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SYNTHESIS OF POTENTIAL AGROCHEMICALS

AND

REACTIONS OF VINAMIDINIUM AND AZAVINAMIDINIUM SALTS
WITH ORGANOMETALLIC/BORANE REAGENTS AND ACTIVATED NITRILES

BY

CHARLES NORWOOD MOOREFIELD
B.S., University of Central Florida, 1982

RESEARCH REPORT

Submitted in partial fulfillment of the requirements
for the Master of Science degree in Industrial Chemistry
in the Graduate Studies Program for the College of Arts and Sciences
University of Central Florida
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Fall Term
1983

ABSTRACT

This report discusses research which was conducted in two areas: the synthesis of potential agrochemicals and the study of vinamidinium and azavinamidinium salt chemistry. Four classes of compounds were synthesized and characterized in the study of new potential agrochemicals. These compounds include diacylhydrazines, semicarbazides, 2,5-disubstituted-1,3,4-oxadiazoles and bis-2,5-disubstituted-1,3,4-oxadiazoles.

The reaction of [3-(dimethylamino)-2-azaprop-2-en-1-ylidene] dimethylammonium chloride (Gold's reagent) with organometallic/borane reagents was examined in efforts to find convenient syntheses for N,N-dimethylamino substituted alkyl and aryl compounds. Additionally, the reaction of 1,5-diazapentadienium chloride (Nair's reagent) with nitrile activated alkanes was examined to find a convenient synthesis of 3-substituted pyridines. Subsequent intramolecular ring closure of the dienaminonitriles was unsuccessful.

Finally, this report reveals the experimental procedures and conditions used for the synthesis of these products and offers explanations of the data as well as recommendations for future research.

ACKNOWLEDGEMENTS

I am deeply indebted to Dr. John T. Gupton III for his guidance and support during my graduate research. His expertise and knowledge were invaluable.

As members of my graduate committee, I am also indebted to Dr. John P. Idoux and Dr. Guy Mattson for their time and patience.

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LIST OF ABBREVIATIONS

bp	boiling point
°C	degrees centigrade
cm ⁻¹	wave numbers (IR spectrum)
δ	delta (NMR spectrum)
d	doublet
DMF	dimethylformamide
DMSO	dimethylsulfoxide
EtOH	ethanol
g	grams
Δ	heat
HMPA	hexamethylphosphoramide
hr	hours
Hz	(Hertz (cycles per second, NMR spectrum))
IR	Infrared
J	coupling constant (NMR spectrum)
m	multiplet (NMR spectrum)
M ⁺	molecular ion (mass spectrum)
m/e	mass to charge ratio (mass spectrum)
MeOH	methanol
ml	milliliters
mol	mole

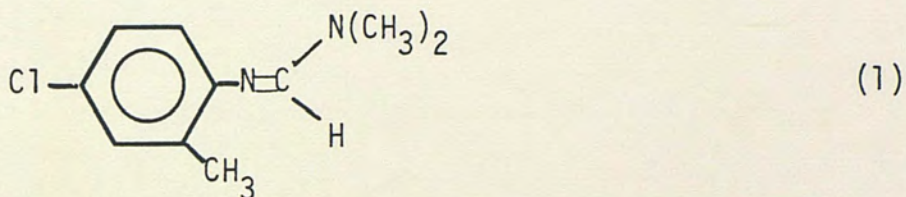
mp	melting point
N	normal (normality)
NMR	Nuclear Magnetic Resonance
pH	$-\log [H^+]$
PPA	polyphosphoric acid
ppm	parts per million (NMR spectrum)
q	quartet (NMR spectrum)
s	singlet (NMR spectrum)
t	triplet (NMR spectrum)
TFA	trifluoroacetic acid
THF	tetrahydrofuran

PART I
SYNTHESIS OF POTENTIAL AGROCHEMICALS

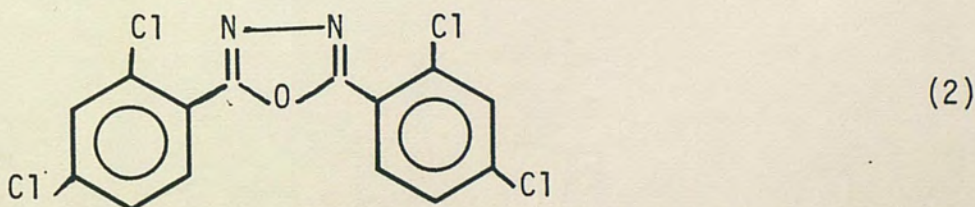
PART I

I. INTRODUCTION

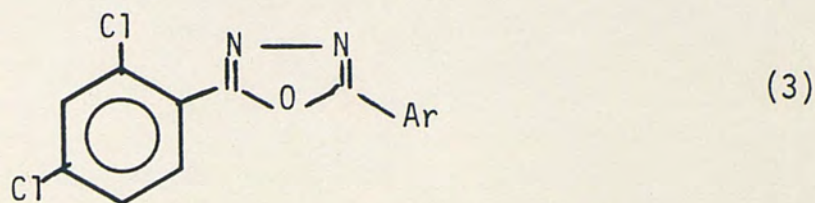
Recently much effort within the chemistry community has been devoted to the search for improved insecticides. In part, this impetus stems from the environmental effects of the insecticides themselves, and from their decomposition products. For example, the commercially available insecticide Chlorodimeform (1)¹ has been demonstrated to form the toxic 2-amino-5-chlorotoluene decomposition product.



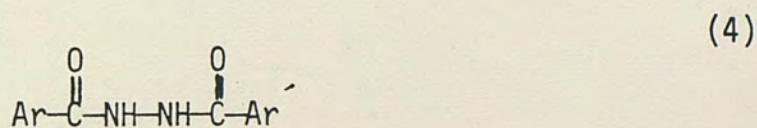
Dow Chemical Company has recently introduced a symmetrical 1,3,4-oxadiazole, DOWCO-416 (2)², which acts as a larvacide. This compound was found effective in the control of manure-breeding insects such as houseflies, hornflies and face flies.



Since this 1980 patent disclosure a number of 2,5-disubstituted 1,3,4-oxadiazoles have been synthesized having the following general formula (3):



where Ar represents 4-(trifluoromethyl)phenyl, 2-chlorophenyl, 4-fluorophenyl or 3,5-dichlorophenyl. It is believed that the biological activity of these insecticides is due to the 1,3,4-oxadiazole moiety. Since analogs of these oxadiazoles may prove to have greater biological activity, it is the purpose of this investigation to synthesize other oxadiazoles which were identified as target compounds by the Dow research group. More specifically, the compounds to be synthesized are as follows:



where Ar is ortho-, meta-, or para-(2,2,2-trifluoroethoxy)benzene and Ar' is 2,4-dichlorobenzene. The corresponding oxadiazoles could then be obtained by dehydration of these diacylhydrazides.

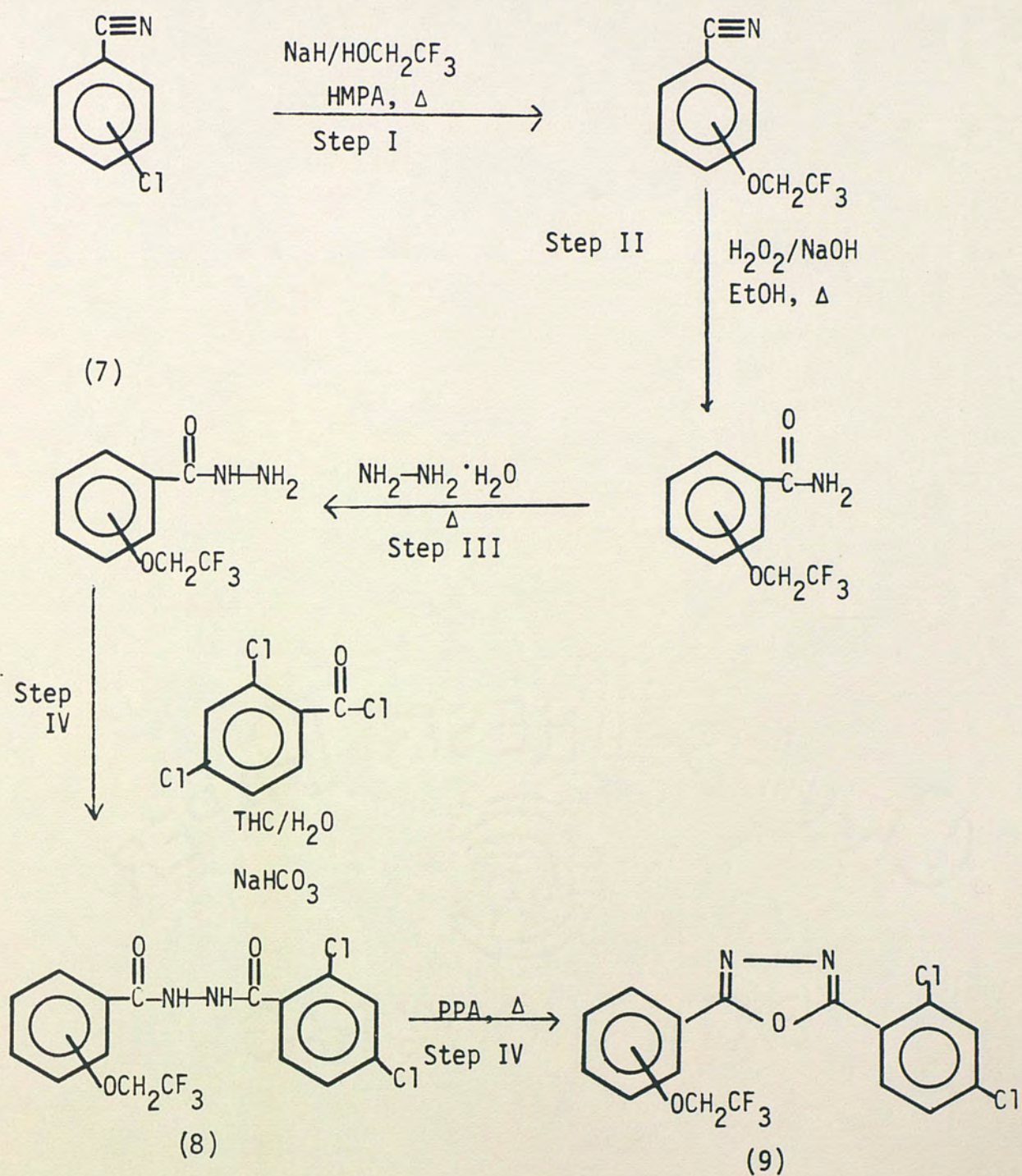


Figure 1. Proposed synthetic scheme for the preparation of diacylhydrazines and 2,5-disubstituted-1,3,4-oxadiazoles.

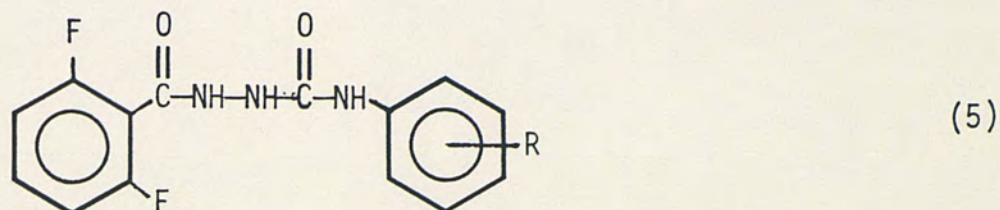
This synthetic scheme is depicted in Figure 1. The characterizations of all products and precursors will be done by NMR and IR spectroscopy as well as the observation of certain physical properties, i.e., H^{\oplus} solubility and melting point.

The reaction sequence which was selected involves the trifluoroethoxylation of chlorobenzonitriles in HMPA as reported by Gupton and Idoux⁵. This aromatic nucleophilic substitution gives good yields for the ortho and para isomers. The meta isomer is obtained only in fair to poor yield due to stabilization of the reaction intermediate via the sigma bond system only. The conversion of the trifluoroethoxybenzonitriles to the corresponding amides would employ the method described by Noller⁶. This method involves the base catalyzed conversion of the nitrile to the amide using 95% EtOH as the solvent. This procedure is much milder than acid hydrolysis of the nitrile and should leave the trifluoroethoxy group intact.

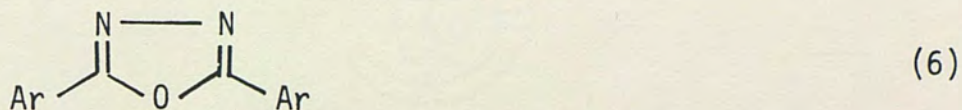
The amide would then be reacted with 85% hydrazine monohydrate to yield the monoacylhydrazide⁷ in Step III. The diacylhydrazide could then be formed by the acylation of the primary amino group. The subsequent cyclization of the diacylhydrazide (8) via polyphosphoric acid (PPA) to the oxadiazole (9) is the final step in the reaction sequence. Phosphorousoxychloride has also been shown to be a good dehydrating agent⁸.

The proposed reaction sequence for the synthesis of the 2,6-difluorophenyl-2,3-dichlorophenyl analog (10) is depicted in Figure 2, and is the same sequence proposed by Lizzi.

The diacylhydrazides (4) where Ar is 2,6-difluorobenzene and Ar' is 2,6-dichlorobenzene will also be synthesized. Some other analogs (5) to be synthesized have the following formula:



where R is para-methyl, ortho-trifluoromethyl, meta-trifluoromethyl and para-fluoro. Finally, this investigator proposes to synthesize bis-2,5-disubstituted-1,3,4-oxadiazoles (6) which have the following formula:



where Ar is 2,6-difluorobenzene, 3-(2,2,2-trifluoroisopropoxy)benzene or 4-(2,2,2-trifluoroisopropoxy)benzene.

The proposed synthetic route to the isomeric trifluoroethoxy diacylhydrazides and the corresponding oxadiazoles was identical to that reported by Lizzi³ except the carboxylic acid was to be synthesized from the corresponding nitrile by acid hydrolysis with 75% sulfuric acid as reported by Clarke and Taylor⁴. An alternate synthetic route is also proposed which allows synthesis of the monoacylhydrazide without synthesizing the carboxylic acid and the methyl ester.

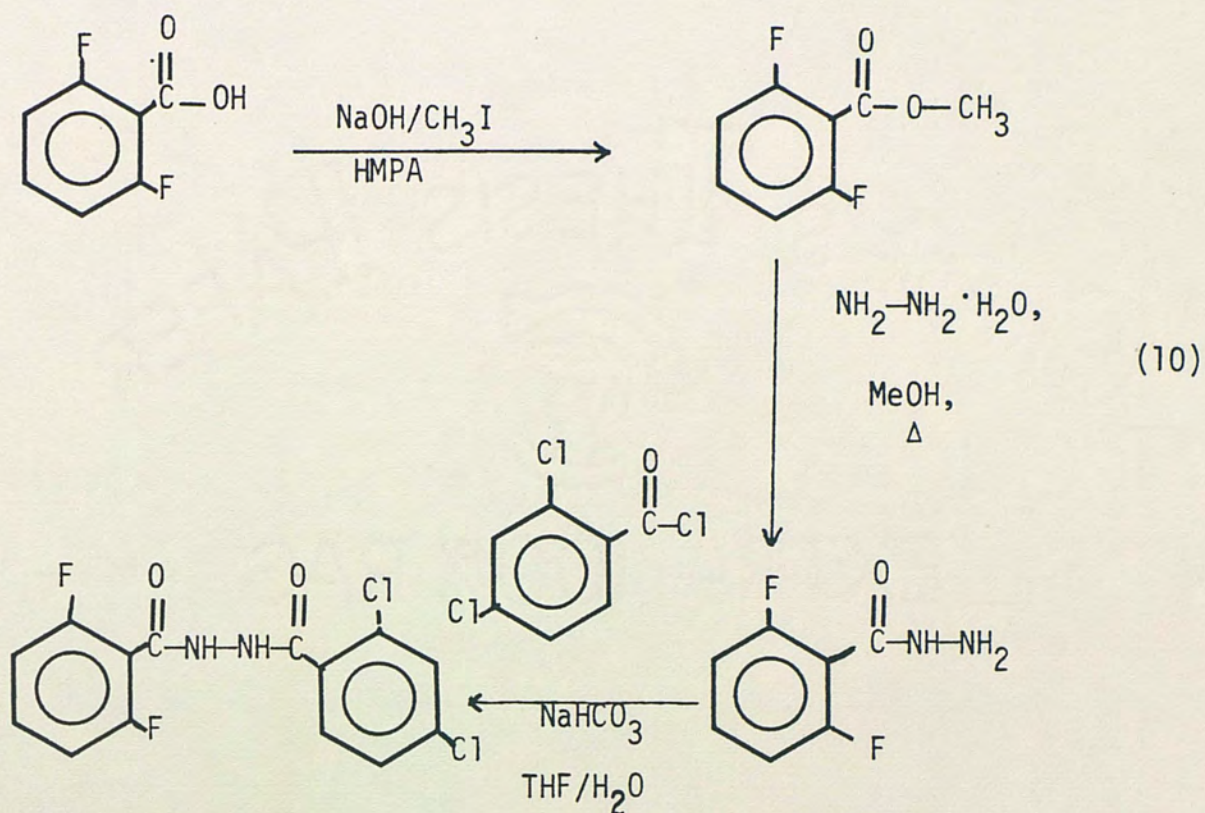


Figure 2. Proposed reaction scheme for the synthesis of N-(2,6-difluorobenzoyl)-N'-(2,4-dichlorobenzoyl)hydrazine.

The proposed synthetic route to the bis-2,5-disubstituted oxadiazoles is given in Figure 3.

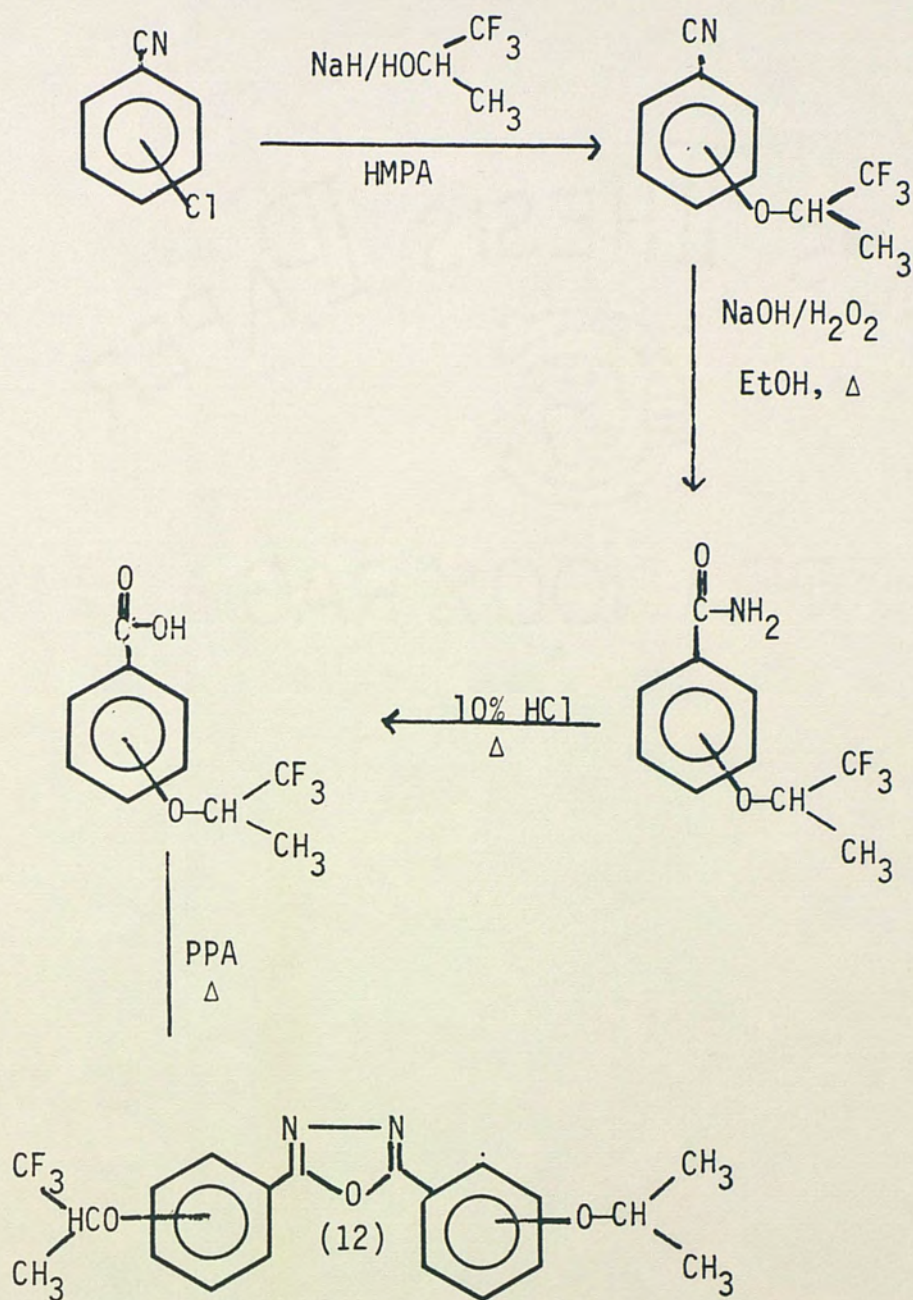


Figure 3. Proposed synthetic scheme for bis- (meta- and para-2,2,2-trifluoroisopropoxyphenyl) oxadiazoles.

This reaction sequence is different from the others previously proposed because it converts the amide to the acid⁹. The conversion of the carboxylic acids to the corresponding 1,3,4-oxadiazoles is readily accomplished by heating two equivalents of the acid and one equivalent of hydrazine monohydrate in PPA². This reaction has been shown to give good to excellent yields of the 1,3,4-oxadiazoles (12). Characterization will be accomplished by NMR and IR spectroscopy as well as mass spectroscopy where necessary.

The proposed synthetic scheme for the substituted acyl semicarbazides^{10,11} is depicted in Figure 4.

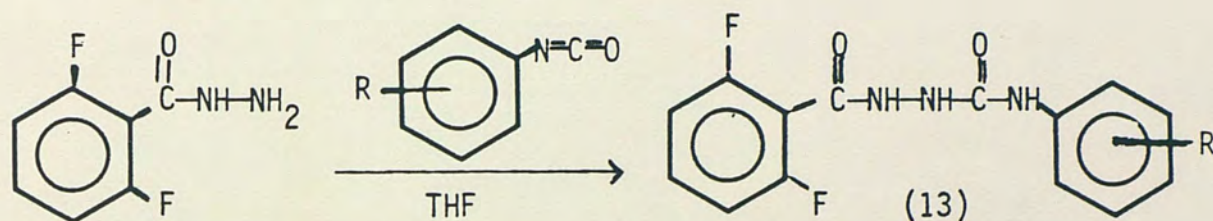


Figure 4. Proposed reaction for the synthesis of substituted semicarbazides.

The synthesis of the starting monoacylhydrazide will be accomplished in the same manner as shown in Figure 2. The R in Figure 4 represents para-methyl, ortho-trifluoromethyl, meta-trifluoromethyl and para-fluoro moieties. The mechanism for the reaction is given in Figure 5. Reviews of the nomenclature¹¹, preparation^{12,13}, properties and reactions^{11,13} of hydrazides and diacylhydrazides are available, as are reviews of the preparation, properties and reactions of 1,3,4-oxadiazoles^{8,14,15}.

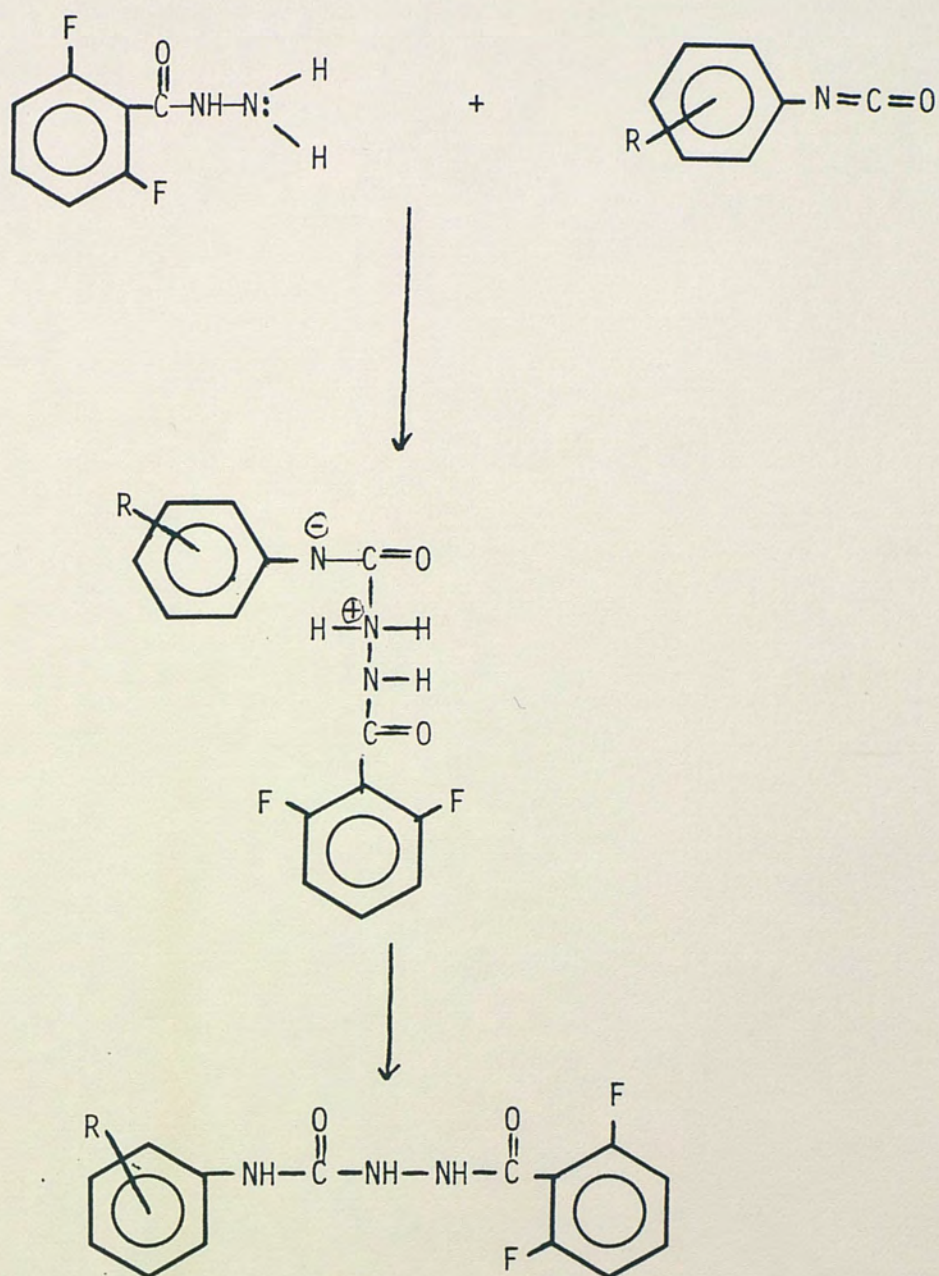


Figure 5. Proposed mechanism for the reaction of an isocyanate with a monoacylhydrazide.

PART I

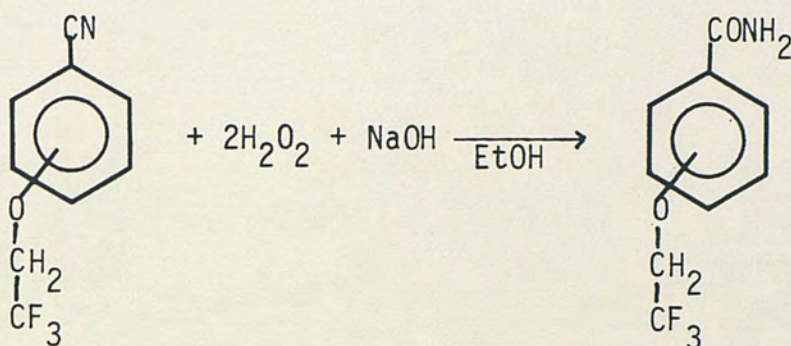
II. EXPERIMENTALA. Preparation of 2,2,2-trifluoroethoxybenzamides

Table I

Experimental Data for the Preparation of Trifluoroethoxybenzamides

Entry	Isomer	Yield (%) ^b	mp, °C ^a
1	ortho ^c	60	148-150
2	meta ^d	85	144-145
3	para ^e	80	182-183

a. The melting points are for the crude products.

b. The percent yields refer to crude yields.

- c. NMR (CDCl_3 , d^6 DMSO) δ 4.79 (q, $J=8\text{Hz}$, 2H), 6.70-7.70 (m, 3H), 8.10 (d of d, $J=2\text{Hz}$, $J=8\text{Hz}$, 1H); IR (nujol mull) 3390, 3195, 1640, 1150, 975, 755 and 668 cm^{-1} .
- d. NMR (d^6 acetone, d^6 DMSO) δ 4.70 (q, $J=8\text{Hz}$, 2H) 6.70-8.10 (m, 4H); IR (nujol mull) 3390, 3195, 1660, 1170 and 795 cm^{-1} .
- e. See the experimental procedure for spectral data.
- f. The yields are for crude products which were analytically pure.
- g. The amount of 6N NaOH used was 30 ml for every .75 mol of starting material. The amount of 95% EtOH used was 400 ml for every .75 mol of starting material. There were 2 equivalents of H_2O_2 used for every 1 equivalent of starting material used.
- h. The products were insoluble in saturated sodium bicarbonate and also in 5% hydrochloric acid.
- i. For spectral data of starting material see reference 5.

4-(2,2,2-trifluoroethoxy)benzamide

To a three-necked, 250 ml, round bottomed flask equipped with a thermometer, stirring bar and reflux condenser was added 40 ml of 95% ethanol, 15.0 g (0.75 mol) of 4-(2,2,2-trifluoroethoxy) benzonitrile and 20.0 g (.15 mol) of 30% hydrogen peroxide. To this was added 3 ml of 6N sodium hydroxide. After a few minutes the solution began to exotherm. A water bath was used to keep the temperature from rising above 50°C . When the exothermic reaction had subsided, the mixture was warmed to $45\text{-}50^\circ\text{C}$ for $4\frac{1}{2}$ hours.

The reaction mixture was cooled to room temperature and the product washed with cold ethanol. This gave 13.1 g (80%) of a white solid: NMR (CDCl_3 , d^6 DMSO), δ 4.60 (q, $J=8\text{Hz}$, 2H), 7.20 d, $J=8\text{Hz}$, 2H), 8.15 (d, $J=8\text{Hz}$, 2H); IR (nujol mull) 3390, 3190, 1643, 865 and 840 cm^{-1} .

B. Preparation of 2,2,2-Trifluoroethoxybenzoylhydrazines

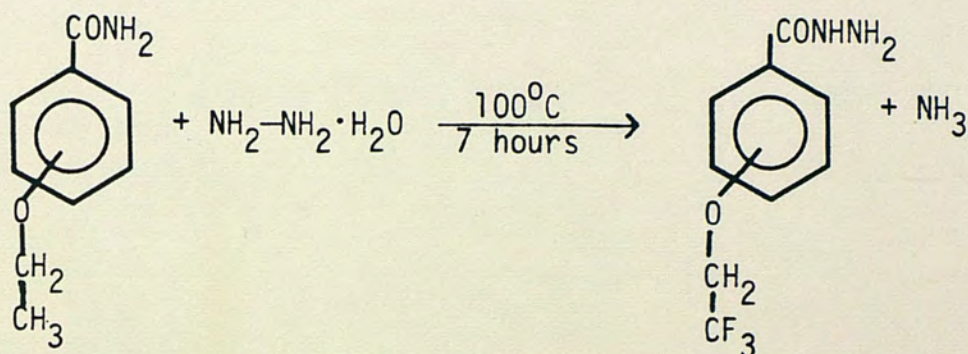


Table II

Experimental Data for the Preparation of Trifluoroethoxyphenyl-monoacylhydrazides

Entry	Isomer	Yield (%) ^a	mp, °C
1	ortho ^b	75	101-103
2	meta ^c	68	107-110
3	para ^d	85	112-115

a. The percent yields refer to crude yields. After filtration, washing and drying the products were pure.

- b. NMR (CDCl_3 , DMSO) δ 4.12 (broad s, 2H), 4.58 (q, $J=8\text{Hz}$, 2H), 6.90-7.60 (m, 3H), 8.10 (d of d, $J=2\text{Hz}$, $J=8\text{Hz}$, 1H), 8.76 (s, 1H); IR (nujol mull) 3318, 1618, 1239, 1158, 950 and 755 cm^{-1} .
- c. NMR (CDCl_3 , d^6 DMSO) δ 3.90 (broad s, 2H), 4.47 (q, $J=8\text{Hz}$, 2H), 6.90-7.70 (m, 4H), 9.62 (broad s, 1H); IR (nujol mull) 3320, 1650, 1350, 801, 761 and 690 cm^{-1} .
- d. See the experimental procedure for spectral data.
- e. All products were soluble in 5% HCl and insoluble in saturated sodium bicarbonate.
- f. The nature of the solubility of the monoacylhydrazides may make it necessary to cool the filtrate and recover product which was not trapped by the first filtration. This procedure was not necessary for the para isomer.

4-(2,2,2-trifluoroethoxy)benzoylhydrazine

The equipment consisted of a three-necked, round bottom flask fitted with a reflux condenser, thermometer and magnetic stirring bar. To the flask was added 12 g (.055 mol) of 4-(2,2,2-trifluoroethoxy)benzamide and 32 g (approximately a 10 fold molar excess) of 85% hydrazine monohydrate. The mixture was heated to 100°C and left to stir for 7 hrs. The reaction mixture was cooled to room temperature and 75 ml of cold water was added. The product was isolated by filtration and dried in vacuo at .5 mm of Hg; NMR (CDCl_3 , d^6 DMSO) δ 4.14 (broad s, 2H), 4.44 (q, $J=8\text{Hz}$, 2H), 6.90 (d, $J=8\text{Hz}$, 2H) and 7.90 (d, $J=8\text{Hz}$, 2H); IR (nujol mull) 3300, 1615, 919, 853 and 838 cm^{-1} .

C. Preparation of Isomeric Diacylhydrazides

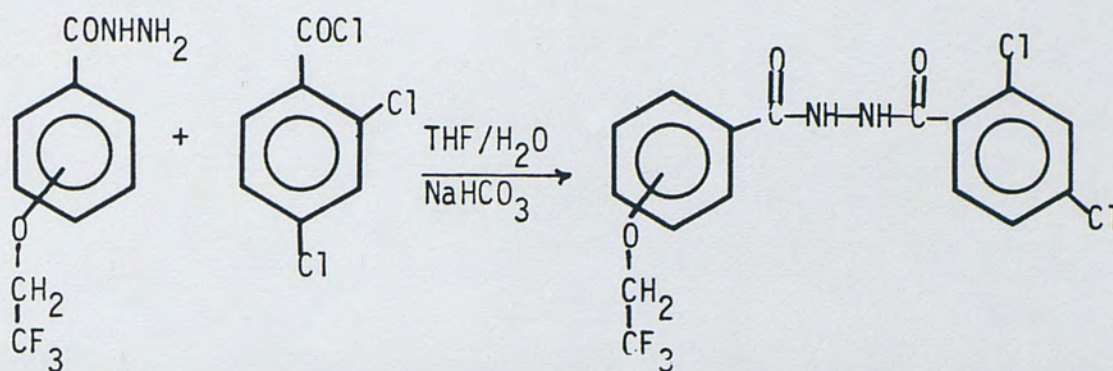


TABLE III

Experimental Data for the Preparation of Diacylhydrazides

Entry	Isomer	Yield (%) ^a	mp, °C ^a
1	ortho ^b	99	151-152
2	meta ^c	89	198-200
3	para ^d	94	212-215

a. All of the reported yields refer to crude yields.

b. NMR (CDCl_3 , d^6 DMSO) δ 4.76 (q, $J=8\text{Hz}$, 2H), 7.00-7.70 (m, 6H) and 7.85 (d of d, $J=2\text{Hz}$, $J=8\text{Hz}$, 1H); IR (nujol mull) 3195, 1600, 1465, 1160, 873, 860, 780 and 750 cm^{-1} .

c. NMR (CDCl_3 , d^6 DMSO) δ 4.73 (q, $J=8\text{Hz}$, 2H), 7.43 (m, 7H); IR (nujol mull) 3233, 1638, 1160, 858 and 850 and 800 cm^{-1} .

- d. See the experimental procedure for spectral data.
- e. One equivalent of sodium bicarbonate is required to neutralize the HCl which is formed as a byproduct.
- f. The volume to volume ratio of THF and H₂O can be modified to allow for precipitation of the product during the course of the reaction. This would eliminate the need to strip off the THF after the reaction and filtration can be performed immediately following the reaction.
- g. All products were found to be insoluble in 5% HCl and saturated NaHCO₃.

N-[4-(2,2,2-trifluoroethoxy)benzoyl]-N'(2,4-dichlorobenzoyl)
hydrazine

The equipment consisted of a 250 ml, three-necked, round-bottomed flask fitted with a reflux condenser, a thermometer and thermometer adapter, stirring bar and 100 ml addition funnel. To the flask was added 100 ml of 50/50 (v/v) mixture of tetrahydrofuran and water. Then 5.0 g (.021 mol) of 4-(2,2,2-trifluoroethoxy)benzoylhydrazine was dissolved in the mixture. Next, 4.37 g (.021 mol) of 2,4-dichlorobenzoylchloride was dissolved in 10 ml of tetrahydrofuran and dripped in slowly via the additions funnel. After stirring for 2 hrs at room temperature the tetrahydrofuran was stripped from the resulting solution. The product then crystallized and was filtered and dried in vacuo at .4 mm of Hg.

No further purification was necessary: NMR δ 4.60 (q, $J=8\text{Hz}$, 2H), 7.00 (d, $J=8\text{Hz}$, 2H), 7.30-7.70 (m, 3H) and 8.00 (d, $J=8\text{Hz}$, 2H); IR (nujol mull) 3210, 1640, 1165, 840, 830, 790 and 760 cm^{-1} .

D. Preparation of Isomeric 2,5-Disubstituted Oxadiazoles

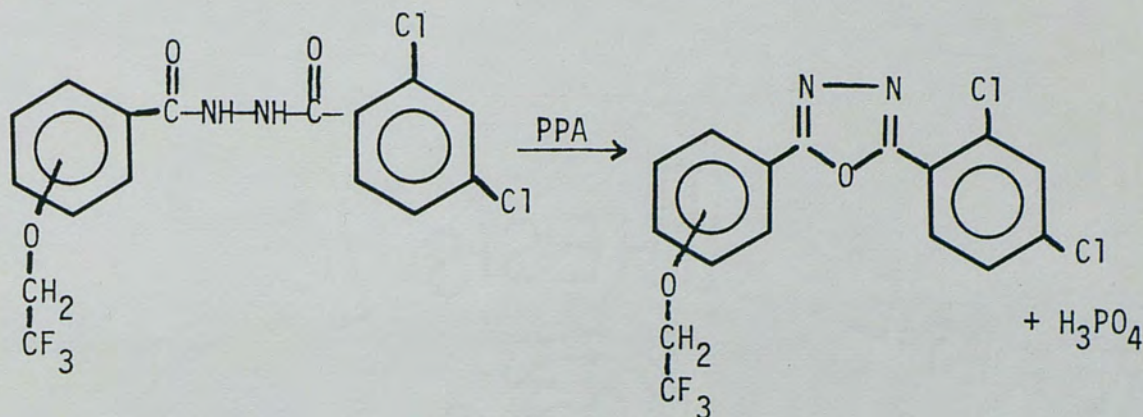


Table IV

Experimental Data for the Preparation of Isomeric 2,5-Disubstituted Oxadiazoles

Entry	Isomer	Yield (%) ^a	mp, °C ^e
1	ortho ^b	89	138-142
2	meta ^c	99	113-118
3	para ^d	93	134-137

a. The reported yields are crude yields which are analytically pure.

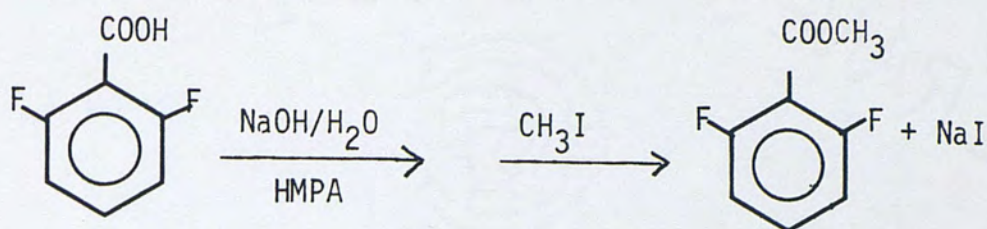
b. NMR (d^6 DMSO, d^6 acetone, CCl_4) δ 4.90 (q, $J=8\text{Hz}$, 2H), 7.30-8.30 (m, 6H) and 8.30 (d, $J=8\text{Hz}$, 1H); IR (nujol mull) 1596, 1480, 1180, 770, 749 and 700 cm^{-1} .

- c. NMR (d^6 DMSO, d^6 acetone, CCl_4) δ 4.82 (q, $J=8\text{Hz}$, 2H), 7.30-7.90 (m, 6H) and 8.30 (d, $J=8\text{Hz}$, 1H); IR (nujol mull) 1595, 1460, 1087, 745 and 740 cm^{-1} .
- d. See the experimental procedure for spectral data.
- e. The wide range for the melting points is attributed to a small amount of water.
- f. The viscosity of PPA makes it necessary to heat it to at least 90°C before proper mixing with a stirring bar can be obtained.

5-[4-(2,2,2-Trifluoroethoxy)phenyl]-2(2,4-dichlorophenyl)
oxadiazole

To a 250 ml, three-necked, round-bottomed flask equipped with a reflux condenser, magnetic stirring bar, thermometer and thermometer adapter was added 4.0 g (.01 mol) of N -[4-(2,2,2-trifluoroethoxy)benzoyl]- N -(2,4-dichlorobenzoyl)hydrazine and 20 g of polyphosphoric acid. The mixture was heated at 130°C for 5 hrs. The solution was cooled to 95°C and 100 ml of water was added. The product precipitated and was filtered through a fritted glass funnel. The tan colored solid product was dried using a Kugelrohr apparatus at $65-70^\circ\text{C}$ at .5 mm for 4 hrs to yield 3.5 g of oxadiazole: NMR (d^6 DMSO) d^6 acetone, CCl_4) δ 4.63 (q, $J=8\text{Hz}$, 2H), 7.10 (d, $J=8\text{Hz}$, 2H), 7.30-7.70 (m, 2H), 8.00 (d, $J=8\text{Hz}$, 2H) and 8.10 (d, $J=8\text{Hz}$, 1H); IR (nujol mull) 1618, 1596, 1500, 1182, 968, 840, 745 and 700 cm^{-1} .

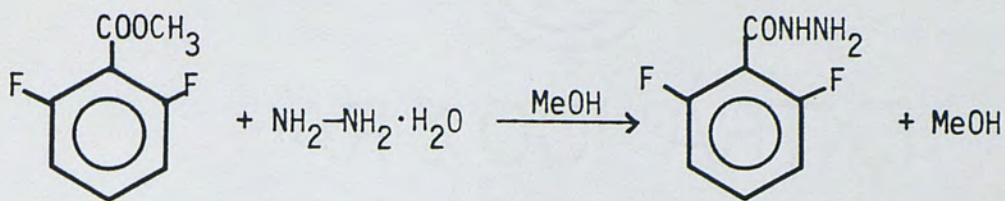
E. Preparation of Methyl(2,6-difluoro)benzoate



Methyl 2,6-Difluorobenzoate

To a 250 ml Erlenmeyer flask equipped with a stirring bar was added 10 g (.063 mol) of 2,6-difluorobenzoic acid, 50 ml of HMPA and 2.77 g (.07 mol) of NaOH. The NaOH was added in the form of a 25% aqueous solution. The mixture was allowed to stir at room temperature for 1-½ hrs at which time 10 ml of water was added and 17.9 g (.126 mol) of methyl iodide was added. The methyl iodide was dripped in slowly. After stirring the reaction mixture at room temperature overnight it was poured into a 500 ml separatory funnel containing 100 ml of a 5% HCl solution. It was then extracted with 3x75 ml portions of diethyl ether. The combined ether extracts were dried over anhydrous magnesium sulfate and concentrated to give an 83% yield of a brown liquid: NMR (CDCl₃) δ 4.00 (s, 3H), 7.31 (m, 3H); IR (thin film) 2965, 1735, 1300, 830, 800, 770 and 600 cm⁻¹.

F. Preparation of 2,6-Difluorobenzoylhydrazine

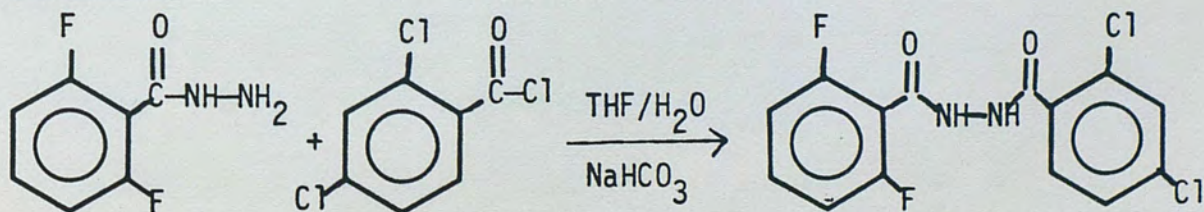


2,6-Difluorobenzoylhydrazine

To a 250 ml, three-necked, round-bottomed flask equipped with a reflux condenser, magnetic stirring bar, thermometer and thermometer adapter was added 60 ml of MeOH, 13.4 (.078 mol) of methyl-2,6-difluorobenzoate and 23.4 g (.468 mol) of hydrazine monohydrate. The mixture was brought to reflux and left to stir overnight. The mixture was then cooled to room temperature and the MeOH was removed in vacuo. The resulting viscous liquid was placed in an ice bath to aid crystal formation. The crystals were removed by filtration washed with 5 ml of cold water and dried in vacuo at .5 mm. This gave a 45% crude yield of a gray-brown solid which had a melting point of 258-263°C and was soluble in 10% HCl: NMR (d^6 DMSO, $CDCl_3$) δ 6.50-7.30 (m, 3H); IR (nujol mull) 3100, 1650, 778 and 730 cm^{-1} ; MS m/e 172 (M^+).

G. Preparation of N-(2,6-Difluorobenzoyl)-N'-(2,4-Dichlorobenzoyl) Hydrazine

Hydrazine



N-(2,6-Difluorobenzoyl)-N-(2,4-dichlorobenzoyl)hydrazine

To a 250 ml, three-necked, round-bottomed flask equipped with a reflux condenser, thermometer, thermometer adapter and 125 ml addition funnel was added .6 g (.0035 mol) of 2,6-difluorobenzoyl hydrazine, 100 ml of a 50/50 (v/v) mixture of tetrahydrofuran and water and .3 g (.0035 mol) of sodium bicarbonate. Next, .728 g (.0035 mol) of 2,4-dichlorobenzoylchloride was dissolved in 10 ml of tetrahydrofuran and added to the reaction mixture. The solution was allowed to stir at room temperature for 18 hrs. The THF was then removed in vacuo which resulted in the formation of a tacky brown solid. This was warmed in 50 ml of ethanol and a lighter colored solid formed. The solid was filtered through a fritted glass funnel and dried in vacuo at .5 mm for 2 hrs. This resulted in a crude product yield of .9 g (75%). The product was re-crystallized from a solution of 5 parts EtOH and 1 part water: NMR (d^6 DMSO, $CDCl_3$, d^6 acetone) δ 7.42 (m, 5H), 8.34 (m, 1H); IR (nujol mull) 3180, 1610, 1468, 870 and 800 cm^{-1} ; MS m/e 344 (M^+).

H. Preparation of Disubstituted Semicarbazides

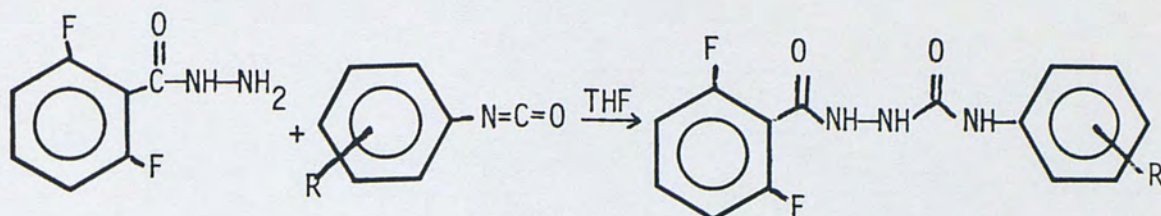


Table V

Experimental Data for the Preparation of Disubstituted Semicarbazides

Entry	R	Yield (%) ⁶	mp, °C ^a
1	p-methyl ^c	85	217-221
2	o-trifluoromethyl ^d	96	196-204
3	m-trifluoromethyl ^e	96	206-209
4	p-fluoro ^f	95	217-221

a. All of the melting points are for the crude products.

b. All of the yields are based on crude products.

c. See the experimental procedure for spectral data.

d. NMR (d⁶ DMSO, CDCl₃) δ 6.90-7.95 (m, 6H), 8.30 (d, J=7Hz, 1H); IR (nujol mu11) 3200, 1710, 1685, 1645, 1615, 795, 760 and 680 cm⁻¹.

e. NMR (d⁶ DMSO, CDCl₃, d⁶ acetone) δ 6.58-7.89 (m, 7H); IR (nujol mu11) 3200, 1705, 1670, 1642, 1620, 800, 750, 730 and 720 cm⁻¹.

f. NMR (d⁶ DMSO, CDCl₃) δ 6.58-7.89 (m, 7H); IR (nujol mu11) 3210, 1705, 1665, 1635, 1615, 800, 760 and 720 cm⁻¹.

- g. All of the products were insoluble in 10% HCl and saturated NaHCO_3 .

N-(2,6-Difluorobenzoyl)-N-(4-methylphenylaminoformyl) hydrazine

To a 250 ml three-necked, round-bottomed flask equipped with a reflux condenser, thermometer, thermometer adapter, magnetic stirring bar and a 125 ml addition funnel was added 50 ml of THF and 1.0 g (.0058 mol) of 2,6-difluorobenzoyl hydrazide. To this solution was added .77 g (.0058 mol) of p-tolylisocyanate. The isocyanate was dissolved in 10 ml THF prior to addition. After stirring overnight at room temperature the THF was removed in vacuo and the resulting solid was collected on a fritted glass filter and washed with 10 ml of cold water. The tan colored solid gave an 85% (1.5 g) yield after drying in vacuo at .5 mm of Hg: NMR (d^6 DMSO, CDCl_3) δ 2.32 (s, 3H) and 6.70-7.88 (m, 7H); IR (nujol mull) 3210, 1715, 1670, 1640, 1610, 860 and 800 cm^{-1} .

I. Preparation of Trifluoroisopropoxybenzonitrile

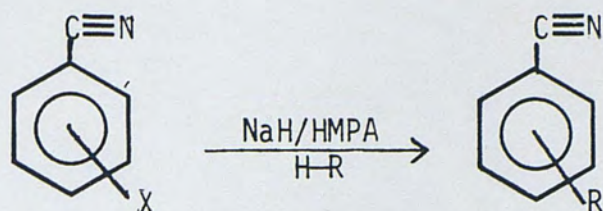


Table VI

Experimental Data for the Preparation of Trifluoroisopropoxybenzonitriles

Entry	R	Yield (%) ^b	mp °C ^a
1	3-(2,2,2-trifluoroisopropoxy) ^c	28	---
2	4-(2,2,2-trifluoroisopropoxy) ^d	49	---

a. The products were liquids at room temperature.

b. The reported yields are for the distilled products.

c. NMR (CDCl₃) δ 1.58 (d, J=6Hz, 3H), 4.73 (heptet, J=6Hz, 1H), 7.11-7.79 (m, 4H).

d. NMR (CDCl₃) δ 1.58 (d, J=6Hz, 3H), 4.87 (heptet, J=6Hz, 1H), 7.11 (d, J=8Hz, 2H), 7.70 (d, J=8Hz, 2H).

e. For a description of the experimental procedure see reference 5.

J. Preparation of Trifluoroisopropoxybenzamides

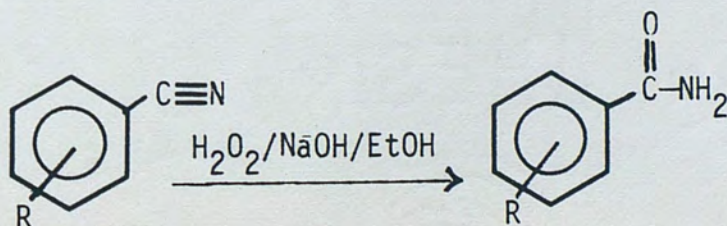


Table VII

Experimental Data for the Preparation of Trifluoroisopropoxybenzamides

Entry	R	Yield (%) ^b	mp °C ^a
1	3-(2,2,2-trifluoroisopropoxy) ^c	75	140-143
2	4-(2,2,2-trifluoroisopropoxy) ^d	73	147-148

- a. The melting points refer to crude products.
- b. The percent yields refer to crude products
- c. NMR (d^6 acetone, $CDCl_3$) δ 1.52 (d, $J=6\text{Hz}$, 3H), 4.98 (heptet, $J=6\text{Hz}$, 1H), 7.00-7.80 (m, 4H); IR (nujol mull) 3370, 3200, 1655, 1245, 950, 780 and 745 cm^{-1} .
- d. NMR (d^6 DMSO, $CDCl_3$) δ 1.56 (d, $J=6\text{Hz}$, 3H), 4.87 (heptet, $J=6\text{Hz}$, 1H), 7.11 (d, $J=8\text{Hz}$, 2H), 8.04 (d, $J=8\text{Hz}$, 2H); IR (nujol mull) 3380, 3200, 1650, 1255, 935, 850, and 795 cm^{-1} .
- e. For a description of the experimental procedure, see section II-A.

K. Preparation of Trifluoroisopropoxybenzoic Acids

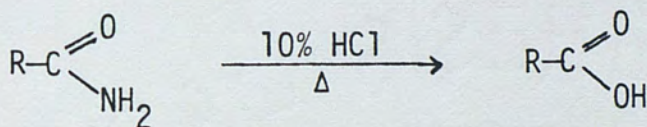


Table VIII

Experimental Data for the Preparation of Trifluoroisopropoxybenzoic Acids

Entry	R	Yield (%) ^b	mp °C ^a
1	3-(2,2,2-trifluoroisopropoxy)phenyl ^c	77	152-156
2	4-(2,2,2-trifluoroisopropoxy)phenyl ^d	96	146-149

a. The reported melting points are for the crude products.

b. The reported yields are for the crude products.

c. NMR (CDCl₃) δ 1.54 (d, J=6Hz, 3H), 4.74 (heptet, J=6Hz, 1H), 7.53 (m, 4H), 9.00 (broad s, 1H); IR (nujol mull) 3200-2500, 1685, 1585, 1155 and 750 cm⁻¹.

d. See the experimental procedure for spectral data.

4-(2,2,2-Trifluoroisopropoxy)benzoic acid

To a 250 ml, three-necked, round-bottomed flask equipped with a thermometer, thermometer adapter, reflux condenser and magnetic stirring bar was added 2.5 g (.011 mol) of 4-(2,2,2-trifluoroisopropoxy)benzamide and 100 ml of 10% HCl. The mixture was allowed to stir overnight, then cooled to room temperature and 100 ml of water was added in one portion. The mixture was stirred for 1 hr and then filtered. The light colored solid was washed with 10 ml of water and dried in vacuo at .5 mm of Hg to yield 2.4 g of product: NMR (CDCl₃) δ 1.52 (d, J=6 Hz, 3H), 4.81 (heptet, J=6Hz, 1H), 6.90

(d, J=8Hz, 2H), 7.20 (broad s, 1H) and 8.00 (d, J=8Hz, 2H); IR (nujol mu11) 3200-2500, 1680, 1585, 1180, 850, 780 and 690 cm^{-1} .

L. Preparation of Bis-disubstituted Oxadiazoles

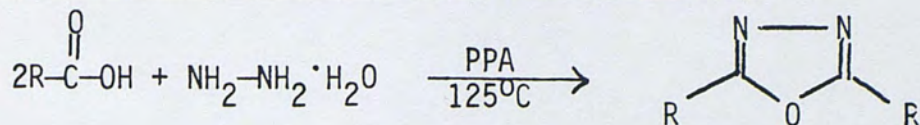


Table IX

Experimental Data for the Preparation of Bis-2,5-disubstituted Oxadiazoles

Entry	R	Yield (%) ^b	mp ^o C ^a
1	2,6-difluorophenyl ^c	22	184-186
2	3-(2,2,2-trifluoroisopropoxy)phenyl ^d	68	140-143
3	4-(2,2,2-trifluoroisopropoxy)phenyl ^e	92	146-149

a. The melting points are for the crude products.

b. The yields are for the crude products.

c. See the experimental procedure for spectral data.

d. NMR (d^6 acetone, CDCl_3) δ 1.58 (d, J=6Hz, 6H), 5.19 (heptet, J=6Hz, 2H), 7.10-7.90 (m, 8H); IR (nujol mu11) 1588, 1490, 1460, 1155, 1025, 960, 740 and 680 cm^{-1} .

e. NMR (d^6 DMSO, CDCl_3) δ 1.52 (d, J=6Hz, 6H), 5.22 (heptet, J=6Hz, 6H), 5.22 (heptet, J=6Hz, 2H), 7.20 (d, J=8Hz, 4H) and 8.00 (d, J=8Hz, 4H); IR (nujol mu11) 1610, 1460, 1175, 1020, 840, 750 and 700 cm^{-1} .

Bis-2,5-(2,6-Difluorophenyl)oxadiazole

To a 100 ml, three-necked, round-bottomed flask equipped with a reflux condenser, thermometer, thermometer adapter and magnetic stirring bar was added 25.3 g of PPA and 2 g (.025 mol) of 2,6-difluorobenzoic acid. The mixture was heated to 45°C and .633 g (.0126 mol) of hydrazine monohydrate was added slowly. The temperature was allowed to rise to 100°C at which point the mixture was mobile enough to allow stirring. The temperature was then equilibrated at 125°C and the mixture was stirred for 5 hr. The solution was cooled to 90°C and 94.5 ml of water was added in one portion. The mixture was then stirred for 15 min. The precipitate which formed was collected on a fritted glass funnel and washed with cold water. The white solid product was then dried in vacuo at .5 mm of Hg for 4 hr giving a 22% yield: NMR (d^6 DMSO) δ 7.10 (t, J=8Hz, 4H) and 7.20-7.70 (m, 2H); IR (nujol mull) 1640, 1600, 1490, 1468, 1250, 1023, 975, 800 and 710 cm^{-1} ; MS m/e 294 (M^+),

PART I

III. DISCUSSION OF RESULTS

Tables I through IV tabulate the ortho-, meta- and para- 2,2,2-trifluoroethoxy isomers of the amides, monoacylhydrazides, diacylhydrazides and 2,5-disubstituted-1,3,4-oxadiazoles. The products were all characterized by NMR and IR spectroscopy^{16,18}. The products were synthesized in adequate purity or were purified by distillation or recrystallization.

Section II-A describes the procedure for the conversion of the isomeric 2,2,2-trifluoroethoxybenzotrioles to their benzamide analogs. The structural assignment of the amide group was based on the presence of a C=O stretch (1640 cm^{-1}) and 1° amide stretching (3390 and 3190 cm^{-1}). The absence of an IR absorption at 2200 cm^{-1} due to $\text{C}\equiv\text{N}$ stretching indicates that all of the starting material was converted. The presence of a quartet at 4.60 ppm in the NMR spectrum is assigned to two hydrogens on the α -carbon of the trifluoroethoxy group. From the data in Section II-B, one can see the 2,2,2-trifluoroethoxybenzotrioles are converted to the corresponding monoacylhydrazides. The IR structural assignments include an N-H 2° amide stretch (3300 cm^{-1}). The absence of the 1° amide stretching at 3390 cm^{-1} and 3190 cm^{-1} and the shift in frequency of the C=O absorption indicate that most if not all of the starting amide was converted. The presence in the NMR spectrum of the characteristic

quartet at 4.40 ppm due to the hydrogens on the α -carbon of the trifluoroethoxy group indicates this group is still intact. Jensen¹⁹, Prevorsek²⁰ and Zabicky²¹ cite these IR absorptions for monoacylhydrazides. These absorptions are also consistent with those reported by Lizzi²².

Section II-C refers to the conversion of the isomeric 2,2,2-trifluoroethoxy monoacylhydrazides to the diacylhydrazides. The infrared spectral characterizations of the diacylhydrazides^{21,22} include a $\text{-NH } 2^\circ$ amide stretch at 3210 cm^{-1} and a broad C=O stretch at 1640 cm^{-1} ; also, absorptions in the regions of 840 cm^{-1} , 830 cm^{-1} , 790 cm^{-1} and 760 cm^{-1} indicate a 1,2,4-trisubstitution pattern which suggests conversion to the diacylhydrazide. The NMR spectrum shows a quartet absorption again at 4.60 ppm indicating the trifluoroethoxy group is still intact²³.

NMR and IR spectroscopy were also used for the characterization of the ortho, meta and para trifluoroethoxy isomeric 2,5-disubstituted-1,3,4-oxadiazoles. Katritsky²⁴ and Barrons²⁵ report infrared absorption bands at 970 and $1020\text{-}1030 \text{ cm}^{-1}$ which are characteristic of the C-O bond and also absorption at $1560\text{-}1640 \text{ cm}^{-1}$ characteristic of a C=N stretch in the oxadiazole heterocyclic ring system. The aryl substituted oxadiazole system²⁶ synthesized in this investigation also reveals a $\text{C}\equiv\text{C}$ absorption band at $1490\text{-}1500 \text{ cm}^{-1}$. Also the absence of a $\text{-NH } 2^\circ$ amide absorption at 3200 cm^{-1} indicates conversion to the oxadiazole system. The distinguishing absorption in the NMR spectrum is again due to the quartet centered at 4.60-4.90 ppm.

The preparation of the N-(2,6-difluorobenzoyl)-N-(2,4-dichlorobenzoyl)hydrazine of Section II-G, the methyl ester and monoacylhydrazide precursor, was successfully carried out. The methyl ester of the carboxylic acid was characterized structurally by the presence of a C=O stretch at 1735 cm^{-1} . The conversion of the methyl ester to the monoacylhydrazide was described in Section II-F. The hydrazide was characterized by the same infrared absorptions described for the previous hydrazides. The absorption of only aromatic hydrogens in the NMR spectrum indicated a need for a molecular weight determination. This was accomplished by mass spectrometry²⁷. The mass spectrum yielded a mass-to-charge ratio of 172. The diacylhydrazide of Section II-G also revealed the same characteristic absorptions as the previous diacylhydrazides. Mass spectrometry was also necessary due to the absence of an identifiable "handle" group in the NMR spectrum. The mass-to-charge ratio was 344. These mass-to-charge ratios indicated molecular ions with a mass of 172 and 344 respectively.

In reference to Section II-H, the semicarbazides were characterized by NMR and IR spectroscopy, the latter being the most useful. The infrared spectrum of these semicarbazides revealed the same IR absorption as the previously obtained diacylhydrazides. The absence of an isocyanate absorption at $2000\text{-}2270\text{ cm}^{-1}$ indicated complete conversion¹⁶.

Sections II-I through II-K reference the spectral data for the characterization of the trifluoroisopropoxy benzonitriles, benzamides and benzoic acids respectively. The major functional group absorptions

in the infrared spectra have been discussed except for the carboxylic acid. The O—H stretch of the acid gives broad absorption from 2500 to 3200 cm^{-1} and C=O absorptions at 1700 cm^{-1} .

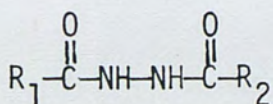
The NMR spectrum of all of these compounds reveals a doublet at 1.58 ppm due to the three geminal hydrogens coupled with the single proton bonded to α -carbon with respect to the oxygen in the trifluoroisopropoxy group. The single proton on this α -carbon is coupled to the three protons as well as the three fluorine atoms to give a heptet at 4.87 ppm.

Similar NMR absorptions are seen in the spectra of the corresponding oxadiazoles. The infrared absorptions were at the same characteristic frequencies as in the previously synthesized oxadiazoles.

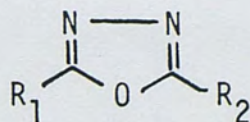
PART I

IV. CONCLUSIONS

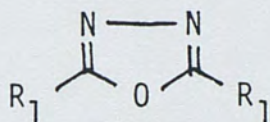
Four classes of compounds were prepared (see below) with the hope of better biological activity than previously synthesized insecticides. These compounds include the diacylhydrazides (14), 2,5-disubstituted-1,3,4-oxadiazoles (15), bis-2,5-disubstituted-1,3,4-oxadiazoles (16) and the semicarbazides (17).



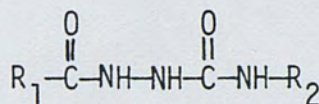
(14)



(15)



(16)



(17)

All of the compounds which were prepared were done under relatively mild conditions which would allow for easy scale-up. In cases where NMR and IR spectroscopy was not conclusive in characterization, mass spectrometry was the definitive tool. All compounds were sent to Dow Chemical Company for biological activity screening.

PART I

V. RECOMMENDATIONS

The following recommendations are suggested for future research:

1. Before any of the fluoroalkoxylation reactions are used industrially (Sections A and I) efforts should be made to find a less toxic solvent than HMPA and a less hazardous base than sodium hydride.
2. Due to the ease of synthesis of the semicarbazides, many more substituted semicarbazides may be rapidly prepared for biological testing.

PART II

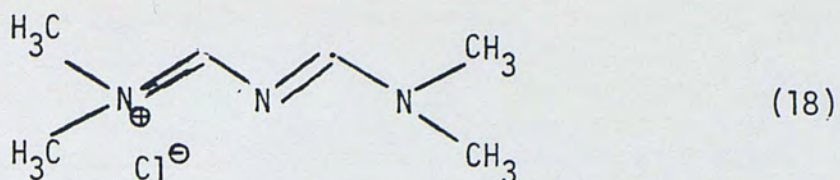
REACTIONS OF VINAMIDINIUM AND AZAVINAMIDINIUM SALTS
WITH ORGANOMETALLIC/BORANE REAGENTS AND ACTIVATED NITRILES

PART II

I. INTRODUCTION

Recently, considerable interest has developed concerning the preparation and use of imminium and vinamidinium salts. Poulter, Roberts and Borromeo²⁸ have demonstrated the reaction of Eschenmoser's salt with Grignard reagents and lithium reagents to give dialkyaminoalkanes which can be converted to alkenes by oxidation or elimination. Nair and Cooper²⁹ have shown that vinamidinium salts react with ketone enolates to give dienaminones. They suggested these dienaminones could be useful in natural product synthesis as intermediates. The reactions of cyclic imminium salts with organometallic reagents has been reported by Moriya³⁰ to yield dialkylaminoalkanes. Gupton³¹ and coworkers recently reported the reaction of phenyl substituted vinamidinium perchlorate salts with organometallic reagents to produce 3-substituted-2-phenyl-acroleins in good yield. Gupton^{32,33} and coworkers also have reported the reaction of azavinamidinium salts with esters and nitrotoluenes as well as arylvinamidinium salts with sodium borohydride and sodium cyanoborohydride.

Additionally, it has been shown^{34,34} that [3-(dimethylamino)-2-azaprop-2-en-1-ylidene] dimethylammonium chloride, hereafter referred to as "Gold's reagent" (18) reacts with ketones and amides to produce enamines and acylamidines.³⁶

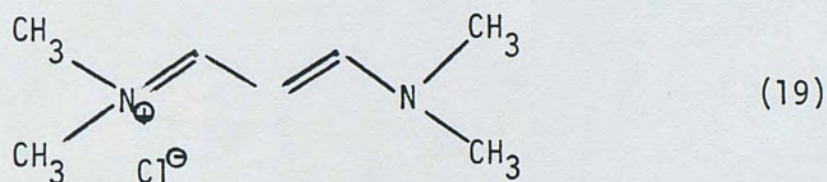


As a consequence of their studies, Gupton and coworkers³⁷ treated Gold's reagent with organometallic reagents and upon dilute acid workup, one carbon elongated aldehydes were obtained.

As a logical extension of these studies, this investigator proposes to react Gold's reagent with organometallic reagents and then reduce the intermediates with borane to the corresponding alkyl and aryl N,N-dimethyl amines. The proposed mechanism for such a reaction is given in Figure 6.

This is a nucleophilic addition at an electrophilic carbon with subsequent borane reduction and conjugate elimination.

Another logical extension of reactions with vinamidinium systems is the reaction of 1,5-diazapentadienium chloride (19), hereafter referred to as "Nair's reagent"³⁸, with new nucleophiles, specifically, nitrile activated alkanes.



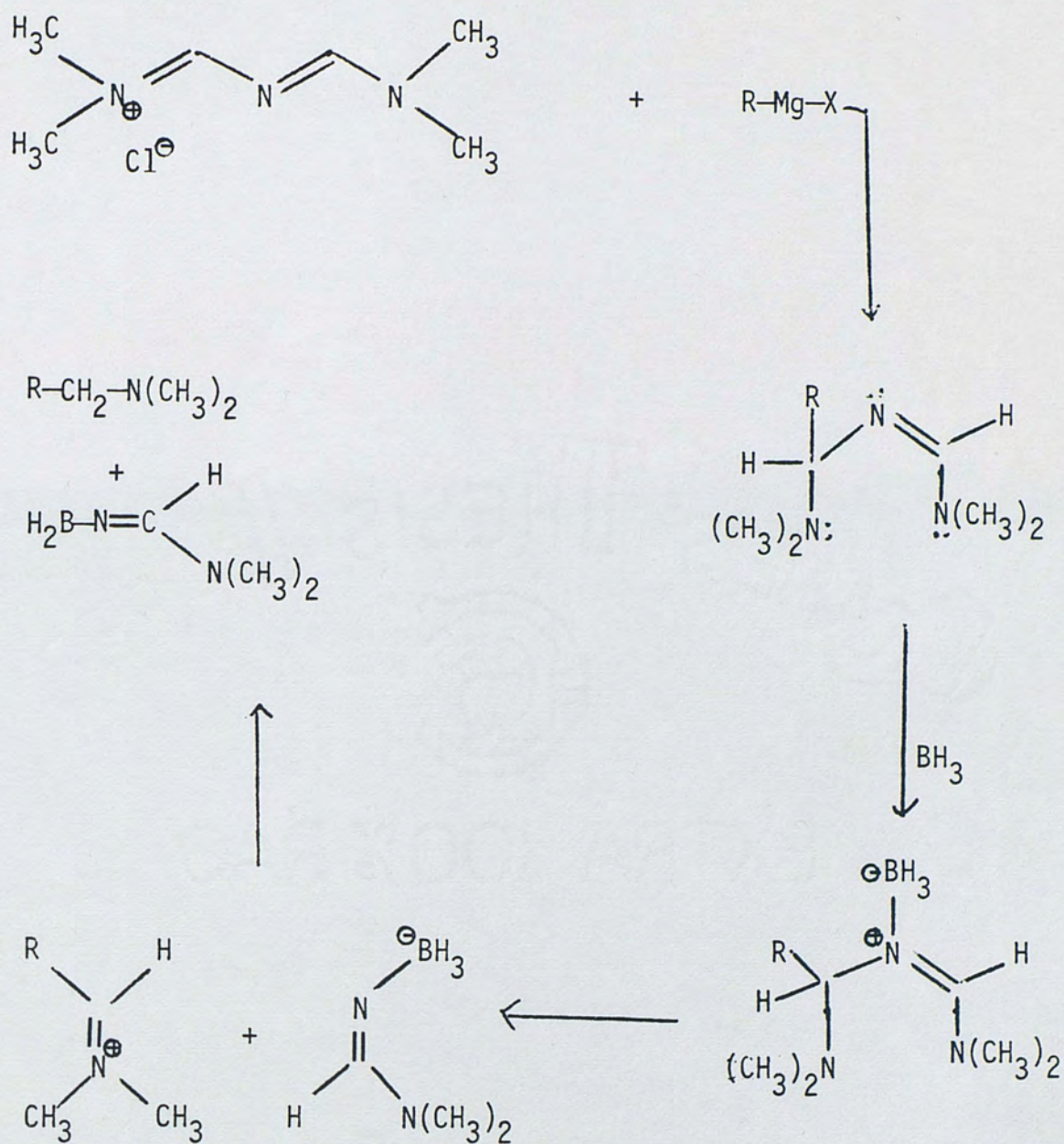


Figure 6. Proposed mechanism for the production of alkyl and aryl N,N-dimethyl amines.

Due to the availability and ease of synthesis, the perchlorate salt analog of Nair's reagent will be used in the proposed syntheses.

The proposed mechanism for these syntheses is given in Figure 7.

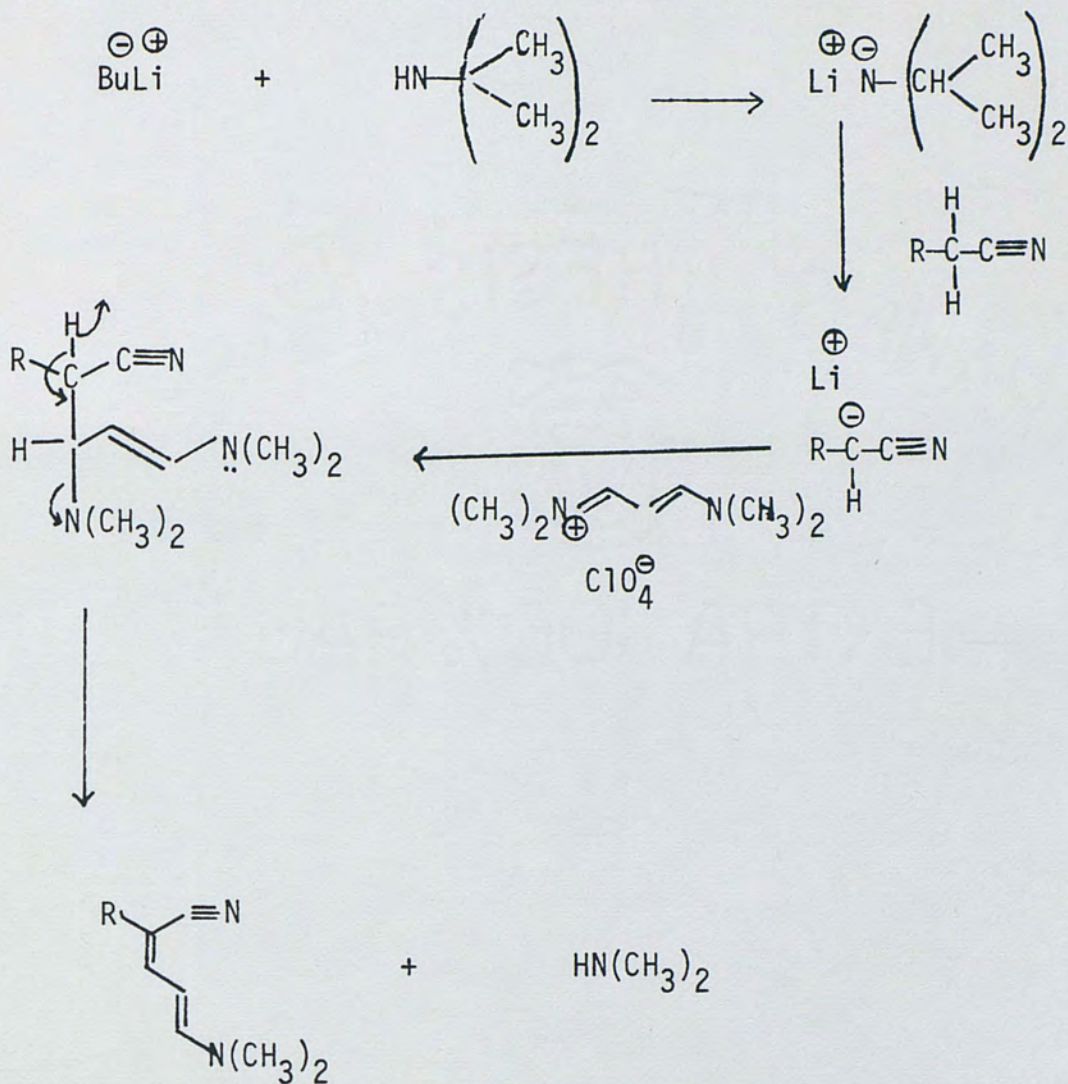


Figure 7. Proposed mechanism for the synthesis of alkyl and aryl dienamino nitriles.

This proposed synthesis is a nucleophilic addition of a carbanion, generated by the abstraction of a weakly acidic hydrogen with diisopropylamide, to an electrophilic carbon with subsequent

elimination of dimethyl amine to yield alkyl and aryl dienamino nitriles. In this instance, the leaving group is dimethylamine due to the relative strengths of the C-N bond and the C-C bond.

Reviews of the nomenclature³⁷ and properties^{38,40} of vinamidinium systems are available. Excellent descriptions of the preparation of Nair's reagent and Gold's reagent are available in the literature^{34,35,38}.

The utility of vinamidinium salts and azavinamidinium salts has been described. The possible use of vinamidinium derivatives as an easy synthesis of alkyl and aryl substituted pyridines is proposed by the investigator. A proposed reaction scheme is given in Figure 8.

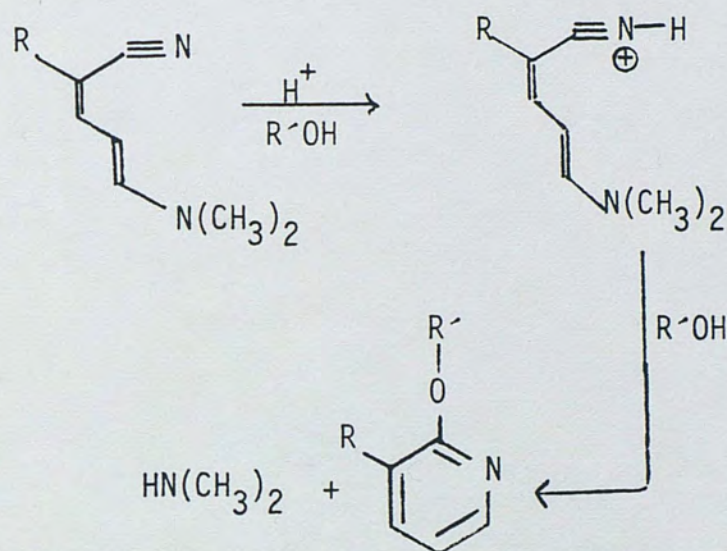


Figure 8. Proposed reaction scheme for the synthesis of alkyl and aryl substituted pyridines.

PART II

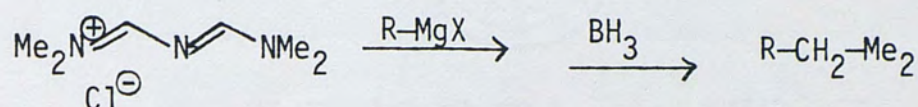
II. EXPERIMENTALA. Preparation of Alkyl and Aryl-N,N-Dimethyl Amines

Table X

Experimental Data for the Preparation of Alkyl and Aryl N,N-Dimethyl Amines

Entry	R	Yield (%) ^b	bp °C ^a
1	n-hexyl ^c	35	78 at 122 mm
2	cyclohexyl ^d	19	64 at 122 mm
3	n-octyl ^e	14	98 at 70 mm
4	phenyl ^f	32	90 at 72 mm
5	benzyl ^j	24	84 at 55 mm

a. The boiling points were obtained using a Kugelrohr apparatus.

b. The yields are distilled yields.

c. NMR (CDCl₃) δ 0.91 (t, J=4Hz, 3H), 1.32 (broad s, 10H), 2.22 (broad s, 8H); IR (thin film) 2925, 2855, 2815, 2760, 1460, 1375, 1155, 1040 and 735 cm⁻¹.

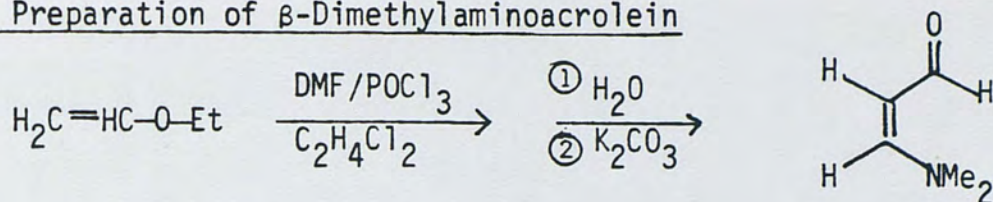
- d. NMR (CDCl_3) δ 1.00-2.00 (broad m, 11H), 2.12 (d, $J=6\text{Hz}$, 2H), 2.20 (s, 6H); IR (thin film) 2950, 2920, 2850, 2815, 2760, 2720, 1450, 1375, 1260, 1030, 850 and 830 cm^{-1} .
- e. NMR (CDCl_3) δ 0.89 (t, $J=4\text{Hz}$, 3H), 1.29 (broad s, 14H), 2.20 (broad s, 8H); IR (thin film) 2920, 2855, 2810, 2760, 2720, 1460, 1378, 1150, 1040 and 735 cm^{-1} .
- f. See the experimental procedure for spectral data.
- g. NMR (CDCl_3) δ 2.29 (s, 6H) 2.50-2.90 (m, 4H, 7.28 (broad s, 5H); IR (thin film) 3065, 3035, 2970, 2940, 2855, 2810, 2760, 1460, 1372, 1263, 1040, 750 and 700 cm^{-1} .

N,N-Dimethylbenzylamine

To a 500 ml, three-necked, round-bottomed flask, under a positive pressure nitrogen atmosphere, equipped with a thermometer, thermometer adapter, reflux condenser and magnetic stirring bar was added 80 ml of dry THF and 6.0 g (.0368 mol) of Gold's reagent. The flask was placed in an ice bath to maintain the temperature between $5\text{-}15^\circ\text{C}$. A syringe and needle were used to add 27.6 ml (.0552 mol) of a 2.0 molar solution of phenylmagnesium chloride. After stirring at room temperature for 3 hr, the solution was again brought to 5°C and the same method was used to add 18.4 ml (.0184 mol or 1.5 equivalents) of a 1.0 molar solution of borane in THF. The solution was then allowed to stir overnight. After cooling the solution in an ice bath, 10 ml of methanol was added. The THF was then removed in vacuo and 150 ml of 5% HCl was added while stirring and cooling. This was extracted with three 40 ml portions of ethyl ether. The aqueous phase was

brought to pH 10-11 and saturated with sodium chloride. The basic aqueous phase was extracted with three 50 ml portions of diethyl ether. The combined ether phases from the second extraction were dried with anhydrous magnesium sulfate and concentrated. The resulting yellow-brown liquid was distilled on a Kugelrohr apparatus at 72 mm of Hg to yield 1.6 g of clear liquid: NMR (CDCl_3) δ 2.23 (s, 6H), 3.43 (s, 2H) and 7.23 (broad s, 5H); IR (thin film) 3065, 3035, 2970, 2943, 2810, 2785, 1453, 1365, 1025, 740 and 700 cm^{-1} .

B. Preparation of β -Dimethylaminoacrolein

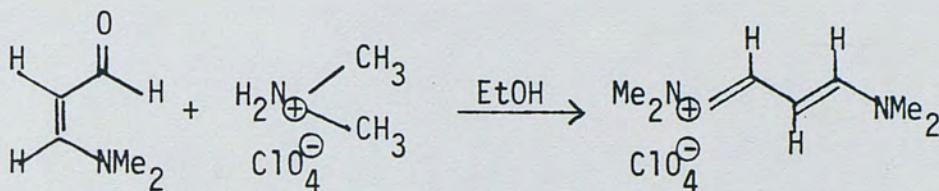


β -Dimethylaminoacrolein

To a 500 ml three-necked, round-bottomed flask equipped with a reflux condenser, thermometer, thermometer adapter, magnetic stirring bar and 125 ml addition funnel was added 29.2 g (0.4 mol) of DMF and 60 ml of 1,2-dichloroethane. The temperature was brought to 0°C using an ice bath. Phosphorous oxychloride (30.6 g, 0.2 mol) dissolved in 1,2-dichloroethane was added through the addition funnel. The solution was allowed to stir for 1 hr. Using a clean addition funnel, 14.4 g (.2 mol) of ethyl vinyl ether in 20 ml of 1,2-dichloroethane was added slowly. The mixture was then heated to 70°C for 3 hr. Next the mixture was cooled to 0°C and 120 ml of water was added slowly. The solution was stirred at room temperature overnight. After cooling to 0°C , 200 ml of saturated potassium carbonate was added slowly. The solution was extracted

in a 1 liter separatory funnel with four 50 ml portions of methylene chloride. The combined organic phases were dried with anhydrous magnesium sulfate and concentrated. The residual DMF was removed by distillation at 40-55°C at .5 mm of Hg and the product was distilled at 60-75°C at .5 mm of Hg using a Kugelrohr apparatus. This gave a 33% yield (6.7 g) of translucent orange liquid: NMR (CDCl₃) δ 2.86 (s, 3H), 5.12 (d of d, J=8Hz, J=13Hz, 1H), 7.19 (d, J=13Hz, 1H), and 9.04 (d, J=8Hz, 1H); IR (thin film) 2810, 2780, 1620 and 1410 cm⁻¹.

C. Preparation of 1,5-Diazapentadienium Perchlorate



1,5-Diazapentadienium Perchlorate

To a 100 ml one-necked, round-bottomed flask equipped with a reflux condenser and magnetic stirring bar was added 6.0 g (.060 mol) of β -(dimethylamino)acrolein 25 ml of EtOH and 9.2 g (.063 mol) of dimethylammonium perchlorate. The mixture was allowed to stir at reflux overnight. The mixture was then cooled in an ice bath to induce crystallization. The crystals were vacuum filtered and washed with 25 ml of cold EtOH. The crude product was then placed on a vacuum pump and dried for 2-½ hr at .5 mm of Hg. This gave 10.1 g (74% yield) of a tan solid.

NMR (CDCl_3 , d^6 DMSO) δ 3.14 (s, 6H), 3.38 (s, 6H), 5.27 (t, $J=12\text{Hz}$, 1H), 7.77 (d, $J=12\text{Hz}$, 2H); IR (nujol mull) 2020, 1615, and 1405 cm^{-1} .

D. Preparation of α -Substituted Dienaminonitriles

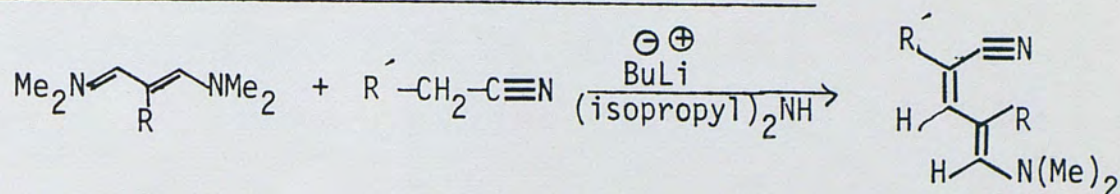


Table XI

Experimental Data for the Preparation of α -Substituted Dienaminonitriles

Entry	R	R'	Yield (%) ^b	bp °C ^a
1	-H	ethyl ^c	50	85 at .4 mm
2	-H	n-propyl ^d	37	98 at .3 mm
3	-H	n-butyl ^e	30	90 at .1 mm

a. The boiling points were obtained by distillation on a Kugelrohr apparatus.

b. The reported yields are distilled yields and are based on the amount of recovered material.

c. See the experimental procedure to spectral data.

d. NMR (CDCl_3) δ 1.00 (broad m, 3H), 1.58 (broad m, 2H), 2.25 (m, 2H), 2.89 (s, 6H), 5.00-5.58 (m, 1H), 6.40-6.87 (m, 2H); IR (thin film) 2960, 2930, 2865, 2805, 2185 and 1625 cm^{-1} .

- e. The NMR spectrum was not as well defined as examples 1 and 2 but was consistent with previous absorption patterns.

4-Cyano-1-Dimethylamino-1,3-Hexadiene

To a 500 ml, three-necked, round-bottomed flask flushed with nitrogen and equipped with a reflux condenser, thermometer, thermometer adapter and magnetic stirring bar was added 75 ml of dry THF and 2.7 g (.027 mol) of diisopropylamine. The solution was cooled to 5°C and 12.4 ml (.0198 mol) of butyl lithium was added via syringe. The solution was allowed to stir 20 min at which time .91 g (.013 mol) of n-butyronitrile was added slowly and allowed to stir for 10-15 min. Next, 3.0 g (.013 mol) of the vinamidinium perchlorate salt was added in one portion. The mixture was stirred at room temperature overnight. The solution was then cooled to 5°C and the THF was removed in vacuo. Then 80 ml of a 50/50 mixture of hexane and THF was added. The solid which precipitated was removed by vacuum filtration and concentrated in vacuo. The resulting dark liquid was poured into 50 ml of water and extracted with three 50 ml portions of methylene chloride. The combined organic phases were then dried over anhydrous magnesium sulfate and concentrated. The dark colored liquid was distilled using a Kugelrohr apparatus at 85°C at .4 mm of Hg. This gave 1.0 g of liquid (50% yield): NMR (CDCl₃) δ 1.11 (t, J=7Hz, 3H), 2.14 (q, J=8Hz, 2H), 2.83 (s, 6H), 4.75-5.50 (m, 1H), 6.38-6.78 (m, 2H); IR (thin film) 2965, 2930, 2855, 2810, 2185 and 1625 cm⁻¹; MS m/e 150 (M⁺).

PART II

III. DISCUSSION OF RESULTS

All characterization of the alkyl and aryl N,N-dimethyl amines was performed via NMR and IR spectroscopy. The IR spectra of these compounds shows similar absorptions at 2785 and 2810 cm^{-1} due to C-H stretching on the methylene group attached to the nitrogen. The aromatic amines show absorption in the 3030 to 3060 cm^{-1} range due to aromatic C-H stretching. The aliphatic amines show absorption in the 1360 and 1450 cm^{-1} regions caused by CH_2 out of plane bending and CH_2 in plane bending, respectively. All of the compounds show absorption at about 1020 cm^{-1} due to C-N stretching.

The NMR spectra of these N,N-dimethyl amines are well documented⁴¹⁻⁴³.

In reference to Sections II-B and II-C, the spectra of β -dimethylaminoacrolein corresponds well with the absorptions reported by Nair and coworkers³⁸.

The IR spectrum of the 4-cyano-1-dimethylamino-1,3-hexadiene compound is typical of the class of compounds in Section II-D. Absorptions are observed at 2930 and 2965 cm^{-1} due to aliphatic C-H stretching, 2185 cm^{-1} caused by the nitrile stretching and 1625 cm^{-1} due to C=C stretching. The NMR spectra of this compound shows a triplet absorption at 1.11 ppm which is due to the three

methyl protons on the number 6 carbon coupled with the methylene protons on the number 5 carbon. A quartet is observed at 2.14 ppm from the methylene protons being coupled with the adjacent methyl protons. A singlet at 2.83 ppm is caused by the $N-(CH_3)_2$ protons which are equivalent. Multiplets from 4.75 to 5.50 ppm and 6.38 to 6.78 ppm are attributed to the vinyl hydrogens and the resulting vinylic coupling. The mass spectrum shows a molecular ion with a mass to charge ratio of 150, which agrees well with the molecular weight of the compound.

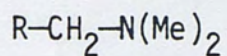
The n-propyl and n-butyl dienaminonitriles show similar NMR absorptions except the aliphatic region is characterized by a hydrocarbon envelope.

The NMR and IR spectra of the reactions to produce 3-substituted pyridines revealed no observable characteristic absorptions.

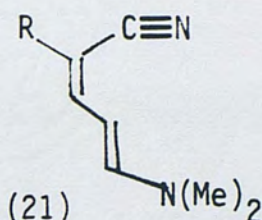
PART II

IV. CONCLUSIONS

Two classes of compounds were synthesized, the alkyl and aryl N,N-dimethyl amines (20) and the dienaminonitriles (21). These classes are depicted below.



(20)



These compounds were characterized by NMR and IR spectroscopy.

Attempts to synthesize 3-substituted pyridines were unsuccessful when the reagents diisobutylaluminum hydride, hydrobromic acid and sulfuric acid, which can all donate a proton, were employed.

PART II

V. RECOMMENDATIONS

The following suggestions may be useful for future work.

1. Reaction conditions should be optimized for the dienaminonitrile synthesis. The NMR spectra of the higher molecular weight compounds indicated some conversion but show the presence of byproducts.
2. In reference to the dienaminonitrile study, reactions involving aromatic nitriles and substituted vinylium salts should be given consideration.
3. Efforts to find a suitable reagent to facilitate intramolecular ring closure should continue.

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