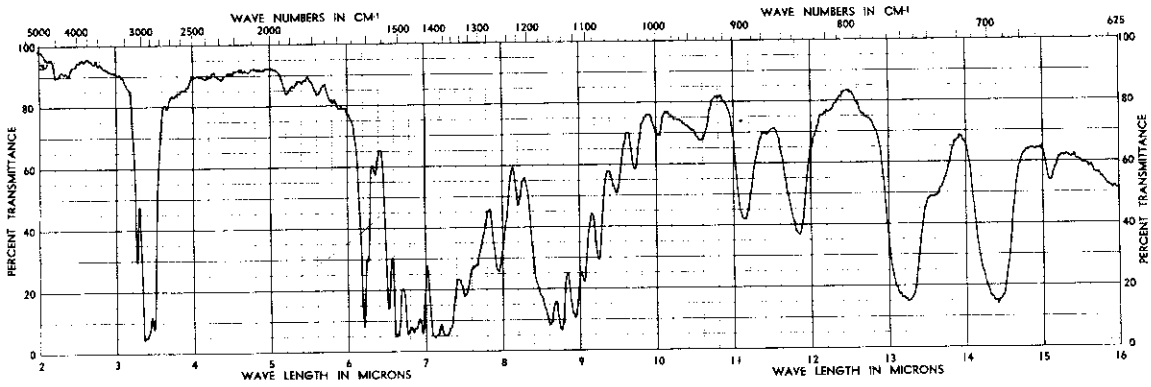
2-(N-Methylanilino)-3-(2-trimethylsilylethyl)pyrazine



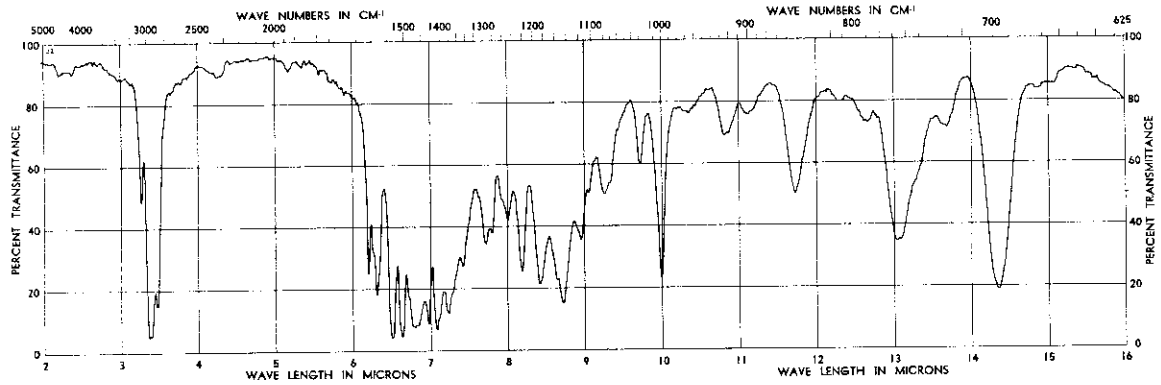
2-(N-Methylanilino)-3-tridecylpyrazine

Approved for Public Release

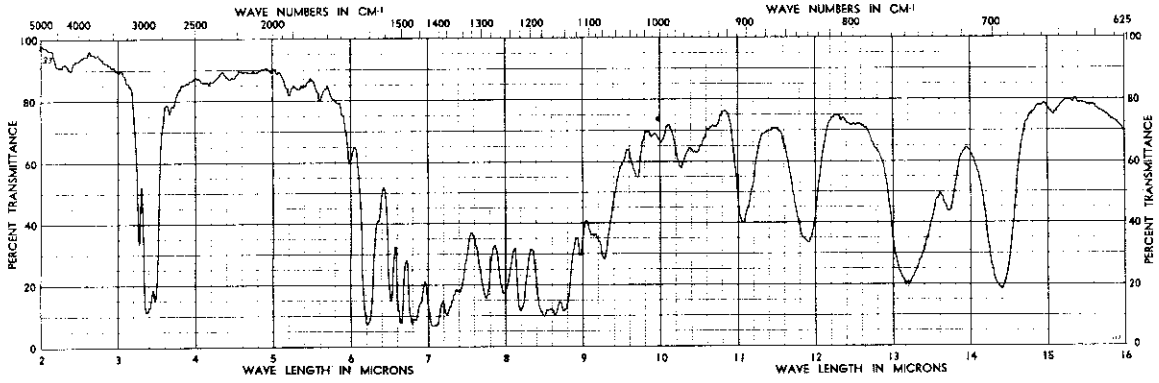
Contrails



2-(N-Butylanilino)-3-pentylpyrazine (from Interaction of 2-(N-Methylanilino)-3-methylpyrazine with 1-Bromobutane)



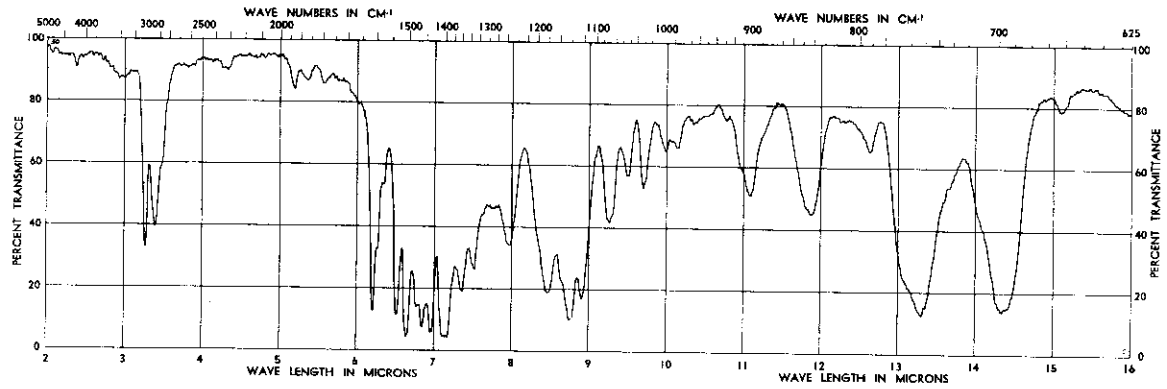
2-(N-Methylanilino)-3-(5-nonyl)pyrazine



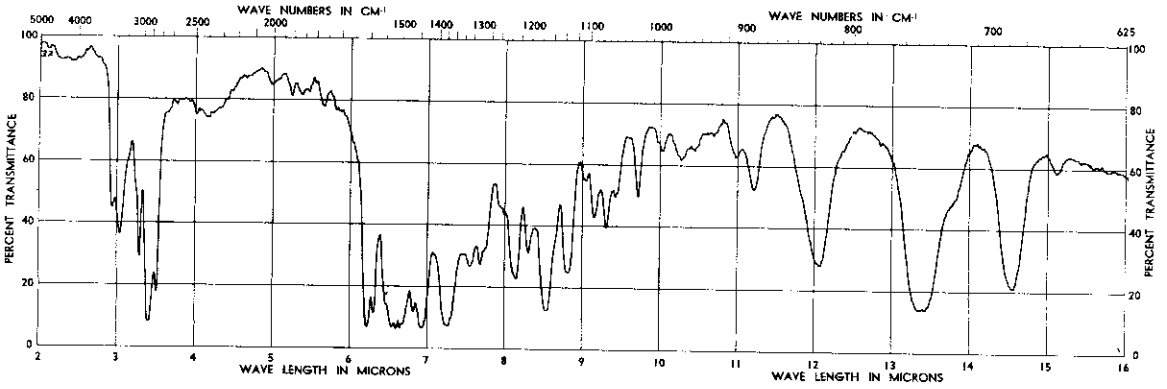
2-(N-Butylanilino)-3-(n-pentyl)pyrazine (from Interaction of 2-Anilino-3-methylpyrazine and 1-Bromobutane)

Approved for Public Release

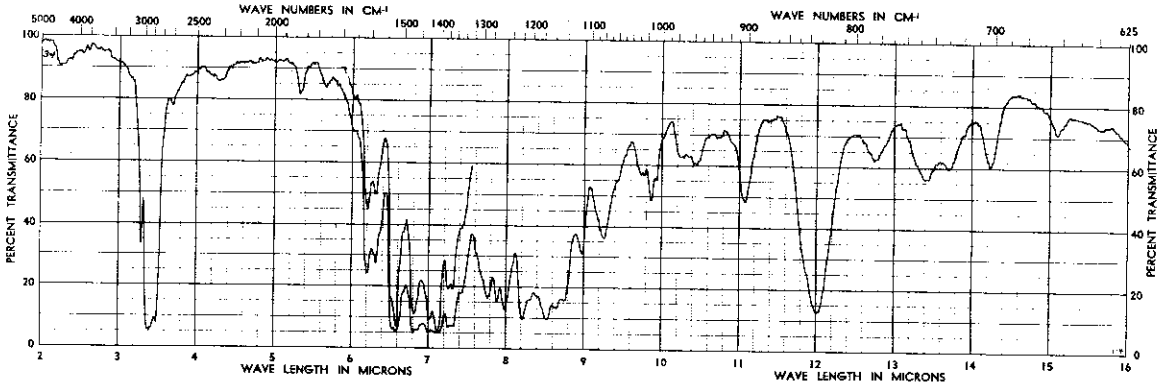
Contrails



2-(N-Methylanilino)-3-(2-phenylethyl)pyrazine



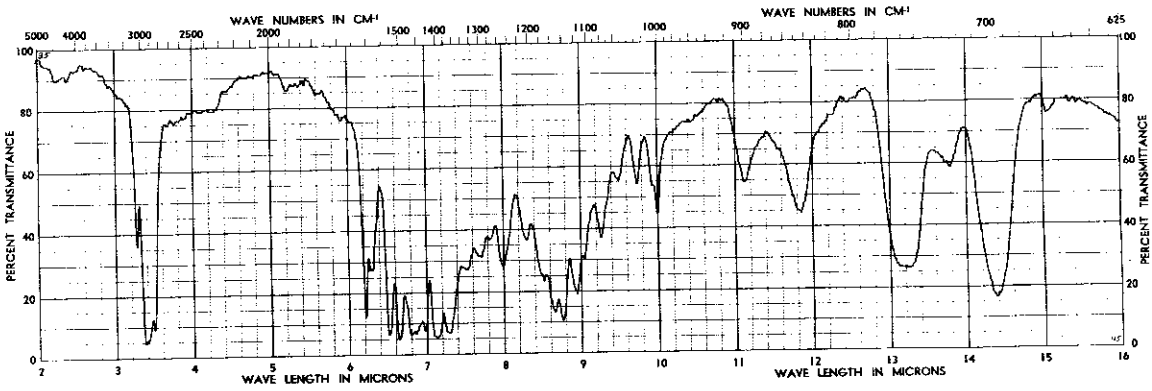
2-Anilino-3-(n-pentyl)pyrazine



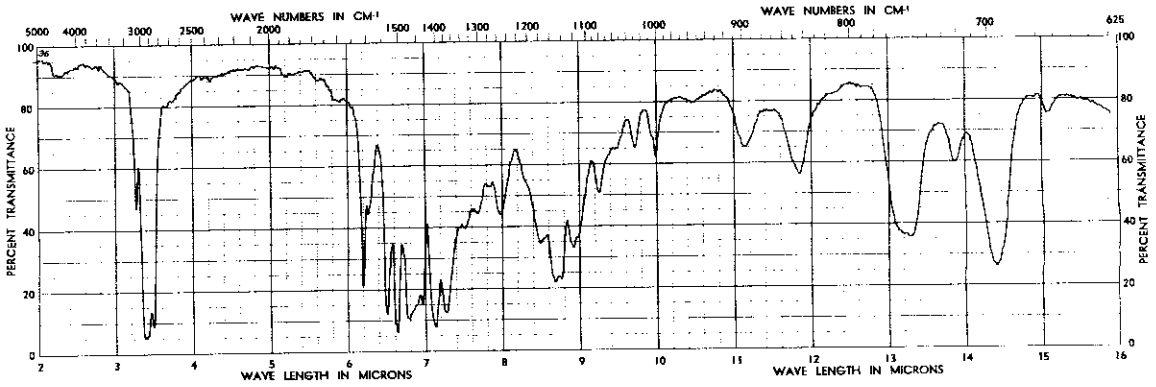
2-(N-Butyl-p-pentylanilino)-3-(n-pentyl)pyrazine

Approved for Public Release

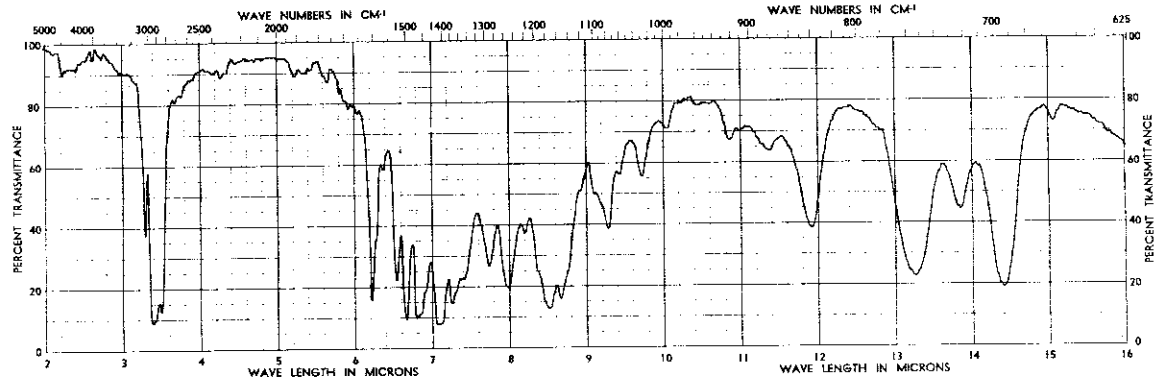
Contrails



2-(N-Methylanilino)-3-(n-hexyl)pyrazine



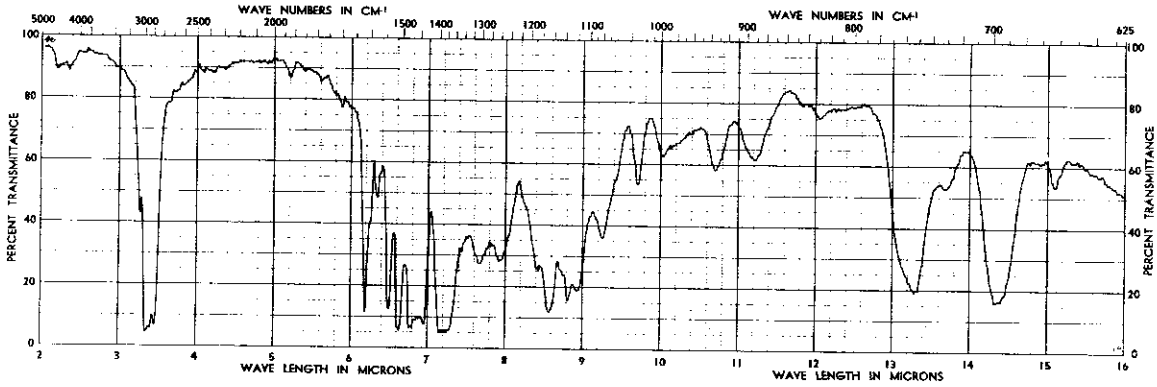
2-(N-Methylanilino)-3-(9-heptadecyl)pyrazine



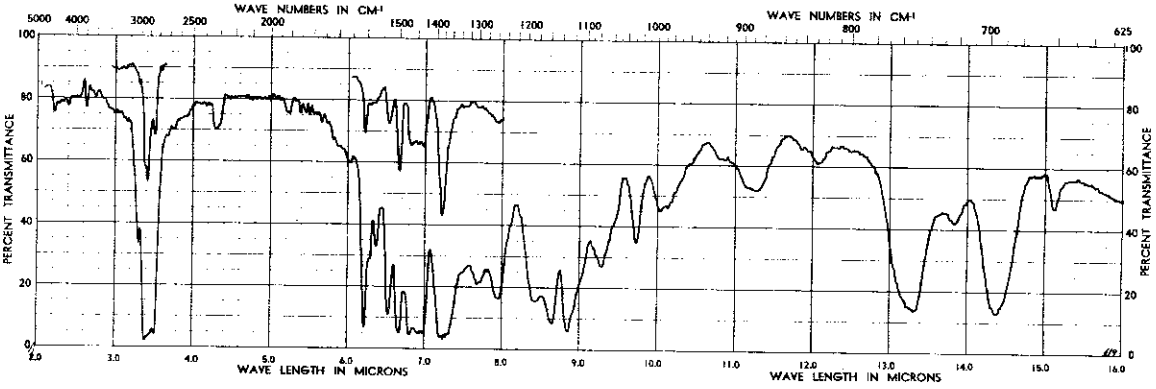
2-(N-n-Hexylanilino)-3-(n-heptyl)pyrazine

Approved for Public Release

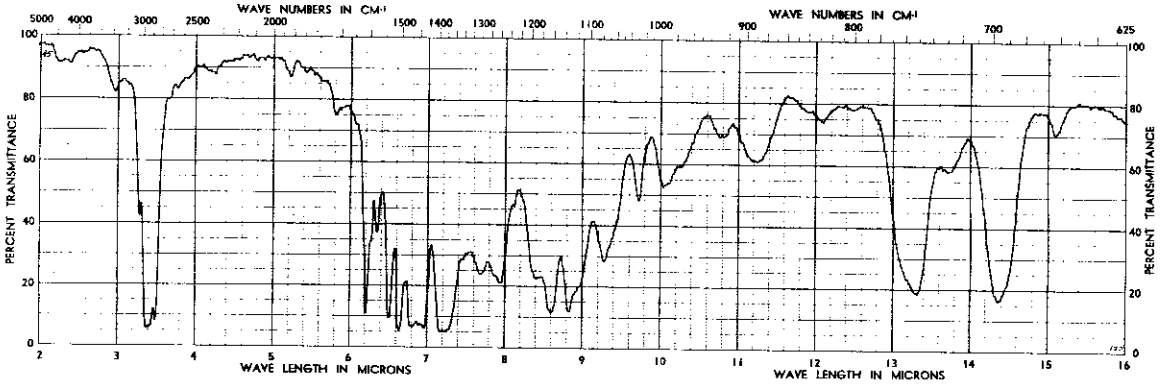
Contrails



2-(N-Methylanilino)-3-(n-pentyl)-6-(5-nonyl)pyrazine



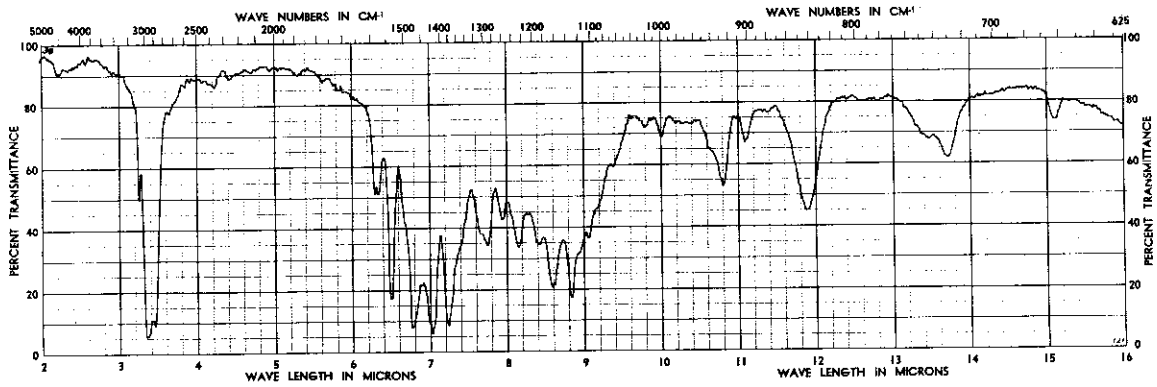
2-(N-Methylanilino)-3-(n-pentyl)-6-(n-heptyl)pyrazine



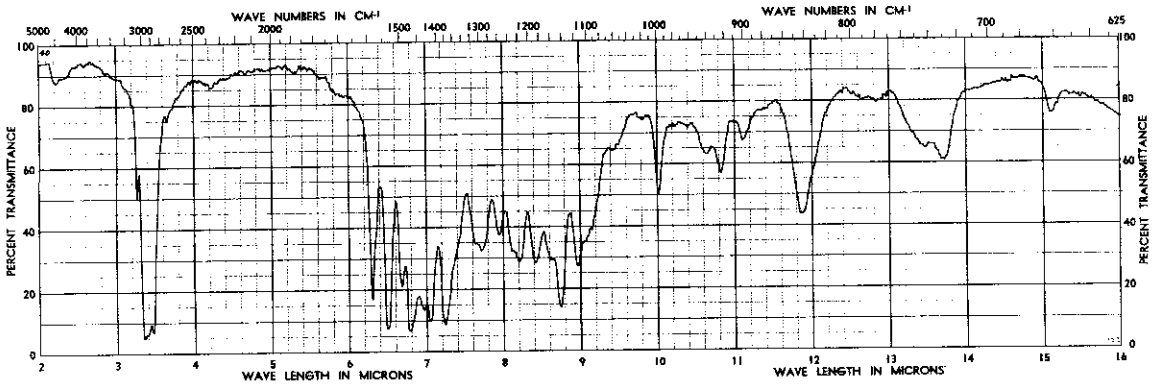
2-(N-Methylanilino)-6-(5-nonyl)pyrazine

Approved for Public Release

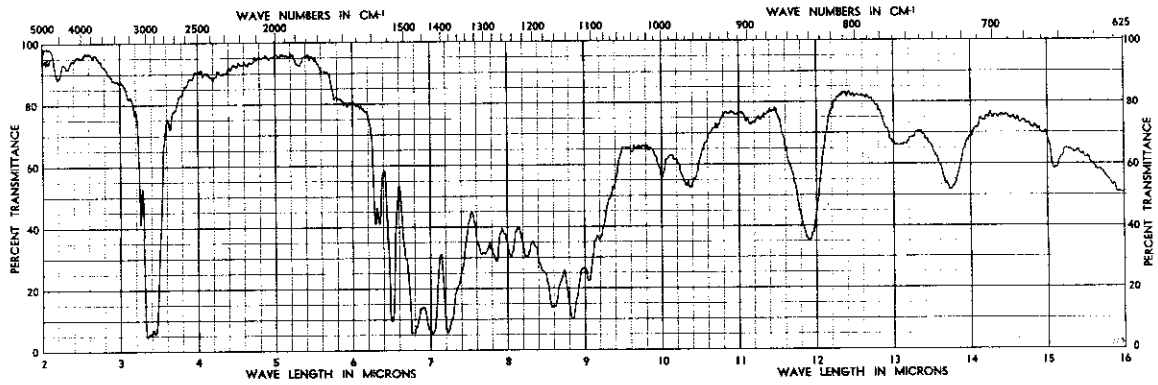
Contrails



2-(N,N-Di-n-butylamino)-3-(n-pentyl)pyrazine



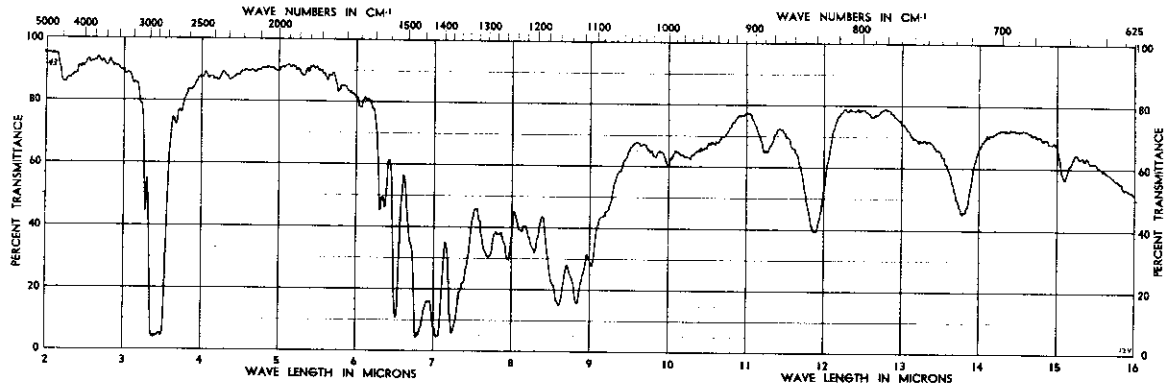
2-(N,N-Di-n-butylamino)-3-(5-nonyl)pyrazine



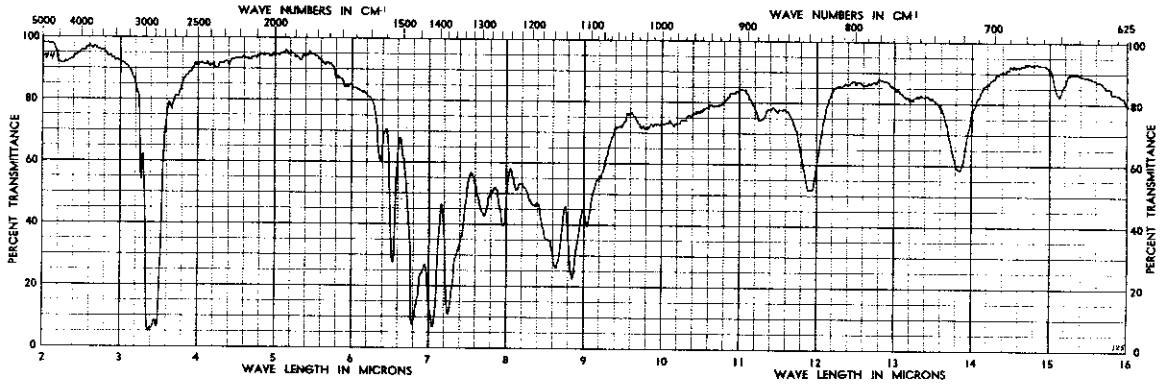
2-(N,N-Di-n-pentylamino)-3-(n-pentyl)pyrazine

Approved for Public Release

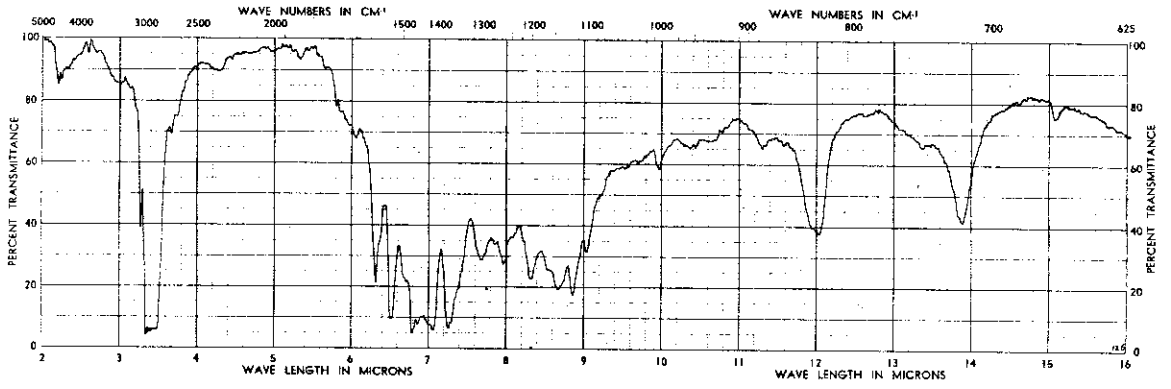
Contrails



2-(N-n-Butyl-N-n-hexylamino)-3-(5-nonyl)pyrazine



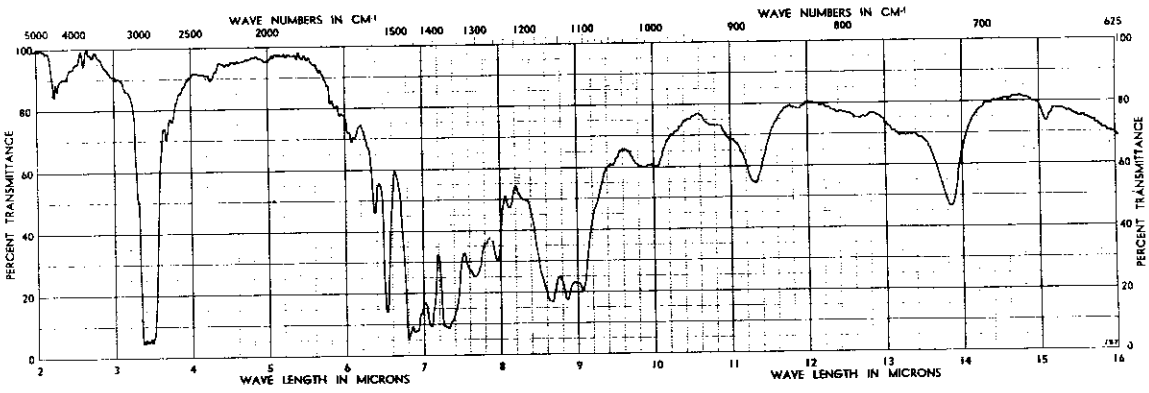
2-(N,N-Di-n-hexylamino)-3-(n-heptyl)pyrazine



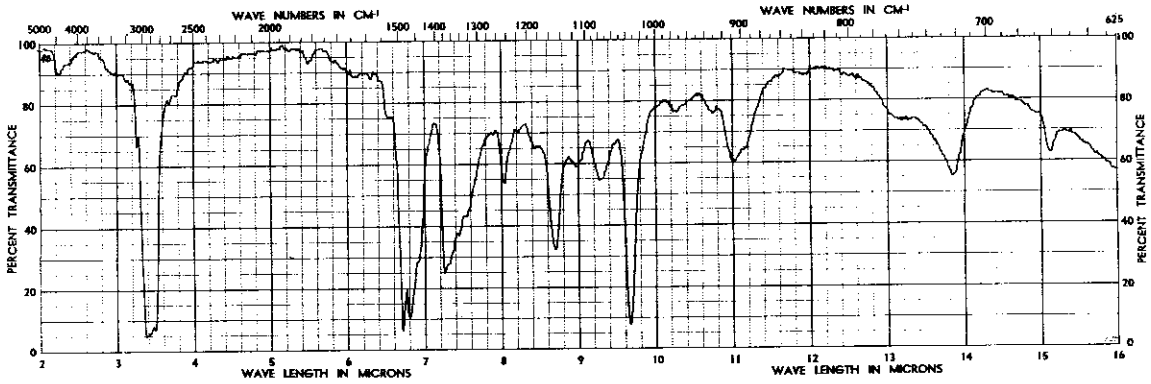
2-(N-n-Hexyl-N-n-octylamino)-3-(n-nonyl)pyrazine

Approved for Public Release

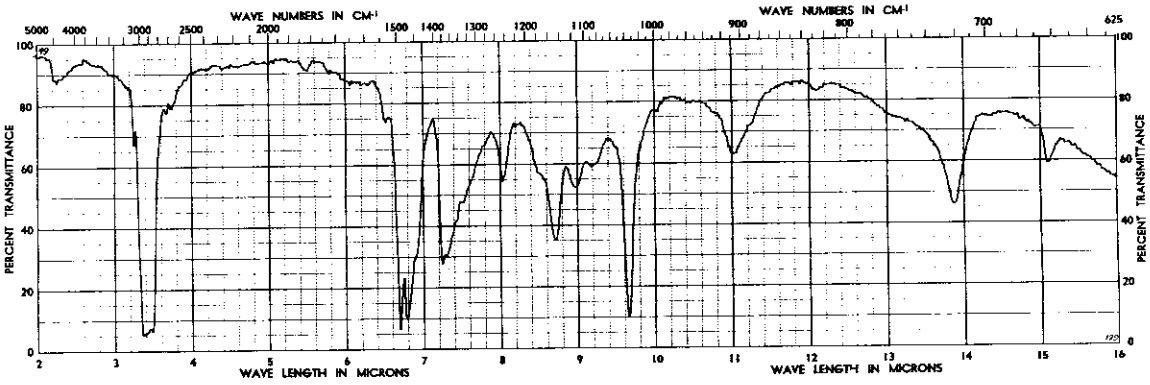
Contrails



2-(N,N-Di-n-hexylamino)-3-(n-pentyl)-6-(n-heptyl)pyrazine



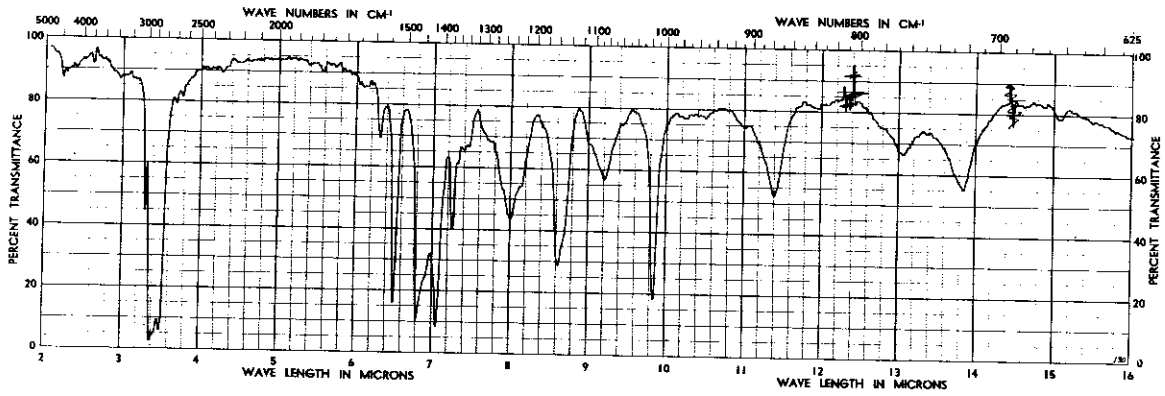
2-n-Heptyl-5-n-pentylpyrazine



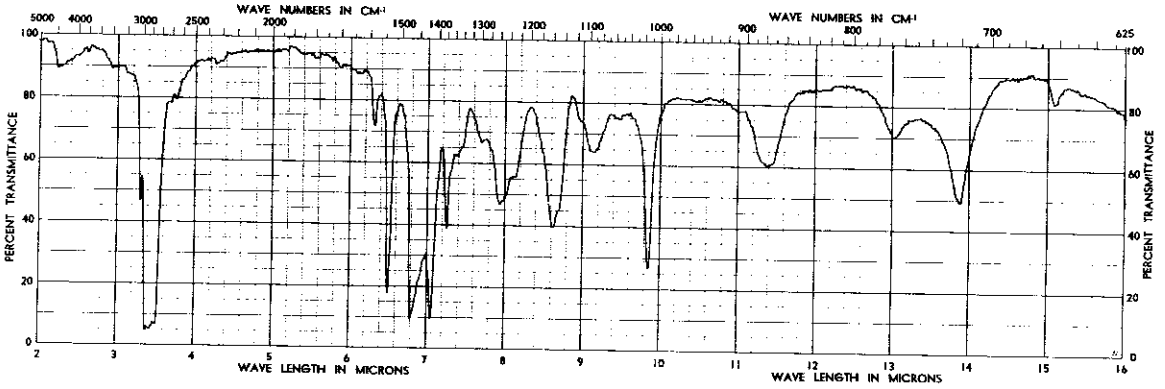
2-n-Heptyl-5-n-nonylpyrazine

Approved for Public Release

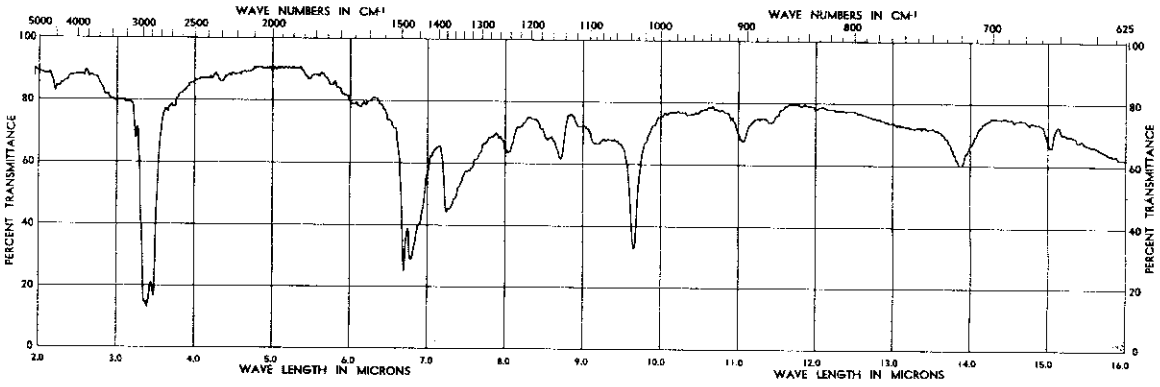
Contrails



2-n-Heptyl-6-n-pentylpyrazine



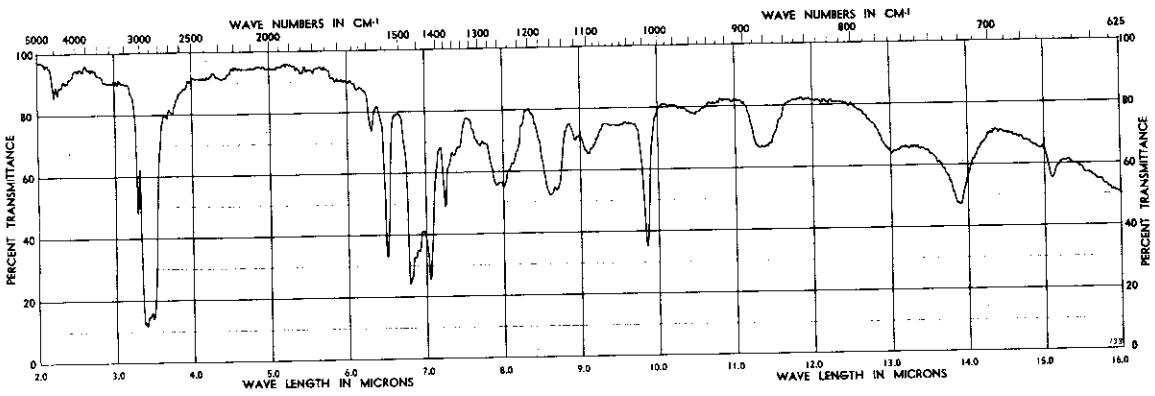
2-n-Heptyl-6-n-nonylpyrazine



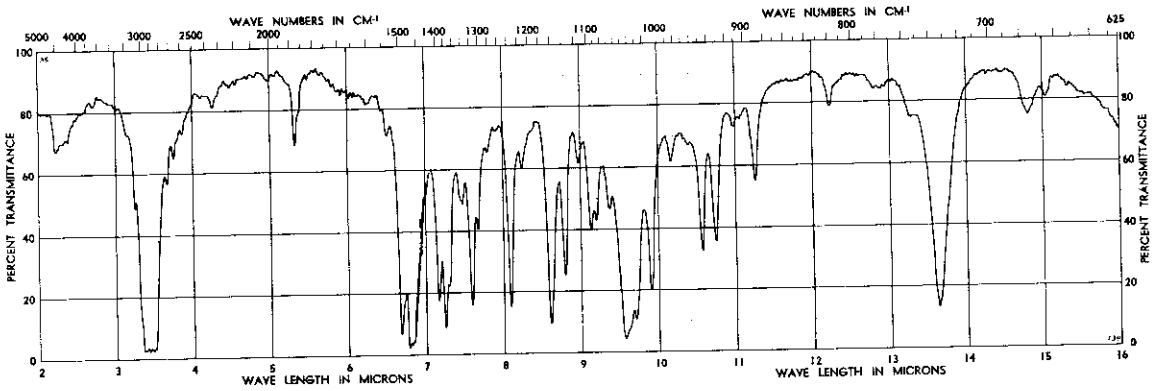
2,5-Di-n-nonylpyrazine

Approved for Public Release

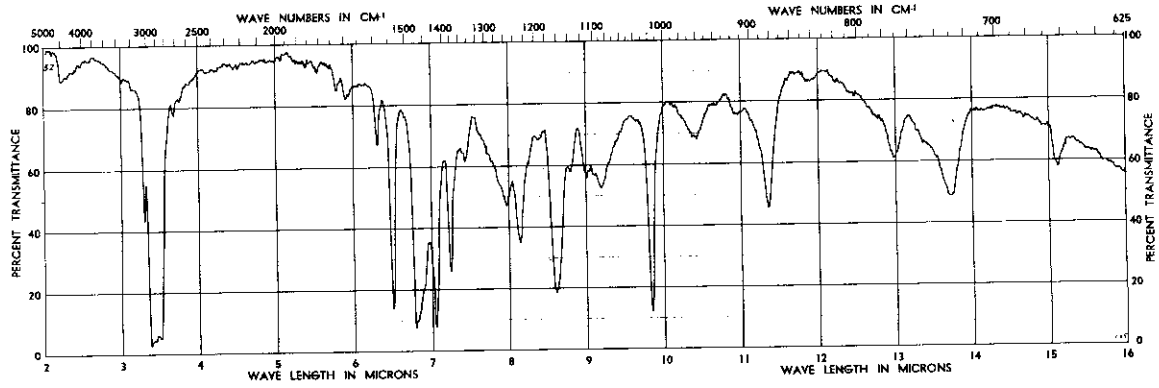
Contrails



2,6-Di-n-nonylpyrazine



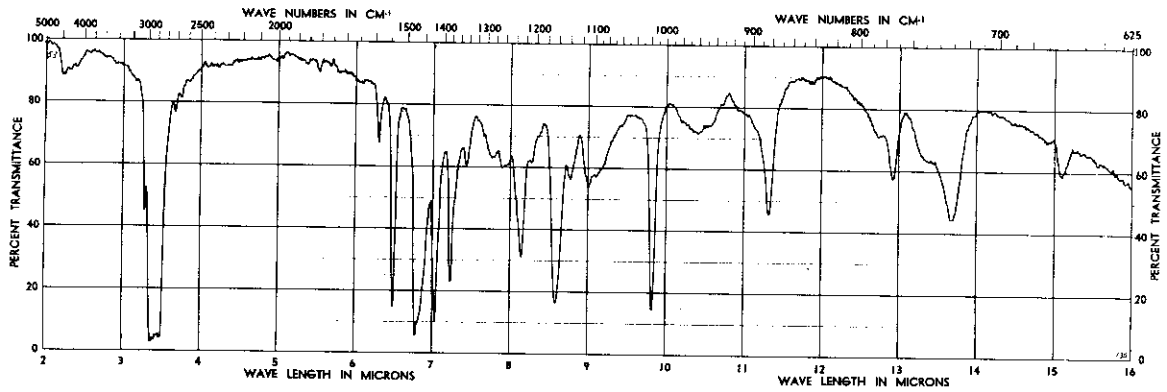
2,5-Di-(5-nonyl)pyrazine



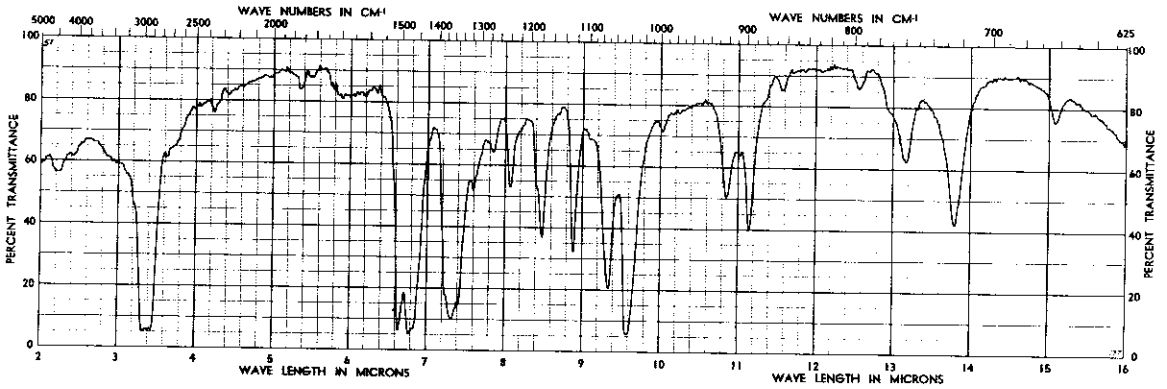
2-(n-Pentyl)-6-(5-nonyl)pyrazine

Approved for Public Release

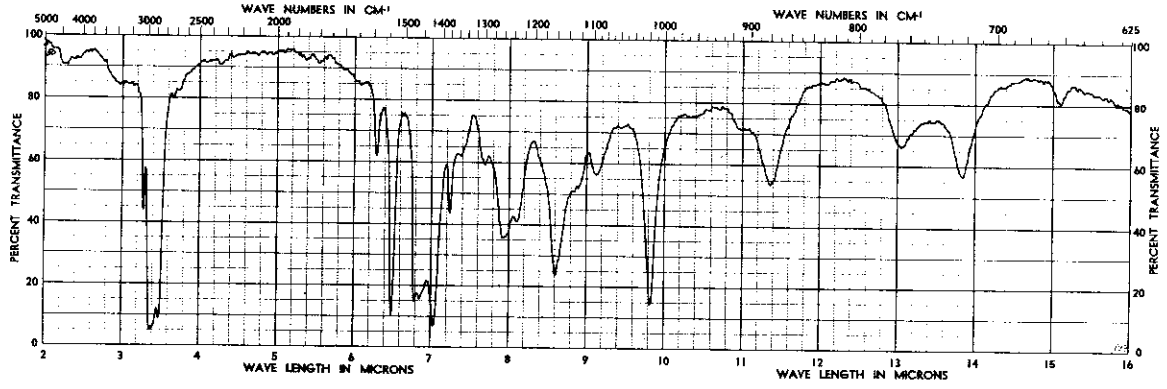
Contrails



2,6-Di-(5-nonyl)pyrazine



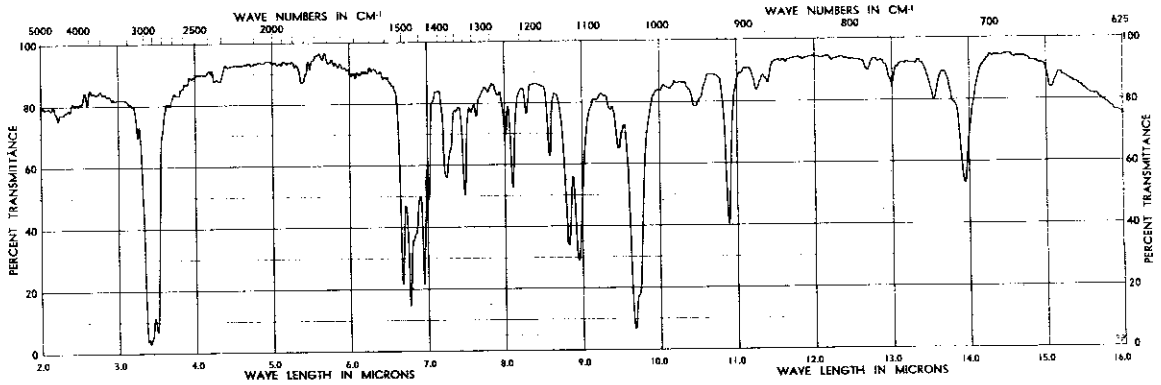
1,4-Bis-[2-(5-n-heptylpyrazyl)] butane



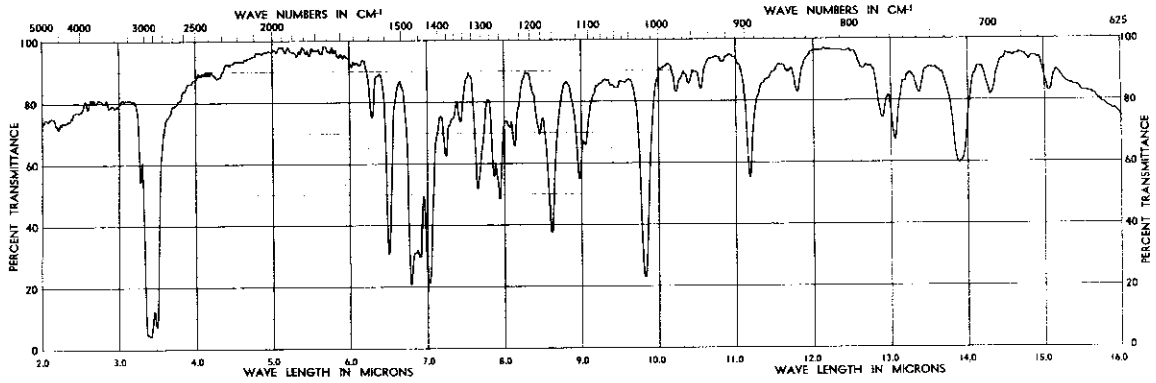
1,4-Bis-[2-(6-n-heptylpyrazyl)] butane

Approved for Public Release

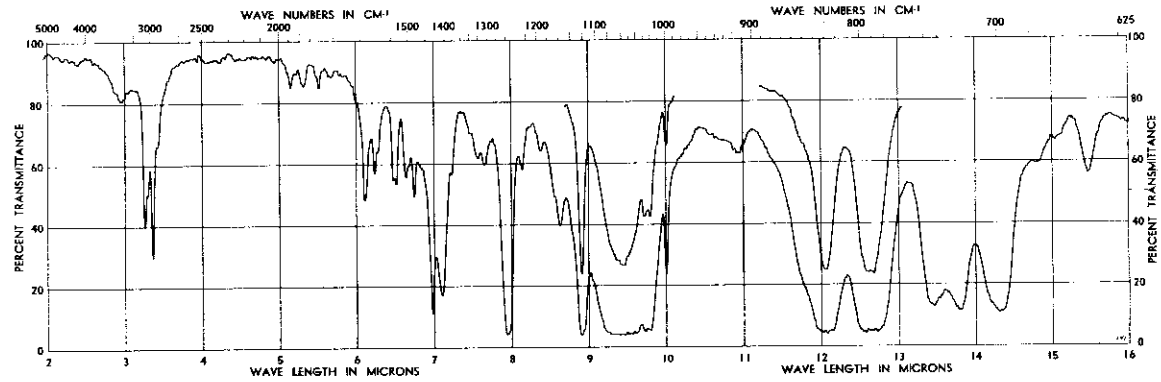
Contrails



1,4-Bis-[2-(5-n-nonylpyrazyl)]butane



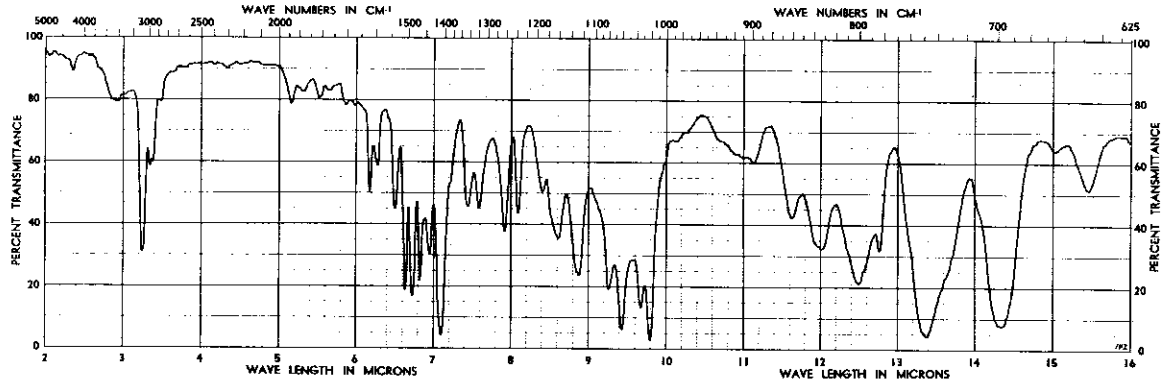
1,4-Bis-[2-(6-n-nonylpyrazyl)]butane



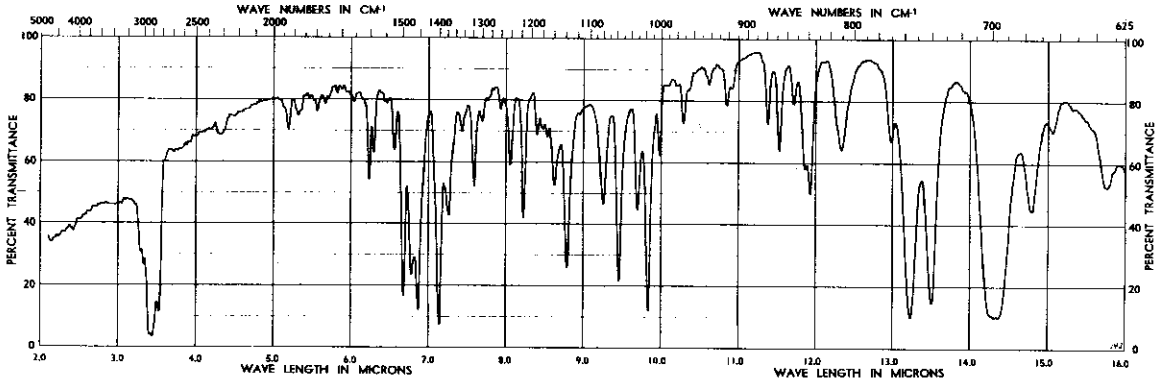
(Phenyldimethylsilyl)methylpyrazine

Approved for Public Release

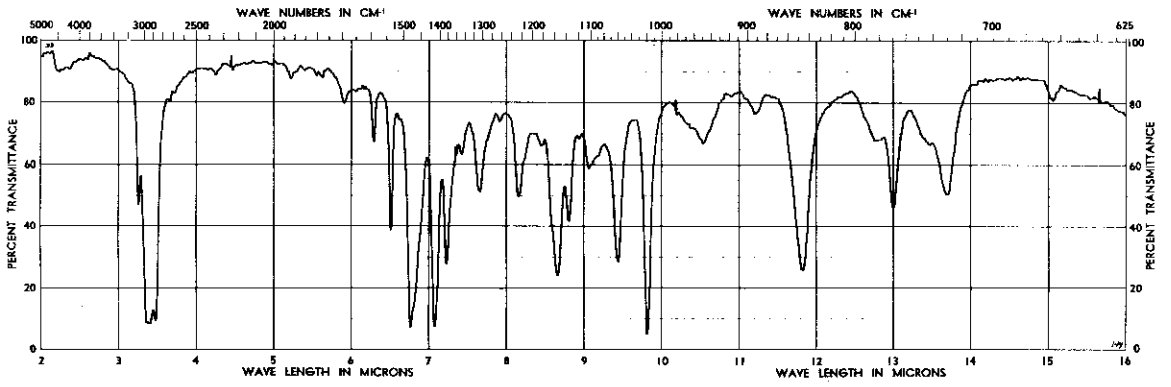
Contrails



Benzylpyrazine



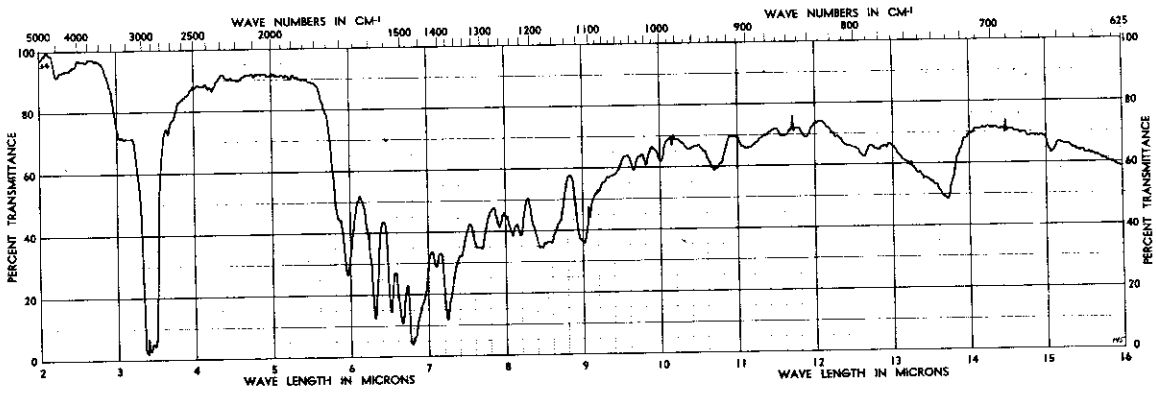
Benzhydrylpyrazine



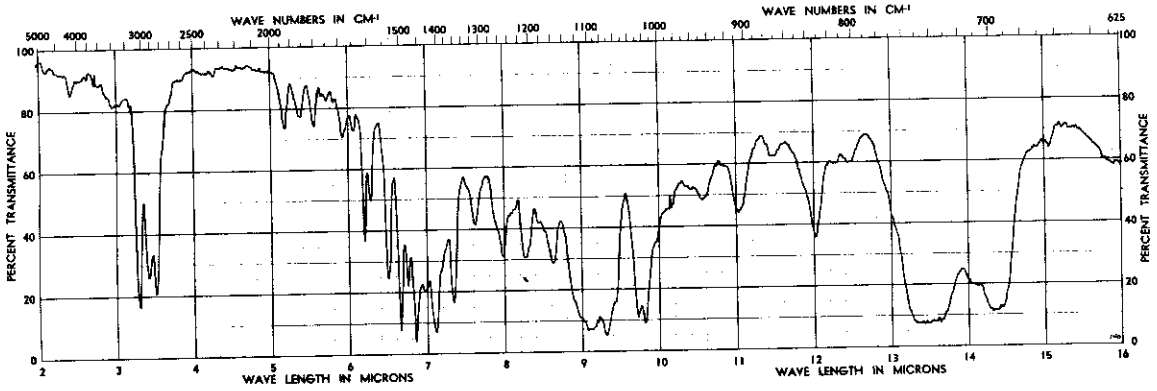
(5-Nonyl)pyrazine

Approved for Public Release

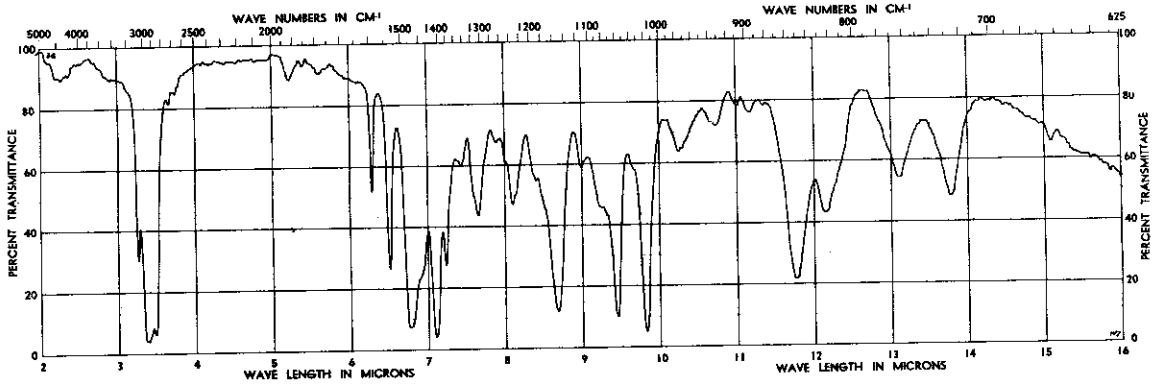
Contrails



(Tributyl)methylpyrazine



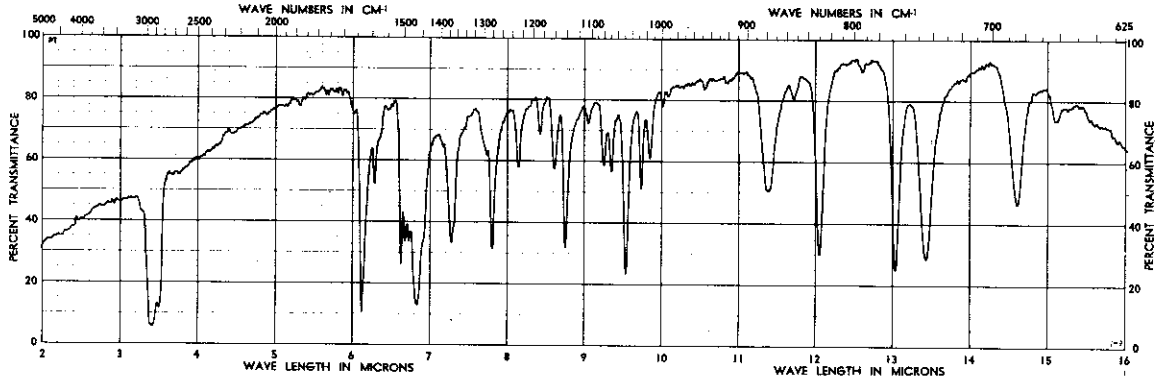
(2-Phenylethyl)pyrazine



n-Pentylpyrazine

Approved for Public Release

Contrails



Phenacylpyrazine

Approved for Public Release

Contrails

BIBLIOGRAPHY

1. Behun, J. D., Kan, P. T., Naqvi, S. M., and Gibson, P. A., WADD Technical Report 60-838, Part I, October 1960.

2. Brown, G. P., Aftergut, S., and Blackington, R. J., J. Chem. and Eng. Data, 6, 125 (1961).

3. Gilman, H., Gaj, B. J., Diehl, J. W., Marrs, O. L., and Trepka, W. J., WADC Technical Report 53-426, Part VI, June 1959, p. 95.

4. Behun, J. D., and Levine, R., J. Org. Chem., 26, 3379 (1961).

5. Bellamy, L. J., "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954.

6. Dale, J. W., Johns, I. B., McElhill, E. A., and Smith, J. O., Paper presented at WADC Materials Laboratory Conference on High Temperature Polymer and Fluid Research, May 20-27, 1959.

7. Blake, E. S., Edwards, J. W., and Hammann, W. C., WADC Technical Report 54-532, March 1955, p. 14.

8. Arne, F., Chem. Economics, 25 January 1960, pp. 60-66.

9. Adams, H. W., WADD Technical Report 60-536, November 1960.

10. Gainer, H., Kokorudz, M., and Langdon, W. K., J. Org. Chem., 26, 2360 (1961).

11. Hirschberg, A., and Spoerri, P. E., J. Org. Chem., 26, 2356 (1961).

12. Gainer, H., Private Communication.

13. Stillson, G. H., Sawyer, D. W., and Hunt, C. K., J. Am. Chem. Soc., 67, 303 (1943).

14. Neville, R. G., J. Org. Chem., 25, 1063 (1960).

15. Benkeser, R. A., and Krysiak, H. R., J. Am. Chem. Soc., 75, 2421 (1953).

16. Levis, W. W., Jr., U. S. 2,541,655, February 13, 1951.

17. Alder, S., Haskeberg, L., and Bergmann, F., J. Chem. Soc., 576 (1940).

18. Leake, W. W., and Levine, R., J. Am. Chem. Soc., 81, 1169 (1959).

Approved for Public Release

Contrails

19. For a detailed discussion, see Eaborn, C., "Organosilicon Compounds," Academic Press, Inc., New York, N. Y., 1960, p. 146.

20. Hauser, C. R., and Hance, C. R., J. Am. Chem. Soc., 74, 1856 (1952).

21. Eaborn, C., and Parker, S. H., J. Chem. Soc., 939 (1954).

22. Gilman, H., Gorsich, R. D., and Gaj, B. J., WADC Technical Report 53-426, Part V, December 1957, p. 40.

23. Gilman, H., and Lichtenwalter, G. D., J. Am. Chem. Soc., 80, 608 (1958).

24. Clinton, R. O., and Laskowski, S. C., J. Am. Chem. Soc., 70, 3135 (1948).

25. Behun, J. D., and Levine, R., J. Am. Chem. Soc., 81, 5157 (1959).

rp

Approved for Public Release