

South Dakota State University

Open PRAIRIE: Open Public Research Access Institutional Repository and Information Exchange

Electronic Theses and Dissertations

1971

The Chemistry of Some Unusual Carbodiimides

Donald Melvin Plautz

Follow this and additional works at: <https://openprairie.sdstate.edu/etd>

 Part of the [Organic Chemistry Commons](#)

Recommended Citation

Plautz, Donald Melvin, "The Chemistry of Some Unusual Carbodiimides" (1971). *Electronic Theses and Dissertations*. 5279.

<https://openprairie.sdstate.edu/etd/5279>

This Dissertation - Open Access is brought to you for free and open access by Open PRAIRIE: Open Public Research Access Institutional Repository and Information Exchange. It has been accepted for inclusion in Electronic Theses and Dissertations by an authorized administrator of Open PRAIRIE: Open Public Research Access Institutional Repository and Information Exchange. For more information, please contact michael.biondo@sdstate.edu.

166

THE CHEMISTRY OF
SOME UNUSUAL CARBODIIMIDES

BY

DONALD MELVIN PLAUTZ

A thesis submitted
in partial fulfillment of the requirements for the
degree, Doctor of Philosophy, Major in
Chemistry, South Dakota
State University

1971

THE CHEMISTRY OF

SOME UNUSUAL CARBODIIMIDES

This dissertation is approved as a creditable and independent investigation by the candidate for the degree, Doctor of Philosophy, and is acceptable as meeting the dissertation requirements for the degree, but without implying that the conclusions reached by the candidate are necessarily the conclusions of the major department.

ABSTRACT

Several N^1 -alkyl- N^2 -(N,N-dialkylamino)carbodiimides, which were found to form dimeric species, were prepared, and the structure of the dimeric species determined. A study of the reaction chemistry of both the monomeric and dimeric carbodiimides led to the conclusion that dimerization occurred via a $(\pi 2s + \pi 2a)$ ground-state, symmetry-allowed mechanism, and that thermal decomposition of the dimeric species occurred via a $(\pi 2s + \pi 2s)$ excited-state, symmetry-allowed mechanism.

Although dialkylphosphoramidates have been shown to be useful intermediates in the preparation of unsaturated organic nitrogen compounds, N-acyl- and N-imino-dialkylphosphorohydrazidates were found to be too unstable, forming trialkylphosphates upon distillation, to be of any synthetic value.

The preparation of several difunctional and bis-carbodiimides was attempted, but no products were isolated. Based on the side reaction products isolated from the reaction mixtures, it was concluded that the desired carbodiimides did form, but that they were too unstable to be isolated under the reaction conditions used.

ACKNOWLEDGEMENTS

To Professor William S. Wadsworth, Jr., without whose guidance and patience this endeavor could not have been completed.

To the faculty and graduate students, whom I have known, who have made my association with S. D. S. U. an unforgettable experience.

To the National Science Foundation for its support through two Summer Traineeships.

And to my family for their patient endurance during this time.

TABLE OF CONTENTS

	Page
Chapter 1. The Chemistry of Some N^1-Alkyl-N^2-Dialkylamino-Carbodiimide -	
Historical	1
Discussion	6
Chapter 2. The Attempted Preparations of Di-functional and <u>Bis</u>-carbodiimides - Historical and Discussion	36
Experimental Section	61
Description of Instruments Used	61
Description of Chemicals Used	61
Preparation of Ethyl- <u>N-tert.</u> -butylcarbamate	62
Preparation of <u>tert.</u> -Butylisocyanate	62
Preparation of Diethyl- N^1, N^1 -dimethylphosphorohydrizate (<u>21a</u>)	63
Preparation of Diethyl- <u>N</u> -piperidinyolphosphorohydrizate (<u>21b</u>)	64
Preparation of Diethyl- <u>N-n</u> -butylphosphoramidate	65
Preparation of Diethyl- <u>N</u> -cyclohexylphosphoramidate	65
Preparation of N^1 - <u>tert.</u> -Butyl- N^2 -(<u>N,N</u> -dimethylamino)-carbodiimide (<u>22</u>)	66
Preparation of N^1 - <u>tert.</u> -Butyl- N^2 -piperdinyldcarbodiimide (<u>23</u>)	67
Preparation of N^1 - <u>tert.</u> -Octyl- N^2 -(<u>N,N</u> -dimethylamino)-carbodiimide (<u>24</u>)	67
Preparation of N^1 - <u>tert.</u> -Butyl- N^2 - <u>n</u> -butylcarbodiimide	68
Preparation of N^1 - <u>tert.</u> -Butyl- N^2 -cyclohexylcarbodiimide	69
Isolation of 1,3-Di-(<u>N,N</u> -dimethylamino)-2,4- <u>bis</u> -(<u>tert.</u> -butylimino)-1,3-diazetidene (<u>22</u> -dimer, <u>30</u>)	69
Isolation of 1,3-Di- <u>N</u> -piperidinyld-2,4- <u>bis</u> -(<u>tert.</u> -butylimino)-1,3-diazetidene (<u>23</u> -dimer)	69

Interconversion of <u>22</u> and <u>30</u>	70
Reaction of <u>22</u> with N^1 - <u>tert.</u> -Butyl- N^2 - <u>n</u> -butylcarbodiimide . . .	70
Reaction of <u>22</u> with N^1 - <u>tert.</u> -Butyl- N^2 -cyclohexylcarbodiimide .	71
Reaction of <u>22</u> with <u>23</u>	71
Preparation of N^1 - <u>tert.</u> -Butyl- N^2 -benzyltrimethylammonium Chloride Carbodiimide (<u>42</u>)	72
Reaction of <u>22</u> with Methyl iodide	72
Preparation of O-Ethyl- N^1 - <u>tert.</u> -butyl- N^2 -(N,N-dimethylamino)- isourea (<u>45</u>)	73
Preparation of N^1 - <u>tert.</u> -Butyl- N^2 - <u>n</u> -butyl- N^3 -(N,N-dimethyl- amino)guanidine (<u>46</u>)	73
Preparation of N^1 - <u>tert.</u> -Butyl- N^2 -piperidinyl- N^3 -(N,N- dimethylamino)guanidine (<u>47</u>)	74
Reaction of <u>30</u> with Cyclopentadiene	74
Reaction of <u>30</u> with Cyclohexene	75
Ultraviolet Photolysis of <u>22</u>	75
Qualitative Study of the Rate of Formation of <u>30</u> from <u>22</u> . . .	75
Preparation of Benzoylhydrazide (<u>94</u>)	76
Preparation of N^1 -Benzoyl- N^2 -benzalhydrazone (<u>95</u>)	76
Preparation of N^1 -Benzoyl- N^1 -methyl- N^2 benzalhydrazone (<u>97</u>) . .	77
Preparation of N^1 -Benzoyl- N^1 -methylhydrazide (<u>98</u>)	77
Preparation of N^1 -Acetyl- N^1 -methylhydrazide (<u>102</u>)	78
Preparation of N^1 -Formyl- N^1 -methylhydrazide (<u>101</u>)	79
Reaction of <u>101</u> with Nitrous Acid	79
Reaction of <u>102</u> with Nitrous Acid	80
Preparation of N^1 -Acetyl- N^1 -methylphosphorohydrazidate (<u>110</u>) .	80
Preparation of N^1 -Formyl- N^1 -methylphosphorohydrazidate (<u>111</u>) .	81
Preparation of Triethylphosphate	82

Reaction of <u>107</u> -residue with Sodium Hydride, then Carbon Dioxide	82
Reaction of <u>107</u> -residue with Sodium Hydride, then Benzaldehyde	83
Reaction of <u>107</u> -residue with Sodium Hydride, then <u>tert.</u> -Butylisocyanate	83
Preparation of Diethylphosphorohydrazidate (<u>113</u>)	84
Preparation of <u>meta</u> -Nitrobenzaliminodiethylphosphorohydrazidate (<u>117</u>)	85
The Attempted Preparation of N^1 - <u>tert.</u> -Butyl- N^2 - <u>meta</u> -nitrobenzaliminocarbodiimide	85
The Attempted Preparation of N^1 - <u>tert.</u> -Butyl-benzaliminocarbodiimide	86
The Attempted Preparation of of N^1 - <u>tert.</u> -Butyl- N^2 -isopropyliminocarbodiimide	87
Preparation of Iminoureas and Iminothioureas	88
Preparation of N^1 - <u>tert.</u> -Butyl- N^2 -isopropylimino-urea	88
Preparation of N^1 - <u>tert.</u> -Butyl- N^2 -isopropyliminothiourea	88
Preparation of N^1 -Phenyl- N^2 -isopropyliminothiourea	88
Preparation of N^1 - <u>tert.</u> -Octyl- N^2 -isopropyliminothiourea	89
Preparation of <u>bis</u> -Ureas and <u>bis</u> -Thioureas	89
Preparation of Di- <u>tert.</u> -butyl- <u>bis</u> -urea	89
Preparation of Di- <u>tert.</u> -butyl- <u>bis</u> -thiourea	90
Preparation of Di- <u>tert.</u> -octyl- <u>bis</u> -urea	90
Preparation of Di- <u>tert.</u> -octyl- <u>bis</u> -thiourea	90
Preparation of Diphenyl- <u>bis</u> -urea	90
Preparation of Dicyclohexyl- <u>bis</u> -urea	91
Preparation of Aminoureas and Aminothioureas	91

Preparation of N ¹ - <u>tert.</u> -Butyl-N ² -(N,N-dimethyl- amino)urea , ,	91
Preparation of N ¹ -Methyl-N ² -(N,N-dimethylamino)urea	92
Preparation of N ¹ - <u>tert.</u> -Butyl-N ² -aminothiourea	92
Preparation of N ¹ -Phenyl-N ² -(N,N-dimethylamino)thiourea	92
Preparation of N ¹ -Phenyl-N ² -aminothiourea	92
Preparation of N ¹ -Cyclohexyl-N ² -(N,N-dimethylamino)- thiourea	93
Preparation of N ¹ - <u>tert.</u> -Octyl-N ² -(N,N-dimethylamino)- thiourea	93
Identification of All Ureas and Thioureas Prepared	93
Preparation of Iminocarbodiimides and <u>bis</u> -Carbodiimides from the Respective Ureas	94
Dehydration Using Phosphorus Pentoxide	94
Dehydration Using Thionyl Chloride	95
Dehydration Using <u>p</u> -Tosyl Chloride	96
Preparation of Iminocarbodiimides and <u>bis</u> -Carbodiimides from the Respective Thioureas	97
Reaction of Phenylisocyanate with <u>21a</u>	98
Reaction of Methylisocyanate with <u>21a</u>	99
Dehydrosulfurization of N ¹ -Phenyl-N ² -(N,N-dimethylamino)- thiourea	99
Literature Cited	101

LIST OF FIGURES

	Page
Figure 1. Possible structures and decomposition products of <u>22</u> -dimer.	10
Figure 2. NMR spectral data for <u>22</u>	12
Figure 3. Possible pathways for nucleophilic addition to <u>30</u>	21
Figure 4. Bonding π and antibonding π^* orbitals of an ethylene moiety.	27
Figure 5. Combinations of approaching ethylene moieties.	27
Figure 6. Possible sigma bond combinations from two ethylene moieties.	27
Figure 7. Correlation diagram for the formation of a cyclobutane moiety from two ethylene moieties.	29
Figure 8. Ground state passage of electrons from cyclobutane bonding orbitals to ethylene bonding orbitals.	31
Figure 9. Orthogonal approach of orbital lobes in ($\pi 2s + \pi 2a$) concerted fashion.	31
Figure 10. Diagram showing the effect of vacant "p" orbital in stabilizing the approaching molecule.	33
Figure 11. A representation of the approach of C=N double bond system to an aminovinylum ion.	33

LIST OF TABLES

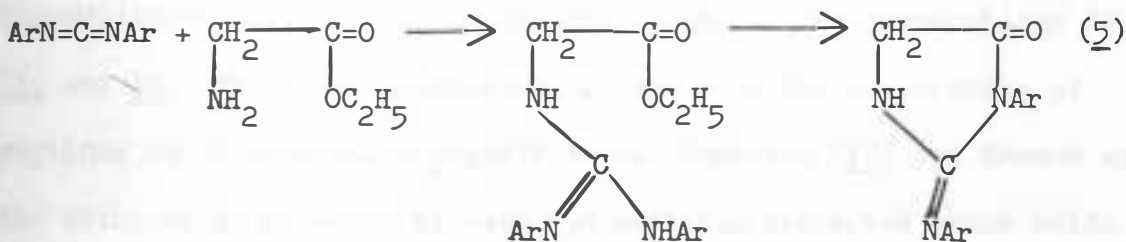
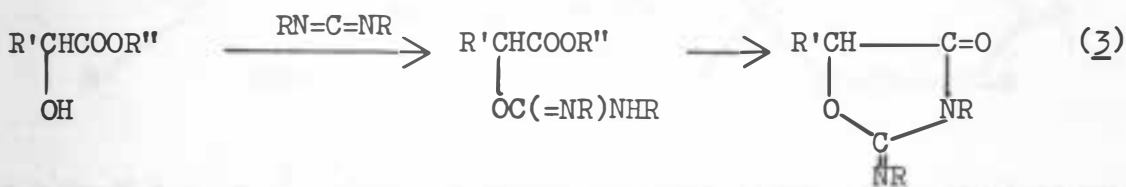
	Page
Table I. Carbodiimides prepared.	8
Table II. Products of reaction.	19
Table III. Carbodiimide photolysis data.	25
Table IV. N-Acyl-N-methylhydrazides.	42
Table V. Crude N-acyl-N-methylphosphorohydrazidates.	45
Table VI. Comparison of data of phosphorohydrazidate distillation product with triethylphosphate.	47
Table VII. Iminoureas and iminothioureas prepared, and reaction used to prepare the carbodiimide.	55
Table VIII. <u>bis</u> -Ureas and <u>bis</u> -thioureas prepared, and reaction used to prepare the carbodiimide.	56
Table IX. Aminothioureas prepared and reacted with HgO.	58

CHAPTER 1

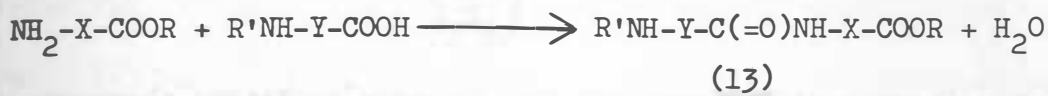
THE CHEMISTRY OF SOME N¹-ALKYL-N²-DIALKYLAMINOCARBODIIMIDES

HISTORICAL

In recent years carbodiimides have attracted increased interest because of their great importance as versatile reagents in organic synthesis. They have been used in the preparation of isoureas¹ (1), isothioureas² (2), oxazolidones³ (3), guanidines⁴ (4), imidazolidones⁵ (5), imidazolines⁶ (6), oxazolines⁷ (7), triazoles⁸ (8), tetrazoles⁹ (9), anhydrides¹⁰ (10), barbiturates¹¹ (11), and diacylperoxides¹² (12).

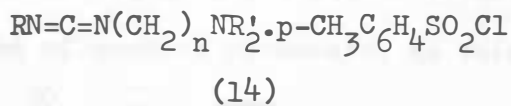


Sheehan and Hess¹³ have reported the use of dicyclohexylcarbodiimide



to bring about this type of condensation, with concomitant formation of dicyclohexylurea.

Sheehan, et al.¹⁴, have also reported the preparation of several



water soluble carbodiimides (14) which have also been shown to be very useful in peptide synthesis.

The first review of carbodiimides was provided by Khorana^{4a} only eighteen years ago. By drawing attention to this class of highly reactive compounds, the paper no doubt contributed significantly to the increased interest in carbodiimides. Kurzer⁵ has provided the most recent review. The fact that his article contains nearly nine hundred references in comparison to the one hundred references in Khorana's article is a measure of the increased activity in the carbodiimide field.

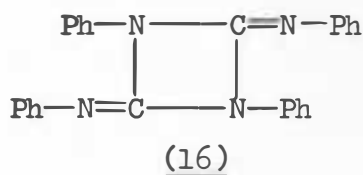
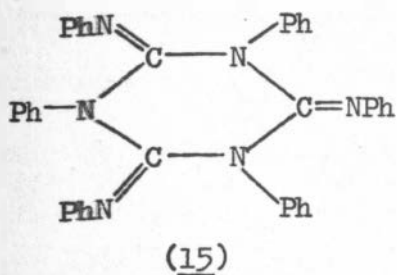
Although first correctly formulated and characterized by Weith¹⁵ in 1873, carbodiimides were undoubtedly obtained by earlier workers. As early as 1852, Hinterberger¹⁶ reported the isolation of a compound, $\text{C}_6\text{H}_{10}\text{N}_2$, from the reaction of N^1 -allyl- N^2 -ethylthiourea with hydrated lead oxide. Zinin¹⁷ in 1852 and Biziro¹⁸ in 1861 also described a compound, $\text{C}_{10}\text{H}_{10}\text{N}_2$, obtained by the action of hydrated lead oxide on N^1 -allyl- N^2 -phenylthiourea. Biziro described it, under the name of

"cyanallylphenylamine", as $\left. \begin{array}{l} \text{CN} \\ \text{C}_6\text{H}_5 \\ \text{C}_3\text{H}_5 \end{array} \right\} \text{N}$. There is little doubt that

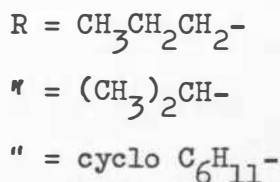
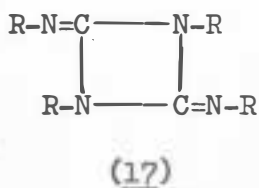
the compounds concerned were in fact the appropriate carbodiimides

$\text{C}_2\text{H}_5\text{N}=\text{C}=\text{NC}_3\text{H}_5$ and $\text{C}_3\text{H}_5\text{N}=\text{C}=\text{NC}_6\text{H}_5$, respectively.⁵

The existence of carbodiimides as dimeric and trimeric species has been known since 1892 when Schall¹⁹ first reported a compound which had twice the molecular weight of the carbodiimide with which he was working. Although he offered no structure, he formulated the dimer as " $(\text{C}\equiv(\text{N-Ph})_2)_2$." Busch²⁰ in 1909 reported the isolation of a trimer of diphenylcarbodiimide (15). Zetzsche and Fredrich²¹ isolated the dimeric form of diphenylcarbodiimide (16). More recently, Brown²² and Richter²³ have reported the characterization of the dimer of diphenylcarbodiimide. Their spectral data support structure 16. Hartke and Rossbach²⁴ have

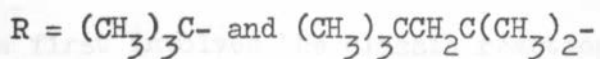


recently reported the isolation and characterization of dimers of dialkylcarbodiimides, (17). The structure of the dimer was deduced



from elemental analysis and spectral data.

Wadsworth and Emmons²⁵ have shown phosphoramidates to be extremely interesting intermediates in laboratory preparations of many unsaturated organic nitrogen compounds, including isocyanates, isothiocyanates, ketenimines and carbodiimides. Several N,N-dialkylaminophosphoramidates (N,N-dialkylphosphorohydrazidates) have been used in the preparation of N,N-dialkylaminocarbodiimides (18). It was noted that the



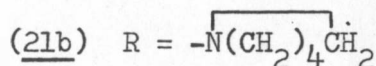
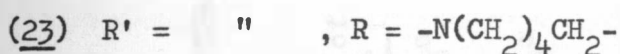
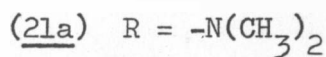
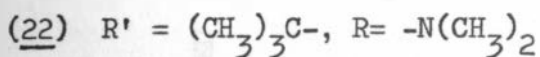
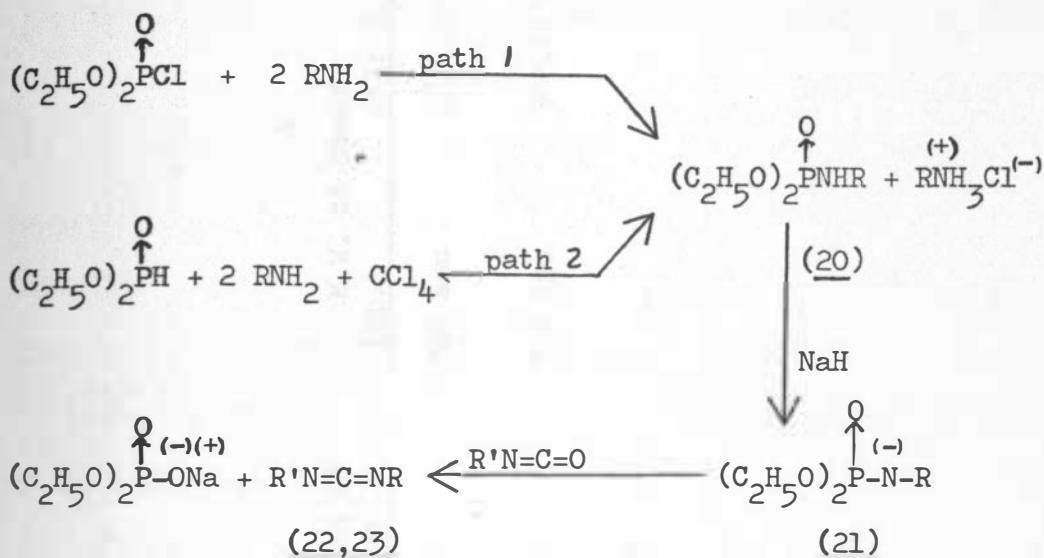
carbodiimides formed solids which were determined to be dimers (19) of unknown structure.

DISCUSSION

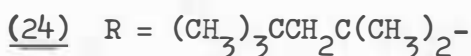
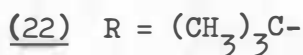
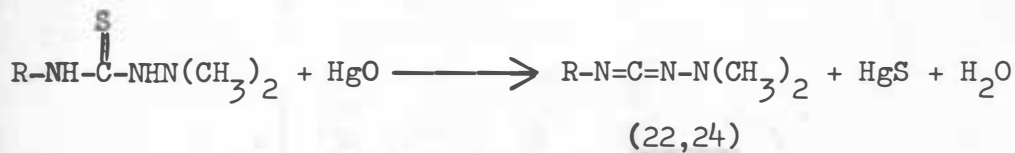
The isolation of unsymmetrically substituted dimeric carbodiimides led to the current investigation of the preparation of several N,N-dialkylaminocarbodiimides, determination of the structure of the dimeric species, investigation of the chemical reactivity of the monomeric and dimeric species, and a proposed mechanism by which dimerization and decomposition of the dimeric species occurs.

Dialkylphosphorohydrazidates, used as intermediates in the preparation of N,N-dialkylaminocarbodiimides, were prepared by two methods. The first involved the classic reaction of diethylphosphorochloridate with the amine (pathway 1), and the second involved the reaction of diethylphosphite with the amine in the presence of carbon tetrachloride²⁶ (pathway 2). Reaction of the dialkylphosphorohydrazidates (20) with sodium hydride produced, in situ, the reactive phosphorohydrazidate anions (21). The reaction of N,N-dimethylphosphorohydrazidate anion (21a) with tert.-butylisocyanate gave N¹-tert.-butyl-N²-(N,N-dimethylamino)carbodiimide (22) in 83% yield. Reaction of N-piperidinylphosphorohydrazidate anion (21b) with the same isocyanate gave N¹-tert.-butyl-N²-piperidinylcarbodiimide (23) in 31% yield.

There are several other methods²⁷ which have been used to prepare carbodiimides. Sheehan²⁸ has prepared several carbodiimides by dehydrosulfurization of thioureas using yellow mercury(II)oxide. Using his method, 22 and N¹-tert.-octyl-N²-(N,N-dimethylamino)carbodiimide (24) were prepared from the appropriate thiourea in 43%

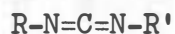


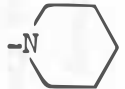

and 51% yields, respectively. The ir spectra of 22, 23 and 24 each contained a strong absorption band at 2120 cm^{-1} , which is characteristic of the $\text{N}=\text{C}=\text{N}$ group²⁹. Generally speaking, Wadsworth's procedure



produced carbodiimides in better yields, but required two weeks to obtain a product. Sheehan's procedure produced poorer yields, but required only twenty-four hours to obtain a product. (See Table I).

TABLE I
CARBODIIMIDES PREPARED



<u>R</u>	<u>R'</u>	<u>B.P. (torr)</u> of monomer	<u>M.P. of</u> <u>dimer</u>	<u>% yield of</u> <u>monomer</u>	<u>M.W. of Dimer</u>	
					<u>Exp.</u>	<u>Calc'd</u>
$(CH_3)_3C-$	$-N(CH_3)_2$	65-7°(11)	142-3°	83.4	280 amu	282.50 amu
$(CH_3)_3C-$		70-2°(0.40)	125-7°	30.8	358 amu	362.64 amu
$(CH_3)_3CH_2C(CH_3)_2-$	$-N(CH_3)_2$	59-60°(0.45)	-	51.3	-	-
$(CH_3)_3C-$	$CH_2CH_2CH_2CH_3$	72-4°(12)	-	33.2		
$(CH_3)_3C-$		65-7°(0.45)	-	36.3		

Carbodiimides 22, 23 and 24 solidified after a period of several days to three weeks, 22 requiring the shortest time and 24, the longest. The ir spectra of the solids contained no absorptions near 2100 cm^{-1} indicating the loss of the N=C=N groups. Molecular weight determinations indicated that the solids from 22 and 23 were dimers (22-dimer and 23-dimer, respectively). Although three carbodiimides were prepared, the majority of the investigation was concerned with 22 and 22-dimer, as they were most readily available.

A priori, there are six possible structures (25-30) for the dimeric species of the carbodiimide. Much information can be obtained as to which structure is correct by studying the products obtained from its decomposition. Decomposition could occur in both the horizontal and vertical planes. Cleavage in the horizontal plane would yield starting monomer from each dimeric structure. Cleavage in the vertical plane of structures 25, 26, 27 and 28 would yield disproportionation products of the starting monomer, but cleavage in the vertical plane of structures 29 and 30 would yield only starting monomer (see Figure 1).

It was observed that distillation at reduced pressure of 22-dimer yielded a distillate whose ir and nmr spectra were identical with the spectra of 22. Gas chromatography indicated that the distillate was pure 22. The distillate, which formed solid after several days, was collected in quantitative yield. The ir and nmr spectra of the solid were identical with the spectra of 22-dimer. The absence of absorption bands near 2100 cm^{-1} in the ir spectrum indicated that 22 had been completely consumed.

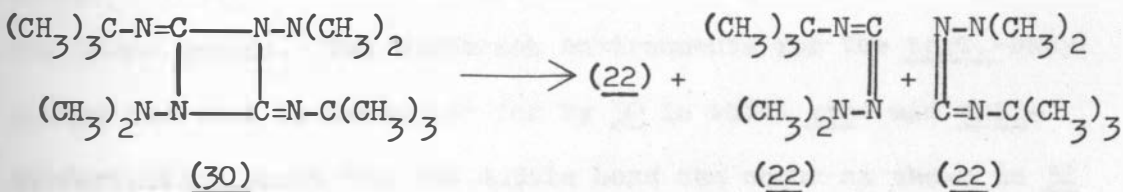
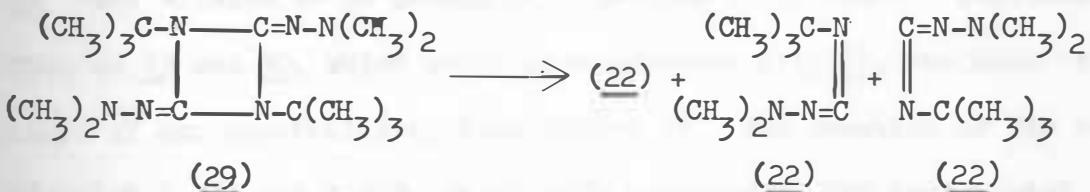
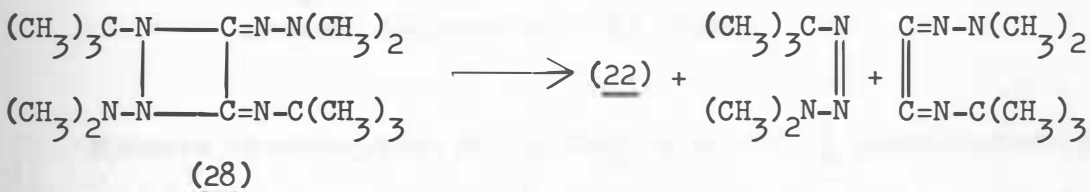
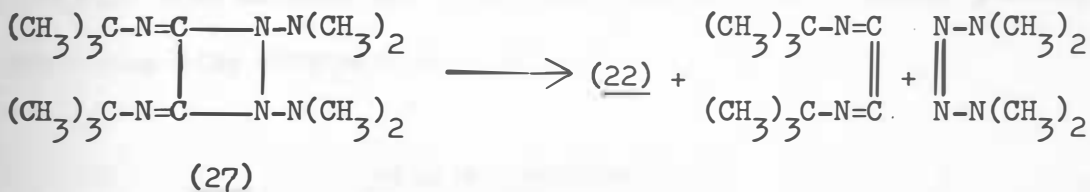
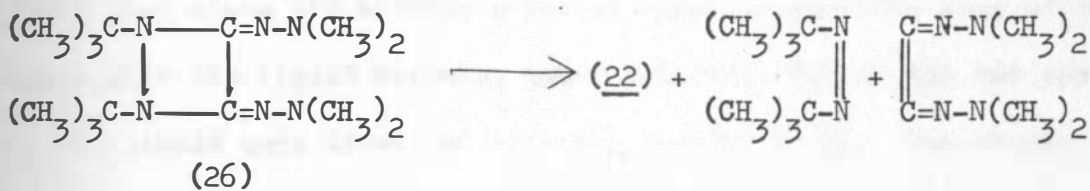
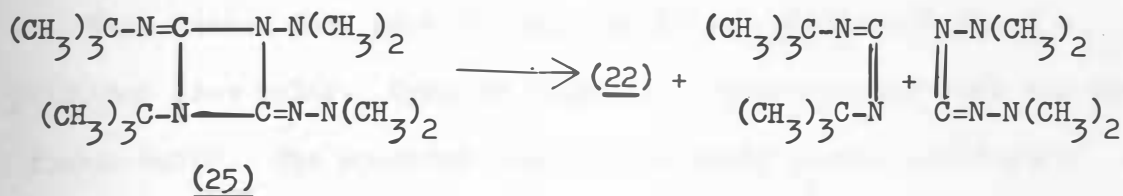
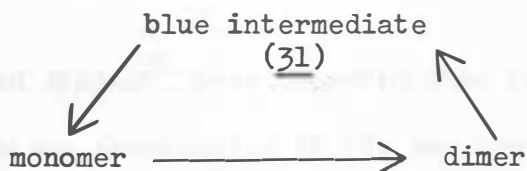


Figure 1. Possible structures and decomposition products of 22-dimer.

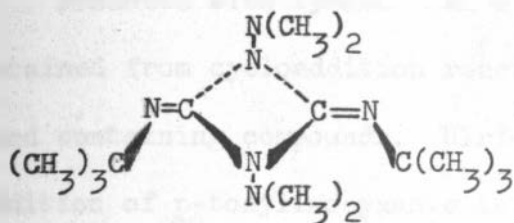
When heated just past its melting point, 22-dimer took on a brilliant blue color. Upon cooling, solid again formed with the loss of blue color. The spectral data of the newly formed solid were identical with those of original 22-dimer. Prolonged heating of the dimer just above its melting point resulted in complete loss of blue color with the liquid becoming amber colored. The ir and nmr spectra of the liquid were identical with the spectra of 22. Gas chromatography indicated the liquid to be about 95% pure 22. The results would indicate that monomer and dimer interconvert via a cyclic pathway involving blue intermediate (31).



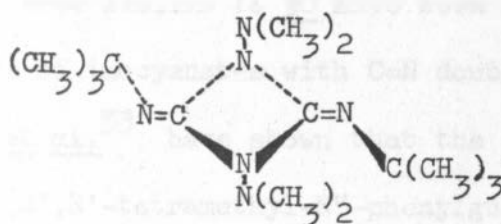
Because decomposition of 22-dimer produced 22 quantitatively, 25, 26, 27 and 28, which would have produced disproportionation products of 22, were eliminated as possible structures of 22-dimer. Differentiation between 29 and 30, which would have produced only 22, was made on the basis of nmr spectral data (see Figure 2). The presence of the two peaks at 1.28 δ and 1.08 δ , which were assigned to the tert.-butyl groups³⁰ would indicate the presence of two different environments for these groups. Two different environments for the tert.-butyl groups can best be accounted for by 30 in which syn- and anti-isomerization about the C=N double bond can occur as shown in 32 and 33, the cis and trans isomers, respectively.

$\delta(\text{ppm})$	ratio	# H's	Group
2.95	1.3	12	2 $-\text{N}(\text{CH}_3)_2$
1.28	1.0	9	2 $-\text{C}(\text{CH}_3)_3$
1.08	1.0	9	

Figure 2. NMR spectral data for 22.

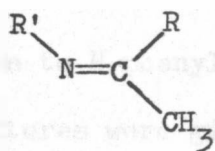


(32) cis

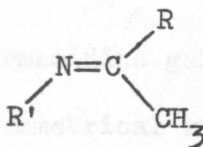


(33) trans

Nelson and Atkins³¹ have reported that the R' group in 34 accounted for two absorption frequencies in the nmr spectrum of trialkylimines as a result of syn- and anti-isomerization about the C=N double bond producing cis and trans isomers.



cis



trans

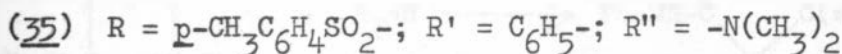
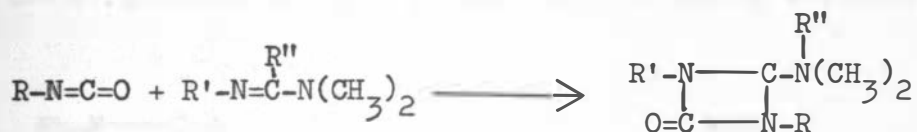
(34)

Symmetrical structure 30 has the following characteristics:

- 1) the heteroatoms are opposite, not adjacent to, each other in the four-membered ring and 2) double bond formation is toward the more electronegative atom. The doubly bonded nitrogens in 29 are more electropositive than the doubly bonded nitrogens in 30 because of the strong negative inductive effect of the attached dialkylamino groups

in 29 compared to the weak negative inductive effect of the tert.-butyl groups in 30³². It should be mentioned that the dimers of diphenylcarbodiimide²¹⁻²³ (15) and dialkylcarbodiimides²⁴ (16) have also been assigned symmetrical structures with the heteroatoms in opposite corners of the ring.

Products with symmetrical structures similar to 30 have been obtained from cycloaddition reactions of isocyanates with C=N double-bond containing compounds. Ulrich, et al.³³, have shown that the addition of p-tosylisocyanate to N,N,N',N'-tetramethyl-N''-phenylguanidine yielded cycloadduct 35. They have also shown that the addition of p-



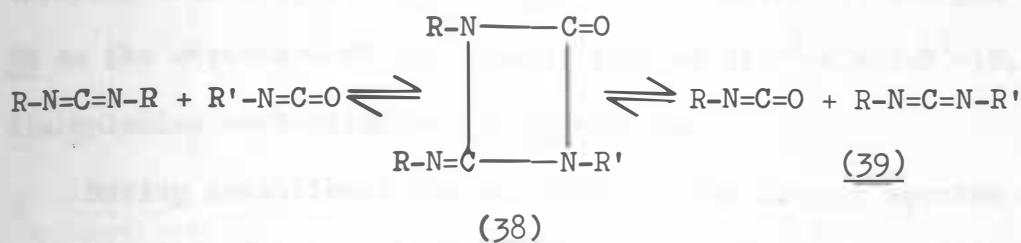
tosylisocyanate to N-phenyl-N'-dimethylformamidine gave cycloadduct 36. The structures were given as being symmetrical with respect to location of the ring nitrogens.

Neumann and Fischer³⁴ have shown that addition of phenylisocyanate to diphenylcarbodiimide at elevated temperatures yielded cycloadduct 37.



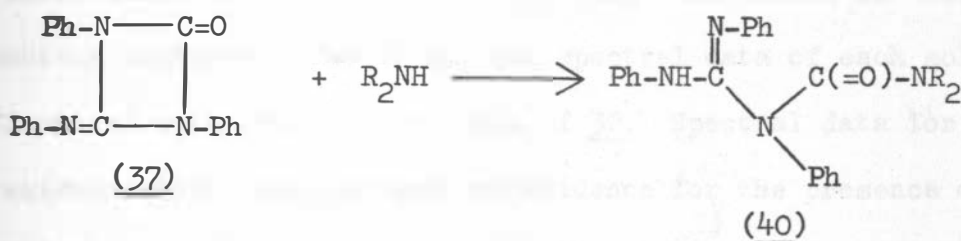
(37)

They have also shown that reaction of isocyanates with carbodiimides is readily reversible producing mixed carbodiimides (39), substantiating

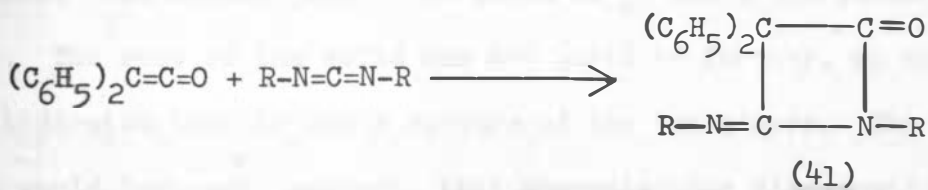


structure 38, and showing that this ring system can decompose in both the horizontal and vertical planes.

Farrisey, et al.³⁵, have shown that amines add to 37 with the formation of guanidines (40), further substantiating structure 37.



Brady and Dorsey³⁶ have recently shown that diphenylketene in reaction with carbodiimide produced an azetidinone (41). Structure 41 is symmetrical with respect to the location of the exocyclic double bonds.



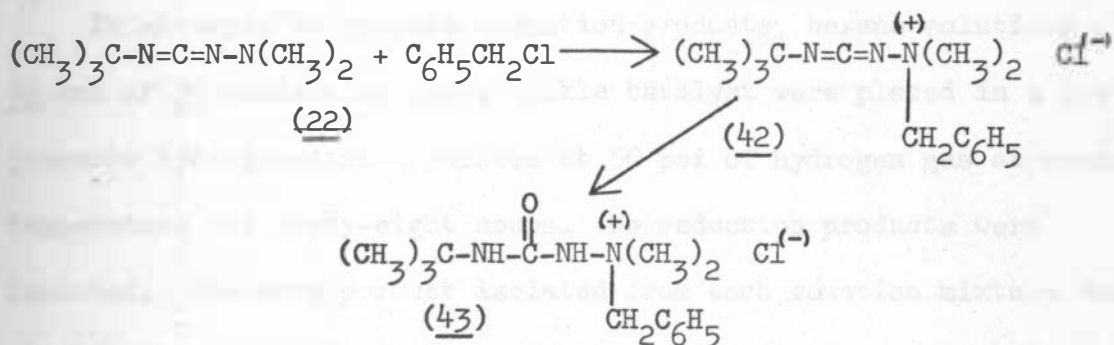
The assignments of symmetrical structures to compounds 15, 16, 35, 36, 37, 38 and 41, together with the evidence for the quantitative interconversion between 22 and 22-dimer, support the assignment of 30 as the structure of the dimeric species of N^1 -alkyl- N^2 -(N,N -dialkylamino)carbodiimides 22, 23 and 24.

Having established the structure of the dimeric species of the carbodiimides, the chemistry of the monomer (22) and the dimer (30) was investigated. Cyclodimerization of 22 to give 30 led to attempts to prepare cycloadducts of 22 with other carbodiimides. Equimolar mixtures of 22 with N^1 -tert.-butyl- N^2 -n-butylcarbodiimide and with N^1 -tert.-butyl- N^2 -cyclohexylcarbodiimide were prepared. (The simple unsymmetrical carbodiimides had been prepared via phosphoramidate anion intermediates.) After two weeks, solid had formed in each of the reaction mixtures. The ir and nmr spectral data of each solid were identical with the spectral data of 30. Spectral data for the oily residues which remained gave no evidence for the presence of heteromolecular cycloadducts, but only the starting, simple carbodiimides with some 22 present as impurity.

As 23 had formed a dimer, it was expected that it would form a heteromolecular adduct with 22. Therefore, an equimolar mixture of 22 and 23 was prepared and set aside. After two weeks, solid had formed in the reaction mixture. Isolation and recrystallization of the solid from hexane gave a 43% yield of 30 and a 30% yield of 23-dimer. The rest of the solid was not purified further, as spectral data indicated that it was a mixture of the two dimers. The data again would indicate, however, that homomolecular dimerization is

preferred to heteromolecular cycloaddition.

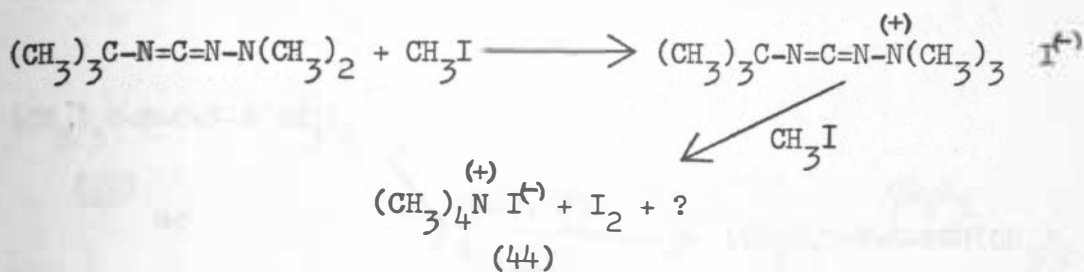
Reactions to prepare water-soluble salts of the monomers, for possible use in biological testing, were carried out on 22. Reaction of 22 with benzylchloride at room temperature gave the benzylammonium chloride salt (42). The ir spectrum of 42 contained a strong absorption band at 2120 cm^{-1} indicating that the $\text{N}=\text{C}=\text{N}$ group had not been destroyed. However, the spectrum also contained weak absorption bands at 3250 and 1700 cm^{-1} , assigned to NH and $\text{C}=\text{O}$ groups, indicating that hydrolysis by atmospheric moisture to produce the urea (43) had occurred. A sample of 42 formed a gummy residue after exposure for fifteen minutes to the atmosphere. The ir spectrum of the gummy



sample contained absorption peaks of nearly equal intensity for $\text{N}=\text{C}=\text{N}$, NH and $\text{C}=\text{O}$ groups. Reaction of 22 with benzylchloride at elevated temperatures did not yield either 42 or 43, but only a tarry residue.

Reaction of 22 with methyl iodide at room temperature was exothermic giving tetramethylammonium iodide (44), some free iodine and tarry residue. The ir spectrum of 44 was identical with that of

authentic tetramethylammonium iodide. The presence, but not the amount, of free iodine was based on comparison of the color of the benzene

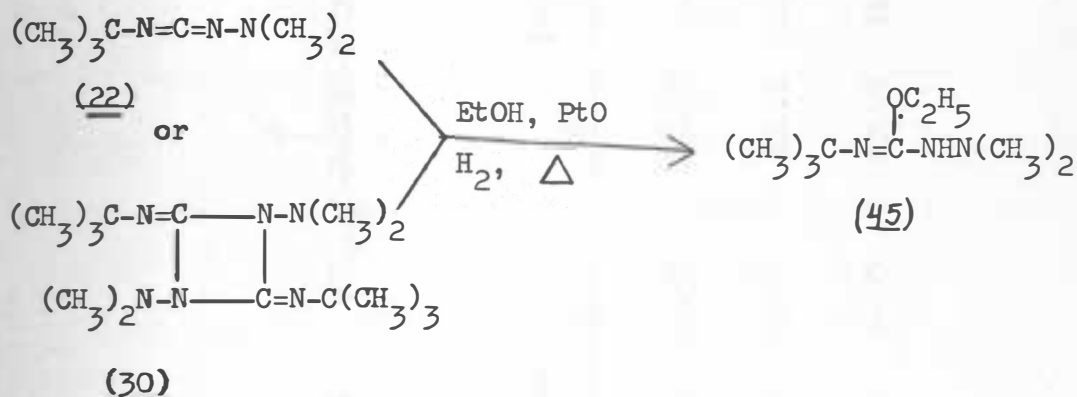


solution with the color of a solution of authentic iodine in benzene. The presence of free iodine would indicate a complicated reaction, which might be free radical in nature and, perhaps, involve oxidation-reduction.

In attempts to prepare reduction products, hexane solutions of 22 and of 30 containing Raney nickle catalyst were placed in a low pressure hydrogenation apparatus at 50 psi of hydrogen gas at room temperature for forty-eight hours. No reduction products were isolated. The only product isolated from each reaction mixture was starting monomer and dimer, respectively. Utilizing more stringent conditions, the reductions were carried out in ethanol in the presence of platinum oxide catalyst at 1000 psi of hydrogen gas and 50° in a high pressure hydrogenation apparatus. The only product isolated from the reaction mixtures was the ethoxyisourea (45), the identity of which was deduced from its ir and nmr spectral data and elemental analysis (see Table II). The significant changes in the ir spectrum of 45 compared to the spectrum of 22 were the loss of an absorption band at 2120 cm⁻¹ for the N=C=N group and the formation of an absorption

band at 1090 cm^{-1} indicative of the presence of a C-O-C group.

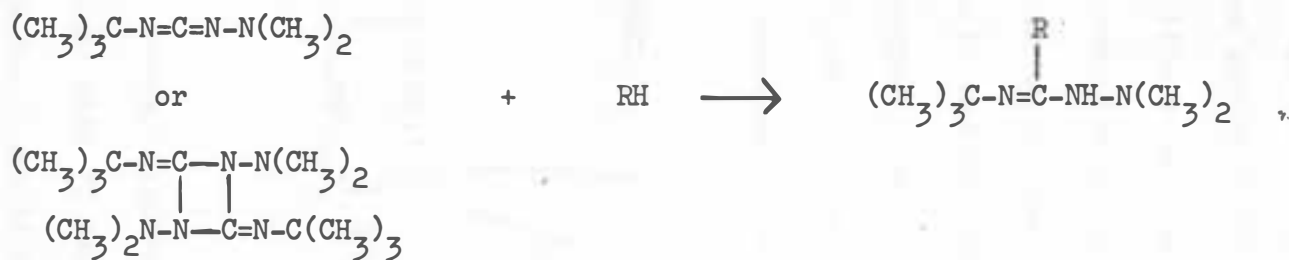
Product 45 was identified as O-ethyl-N¹-tert.-butyl-N²-(N,N-dimethylamino)isourea.

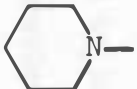


The addition of alcohols to carbodiimides to give isoureas in high yields has been shown to occur readily and exothermically under the influence of certain ionic catalysts such as copper(I) and copper(II)chloride^{3,37}. However, in the absence of catalyst, alcohols have been shown to be fairly inert towards carbodiimides unless the reaction is carried out under conditions of high pressure and temperature, as in a sealed tube reaction³⁸.

To determine if the reduction reaction conditions were necessary to induce formation of the isourea (45), 22 and 30 were each maintained at gentle reflux in ethanol for several hours with no catalyst being present. Isourea (45) was found to be the only product of each reaction. Product identification was based on spectral data. Formation of isourea under mild reaction conditions indicated that 22 was more reactive towards alcohols than the carbodiimides previously described,

TABLE II
PRODUCTS OF REACTION



<u>R</u>	<u>B.P.(terr)</u>	<u>Calculated</u>			<u>Found</u>		
		<u>%C</u>	<u>%H</u>	<u>%N</u>	<u>%C</u>	<u>%H</u>	<u>%N</u>
C ₂ H ₅ O-	46-8°(0.50)	57.70	11.32	22.45	57.60	11.28	22.61
CH ₃ CH ₂ CH ₂ CH ₂ NH-	98-102°(11)	61.62	12.25	26.14	62.08	12.22	25.82
 -	84-6°(0.50)	63.50	11.60	24.75	63.09	11.16	27.08

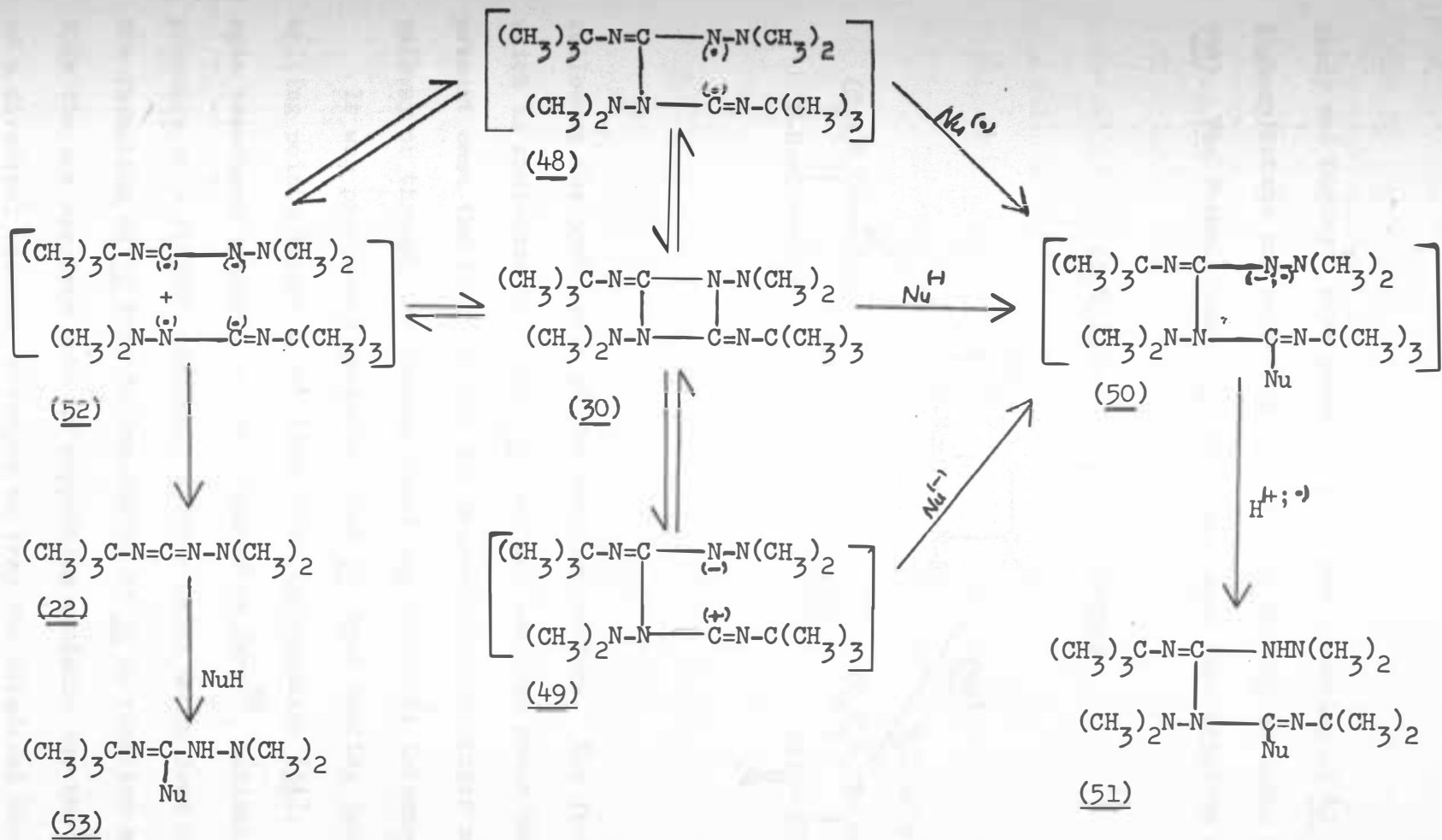
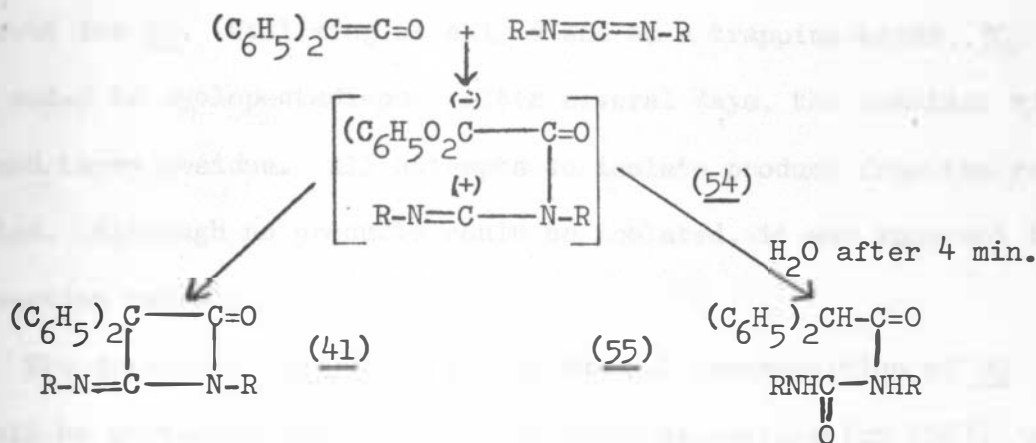


Figure 3. Possible pathways for nucleophilic addition to 30.

Brady and Dorsey³⁶ have proposed that the formation of 41 from diphenylketene and carbodiimide occurred through an ionic intermediate (54). The formulation of 54 was based upon the isolation of urea 55

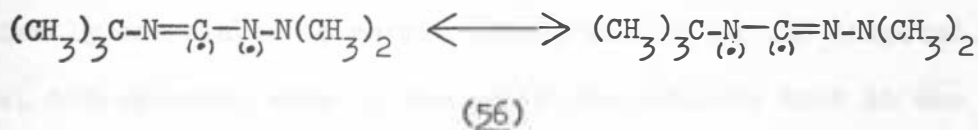


following the hydrolysis of the reaction mixture. The fact that 51, which is analogous to 40 and 55, was not isolated meant that in the present case the reaction did not proceed through either an ionic pathway or through the pathway involving diradical intermediate 48.

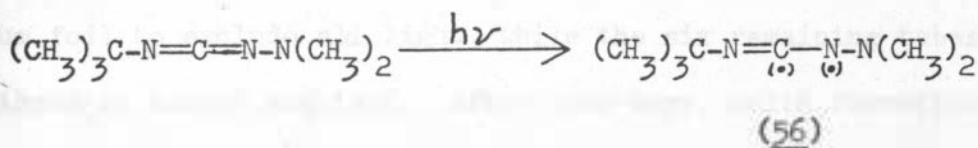
It was previously mentioned that 30, upon heating just past its melting point, formed a brilliant blue intermediate (31). The electron spin resonance spectrum, as interpreted by Farr³⁹, indicated the presence of a triplet diradical species which would lend credence to the formation of 52 from decomposition of 30 in reaction mixtures. With the esr spectrum data as supporting evidence for the existence of a diradical species, attempts to trap the diradical were carried out. The use of alkenes and alkyldienes to trap carbene and nitrene

triplet diradicals is well known⁴⁰. Therefore, a sample of 30 was dissolved in cyclohexene and the mixture refluxed for several hours. No products, except starting material, were isolated from the mixture. Cyclohexene was found to actually be an excellent recrystallizing solvent for 30. Utilizing an aklyldiene as a trapping agent, 30 was added to cyclopentadiene. After several days, the reaction mixture formed tarry residue. All attempts to isolate product from the residue failed. Although no products could be isolated, it was apparent that a reaction had occurred.

The diradical (52) found in the thermal decomposition of 30 should be partially stabilized by electron delocalization (56). As the radical is a triplet, in which the spins of unpaired electrons are



parallel, it must be of fairly high energy. A number of attempts were made to produce this species by photolysis of 22 with ultraviolet light. If dimerization occurs via a similar diradical, the rate of



formation of 30 should be enhanced. Boyer and Frints⁴¹ have reported

the isolation of cyanamides ($R_2-N-C\equiv N$) from the photolysis of carbodiimides. Therefore, the formation of a cyanamide from the photolysis of 30 was considered possible. During the course of the photolysis reaction, samples were removed and their ultraviolet spectra obtained. Both monomer (22) and dimer (30) show uv absorptions at 250 and 218 nm. with ϵ_{\max} of 1630 and 7900 for $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions⁴², respectively. The uv spectra of the various photolysate samples were all identical. They contained the two absorptions found for 22 and 30 plus two additional bands at 284 and 272 nm. with ϵ_{\max} of 670 and 1030, respectively. The small ϵ_{\max} values could be indicative of forbidden transitions, but the type of chromophore(s) is (are) unknown. A small amount of solid product was isolated from the photolysate reaction mixture, but the data collected for the solid could not be sufficiently correlated to permit identification of the compound. However, the spectral data of the solid did indicate that it was not monomer or dimer or cyanamide because there were no absorption bands near 2100 cm^{-1} in their ir spectrum. (See Table IV)

To determine the effect of light and dark conditions on the rate of dimerization, twelve sample tubes of freshly distilled 22 were prepared. Six of the tubes were placed in a container wrapped in aluminum foil to exclude all light, while the six remaining tubes were placed in direct sunlight. After four days, solid formation occurred in all six tubes placed in the sunlight. Subsequent examination of the six dark tubes revealed that solid formation had also occurred in the same span of time. Therefore, it was concluded that

TABLE III

CARBODIIMIDE PHOTOLYSIS DATA

Ultraviolet data:

<u>Time</u>	<u>λ_{\max}</u>	<u>ϵ_{\max}</u>
0 hr.	250	1,630
	218	7,930
20 "	284	750
	272	950
	255	1,450
	217	-
42 "	283	810
	272	1,550
	255	1,950
	218	-
66 "	284	450
	272	600
	257	1,560
	218	-

Physical data for solid product isolated:

Melting point----- 123-5°

Molecular weight - potentiometric titration - 154 to 159 amu.

<u>Infrared data</u>		<u>NMR data</u>		
<u>Absorption (cm⁻¹)</u>	<u>Group (?)</u>	<u>δ(ppm)</u>	<u>#H's</u>	<u>Group(?)</u>
3250	-NH	7.67	1 - singlet	-NH or =CH
3050	=C-H	3.80	3 or 4 - singlet	CH ₃ N- or 2 - CH ₂ N-
		1.42	9 - singlet	-C(CH ₃) ₃

the dimerization of 22 to 30 was not a photolytic process.

Because 30 gave the same products as 22 under identical reaction conditions, it was concluded that 30 did not decompose via a two-step ionic mechanism. Even though 30 passed through an excited-state intermediate during thermal decomposition, no cycloaddition products could be isolated from reactions with diradical trapping agents. Because the rate of dimerization of 22 to form 30 was not affected by light or dark conditions, dimerization did not occur via an excited-state intermediate. These observations and partial conclusions led to the overall conclusion that N^1 -alkyl- N^2 -(N,N-dialkylamino)carbodiimides dimerized and decomposed, under various reaction conditions, via a concerted one-step mechanism.

The dimerization through the C=N double bonds of two molecules of 22 to produce 30 is a ($\pi^2 + \pi^2$) cycloaddition reaction. Woodward and Hoffman⁴³ have established a set of rules concerning the conservation of orbital symmetry in cycloaddition reactions. The cycloaddition of C=N double bonds is formally analogous to the cycloaddition of two C=C double bonds, as in the dimerization of two ethylene molecules to produce one cyclobutane molecule⁴⁴. The bonding π (57) and anti-bonding π^* (58) orbitals of an ethylene molecule may approach those of another ethylene molecule in four different manners giving the four combinations $\pi_1 + \pi_2$, $\pi_1 - \pi_2$, $\pi_1^* + \pi_2^*$, and $\pi_1^* - \pi_2^*$ (59-62). The π orbitals may then combine forming four σ bonds, two being bonding σ orbitals, $\sigma_1 + \sigma_2$ and $\sigma_1 - \sigma_2$ (63,64) and two being anti-bonding σ^* orbitals, $\sigma_1^* + \sigma_2^*$ and $\sigma_1^* - \sigma_2^*$ (65,66). Included with all

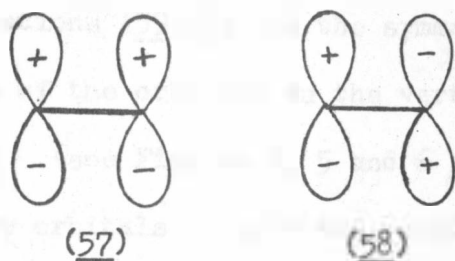


Figure 4. Bonding π (54) and antibonding π^* (55) orbitals of an ethylene moiety.

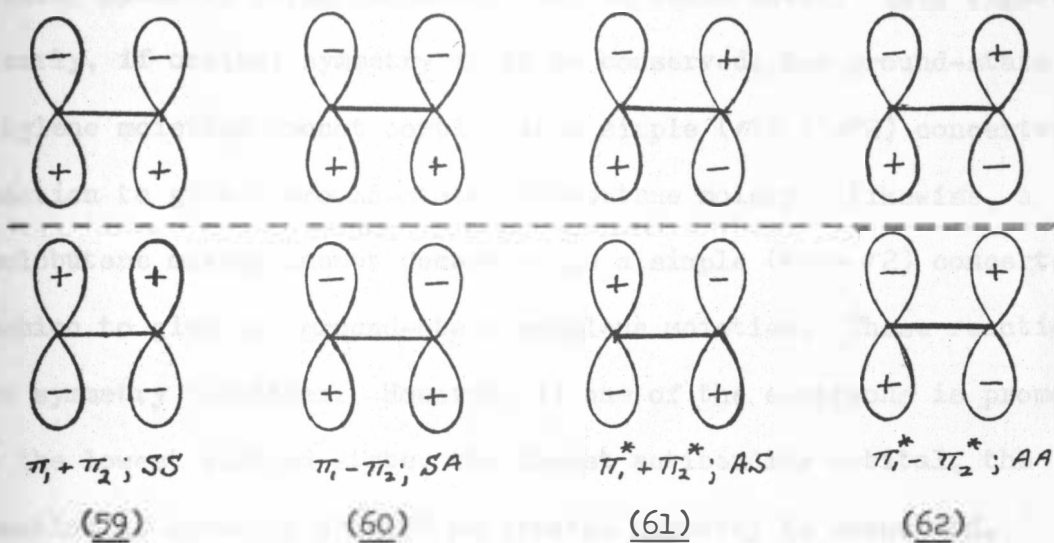


Figure 5. Combinations of approaching ethylene moieties.

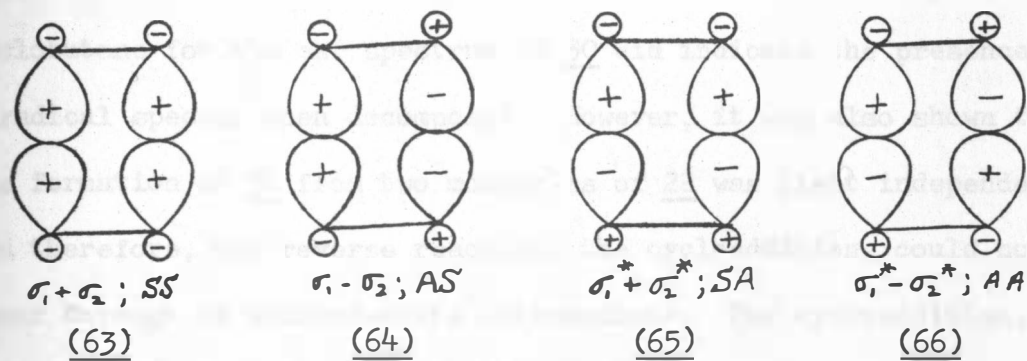


Figure 6. Possible sigma bond combinations from two ethylene moieties.

eight orbital combinations (59-66) are the symmetric, S, and anti-symmetric, A, states of the orbitals in the vertical and horizontal planes, respectively. (see Figures 4, 5 and 6 for 57 to 66.)

By arranging the orbitals of both the reactant and product states in order of increasing stability, the correlation diagram of the approaching ethylene moieties with the cyclobutane moieties, with orbital symmetry being conserved, may be constructed. (See Figure 7.) Clearly, if orbital symmetry is to be conserved, two ground-state ethylene moieties cannot combine in a simple ($\pi 2 + \pi 2$) concerted reaction to give a ground-state cyclobutane moiety. Likewise, a cyclobutane moiety cannot decompose in a simple ($\pi 2 + \pi 2$) concerted fashion to give two ground-state ethylene moieties. These reactions are symmetry forbidden. However, if one of the electrons is promoted to the lowest excited state, the lowest antibonding orbital, the reaction is symmetry allowed as orbital symmetry is conserved.

The decomposition of 30 to produce two molecules of 22 does indeed conform to the symmetry-allowed excited-state decomposition of cyclobutane for the esr spectrum of 30 did indicate the presence of a diradical species when decomposed. However, it was also shown that the formation of 30 from two molecules of 22 was light independent, and therefore, the reverse reaction, the cycloaddition, could not occur through an excited-state intermediate. The cycloaddition, therefore, must be a ground-state reaction.

In the forbidden ground-state cyclobutane-ethylene system just discussed, the bonds that were broken and formed were all on the same

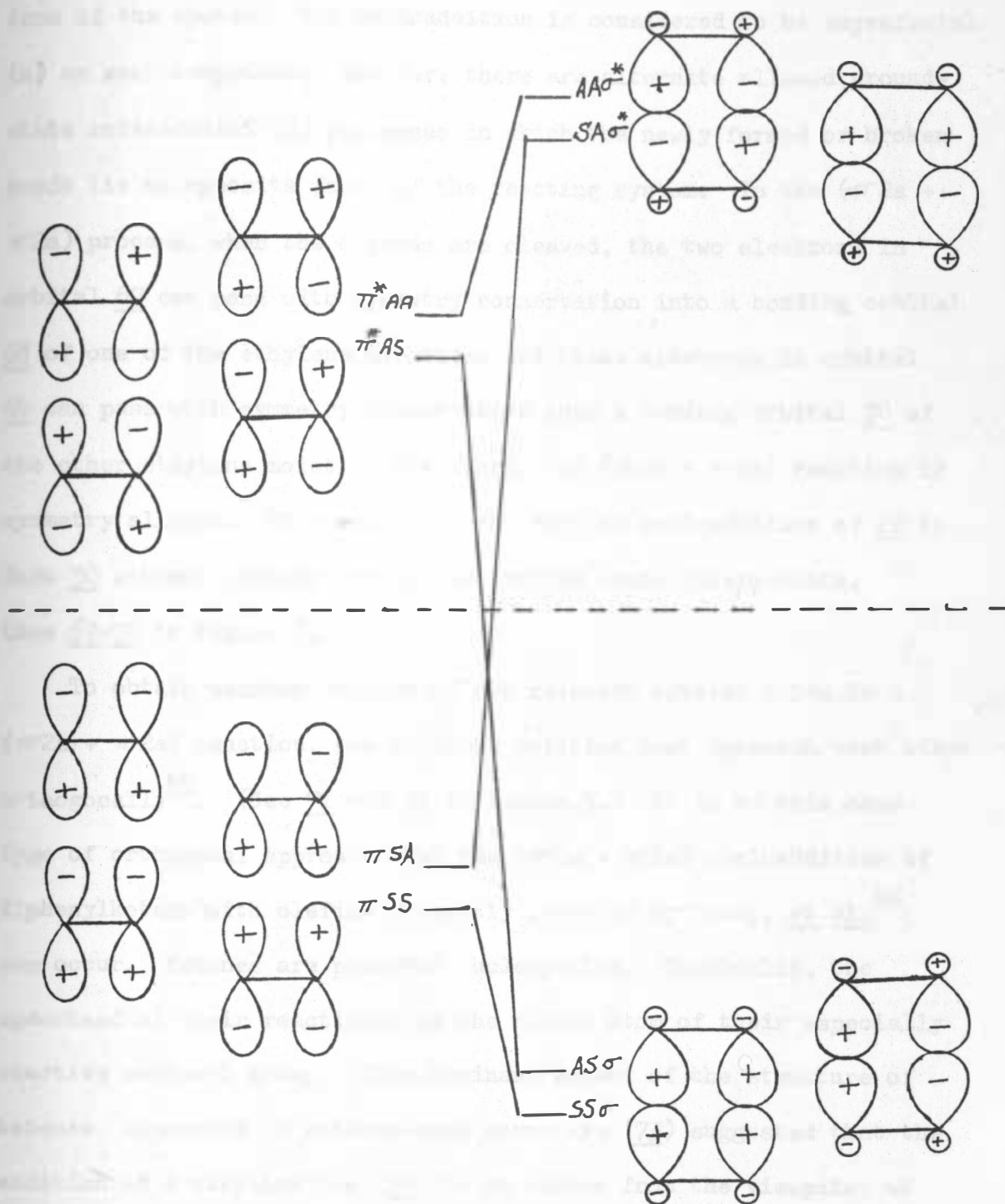


Figure 7. Correlation diagram for the formation of a cyclobutane moiety from two ethylene moieties.

face of the system. The cycloaddition is considered to be suprafacial (s) on each component. However, there are alternate allowed ground-state antarafacial (a) processes in which the newly formed or broken bonds lie on opposite faces of the reacting system. In the ($\pi 2s + \pi 2a$) process, when the σ bonds are cleaved, the two electrons in orbital 67 can pass with symmetry conservation into a bonding orbital 68 of one of the ethylene moieties, and those electrons in orbital 69 can pass with symmetry conservation into a bonding orbital 70 of the other ethylene moiety. Therefore, the ($\pi 2s + \pi 2a$) reaction is symmetry allowed. This would account for the cycloaddition of 22 to form 30 without passing through an excited state intermediate.

(See 67-70 in Figure 8.)

To obtain maximum overlap of the relevant orbital lobes in a ($\pi 2s + \pi 2a$) reaction, the ethylene moieties must approach each other orthogonally⁴⁵. (See 71 and 72 in Figure 9.) It is by this same type of orthogonal approach that the ($\pi 2s + \pi 2a$) cycloaddition of diphenylketene with olefins, recently reported by Brady, *et al.*⁴⁶, can occur. Ketenes are powerful nucleophiles. Chemically, the spearhead of their reactivity is the carbon atom of their especially reactive carbonyl group. This dominant aspect of the structure of ketenes, expressed in valence-bond structure (73) suggested that the addition of a vinylum ion (74) to an olefin from the viewpoint of orbital symmetry be analyzed, as was done by Woodward and Hoffman⁴⁷. The relevant diagrams are 75 and 76 in Figure 10. The significant differences here, compared to simple olefin-olefin combinations, is

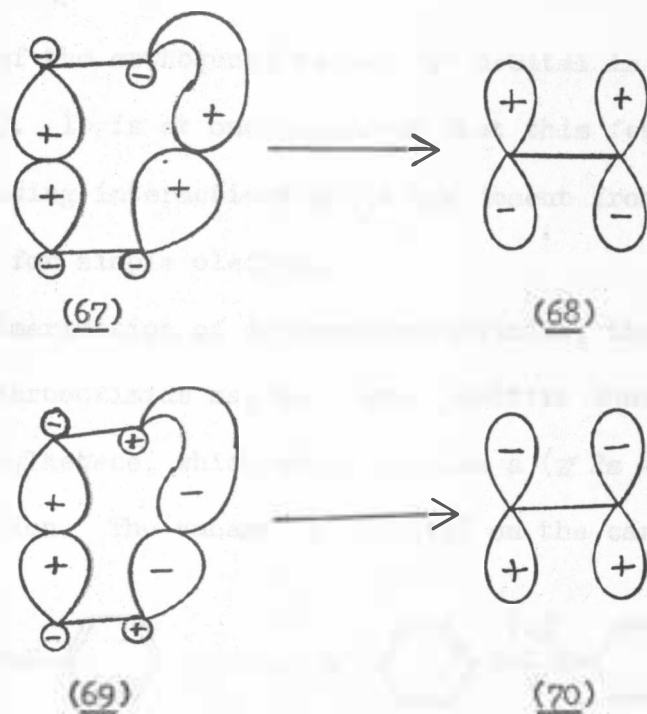


Figure 8. Ground state passage of electrons from cyclobutane bonding orbitals to ethylene bonding orbitals.

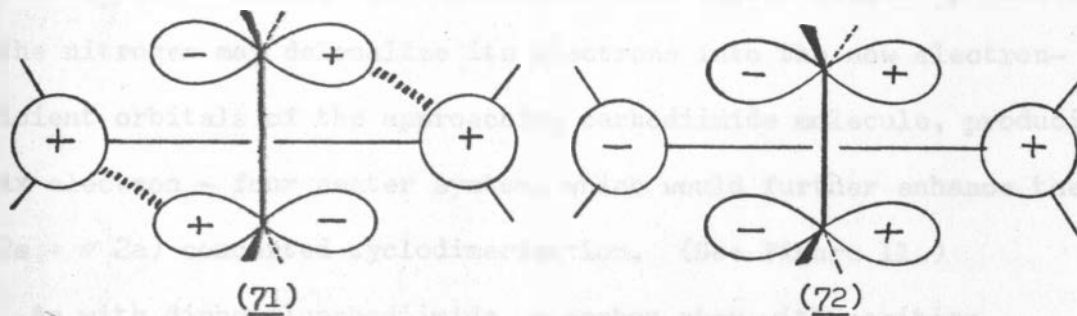
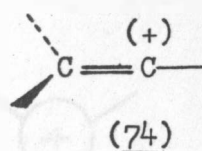
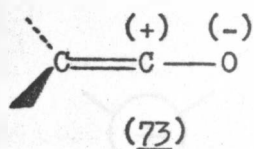
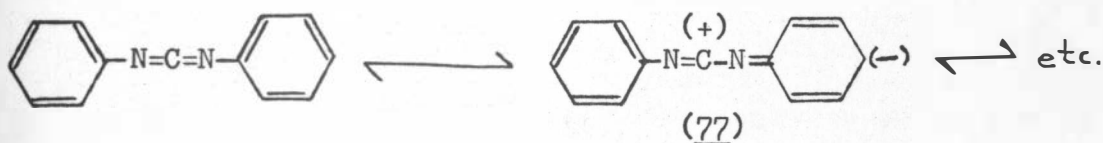


Figure 9. Orthogonal approach of orbital lobes in $(\pi 2s + \pi 2a)$ concerted fashion.



the presence of the orthogonal vacant "p" orbital in the vinyl cation (stippled). It is at once apparent that this feature contributes two strong bonding interactions which are absent from the ($\pi 2s + \pi 2a$) reaction path for simple olefins.

In the dimerization of diphenylcarbodiimide, the carbon atom of the starting carbodiimide may have some positive character, as it does in diphenylketene, which would enhance a ($\pi 2s + \pi 2a$) concerted cyclodimerization. The vacant "p" orbital on the carbon atom can



help stabilize the orbitals of the second approaching carbodiimide molecule. In addition, the like-signed lobe of the filled "p" orbital of the nitrogen may delocalize its electrons into the now electron-deficient orbitals of the approaching carbodiimide molecule, producing a six electron - four center system, which would further enhance the ($\pi 2s + \pi 2a$) concerted cyclodimerization. (See Figure 11.)

As with diphenylcarbodiimide, a carbon atom with positive character (78) may also exist for N^1 -alkyl- N^2 -(N,N-dialkylamino) carbodiimide, using valence bond structures. The positive character on carbon may be less than that in diphenylcarbodiimide, but it is

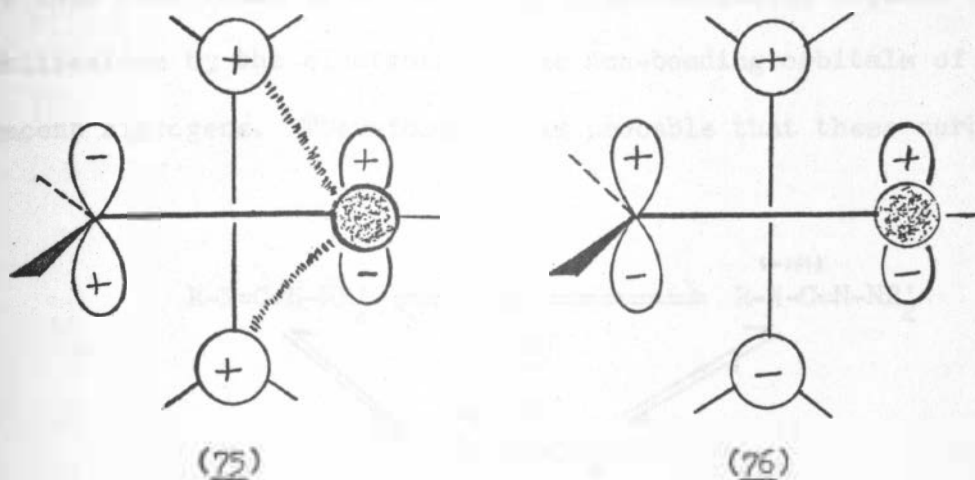


Figure 10. Diagram showing effect of vacant "p" orbital (stippled) in stabilizing the approaching molecule.

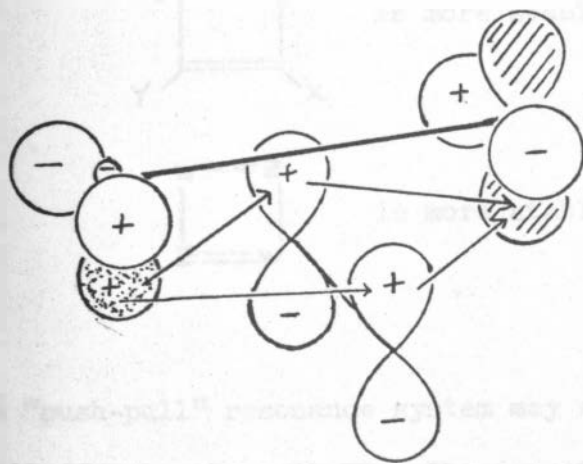
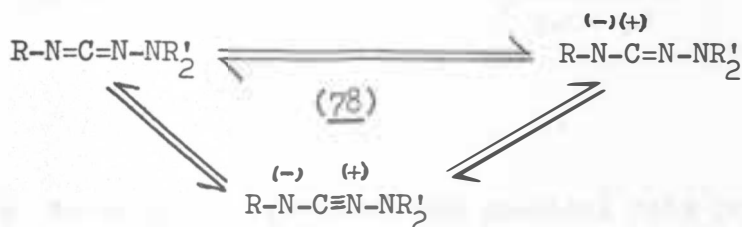


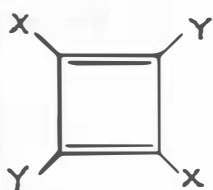
Figure 11. A representation of the approach of a C=N double bond system to an aminovinyl cation. The arrows represent initial electron flow towards the vacant "p" orbital (shaded) on the carbonium ion. The stippled orbital represents the filled "p" orbital on the nitrogen atom.

more than that found in a simple dialkylcarbodiimide because of ion stabilization by the electrons in the non-bonding orbitals of the adjacent nitrogens. Therefore, it is probable that these carbodiimides

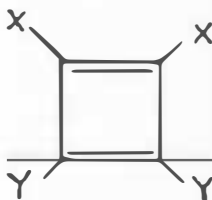


undergo a concerted ($\pi 2s + \pi 2a$) cyclodimerization through the same type of intermediate as shown in Figure 10.

Additional supporting evidence for the existence of a stable ion as shown in 78 may be found in an article by Hoffman⁴⁸ in which he has reported that symmetrical cyclobutadiene systems are stable if a "push-pull" resonance system exists in the molecule. That is,



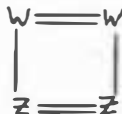
is more stable than



, and

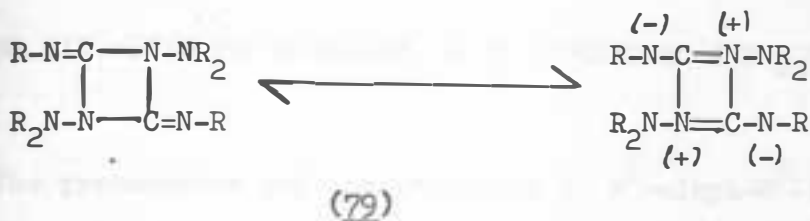


is more stable than



A "push-pull" resonance system may exist for N,N-dialkylaminocarbodiimides as shown in 79. The important feature of this system in comparison with the equilibrium shown in 78 is that a negatively

charged nitrogen atom is present in an identical position.

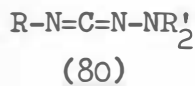


Therefore, based on the physical and chemical data presented, the N^1 -alkyl- N^2 -(N,N-dimethylamino)carbodiimides form dimers with symmetrical structures, as 30. These carbodiimides, like diphenylcarbodiimide and the simple olefinic system discussed, do conform to the Woodward-Hoffman rules for orbital symmetry conservation, and therefore, the cyclodimerization may indeed occur via a $(\pi 2s + \pi 2a)$ concerted one-step reaction mechanism. In addition, the observation of an excited intermediate from the thermal decomposition of 30 would conform to a $(\pi 2s + \pi 2s)$ concerted decomposition.

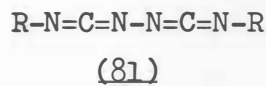
CHAPTER 2

THE ATTEMPTED PREPARATIONS OF DI-FUNCTIONAL AND BIS-CARBODIIMIDES

The preparation and investigation of N^1 -alkyl- N^2 -(N,N -dialkylamino)-carbodiimides led to an investigation of carbodiimides containing at least one non-alkyl substituent (80) and of bis-carbodiimides (81).

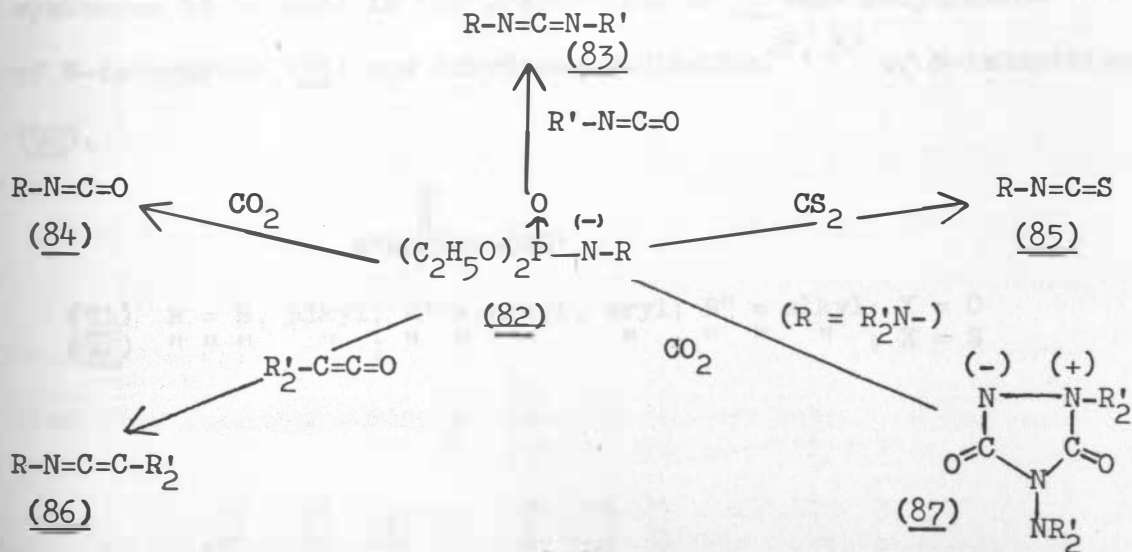


if $R = \text{alkyl}$, $R' \neq \text{alkyl}$
if $R' = \text{alkyl}$, $R \neq \text{alkyl}$

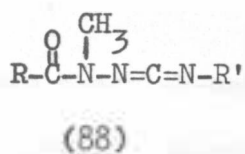


$R = \text{alkyl}$, or aryl

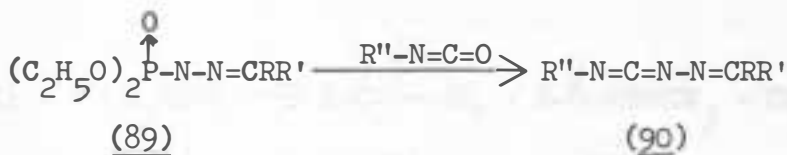
The utility of phosphoramidate anions (82) as intermediates in laboratory preparations of many unsaturated organic nitrogen compounds²⁵ was mentioned in Chapter 1. Phosphoramidates were found to be useful not only in the synthesis of carbodiimides (83), but also in the



synthesis of isocyanates (84), isothiocyanates (85) ketenimines (86), and hydrazinium "ylides" (87), which could rearrange to form tetrazoles⁴⁹. As an extension of this work, it was intended to prepare a series of N-acyl-N-methylphosphorohydrazidates with respect to their possible use as intermediates in the preparations of N-acyl-N-methylcarbodiimides (88) and other unsaturated organic nitrogen compounds analogous to 84-87.



It was also intended to prepare a series of N-iminocarbodiimides (90) utilizing N-iminophosphorohydrazidate anions (89). Alternate



syntheses to be used in the preparation of 90 were dehydration^{14, 50, 51} of N-iminoureas (91) and dehydrosulfurization^{28, 52} of N-iminothioureas (92).



(91) R = H, alkyl; R' = alkyl, aryl; R'' = alkyl; X = O

(92) " " " " " " " " " " " " " " ; X = S

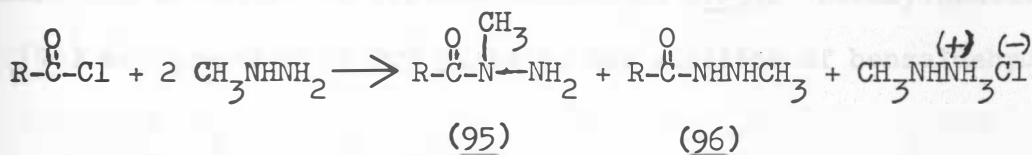
The syntheses to be used in the preparation of bis-carbodiimides (81) were dehydration of bis-ureas (93) and dehydrosulfurization of bis-thioureas (94).



(93) R = alkyl; X = O

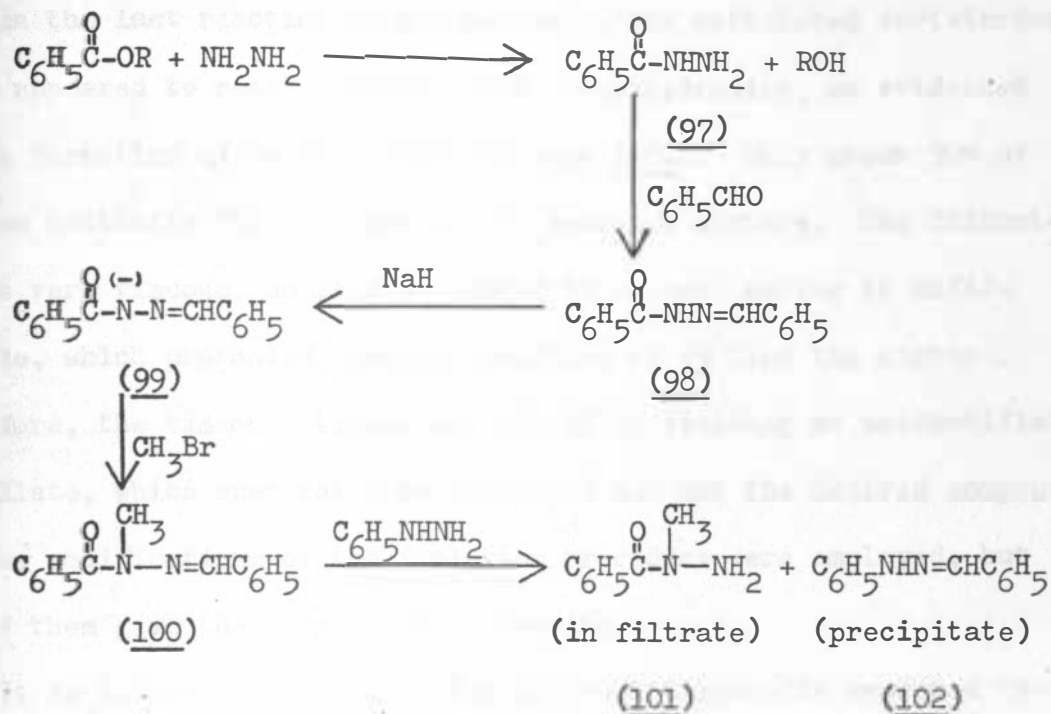
(94) " " " ; X = S

In order to prepare N-acyl-N-methylphosphorohydrazidates, it was first necessary to prepare N-acyl-N-methylhydrazides, for which there were four major synthetic procedures. The first procedure was the direct reaction of acyl halides with methylhydrazine in a mole ratio of one-to-two, respectively⁵³. Both the unsymmetrical (95)



and the symmetrical (96) isomers could be obtained with 96 predominating with large bulky R groups. The acetyl analogue of 95 (R = CH₃-) was prepared in 44% yield. Several attempts to prepare the benzoyl analogue of 95 (R = C₆H₅-) did not yield the desired compound.

The second procedure, used in attempts to prepare the benzoyl analogue of 95, was that reported by Cignarella⁵⁴. The proposed reaction sequence was as follows:



Benzoylhydrazide (97) was prepared in 75% yield by the addition of methyl benzoate to excess hydrazine. Excess hydrazine was used to minimize the formation of dibenzoylhydrazide (103). Benzoylbenzalhydrazone (98) was prepared in 96% yield by the addition of benzaldehyde



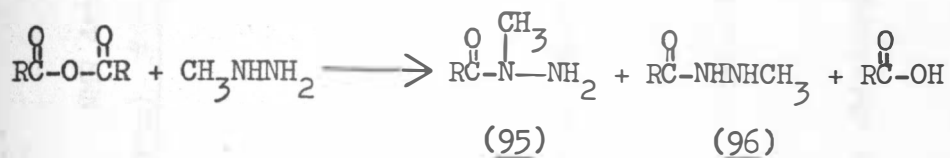
to 97 dissolved in ethanol. Reaction of 98 with sodium hydride in dry dioxane led to the in situ formation of the benzoylbenzalhydrazone anion (99), which readily reacted with excess methylbromide forming the methylated derivative (100) in 63% yield.

In the last reaction of the sequence, the methylated derivative (100) appeared to react smoothly with phenylhydrazine, as evidenced by the formation of benzalphenylhydrazone (102). Only about 50% of 102 was initially filtered out of the reaction mixture. The filtrate became very viscous, as it was reduced in volume, making it unfilterable, which prevented further isolation of 99 from the mixture. Therefore, the viscous residue was distilled yielding an unidentifiable distillate, which spectral data indicated was not the desired compound. Various modifications of the isolation procedure were employed, but all of them gave the same negative results.

It is interesting to note that although Cignarella reported the preparation of eight different analogues of the general formula $RC(O)-N(R')NH_2$, where R was acyl and R' was alkyl, none of the derivatives contained both benzoyl and methyl as R and R', respectively. Either he did not attempt the preparation of the benzoyl analogue, or else he obtained the same negative results.

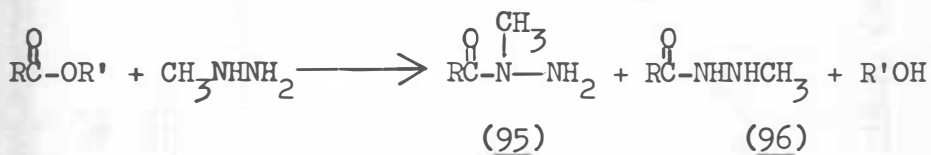
The third procedure, used in attempts to prepare the benzoyl analogue of 95, was that reported by Hinman and Fulton⁵⁵. The procedure involved the reaction of methylhydrazine with symmetrical anhydrides which were used to eliminate a mixture of products. Hinman and Fulton never isolated pure hydrazide, but rather, the benzalhydrazine and phenylsemicarbazone derivatives. Dibenzoyl anhydride was added to a 30% aqueous solution of methylhydrazine. Attempts to isolate pure hydrazide, using crystallization, extraction, and distillation procedures, did not afford pure product. The only

identifiable product isolated was benzoic acid.



As N^1 -benzoyl- N^1 -methylhydrazide could not be isolated by any of the above three procedures, no further attempts to prepare this compound were made.

The fourth procedure used for the preparation of acylhydrazides was that reported by Pedersen⁵⁶, involving the reaction of esters with methylhydrazine. As with the acyl halide and anhydride procedures, the ratio of products is affected by the size of the R group. The

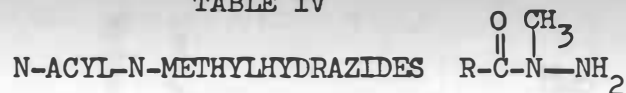


(104) R = H-

(105) R = CH₃-

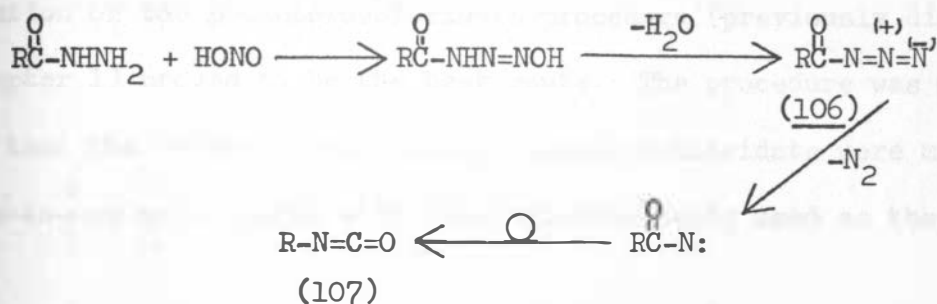
reaction of methylhydrazine with methylformate and with ethylacetate produced N^1 -formyl- N^1 -methylhydrazide (104) and N^1 -acetyl- N^1 -methylhydrazide (105) in 89% and 17% yields, respectively. Product identification was based upon spectral data and positive tests for the presence of an NH₂ group, using meta-nitrobenzaldehyde. (See Table IV.)

TABLE IV

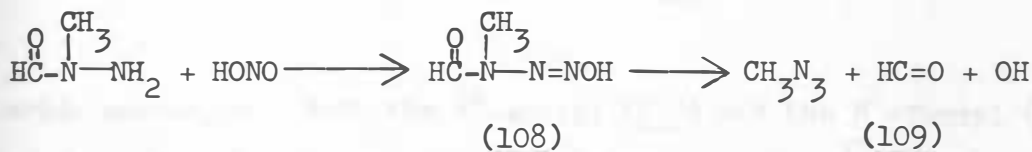


R	B.P. (mm. Hg) or M.P.		IR data		NMR data		
	Exp.	Lit.	Absorption (cm^{-1})	Group	δ (pattern)	# H's	Group
C_6H_5-	(Desired compound not obtained)						
a. $\text{C}_6\text{H}_5-\overset{\text{O}}{\parallel}{\text{C}}-\text{NHNH}_2$	111-3	112 ⁶⁶	3250 ^a 3100 1650 3020, 1600, 1500 760, 690	NH_2 NH $\text{C}=\text{O}$ C_6H_5	nmr not obtained		
b. $\text{C}_6\text{H}_5-\overset{\text{O}}{\parallel}{\text{C}}-\text{NHN}=\text{CHC}_6\text{H}_5$	206-8		3100 1620 3020, 1600, 1495 760, 690	NH $\text{C}=\text{O}$ C_6H_5	nmr not obtained		
c. $\text{C}_6\text{H}_5-\overset{\text{O}}{\parallel}{\text{C}}-\overset{\text{CH}_3}{\text{N}}-\text{N}=\text{CHC}_6\text{H}_5$	83-5	84-5 ⁶⁷	1630 1600, 1495 760, 690	$\text{C}=\text{O}$ C_6H_5	nmr not obtained		
CH_3	97-100 (12)	118-20 (24) ⁵⁵	3250 3170 1650	NH_2 $\text{C}=\text{O}$	nmr not obtained		
H	90-3 (12)	80 (1) ⁵⁶	3300 3200 1670	NH_2 $\text{C}=\text{O}$	7.95(sing.) 7.75(") 4.60(broad) 2.84(sing.) 2.80(")	1 1 2 3 3	$\text{HC}=\text{O}$ NH_2 CH_3
(a) Identical with Sadtler IR #15671 ⁶⁸							

N-Acyl-N-methylhydrazides differ from N-acylhydrazides, which may undergo Curtius rearrangement, by the presence of the methyl group. Therefore, it was of interest to subject 104 to Curtius rearrangement reaction conditions. The Curtius rearrangement⁵⁷ involves the reaction of an acylhydrazide with nitrous acid to form the azide (106). The azide loses nitrogen, and the formed nitrene rearranges to an isocyanate (107). The reaction of 104 with nitrous acid did not produce an



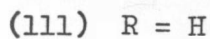
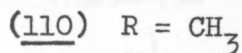
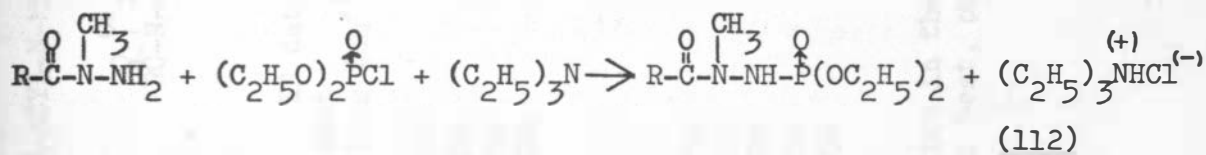
isocyanate, but rather, methylazide (109). The formyl group and the hydroxyl group, the fragments remaining from the decomposition of



intermediate 108, could have combined to form formic acid. Titration of the solution, using aqueous base, indicated that no excess acid was present. Therefore, the formyl and hydroxyl fragments possibly decomposed further, forming water and carbon monoxide. To confirm

the identity of 109 as the reaction product, its spectral data were compared with, and found to be identical with, the spectral data of authentic methylazide prepared by the reaction of sodium azide with dimethylsulfate⁵⁸. The apparent reason for the difference in reactivities of the two types of acylhydrazides is the lack of an acidic hydrogen in 104.

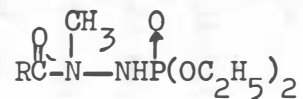
To pursue the chemistry of N¹-acyl-N¹-methylphosphorohydrazidates required their preparation from N¹-acyl-N¹-methylhydrazides. Utilization of the phosphorochloridate procedure (previously discussed in Chapter 1) proved to be the best route. The procedure was modified in that the hydrazide and diethylphosphorochloridate were mixed in a one-to-one molar ratio with triethylamine being used as the hydrogen



chloride scavenger. Both the N¹-acetyl (110) and the N¹-formyl (111) phosphorohydrazidates were prepared. In each case the ammonium salt (112) was isolated in 60-70% yield. The spectral data of the crude residues of 110 and 111 indicated that the desired compounds were present. (See Table V.) However, upon vacuum distillation, both the N¹-formyl and N¹-acetyl residues gave distillates with identical

TABLE V

CRUDE N-ACYL-N-METHYLPHORPHOROHYDRAZIDATES



R	IR data		NMR data ^(a)	
	Significant Absorptions (cm ⁻¹)	Group	δ (pattern)	Group
CH ₃	3300	NH	4.75(broad)	NH
	1670	C=O	3.90(split quartet)	P-O-CH ₂
	1250	P=O	2.87(singlet with impurity peaks)	CH ₃ C=O ²
	1050	P-O-C	1.85(singlet with impurity peaks)	N-CH ₃
H			1.08(triplet)	-CH ₃
	3250	NH	7.90(singlet)	HC=O
	2820	HC=O	3.90(split quartet)	P-O-CH ₂
	1680	C=O	3.0-1.6(many small peaks)	
	1250	P=O	1.10(triplet)	-CH ₃
	1050	P-O-C		

(a) Due to the presence of impurities in the samples, integration of peak areas was impossible. Also, group assignments are, at best, only tenuous.

boiling points and spectral data. The lack of NH and C=O absorptions in the ir spectra of the distillates, whereas these absorptions were present in the ir spectra of the undistilled residues, indicated that the phosphorohydrazidates had decomposed upon distillation. The spectral data of the distillates, which were identical, did indicate the presence of ethoxy groups and a phosphorus-oxygen group, indicating that the distillate was a phosphate ester. The three possible esters that could have formed were 1) tetraethylhypophosphate, 2) tetraethylpyrophosphate and 3) triethylphosphate. The boiling points of the three esters are 1) 116-7° (2mm. Hg)⁵⁹, 2) 166-70° (8mm. Hg)⁵⁹, and 3) 99.2° (13 mm. Hg) and 108° (25 mm. Hg)⁶⁰. As the boiling point of the distillation product was 101-3° (15 mm. Hg), phosphate esters 1) and 2) were eliminated. Comparison of the data obtained for an authentic sample of triethylphosphate⁶¹ with the experimental data obtained for the distillation products of the phosphorohydrazidates confirmed that the distillation product was triethylphosphate. (See Table VI.) The mechanism by which triethylphosphate was formed is unknown.

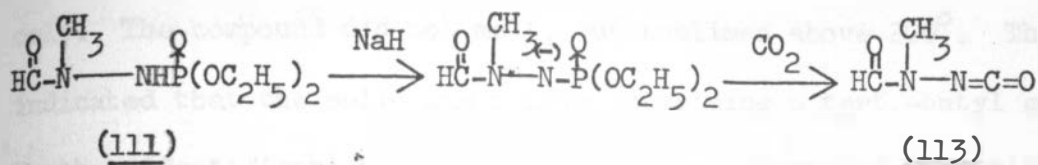
Because the acylphosphorohydrazidates could not be purified, several reactions were carried out on the impure undistilled residues. The first was reaction with carbon dioxide, with the expected product being the isocyanate (113). The reaction was carried out several times. Each time, the reaction appeared to proceed smoothly with the formation of gummy residue. However, attempts to isolate product from both the filtrates and gummy residues did not yield any identifiable products.

TABLE VI

COMPARISON OF DATA OF PHOSPHOROHYDRAZIDATE
DISTILLATION PRODUCT WITH TRIETHYLPHOSPHATE

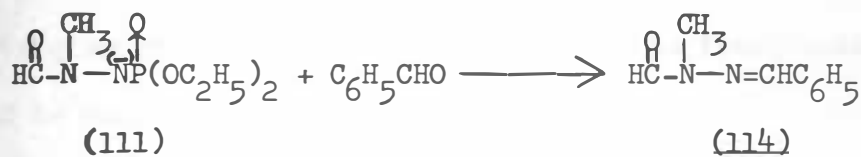
<u>Data type</u>	<u>Distillate</u>	<u>Triethylphosphate</u>
IR	No NH or C=O absorptions P→O at 1250 cm ⁻¹ P-O-C at 1050 cm ⁻¹	No NH or C=O absorptions P→O at 1250 cm ⁻¹ P-O-C at 1050 cm ⁻¹
NMR	Split quartet at 3.97δ (J = 8.2 Hz.) Split triplet at 1.15δ (J is too small to measure) $\delta_q - \delta_t = 2.82\delta$	Split quartet at 4.11δ (J = 7 Hz. ^a) Split triplet at 1.35δ (J is too small to measure) $\delta_q - \delta_t = 2.76\delta$
MW	VPO in benzene 184 and 182 amu	Calculated = 182.18 amu
BP	74-5° at 1.5 mm. Hg 101-3° at 15 mm. Hg 104-7° at 18 mm. Hg	77-9° at 2 mm. Hg (exp.) 99.2° at 13 mm. Hg ⁶⁰ 108° at 25 mm. Hg ⁶⁰
$\eta_D^{25^\circ}$	1.4055	1.4059 ⁶⁰
Analysis	Found: C, 39.72; H, 8.36 C, 40.01; H, 8.55	Calculated: C, 39.55; H, 8.32

a. J = 6.5-10 for P-O-CH₂⁶⁹



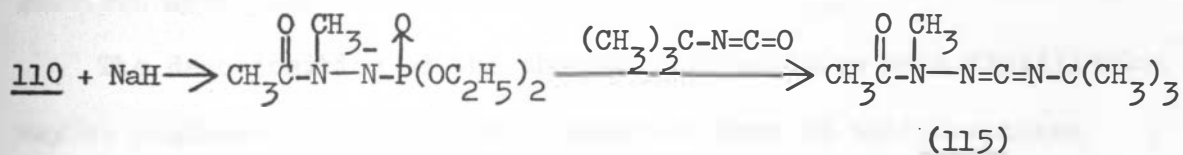
The isocyanate may rapidly polymerize and be too unstable to isolate.

The reaction of 111 with benzaldehyde to produce the benzalhydrazone (114) was carried out. The only product isolated from the



reaction was 0.04 g. of a high melting (above 250°) solid which was not identifiable.

In an attempt to prepare N¹-acetyl-N¹-methyl-N²-tert.-butylcarbodiimide (115), sodium hydride was added to 110 producing, in situ,



the phosphorohydrazidate anion. tert.-Butylisocyanate was added to the reaction mixture. After several days, upon work-up of the reaction mixture, a small amount of white solid was isolated. The ir spectrum of the solid indicated the presence of NH, C=O and alkyl groups.

The nmr spectrum indicated the presence of NH and tert.-butyl protons,

only. The compound did not melt, but sublimed above 200° . The data indicated that the solid was a urea containing a tert.-butyl group. Further identification of the solid was not attempted. Distillation of the solvent-stripped filtrate residue gave a very small amount of distillate. Spectral data of the distillate indicated the presence of ethoxy, carbonyl, N-methyl, phosphate ester, phosphorus oxide, and tert.-butyl groups in addition to other unassignable impurity peaks. Therefore, it appeared that the product was a mixture of starting materials, as no correlations of the integrated nmr spectrum could be made.

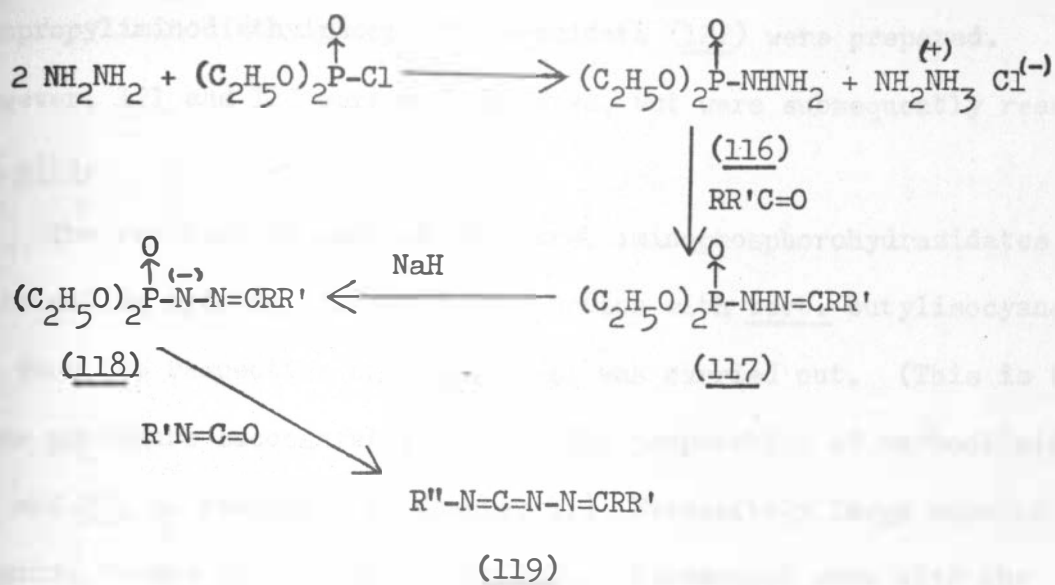
The results of the experimentation have indicated that a variety of N-acyl-N-methylphosphorohydrazidates were not to be made. The two crude phosphorohydrazidates that were prepared were either too unstable in the anionic form, to be available for reaction in situ, or that the anions, because of the presence of electron-withdrawing groups on both ends of the molecule, were not basic enough to undergo reaction with electrophiles.

The decomposition of the phosphorohydrazidates upon distillation may be analogous to the thermal decompositions of halophosphates (phosphorohalidates) and polyphosphates. According to Kosolapoff⁶², "the basic principle of this (thermal decomposition) reaction, which yields various polyphosphate esters as the end products, consists of the elimination of alkyl halide from reaction mixtures in which substances with halophosphate groups and with phosphate ester groups are present." The phosphorohydrazidate reaction mixture, which contained

acylphosphorohydrazidate, acylphosphorohydrazidate anions, ammonium chloride salts, and unreacted hydrazide and phosphorochloridate, may have produced various chlorophosphates, which decomposed forming phosphites. The phosphites could have dimerized forming hypophosphates, which could undergo oxidation-reduction giving pyrophosphites and pyrophosphates. The pyrophosphates could then decompose giving phosphates (i.e., triethylphosphate) and "by-products that are usually named metaphosphates or 'decomposition' products." It is quite possible that these same phosphate decompositions occurred in the phosphorohydrazidate anion reaction mixtures, which could have produced the large amounts of gummy residues, making product isolation difficult.

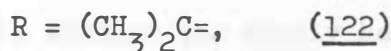
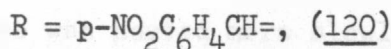
Having had no success in the preparation of N-acylcarbodiimides, the preparation of N-iminocarbodiimides was attempted. Utilization of N-iminophosphorohydrazidate anions to prepare N-iminocarbodiimides required the preparation of diethylphosphorohydrazidate (116), conversion of 116 to the appropriately substituted N-iminodiethylphosphorohydrazidate (117), formation of the anion (118), and finally, reaction of 118 with isocyanate to produce the N-iminocarbodiimide (119).

In the preparation of 116, the reaction of diethylphosphorochloridate with hydrazine in a one-to-two molar ratio gave a residue product that, when distilled for purification, decomposed, giving triethylphosphate. The ir and nmr spectra of the distillate compared with the spectral data of authentic triethylphosphate. It should be recalled that triethylphosphate was also obtained from the distillations



of N-acyl-N-methylphosphorohydrazidates. Therefore, the reactions to form N-iminophosphorohydrazidates (117) were carried out on the undistilled residue of 116, as the spectral data of the residue and a positive test for the NH_2 group, using meta-nitrobenzaldehyde, indicated that 116 was present in the residue.

The reaction of para-nitrobenzaldehyde with the residue gave a 71% yield of para-nitrobenzaliminodiethylphosphorohydrazidate (120). (The per cent yield was based on the assumption that 116 was pure compound.) The identity of 120 was based on spectral data. In



similar reactions, benzaliminodiethylphosphorohydrazidate (121) and

isopropyliminodiethylphosphorohydrazidate (122) were prepared.

However, 121 and 122 were not isolated, but were subsequently reacted in situ.

The reaction of each of the three iminophosphorohydrazidates with sodium hydride, followed by reaction with tert.-butylisocyanate to form the respective carbodiimides, was carried out. (This is the same procedure successfully used in the preparation of carbodiimides 22 and 23, as mentioned in Chapter 1.) Excessively large amounts of residue formed in all three reactions. Subsequent work with the filtrates and residues from all three reactions did not yield any products.

Having had no success in preparing N-iminocarbodiimides via N-iminophosphorohydrazidate anions, the dehydration of a series of N-imino- (91), and bis- (93) ureas (see Tables VII and VIII.) to produce N-imino- (90) and bis- (81) carbodiimides was attempted using three different dehydrating agents. The first reagent used for dehydration was phosphorus pentoxide⁵⁰. The reaction procedure was carried out by four different methods: 1) an intimate mixture of phosphorus pentoxide and urea was heated with an open flame with the products being distilled away from the reaction mixture at atmospheric pressure; 2) an identical intimate mixture was heated more slowly with the products being distilled away from the reaction mixture under aspirator vacuum; 3) an identical intimate mixture was slowly heated with the products being distilled away from the reaction mixture at pressures of less than one millimeter of Hg; 4) an identical intimate mixture

suspended in n-octane was maintained at reflux temperature for forty-eight hours followed by vacuum distillation of the filtrate. The first reaction yielded less than one milliliter of distillate. The ir spectrum of the distillate contained absorption bands at 2200 and 2120 cm^{-1} , indicative of the presence of N=C=O and N=C=N groups. Subsequent attempts at duplicating this reaction did not yield any product. No products were isolated from any of the other reactions.

The second reagent used for dehydration was thionyl chloride⁵¹. The reaction procedure was carried out by two different methods. In the first procedure thionyl chloride and urea were mixed in a one-to-one molar ratio in dry benzene, the mixture brought to reflux for several hours, and the products distilled away. In the second method excess thionyl chloride was added as both reactant and solvent to the urea, the mixture maintained at reflux for several hours and then distilled. No carbodiimides were obtained on distillation of either of the reaction mixtures. However, phenylisocyanate was isolated in 71% yield from the reaction of thionyl chloride with diphenyl-bis-urea, and tert.-octylisocyanate was isolated from the reaction of thionyl chloride with di-tert.-octyl-bis-urea.

The third reagent used for dehydration was para-tosyl chloride following Sheehan's procedure¹⁴. In this procedure urea and freshly recrystallized para-tosyl chloride were mixed together in methylene chloride with triethylamine present as the hydrogen chloride scavenger. After three hours of refluxing, the mixture was neutralized with 40% aqueous potassium carbonate, extracted with methylene chloride, and

product isolation from methylene chloride attempted. One problem with the procedure was the attempt to extract a carbodiimide from an aqueous solution, under which conditions, the carbodiimide should again form the urea. Another problem was the handling of excessive amounts of solid that formed upon neutralization with potassium carbonate. Even though Sheehan had reported the preparation and isolation of several carbodiimides(14), as discussed in Chapter 1, all attempts to prepare imino- and bis-carbodiimides by this method failed. The attempted preparation of 22 from N^1 -tert.-butyl- N^2 -(N,N-dimethylamino)urea did not yield any product, except a small amount of solid, m.p. $137-9^{\circ}$, whose spectral data indicated that it was a para-tosyl derivative of the urea. The small amount of compound did not allow for exact product identification.

There are several equally useful procedures for the dehydro-sulfurization of thioureas⁶³. The use of yellow mercury(II)oxide, following Sheehan's procedure²⁸, was the most convenient method. (The procedure was used successfully in the preparation of carbodiimides 22 and 24, as discussed in Chapter 1.) The reactions of several imino-(92) and bis-(94) thioureas (see Tables VII and VIII.) with mercury(II) oxide were carried out. The only product isolated was a small amount of tert.-octylisothiocyanate from the reaction of mercury(II)oxide with di-tert.-octyl-bis-thiourea. No other products were isolated from any of the reactions.

The isolation of several isocyanates and isothiocyanates from the various reaction mixtures indicated that the desired carbodiimides

TABLE VII


IMINOUREAS AND IMINOTHIOUREAS PREPARED, AND REACTION USED TO PREPARE THE CARBODIIMIDE



R	X	M.P.	% yield	P_2O_5	SOCl_2	$\text{p-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{Cl}$	HgO	Product	
								yes	no
$(\text{CH}_3)_3\text{C-}$	O	117-8°	31.6	x	x	x			?
$(\text{CH}_3)_3\text{C-}$	S	121-6°	10.9				x		x
$\text{C}_6\text{H}_5\text{-}$	S	127-9°	40.2				x		x
$(\text{CH}_3)_3\text{CCH}_2\text{C(CH}_3)_2$	S	78-81°	26.7				x		x

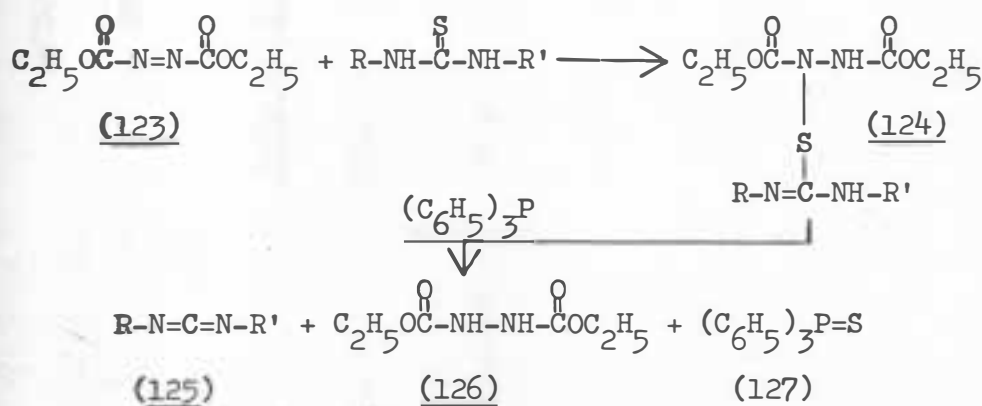
TABLE VIII

BIS-UREAS AND BIS-THIOUREAS PREPARED, AND REACTION USED TO PREPARE CARBODIIMIDES

<u>R</u>	<u>X</u>	<u>M.P.</u>	<u>% yield</u>	<u>GENERAL FORMULA RNHC(=X)NHNHC(=X)NHR</u>			<u>Product</u>	
				<u>SOCl₂</u>	<u>p-CH₃C₆H₄SO₂Cl</u>	<u>HgO</u>	<u>yes</u>	<u>no</u>
(CH ₃) ₃ C-	O	190-2°	80.0		x			x
(CH ₃) ₃ C-	S	153-5°	67.3			x		x
(CH ₃) ₃ CCH ₂ C(CH ₃) ₂ -	O	170-2°	85.6	x				x
(CH ₃) ₃ CCH ₂ C(CH ₃) ₂ -	S	134-8°	62.5			x		x
C ₆ H ₅ -	O	242-4°	95.5	x				x
	O	196-8°	90.7	x				x

had formed, but were too unstable under the reaction conditions used. Having had no success in isolating di-functional and bis-carbodiimides, it was intended to determine if any N-aminocarbodiimides, other than those already prepared, (i.e. 22,23 and 24) could be prepared either via phosphorohydrazidate anion intermediates or from ureas or thioureas. (See Table IX). The reaction of phenylisocyanate with N,N-dimethylphosphorohydrazidate anion (21a) did not yield any product. The reaction of methylisocyanate with 21a gave trimethylisocyanurate, apparently because of the basicity of the reaction mixture⁶⁴. The dehydrosulfurization of N¹-phenyl-N²-(N,N-dimethylamino)thiourea using mercury(II)oxide yielded a very small amount of an ethanol-soluble solid, whose elemental analysis and spectral data indicated that it was N¹-phenyl-N²-(N,N-dimethylamino)carbodiimide, but attempts to duplicate the reaction did not yield any more product.

Mitsunobu, et al.⁵², have recently reported the preparation of carbodiimides from the reaction of thioureas with diethylazodicar-



boxylate (123) to produce isothioureas (124), followed by reaction

TABLE IX

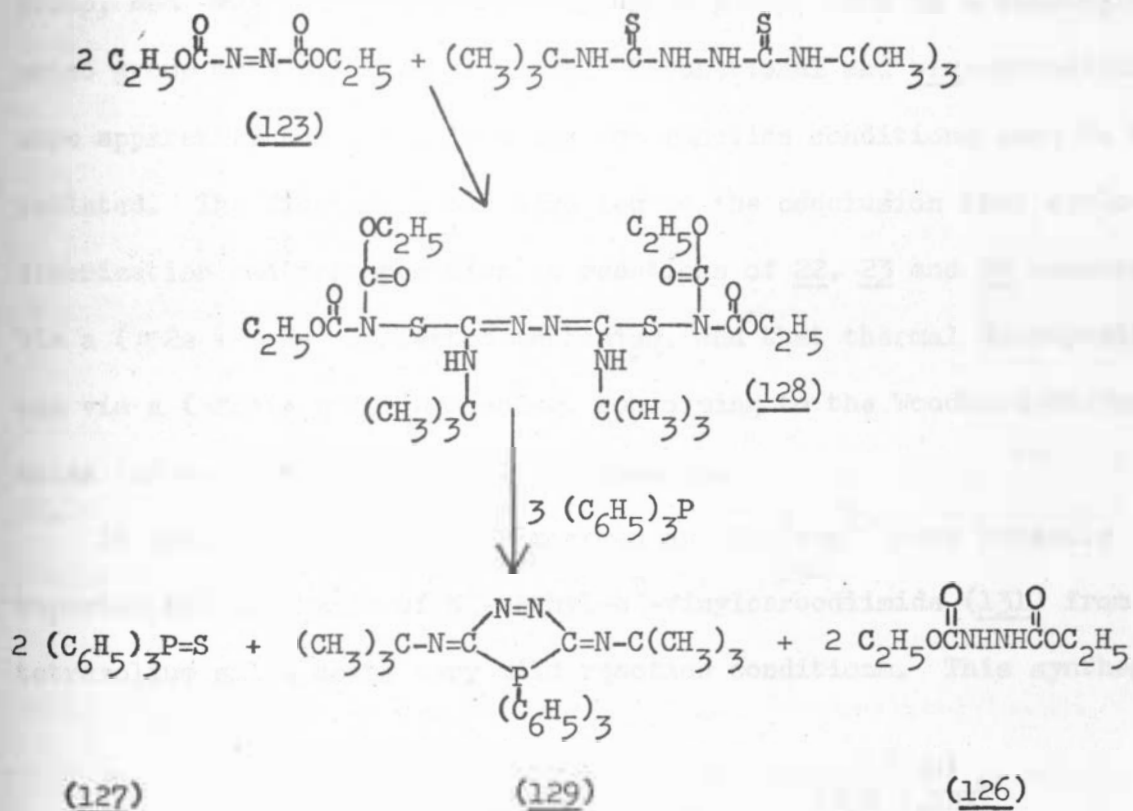
AMINOTHIUREAS PREPARED AND REACTED WITH HgO



<u>R</u>	<u>M.P.</u>	<u>% yield</u>	<u>Product obtained</u>	<u>Calculated</u>			<u>Found</u>			
				<u>%C</u>	<u>%H</u>	<u>%N</u>	<u>%C</u>	<u>%H</u>	<u>%N</u>	
$(\text{CH}_3)_3\text{C-}$	150-3°	61.2	$(\text{CH}_3)_3\text{C-N=C=N-N(CH}_3)_2$				a.			
$(\text{CH}_3)_3\text{CCH}_2\text{C(CH}_3)_2\text{-}$	108-11°	86.2	$(\text{CH}_3)_3\text{CCH}_2\text{C(CH}_3)_2\text{-N=C=N-N(CH}_3)_2$				a.			
$\text{C}_6\text{H}_5\text{-}$	180-2°	73.1	(?) $\text{C}_6\text{H}_5\text{-N=C=N-N(CH}_3)_2$	67.04	6.89	26.07	66.86	6.87	25.85	

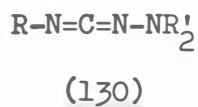
a. See Table I

with triphenylphosphine to yield carbodiimide (125), diethyldihydrozodicarboxylate (126) and triphenylphosphine sulfide (127). Having determined from previous reactions that bis-carbodiimides were too unstable to be isolated, it was thought that reaction of 123 with di-tert.-butyl-bis-thiourea could yield azine (128) which, upon reaction with excess triphenylphosphine, could yield the phosphine adduct of the bis-carbodiimide (129). Preliminary investigations



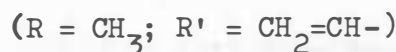
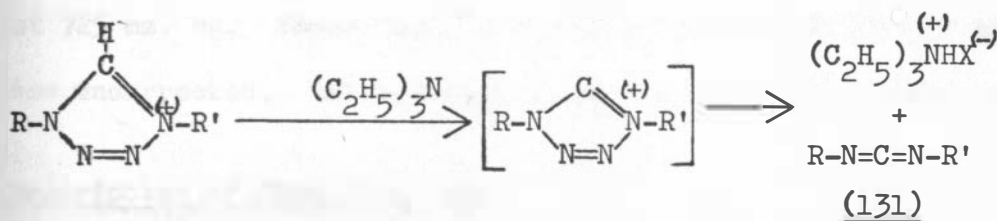
of the reaction have shown that 126 did form and was isolated in 90% yield. Another solid has also been isolated. The spectral data tenuously indicated that the solid could be 129, but all purification procedures have not produced any product purer than the original solid.

The data presented has indicated that N-substituted carbodiimides of general formula (130) could not be prepared from phosphorohydrazidates,



ureas, or thioureas, under the reaction conditions used, unless R was a bulky alkyl group, such as a tert.-butyl group or a tert.-octyl group, and -NR'₂ was a tertiary alkylamino group, such as a dimethylamino group or a piperidinyll group. Difunctional and bis-carbodiimides were apparently too unstable under the reaction conditions used to be isolated. The discussion has also led to the conclusion that cyclo-dimerization and decomposition in reactions of 22, 23 and 24 occurred via a ($\pi 2s + \pi 2a$) concerted mechanism, and that thermal decomposition was via a ($\pi 2s + \pi 2s$) mechanism, conforming to the Woodward-Hoffman rules for conservation of orbital symmetry.

It should be noted that Zimmerman and Olofson⁶⁵ have recently reported the synthesis of N¹-methyl-N²-vinylcarbodiimide (131) from a tetrazolium salt, using very mild reaction conditions. This synthesis,



and possibly others involving mild reaction conditions, may prove to be useful in the synthesis of other difunctional carbodiimides.

EXPERIMENTAL

Description of Instruments Used

The infrared (ir) spectra were obtained on either a Beckman IR-5 Infrared Spectrophotometer or a Perkin-Elmer 700 Infrared Spectrophotometer either as nujol mulls or as neat samples.

The nuclear magnetic resonance (nmr) spectra were obtained on a 60 MHz Varian A-60A Spectrophotometer as either solutions or as neat samples with tetramethylsilane used as an external standard.

The ultraviolet (uv) spectra were obtained on a Beckman DK-2A Spectrophotometer.

Gas chromatography analyses were carried out on a Beckman GC-2A using a column (20 ft. x 3/8 in.) packed with 30 g. of Dow-Corning fluid type 550 silicone on 100 g. of 42/60 C-2 firebrick.

Melting points were taken either on a Thomas Hoover capillary melting point apparatus or on a Thiele tube apparatus. All temperatures are in degrees centigrade and are uncorrected.

Brookings, South Dakota, where this research was performed, is at an elevation of 1,620 feet with an average barometric pressure of 725 mm. Hg. Those boiling points given at atmospheric pressure are uncorrected. All boiling points are given in degrees centigrade.

Description of Chemicals Used

All chemicals were used without purification as they were received from the manufacturers. All solvents that had to be anhydrous were

stored over anhydrous calcium chloride for at least two weeks before use.

Preparation of Ethyl-N-tert.-butylcarbamate

Ethylchloroformate, 108 g. (1.0 mole), was added slowly with stirring to a mixture of tert.-butylamine, 73.0 g. (1.0 mole), potassium carbonate, 150 g. (1.1 moles), 300 ml. of water and 100 ml. of xylene. (Note: enough potassium carbonate was used so that the solid did not completely dissolve.) The mixture was allowed to stir two hours and was filtered. The organic and aqueous layers of the filtrate were separated. The organic phase was washed three times with 20 ml.-portions of water. The combined water phase was then washed three times with 20 ml.-portions of xylene. The xylene fractions were combined and dried over anhydrous magnesium sulfate for several hours. The mixture was then filtered, the filtrate stripped of solvent at the aspirator, and the residue distilled, giving 109.30 g. (75.4% yield) of distillate, b.p. 65-6° (11 mm. Hg).

Preparation of tert.-Butylisocyanate

Calcium oxide, 20 g., was added to ethyl-N-tert.-butylcarbamate, 80.79 g. (0.5 mole), and the mixture brought to reflux (oil bath at 175°). Distillate was collected periodically at an equilibrium vapor temperature of 70°. As each portion of distillate was collected, it was quickly washed with water, the layers separated, and the organic layer dried over anhydrous calcium chloride. The combined dried distillates were filtered and the filtrate redistilled, giving 26.20 g. (53% yield) of distillate, b.p. 71-3° (atm.). The ir spectrum of the

distillate was identical with that of commercial tert.-butylisocyanate.

Preparation of Diethyl-N¹,N¹-dimethylphosphorohydrazidate (21a)

Method A. N¹,N¹-Dimethylhydrazine, 120 g. (2 moles) was added slowly with stirring to a mixture of diethylphosphite, 138 g. (1 mole), dry carbon tetrachloride, 154 g. (1 mole) and 250 ml. of dry xylene. The reaction flask condenser was fitted with an anhydrous calcium chloride drying tube to exclude atmospheric moisture. The temperature of the reaction mixture was kept below 40° by external cooling with an ice bath. After the addition was completed, the mixture was allowed to stir for one hour while coming to room temperature. The mixture was immediately filtered, giving 92 g. (96% yield) of white crystalline solid. The solid, which was hygroscopic, gave a positive halide ion test upon the addition of aqueous silver nitrate and was assumed to be N¹,N¹-dimethylhydrazinium chloride. The filtrate was stripped of solvent at the aspirator and the residue distilled, giving 129.17 g. (66% yield) of distillate, b.p. 110-4° (0.5 mm. Hg). The ir and nmr spectra supported the identification of the compound.

Method B. Diethylphosphorochloridate, 86.28 g. (0.5 moles) was added slowly with stirring to a mixture of N¹,N¹-dimethylhydrazine, 60.10 g. (1.0 moles), and triethylamine, 50.55 g. (0.5 moles), in 200 ml. of dry benzene. The temperature of the reaction mixture was kept below 40° by external cooling with an ice bath. After the addition was completed, the mixture was allowed to stir for four hours while coming to room temperature. The mixture was filtered, giving 63.74 g.

(92.5% yield) of white crystalline solid, m.p. 247-50°. The ir spectrum of the solid was identical with that of authentic triethylammonium chloride prepared from triethylamine and hydrogen chloride gas. The filtrate was stripped of solvent at the aspirator and the residue distilled, giving 54.59 g. (55.9% yield) of distillate, b.p. 110-5° (0.8 mm. Hg). The ir spectrum of the distillate was identical to the spectrum of the distillate obtained by Method A.

Preparation of Diethyl-N-piperdinyolphosphorohydrazidate (21b)

(Method A.) N-Aminopiperidine, 50.1 g. (0.5 moles), was added slowly with stirring to a mixture of diethylphosphite, 34.5 g. (0.25 moles), and dry carbon tetrachloride, 39.0 g. (0.25 moles) in 100 ml. of dry xylene. The reaction flask condenser was fitted with an anhydrous calcium chloride drying tube to exclude atmospheric moisture. The temperature of the reaction mixture was kept below 40° by external cooling with an ice bath. After the addition was completed, the mixture was stirred for one hour while coming to room temperature. The mixture was immediately filtered, giving 33.24 g. (expected - 34.17 g.) of moist solid. The water-soluble solid gave a positive halide ion test with aqueous silver nitrate and was assumed to be N-methylpiperidinium chloride. The filtrate was stripped of solvent at the aspirator and the residue recrystallized from heptane, giving 30.41 g. (83.1% yield) of white crystalline solid, m.p. 70-2°. The ir and nmr spectra supported the identification of the compound.

Preparation of Diethyl-N-n-butylphosphoramidate

(Method A.) n-Butylamine, 29.2 g. (0.4 moles), was added slowly with stirring to a mixture of diethylphosphite, 27.6 g. (0.2 moles), and dry carbon tetrachloride, 30.8 g. (0.2 moles), in 100 ml. of dry xylene. The reaction flask condenser was fitted with an anhydrous calcium chloride drying tube to exclude atmospheric moisture. The temperature of the reaction mixture was kept below 40° by external cooling with an ice bath. After the addition was completed, the mixture was stirred for one hour while coming to room temperature. The mixture was immediately filtered, giving 16.7 g. (expected - 21.92 g.) of moist solid. The water-soluble solid gave a positive halide ion test with aqueous silver nitrate and was assumed to be n-butylammonium chloride. The filtrate was stripped of solvent at the aspirator and the residue distilled, giving 27.07 g. (63.4% yield) of distillate, b.p. 114-6° (0.15 mm. Hg). The ir and nmr spectra supported the identification of the compound.

Preparation of Diethyl-N-cyclohexylphosphoramidate

(Method A.) Cyclohexylamine, 39.6 g. (0.4 moles), was added slowly with stirring to a mixture of diethylphosphite, 27.6 g. (0.2 moles), and carbon tetrachloride, 30.8 g. (0.2 moles), in 100 ml. of dry xylene. The reaction flask condenser was fitted with an anhydrous calcium chloride drying tube to exclude atmospheric moisture. The temperature of the reaction mixture was kept below 40° by external cooling with an ice bath. After the addition was completed, the mixture was stirred

for one hour while coming to room temperature. The mixture was immediately filtered, but the isolated solid was not weighed. The filtrate was stripped of solvent at the aspirator and the residue recrystallized from hexane, giving 33.56 g. (71.3% yield) of white crystalline solid, m.p. 71-4°. The ir and nmr spectra supported the identification of the compound.

Preparation of N¹-tert.-Butyl-N²-(N,N-dimethylamino)carbodiimide (22)

Method A. Sodium hydride (50% in oil), 14.4 g. (0.3 moles), was slowly added to diethyl-N¹,N¹-dimethylphosphorohydrazidate, 58.86 g. (0.3 moles), dissolved in 250 ml. of dry benzene under a dry nitrogen atmosphere. The mixture was stirred for twelve hours until gas evolution had ceased. tert.-Butylisocyanate, 29.7 g. (0.3 moles), was added to the reaction mixture, cooled in an ice bath. The mixture was allowed to stir until the stir bar "froze" in the formed residue. The reaction flask was sealed under a dry nitrogen atmosphere and set aside. Fourteen days later, the reaction mixture was filtered, the filtrate stripped of solvent at the aspirator, and the residue distilled, giving 35.33 g. (83.4% yield) of distillate, b.p. 65-7° (11 mm. Hg). Analysis for C₇H₁₅N₃- Calculated: C, 59.52; H, 10.74. Found: C, 60.00, H, 10.61. The ir spectrum of the distillate contained an absorption band at 2120 cm⁻¹ which is characteristic of the N=C=N group.

Method B. Yellow mercury(II)oxide (Merck), 25 g., was added to N¹-tert.-butyl-N²-(N,N-dimethylamino)thiourea, 17.53 g. (0.1 moles), dissolved in 100 ml. of benzene. The mixture was refluxed for six hours

with the water being azeotroped off. The mixture was filtered and the filtrate was refluxed with an additional 20 g. of mercury(II)oxide for six hours. The mixture was filtered, the filtrate stripped of solvent at the aspirator, and the residue distilled, giving 6.04 g. (43% yield) of distillate, b.p. 65-8° (11 mm. Hg). The spectral data for the sample were identical with the spectral data for the sample obtained by Method A.

Preparation of N¹-tert.-Butyl-N²-piperidinyldiimidate (23)

(Method A.) Sodium hydride (50% in oil), 4.8 g. (0.1 mole) was added portionwise to diethyl-N-piperidinyldiimidate, 23.6 g. (0.10 mole), dissolved in 200 ml. of dry benzene under a dry nitrogen atmosphere. The mixture was stirred for eight hours until gas evolution had ceased. tert.-Butylisocyanate, 9.9 g. (0.10 moles), was added to the reaction mixture, cooled in an ice bath. The reaction mixture was allowed to stir until the stir bar "froze" in the formed residue. The reaction flask was sealed under a dry nitrogen atmosphere and set aside. After five hours, the reaction mixture was filtered, the filtrate stripped of solvent at the aspirator, and the residue distilled, giving 5.58 g. (30.8% yield) of distillate, b.p. 68-70° (0.40 mm. Hg). The ir spectrum of the distillate contained a strong absorption band at 2120 cm⁻¹, which is characteristic of the N=C=N group.

Preparation of N¹-tert.-Octyl-N²-(N,N-dimethylamino)diimidate (24)

(Method B.) Yellow mercury(II)oxide, 22 g., was added to

N¹-tert.-octyl-N²-(N,N-dimethylamino)thiourea, 23.14 g. (0.1 moles), dissolved in 100 ml. of dry benzene. The mixture was maintained at reflux for eight hours with the water being azeotroped off. The mixture was filtered and the filtrate maintained at reflux with an additional 20 g. of mercury(II)oxide for six hours. The mixture was filtered, the filtrate stripped of solvent at the aspirator and the residue distilled, giving 10.51 g. (51.3% yield) of distillate, b.p. 59-60° (0.45 mm. Hg). The ir spectrum of the distillate contained a strong absorption band at 2120 cm⁻¹ for the N=C=N group.

Preparation of N¹-tert.-Butyl-N²-n-butylcarbodiimide

(Method A.) Sodium hydride (50% in oil), 4.8 g. (0.1 moles) was added portionwise to N-n-butylphosphoramidate, 21.03 g. (0.1 moles), dissolved in 100 ml. of dry benzene under a dry nitrogen atmosphere. The mixture was allowed to stir for eight hours until gas evolution had ceased. tert.-Butylisocyanate, 9.9 g. (0.1 moles) was added to the reaction mixture cooled in an ice bath. The reaction mixture was stirred until the stir bar "froze" in the formed residue. After four hours, the reaction mixture was filtered, the filtrate stripped of solvent at the aspirator, and the residue distilled, giving 5.13 g. (33.2% yield) of distillate, b.p. 72-4° (12 mm. Hg). The ir spectrum of the distillate contained a strong absorption band at 2120 cm⁻¹, characteristic of the N=C=N group.

Preparation of N¹-tert.-Butyl-N²-cyclohexylcarbodiimide

(Method A.) Sodium hydride (50% in oil), 4.8 g. (0.1 moles), was added portionwise to N-cyclohexylphosphoramidate, 23.5 g. (0.1 moles), dissolved in 100 ml. of dry benzene under a dry nitrogen atmosphere. The mixture was stirred for three hours until the stir bar "froze" in the formed residue. The reaction mixture was filtered, the filtrate stripped of solvent at the aspirator, and the residue distilled, giving 6.55 g. (36.3% yield) of distillate, b.p. 65-7° (0.45 mm. Hg). The ir spectrum of the distillate contained a strong absorption band at 2120 cm⁻¹, characteristic of the N=C=N group.

Isolation of 1,3-Di-(N,N-dimethylamino)-2,4-bis-(tert.-butylimino)-1,3-diazatidine (22-dimer, 30)

Carbodiimide 22 formed a solid after several days. The solid was recrystallized from hexane, giving a white crystalline solid, m.p. 142-3°. Analysis for C₁₄H₃₀N₆ - calculated: C, 59.52; H, 10.74. Found: C, 59.21; H, 10.35. Their spectrum showed the loss of the 2120 cm⁻¹ absorption band, present in the ir spectrum of 22. Molecular weight determination in benzene by vapor pressure osmometry gave a weight of 280 amu. The theoretical value is 282.50 amu.

Isolation of 1,3-Di-N-piperidinyl-2,4-bis-(tert.-butylimino)-1,3-diazetidine (23-dimer)

Carbodiimide 23 formed a solid after several days. The solid was

recrystallized from hexane, giving a white crystalline solid, m.p. 125-7°. The ir spectrum showed the loss of the 2120 cm^{-1} absorption band, present in the ir spectrum of 23. Molecular weight determination in benzene by vapor pressure osmometry gave a weight of 355 amu. The theoretical value is 362.64 amu.

Interconversion of 22 and 30

Dimer 30, 5.0 g. (0.018 moles) was distilled, giving 4.85 g. (97% yield) of distillate, b.p. 66-8° (11 mm. Hg). The ir and nmr spectra of the distillate were identical with the spectral data of 22. After several days, solid formed in the distillate. The solid was recrystallized from hexane, giving 4.53 g. (93.5% yield) of white crystalline solid, m.p. 142-3°. The ir and nmr spectra of the solid were identical with the spectra of 30. Heating of 30 just above its melting point gave a brilliant blue colored liquid which became pale yellow colored after several minutes of heating. The ir and nmr spectra of the pale yellow liquid were identical with the spectra for 22. Gas chromatography indicated the compound to be 95% pure 22.

Reaction of 22 with N^1 -tert.-Butyl- N^2 -n-butylcarbodiimide

A mixture of 22, 2.82 g. (0.02 moles), and N^1 -tert.-butyl- N^2 -n-butylcarbodiimide, 3.08 g. (0.02 moles), was placed in a sealed vial and set aside. After fifteen days, the formed solid was removed and air dried by vacuum filtration. The ir and nmr spectra of the solid, m.p. 138-40°, were identical with the spectra of 30. The nmr

spectrum of the oily residue was identical with the spectrum of original N^1 -tert.-butyl- N^2 -n-butylcarbodiimide, but also showed the presence of a small amount of 22, as impurity peaks.

Reaction of 22 with N^1 -tert.-Butyl- N^2 -cyclohexylcarbodiimide

A mixture of 22, 2.82 g. (0.02 moles), and N^1 -tert.-butyl- N^2 -cyclohexylcarbodiimide, 3.61 g. (0.02 moles), was placed in a sealed vial and set aside. After fifteen days, the formed solid was removed and air dried by vacuum filtration. The ir and nmr spectra of the solid, m.p. $136-9^{\circ}$, were identical with the spectra of 30. The nmr spectrum of the oily residue was identical with the spectrum of original N^1 -tert.-butyl- N^2 -cyclohexylcarbodiimide, but also showed the presence of a small amount of 22, as impurity.

Reaction of 22 with 23

A mixture of 22, 1.41 g. (0.01 moles), and 23, 1.65 g. (0.01 moles), was placed in a sealed vial and set aside. After fifteen days, the formed solid was removed. Recrystallization from dilute hexane solution gave 0.61 g. (43% yield) of 22, m.p. $137-40^{\circ}$, whose identity was confirmed by spectral data. Concentration of the hexane filtrate gave solid, m.p. $105-20^{\circ}$. The last solid to be isolated from the hexane melted at $122-5^{\circ}$. The spectral data of the 0.49 g. (30% yield) compared with the spectral data of 23.

Preparation of N¹-tert.-Butyl-N²-benzyldimethylammonium Chloride

Carbodiimide (42)

Benzyl chloride, 1.26 g. (0.01 moles), was added to 22, 1.41 g. (0.01 moles), dissolved in 10 ml. of dry benzene and the solution allowed to stand for eight hours. The solid which had formed was filtered out, giving 0.88 g. (33% yield). The melting point of the solid was 123-6° (lit. 128-9°^{25b}). The ir spectrum of the solid contained a strong absorption band at 2120 cm⁻¹, indicating that the N=C=N group was still present. The presence of absorption bands at 3200 and 1700 cm⁻¹, indicated that the solid had been partially hydrolyzed to the urea.

When the reagents were mixed as above, but the mixture maintained at reflux for several hours, the mixture became a dark gummy residue of unknown composition.

Reaction of 22 with Methyl iodide

Methyl iodide, 1.62 g. (0.01 moles), was added to 22, 1.41 g. (0.01 moles), dissolved in 50 ml. of dry benzene. The exothermic reaction produced a brown solid, 1.34 g., which did not melt below 240°. The ir spectrum of the solid was identical with the published spectrum of tetramethylammonium iodide⁷⁰. No other product could be isolated from the tarry residue.

Preparation of O-Ethyl-N¹-tert.-butyl-N²-(N,N-dimethylamino)isourea (45)

Compound 30, 2.0 g. (0.14 moles) was dissolved in 10 ml. of ethanol and the mixture maintained at gentle reflux for three hours. The mixture was stripped of solvent and distilled, giving a colorless distillate, b.p. 46-8° (0.50 mm. Hg). Analysis for C₉H₂₁N₃O - Calculated: c, 57.70; H, 11.32; N, 22.45. Found: C, 57.60; H, 11.28; N, 22.61.

The identical reaction of 22 with ethanol also gave 45 with product identification based on identical spectral data of the distillates from both reactions.

Product 45 was also obtained when 22 and 30 were dissolved in ethanol and placed in the Parr bomb high pressure hydrogenation apparatus at 50° and 1000 psi of hydrogen gas. Product identification was based on spectral data of the distillate products.

Preparation of N¹-tert.-Butyl-N²-n-butyl-N³-(N,N-dimethylamino)-guanidine (46)

n-Butylamine, 1.02 g. (0.014 moles), was added to 22, 2.0 g. (0.014 moles), dissolved in 10 ml. of hexane. The exothermic reaction was stirred while coming to room temperature. The mixture was filtered, the filtrate stripped of solvent at the aspirator and the residue distilled. Only enough product, b.p. 98-102 (11 mm. Hg), was collected for spectral and elemental analysis. Analysis for C₁₁H₂₆N₄ - Calculated: C, 61.62; H, 12.25; N, 26.14. Found: C, 62.08;

H, 12.22; N, 25.82. The ir and nmr spectra supported the identification of the compound.

The same reaction with 30, 2.0 g. (0.007 moles), also produced 46 with identification based on spectral data.

Preparation of N¹-tert.-Butyl-N²-piperidiny1-N³-(N,N-dimethylamino)-guanidine (47)

A mixture of 30, 2.82 g. (0.01 moles), and piperidine, 0.85 g. (0.01 moles), was slowly warmed in an oil bath until all solid had disappeared. The mixture was maintained at this temperature for several hours, and then distilled, giving distillate, b.p. 84-6° (0.50 mm. Hg). Only enough distillate was collected for spectral and elemental analysis. Analysis for C₁₂H₂₆N₄ - Calculated: C, 63.50; H, 11.60; N, 24.75. Found: C, 63.09; H, 11.16; N, 27.08. The ir and nmr spectra supported the identification of the compound.

The same reaction with 22, 1.41 g. (0.01 moles), also produced 47 with identification based on spectral data.

Reaction of 30 and Cyclopentadiene

A mixture of 30, 2.82 g. (0.01 moles), and cyclopentadiene, 1.32 g. (0.02 moles) was prepared and set aside. After several days, the mixture had become a dark gummy residue. No products could be isolated from the residue mixture. The spectral data of the residue mixture were poor and inconclusive.

Reaction of 30 with Cyclohexene

Carbodiimide dimer 30, 2.82 g. (0.01 moles), was dissolved in 10 ml. of cyclohexene and the mixture maintained at gentle reflux for forty-eight hours. Upon cooling of the mixture, 2.57 g. (91% yield) of solid, m.p. 140-2°, was collected. The spectral data of the solid were identical with the spectral data of 30.

Ultraviolet Photolysis of 22

A solution of 22, 5.0 g. (0.035 moles), dissolved in 800 ml. of hexane was placed in the photolysis apparatus and irradiated with a mercury lamp at 2537Å. Aliquots of the photolysate were removed and the uv spectra obtained at 0, 20, 42, and 66 hours. (See Table III for uv spectral data.) The photolysate was stripped of solvent at the aspirator giving 0.1 g. of solid, m.p. 123-5°. Data were collected (see Table III), but the identity of the compound could not be deduced.

Qualitative Study of the Rate of Formation of 30 from 22

Twelve sample tubes containing freshly distilled 22 were prepared. Six of the tubes were placed in a box completely wrapped in aluminum foil to exclude all light, and six of the tubes were placed in direct sunlight. After four days, solid formed in all six of the light-exposed tubes. A sample of this solid had a melting point of 139-41° and spectral data that were identical with the spectral data of 30. Examination of the tubes not exposed to light, revealed that solid had also formed in all six tubes. A sample of this solid had a melting

point of $140-2^{\circ}$ and spectral data that was identical with the spectral data of 30.

Preparation of Benzoylhydrazide (94)

A solution of methylbenzoate, 136 g. (1.0 moles), dissolved in 200 ml. of dry benzene was added to a mixture of hydrazine (95⁺%), 128 g. (4.0 moles), in 100 ml. of dry benzene. The mixture was stirred, while coming to room temperature. Two layers were present in the reaction mixture, the lower being yellow in color, and the upper being colorless. Cooling the reaction mixture in an ice bath caused the formation of solid in the lower layer. Separation of the layers in the warm mixture, removal of solvent at the aspirator from the lower layer, and recrystallization of the residue from benzene, gave 104.48 g. (77% yield) of white crystalline solid, m.p. $111.5-113^{\circ}$. The ir spectrum of 94 was identical with Sadtler spectrum #15671 of benzoylhydrazide.

Preparation of N¹-Benzoyl-N²-benzalhydrazone (95)

Benzaldehyde, 42.4 g. (0.4 moles) was slowly added to a solution of 94, 54.4 g. (0.4 moles), dissolved in 400 ml. of ethanol. Solid began forming as the addition was completed. The mixture was maintained at reflux for several hours to insure completion of reaction. The mixture was reduced in volume at the aspirator, cooled in an ice bath, and the solid filtered out, giving 85.70 g. (95.7% yield) of white crystalline solid, m.p. $206-8^{\circ}$. The ir spectrum of the solid showed

the disappearance of the NH_2 absorption band at 3250 cm^{-1} , which was present in the ir spectrum of 94.

Preparation of N^1 -Benzoyl- N^1 -methyl- N^2 -benzalhydrazone (97)

Sodium hydride (50% in oil), 20.2 g. (0.42 moles), was slowly added to a solution of 95, 85.5 g. (0.38 moles), dissolved in 250 ml. of dry dioxane and the mixture was stirred for twelve hours. (The reaction flask condenser was fitted with an anhydrous calcium chloride drying tube to exclude excess atmospheric moisture from the reaction mixture.) The mixture was maintained at reflux for an additional two hours to insure completion of reaction. After cooling the reaction mixture in an ice bath, excess methyl bromide (about 100 ml.) was added. The reaction mixture was allowed to slowly come to room temperature, and was then maintained at reflux for twelve hours. The resultant slurry was allowed to cool to room temperature and the solid filtered out, giving 38.82 g. (94.3% yield) of sodium bromide. The filtrate was stripped of solvent at the aspirator, and the residue recrystallized from ethanol, giving 56.14 g. (63% yield) of white crystalline solid, m.p. $83-5^\circ$. The ir and nmr spectra confirmed the identity of the compound.

Preparation of N^1 -Benzoyl- N^1 -methylhydrazide (98)

Phenylhydrazine, 26 g. (0.24 moles), was slowly added to a mixture of 97, 56.1 g. (0.24 moles), in 500 ml. of ethanol containing 3 ml. of concentrated hydrochloric acid. The reaction mixture was maintained at

reflux for two hours, then cooled in an ice bath and solid filtered out, giving 20.81 g. (44.4% yield), of benzalphenylhydrazone, m.p. 154-6°. The filtrate, upon reduction in volume at the aspirator, became very viscous and unfilterable, which prevented the isolation of more benzalphenylhydrazone. Therefore, the residue mixture was distilled, giving 18.76 g. of a viscous oil, b.p. 178-84° (12 mm. Hg). The ir spectrum of the oil had no absorption bands in the 3300 cm^{-1} region, which indicated that the NH_2 group was not present in the material. Qualitative tests for the presence of NH_2 , using acetophenone and benzaldehyde, were negative; therefore, it was concluded that the desired compound had not been prepared.

Preparation of N¹-Acetyl-N¹-methylhydrazide (102)

Method A. Acetyl chloride, 78.5 g. (1.0 moles), was slowly added to a solution of methylhydrazine, 92.0 g. (2.0 moles), dissolved in 75 ml. of ethanol. The temperature of the reaction mixture was kept below 40° by external cooling in an ice bath. After the addition was complete, the mixture was allowed to come to room temperature, during which time, a white solid formed. The solid, methylhydrazinium chloride, m.p. 79-82°, was isolated in quantitative yield. The filtrate was stripped of solvent at the aspirator and the residue distilled, giving 39.4 g. (44.8% yield) of colorless distillate, b.p. 97-100° (12 mm. Hg). The ir spectrum of the solid confirmed the identification of the product.

Method B. Ethyl acetate, 17.6 g. (0.20 moles), was slowly added to a solution of methylhydrazine, 9.2 g. (0.20 moles), dissolved in 15 ml. of ethanol. The mixture was maintained at reflux for nine hours, the solvent removed at the aspirator, and the residue distilled, giving 2.97 g. (16.9% yield) of colorless distillate, b.p. 98-100° (12 mm. Hg). The ir spectrum of the distillate was identical to that of 102 prepared by Method A.

Preparation of N¹-Formyl-N¹-methylhydrazide (101)

Methyl formate, 132.12 g. (2.2 moles), was slowly added to methylhydrazine, 92.18 g. (2.0 moles), in the absence of solvent. The temperature of the reaction mixture was kept below 40° by external cooling in an ice bath. The mixture was allowed to come to room temperature, the formed methanol removed at the aspirator, and the residue distilled, giving 131.64 g. (88.7% yield) of colorless distillate, b.p. 90-3° (12 mm. Hg). The ir and nmr spectra supported the identity of the product.

Reaction of 101 with Nitrous Acid

Hydrochloric acid, 10 ml. of a 30% solution in water, was slowly added to a mixture of 101, 7.4 g. (0.10 moles), and sodium nitrite, 7.9 g. (0.10 moles). The gases formed in the exothermic reaction were fractionally collected (an ice bath trap followed by a Dry Ice-acetone bath). A total of 4.54 g. (82.4% yield) of methyl azide with trace impurity was collected in the ice bath trap.

Distillation of the residual reaction mixture gave water as the only distillate with sodium chloride being left in the distillation flask. The ir spectrum of the distillate was identical with that of water. The distillate was found to be neutral, when titrated with aqueous base.

Note 1. An authentic sample of methyl azide, for comparative purposes, was prepared by adding slowly dimethylsulfate, 12.6 g. (0.01 moles), to sodium azide, 10.7 g. (0.1 moles), dissolved in 50 ml. of water. The evolved gas was collected in an ice bath trap. The ir spectrum of the gas was identical with the gas obtained above, except for several impurity peaks.

Note 2. The nitrogen dioxide impurity was verified by comparing the extraneous absorption bands in the ir spectrum of methyl azide with the ir spectrum of authentic nitrogen dioxide, prepared by the reaction of hydrochloric acid with sodium nitrite.

Reaction of 102 with Nitrous Acid

The same reaction was carried out with 102 as was carried out with 101. Because of the small amount of 102 available, not enough product was obtained to be identified.

Preparation of N¹-Acetyl-N¹-methylphosphorohydrazidate (110)

Diethylphosphorochloridate, 17.25 g. (0.1 moles), was slowly added to an ice-cooled mixture of 102, 8.81 g. (0.1 moles) and triethylamine, 10.12 g. (0.1 moles), in 50 ml. of dry benzene. The

reaction mixture temperature was maintained at 25° by controlling the rate of addition of the phosphorochloridate. The reaction mixture was stirred for a period of four hours, after which time, the solid was filtered out giving, 8.42 g. (61.2% yield) of triethyl ammonium chloride, m.p. 243-5°. The filtrate was stripped of solvent at the aspirator, leaving an oily residue. The ir and nmr spectra of the residue indicated that 110 was present in the residue. Distillation of the residue gave 15 ml. of light yellow distillate, b.p. 58-60° (0.25 mm. Hg). The ir spectrum of the distillate contained no absorption bands to indicate the presence of NH or C=O groups, which were present in the ir spectrum of the undistilled residue.

Preparation of N¹-Formyl-N¹-methylphosphorohydrazidate (111)

Diethylphosphorochloridate, 86.25 g. (0.5 moles), was slowly added to an ice-cooled mixture of 101, 37.0 g. (0.50 moles), and triethylamine, 50.6 g. (0.5 moles) in 300 ml. of dry benzene. The reaction mixture temperature was maintained at 25° by controlling the rate of addition of the phosphorochloridate. The reaction mixture was stirred for six hours, after which time, the solid was filtered out, giving 45.75 g. (66.5% yield) of triethylammonium chloride. The filtrate was stripped of solvent at the aspirator, leaving an oily residue. The ir and nmr spectra indicated that 111 was present in the residue. Distillation of the residue gave 25 ml. of light yellow distillate, b.p. 90-1° (12 mm. Hg). The ir and nmr spectra of the distillate were identical with the spectra for the distillate obtained from the distillation of 110-residue.

Preparation of Triethylphosphate

Phosphorus oxytrichloride, 15.33 g. (0.1 moles), was slowly added to a mixture of ethanol, 13.82 g. (0.3 moles), and pyridine, 23.73 g. (0.3 moles) in 100 ml. of dry benzene. The temperature of the reaction mixture was kept below 40° by external cooling with an ice bath. After the reaction mixture had come to room temperature, the solid was filtered out, giving 29.40 g. (84.8% yield) of pyridinium chloride, m.p. 138-41°. The filtrate was stripped of solvent at the aspirator and the residue distilled. Only enough distillate, b.p. 95-6° (13 mm. Hg) was collected for identification and comparison purposes. The ir and nmr spectral data of the distillate were identical with the spectra of the distillates from 110-residue and 111-residue. (See Table VI).

Reaction of 111-residue with Sodium Hydride, then Carbon Dioxide

Sodium hydride (50% in oil), 9.6 g. (0.2 moles), was slowly added to undistilled residue-111, 42.04 g. (0.2 moles), dissolved in 200 ml. of dry benzene under a dry nitrogen atmosphere. The mixture was stirred for twelve hours, until gas evolution had ceased. Carbon dioxide, from the sublimation of Dry Ice, was allowed to bubble through the reaction mixture with stirring for three hours. The reaction flask was then sealed under a dry nitrogen atmosphere and set aside. After seven days, the liquid was decanted from the gummy residue, the decantate filtered several times, and the filtrate stripped of solvent at the aspirator. Distillation of the residue did not yield any distillate that could be identified.

Reaction of 111-residue with Sodium Hydride, then Benzaldehyde

Sodium hydride (50% in oil), 2.4 g. (0.05 moles), was slowly added to undistilled residue-111, 10.5 g. (0.05 moles) dissolved in 100 ml. of dry benzene under a dry nitrogen atmosphere. The mixture was stirred for a six hour period until gas evolution had ceased. Benzaldehyde, 5.36 g. (0.05 moles) was added to the mixture under a dry nitrogen atmosphere and the mixture was allowed to stir for twelve hours. The reaction mixture was filtered and the filtrate reduced at the aspirator to a volume of 15 ml. Only 0.04 g. of a high melting (above 250°) solid was isolated. The solid could not be identified because of the small amount obtained.

Reaction of 110-residue with Sodium hydride, then tert.-Butylisocyanate

Sodium hydride (50% in oil), 4.9 g. (0.1 moles), was slowly added to undistilled residue-110, 22.2 g. (0.1 moles), dissolved in 200 ml. of dry benzene under a dry nitrogen atmosphere. The mixture was stirred for an eight hour period until gas evolution had ceased. tert.-Butylisocyanate, 9.9 g. (0.1 moles), was added to the reaction mixture under a dry nitrogen atmosphere and the mixture allowed to stir until the stirring bar "froze" in the gummy residue. The reaction flask was sealed under a dry nitrogen atmosphere and set aside. After two weeks, the entire contents of the flask had formed a gummy residue. The mixture was heated with most of the residue going into solution. The hot mixture was filtered and the filtrate stripped of solvent at the aspirator, yielding a small amount of white solid, which

sublimed above 200° . The spectral data of the solid indicated that the solid was a urea containing at least one tert.-butyl group. Further identification could not be made because of the small amount of sample. No other products could be isolated.

Preparation of Diethylphosphorohydrazidate (113)

Method A. Diethylphosphorochloridate, 17.2 g. (0.1 moles), was added to a mixture of hydrazine (95⁺%), 3.36 g. (0.1 moles), and sodium hydroxide pellets, 4.0 g. (0.1 moles), dissolved in 50 ml. of methanol. The temperature of the reaction mixture was kept below 40° by controlling the rate of addition of the phosphorochloridate. The mixture was stirred while coming to room temperature. The solid was filtered out of the reaction mixture, giving 3.40 g. (58.2% yield) of sodium chloride. The filtrate was stripped of solvent at the aspirator and the oily residue was decanted from the remaining solid. The ir and nmr spectra of the oil indicated that the desired compound, 113, was present. The distillation of the oil gave a small amount of distillate, b.p. $68-70^{\circ}$ (0.70 mm. of Hg). The ir spectrum of the distillate was identical with that of triethylphosphate.

Method B. Diethylphosphorochloridate, 17.2 g. (0.10 moles), was slowly added to a mixture of hydrazine (95⁺%), 6.72 g. (0.20 moles), dissolved in 50 ml. of dry benzene. The mixture was stirred for two hours while coming to room temperature. The solid was filtered out, giving 4.70 g. (67% yield) of hydrazinium chloride. The filtrate was stripped of solvent at the aspirator. The ir spectrum

of the oily residue was the same as the spectrum of the residue in Method A. Attempted distillation of the residue gave no product.

Preparation of meta-Nitrobenzaliminodiethylphosphorohydrazidate (117)

An excess of 5% meta-nitrobenzaldehyde in benzene was added to undistilled residue-113, 10 g. (0.06 moles), dissolved in 50 ml. of ethanol. An excess of the benzene solution was used to ensure complete removal of unreacted hydrazine. After several minutes of stirring, a yellow solid formed, which was filtered out. The ir spectrum of the solid, m.p. 187-90°, indicated that the solid was meta-nitrobenzalazine. The filtrate was stripped of solvent at the aspirator and the residue recrystallized from ethanol, yielding 13.05 g. (71.5% yield) of white crystalline solid, m.p. 138-41°. The ir and nmr spectra of the solid supported the identity of the compound as 117.

The Attempted Preparation of N¹-tert.-Butyl-N²-meta-nitrobenzalimino-carbodiimide

Sodium hydride (50% in oil), 2.45 g. (0.05 moles), was added to a solution of 117, 15.1 g. (0.05 moles), dissolved in dry benzene under a dry nitrogen atmosphere. The mixture was stirred for one hour while coming to room temperature. When the rate of gas evolution had visibly lessened, tert.-butylisocyanate, 4.95 g. (0.05 moles) was slowly added to the reaction mixture. The mixture took on a deep red color with the formation of solid. The mixture was stirred until the stirring bar became "frozen" in the residue. The

flask was sealed under a dry nitrogen atmosphere and set aside. Six days later, the flask was opened, but all attempts to isolate product were without success.

The Attempted Preparation of N¹-tert.-Butyl-N²-benzaliminocarbodiimide

Diethylphosphorochloridate, 17.2 g. (0.10 moles), was added to a mixture of hydrazine, (95⁺%), 6.72 g. (0.20 moles), in 50 ml. of dry benzene. The mixture was stirred for a one hour period and the solid filtered out. Benzaldehyde, 10.61 g. (0.10 moles), was added to the filtrate. The reaction mixture was maintained at reflux with the water being azeotroped off for a period of five hours. Sodium hydride (50% in oil), 4.9 g. (0.10 moles), was added to the mixture which was stirred for a one hour period, until gas evolution had diminished. tert.-Butylisocyanate, 9.9 g. (0.10 moles), was added to the reaction mixture, which was stirred while warming to room temperature. As the isocyanate was added, the reaction mixture thickened turning dark reddish-orange in color. After several hours of stirring, the mixture began to solidify. After twenty-four hours, the mixture was filtered and the filtrate stripped of solvent at the aspirator, giving a solid residue, m.p. 87-92^o. The ir spectrum of the solid was identical with that of authentic dibenzalazine. All attempts to isolate product from the residues were without success.

The Attempted Preparation of N¹-tert.-Butyl-N²-isopropyliminocarbodiimide

Diethylphosphorochloridate, 17.2 g. (0.10 moles), was added to a mixture of hydrazine (95⁺%), 6.72 g. (0.20 moles), in 50 ml. of dry benzene. The mixture was stirred for a one hour period and the solid filtered out. Acetone, 5.8 g. (0.10 moles), was added to the reaction mixture which was maintained at reflux for a period of five hours with the water being azeotroped off. The reaction mixture was reduced in volume at the aspirator to remove unreacted acetone. The residue was redissolved in dry benzene and sodium hydride (50% in oil), 4.9 g. (0.1 moles) was added under a dry nitrogen atmosphere and the mixture was stirred for six hours, until gas evolution had ceased. tert.-Butylisocyanate, 9.9 g. (0.10 moles), was added to the ice bath cooled mixture and the mixture was stirred while warming to room temperature. The mixture was brought to reflux and maintained at that temperature for two days. After cooling to room temperature, the solid was filtered out, the filtrate reduced in volume at the aspirator, and the residue distilled, yielding only a few drops of distillate, which was not enough sample to be identified. Near the end of the distillation, solid began collecting in the distillation head. The ir and nmr spectra of the solid were identical with the spectra of authentic di-tert.-butylurea. No other products were isolated from the reaction mixture.

Preparation of Iminoureas and Iminothiureas

General Procedure: Acetone was added to hydrazine in benzene and the mixture maintained at reflux for twelve hours with the water being azeotroped off. The desired isocyanate or isothiocyanate was added to the reaction mixture, which was maintained at reflux for several hours. The reaction mixture was stripped of solvent and the residue isolated, and recrystallized, if necessary.

Preparation of N¹-tert.-Butyl-N²-isopropyliminourea

Acetone, 5.81 g. (0.10 moles), and hydrazine (80⁺%), 4.0 g. (0.1 moles), were mixed together. tert.-Butylisocyanate, 9.91 g. (0.10 moles) was added to the mixture. The isolated solid, recrystallized by dissolving in ethanol and precipitating with water, gave 5.42 g. (31.6% yield) of white solid, m.p. 117-8^o.

Preparation of N¹-tert.-Butyl-N²-isopropyliminothiurea

Acetone, 5.81 g. (0.10 moles), and hydrazine (95⁺%), 3.30 g. (0.10 moles), were mixed together. tert.-Butylisothiocyanate, 11.5 g. (0.10 moles), was added to the mixture. Isolated was 2.04 g. (10.9% yield) of white crystalline solid, m.p. 121-6^o.

Preparation of N¹-Phenyl-N²-isopropyliminothiurea

Acetone, 11.6 g. (0.20 moles), and hydrazine (95⁺%), 6.60 g. (0.20 moles), were mixed together. Phenylisothiocyanate, 27.04 g. (0.20 moles), was added to the mixture. The isolated solid,

recrystallized from ethanol, gave 16.65 g. (40.2% yield) of white crystalline solid, m.p. 127-9°.

Preparation of N¹-tert.-Octyl-N²-isopropyliminothiourea

Acetone, 11.6 g. (0.20 moles), and hydrazine (95⁺%), 6.60 g. (0.20 moles), were mixed. tert.-Octylisothiocyanate, 39.47 g. (0.20 moles), was added to the mixture. The isolated solid, recrystallized from ethanol, gave 13.02 g. (26.7% yield) of white crystalline solid, m.p. 78-81°.

Preparation of bis-Ureas and bis-Thioureas

General Procedure: Two parts of the desired isocyanate or isothiocyanate were slowly added to one part of hydrazine in benzene. The mixture was maintained at reflux for several hours to insure completion of the reaction. The solid was filtered out of the reaction mixture, and recrystallized, if necessary.

Preparation of Di-tert.-Butyl-bis-urea

tert.-Butylisocyanate, 99.13 g. (1.0 moles), was added to hydrazine (95⁺%), 17.0 g. (0.50 moles). Refluxing of the reaction mixture was not required. The solid was filtered out, and recrystallized from ethanol, giving 92.90 g. (80.0% yield) of white crystalline solid, m.p. 190-2°.

Preparation of Di-tert.-butyl-bis-thiourea

tert.-Butylisothiocyanate, 49.02 g. (0.42 moles) was added to hydrazine (95⁺%), 7.15 g. (0.21 moles), and the mixture maintained at reflux for two hours. The solid was isolated from the cooled mixture and recrystallized from ethanol, giving 37.83 g. (67.3% yield) of white crystalline solid, m.p. 153-5°.

Preparation of Di-tert.-octyl-bis-urea

tert.-Octylisocyanate, 31.05 g. (0.20 moles), was added to hydrazine (95⁺%), 3.4 g. (0.10 moles), and the mixture maintained at reflux for three hours. The solid was isolated from the cooled mixture giving 29.15 g. (85.6% yield) of unrecrystallized white crystalline solid, m.p. 170-1.5°.

Preparation of Di-tert.-octyl-bis-thiourea

tert.-Octylisothiocyanate, 23.17 g. (0.136 moles), was added to hydrazine (90⁺%), 2.42 g. (0.078 moles), and the mixture maintained at reflux for three hours. The solid was isolated from the cooled mixture, giving 15.99 g. (62.5% yield) of unrecrystallized white crystalline solid, m.p. 134-8°.

Preparation of Di-phenyl-bis-urea

Phenylisocyanate, 59.56 g. (0.50 moles), was added to hydrazine (95⁺%), 8.43 g. (0.25 moles), and the mixture maintained at reflux for two hours. The solid was isolated from the cooled mixture, giving

64.90 g. (95.5% yield) of unrecrystallized white crystalline solid, m.p. $242-4^{\circ}$.

Preparation of Di-cyclohexyl-bis-urea

Cyclohexylisocyanate, 12.52 g. (0.10 moles), was added to hydrazine (95⁺%), 1.69 g. (0.05 moles), and the mixture maintained at reflux for two hours. The solid was isolated from the cooled reaction mixture, giving 12.90 g. (90.7% yield) of unrecrystallized white crystalline solid, m.p. $196-8^{\circ}$.

Preparation of Aminoureas and Aminothiureas

General Procedure: One part of the selected isocyanate or isothiocyanate was added to one part of the selected amine or hydrazine dissolved in benzene. The reaction mixture was maintained at reflux for several hours to insure completion of the reaction. The reaction mixture was stripped of solvent at the aspirator and the residue isolated and recrystallized, if necessary.

Preparation of N¹-tert.-Butyl-N²-(N,N-dimethylamino)urea

tert.-Butylisocyanate, 49.56 g. (0.5 moles), was added to unsym.-dimethylhydrazine, 30.05 g. (0.5 moles), and the mixture maintained at reflux for one hour. The mixture was stripped of solvent at the aspirator, giving 78.50 g. (98.5% yield) of unrecrystallized white crystalline solid, m.p. $88-91^{\circ}$.

Preparation of N¹-Methyl-N²-(N,N-dimethylamino)urea

Methylisocyanate, 28.54 g. (0.50 moles), was added to unsym.-dimethylhydrazine, 36.57 g. (0.50 moles), and the mixture maintained at reflux for one hour. The solid, isolated from the cooled mixture, was recrystallized from chloroform-hexane, giving 42.96 g. (66.1% yield) of white crystalline solid, m.p. 143-5°.

Preparation of N¹-tert.-Butyl-N²-aminothiourea

tert.-Butylisothiocyanate, 5.76 g. (0.05 moles), was added to hydrazine (95⁺%), 1.7 g. (0.05 moles), and the mixture maintained at reflux for one hour. The mixture was stripped of solvent at the aspirator, giving 7.27 g. (97.5% yield) of unrecrystallized white crystalline solid, m.p. 135-8°.

Preparation of N¹-Phenyl-N²-(N,N-dimethylamino)thiourea

Phenylisothiocyanate, 13.52 g. (0.10 moles) was added to unsym.-dimethylhydrazine, 6.01 g. (0.10 moles), and the mixture maintained at reflux for one hour. The solid, isolated from the cooled mixture, was recrystallized from ethanol, giving 13.76 g. (74.2% yield) of white crystalline solid, m.p. 180-2°.

Preparation of N¹-Phenyl-N²-aminothiourea

Phenylisothiocyanate, 13.52 g. (0.10 moles), was added to hydrazine (95⁺%), 6.6 g. (0.20 moles), and the mixture maintained at reflux for one hour. The solid was isolated from the cooled reaction

mixture, giving 12.29 g. (73.1% yield) of unrecrystallized white crystalline solid, m.p. 139-42°.

Preparation of N¹-Cyclohexyl-N²-(N,N-dimethylamino)thiourea

Cyclohexylisothiocyanate, 8.60 g. (0.061 moles) was added to unsym.-dimethylhydrazine, 3.7 g. (0.061 moles), and the mixture maintained at reflux for one hour. The solid, isolated from the cooled reaction mixture, was recrystallized from ethanol, giving 4.67 g. (38.0% yield) of white crystalline solid, m.p. 149-52°.

Preparation of N¹-tert.-Octyl-N²-(N,N-dimethylamino)thiourea

tert.-Octylisothiocyanate, 34.26 g. (0.20 moles), was added to unsym.-dimethylhydrazine, 12.02 g. (0.20 moles), and the mixture maintained at reflux for two hours. The solid was isolated from the cooled reaction mixture, giving 39.87 g. (86.2% yield) of unrecrystallized white crystalline solid, m.p. 108-11°.

Identification of all Ureas and Thioureas Prepared

The identification of the N-iminoureas, N-iminothioureas, bis-ureas, bis-thioureas, N-aminoureas and N-aminothioureas was based on their ir and nmr spectra and qualitative tests for the presence of NH₂ groups, using meta-nitrobenzaldehyde.

Preparation of Iminocarbodiimides and bis-carbodiimides from the
Respective Ureas

Dehydration Using Phosphorus Pentoxide

Method A. An intimate mixture of phosphorus pentoxide, 21.3 g. (0.15 moles) and N^1 -tert.-butyl- N^2 -(N,N-dimethylamino)urea, 17.3 g. (0.10 moles), was placed in a flask fitted with a distillation head, condenser and receiving flask. The mixture was heated with a flame. The mixture became very dark brown in color and began frothing with about 2 ml. of distillate being collected at a very erratic temperature. The ir spectrum of the distillate contained absorption bands for N=C=O and N=C=N groups at 2250 and 2080 cm^{-1} , respectively. The attempted redistillation of the distillate gave no product. Subsequent attempts to duplicate this procedure gave no product.

Method B. An identical intimate mixture, as used in Method A, was prepared. The mixture was heated more slowly with a heating mantle and an aspirator vacuum was applied to the system. No product was isolated after several attempts using this method.

Method C. An identical intimate mixture was again prepared. Vacuums of less than 1 mm. Hg were applied to the system. No products were isolated, except some starting urea which sublimed up into the distillation head.

Method D. An identical intimate mixture was prepared and was placed in 200 ml. of n-octane. The mixture was maintained at reflux for 48 hours. The residue solid was removed, the filtrate stripped of solvent and the residue distilled, but no product was collected.

Dehydration Using Thionyl Chloride

Reaction 1. Excess thionyl chloride was slowly added to N¹-tert.-butyl-N²-(N,N-dimethylamino)urea, 5 g. (0.03 moles), the thionyl chloride acting as both reactant and solvent. The mixture was maintained at reflux for twenty-four hours, at which time the excess thionyl chloride was distilled off at the aspirator. Subsequent vacuum distillation of the residue gave no product.

Reaction 2. Excess thionyl chloride was slowly added to di-phenyl-bis-urea, 27.03 g. (0.1 moles), the thionyl chloride acting as both reactant and solvent. The mixture was maintained at reflux for twenty-four hours, at which time the excess thionyl chloride was distilled off at the aspirator. Subsequent vacuum distillation gave 17.10 g. (71% yield) of distillate, b.p. 65-75° (1.5 mm. of Hg). The ir and nmr spectral data were identical with the data of authentic phenylisocyanate. No other products were isolated.

Reaction 3. Excess thionyl chloride was slowly added to di-cyclo-hexyl-bis-urea, 28.24 g. (0.1 moles), the excess thionyl chloride acting as both reactant and solvent. The mixture was maintained at reflux for twenty-four hours, at which time the excess thionyl chloride was distilled off at the aspirator. Subsequent vacuum distillation of the residue gave no product.

Reaction 4. Excess thionyl chloride was slowly added to di-tert.-octyl-bis-urea, 34.26 g. (0.1 moles), the excess thionylchloride

acting as both reactant and solvent. The mixture was maintained at reflux for twenty-four hours, at which time the excess thionyl chloride was distilled off at the aspirator. Subsequent vacuum distillation of the residue gave no product.

Reaction 5. Thionyl chloride, 9.54 g. (0.09 moles), was slowly added to di-tert.-octyl-bis-urea, 13.7 g. (0.04 moles), in dry benzene. The mixture was maintained at reflux for several days, and the mixture stripped of solvent at the aspirator. Distillation of the residue gave 6.10 g. (49% yield) of tert.-octylisothiocyanate, b.p. 27-9° (0.80 mm. Hg). The ir and nmr spectra were identical with the spectra of authentic tert.-octylisothiocyanate. No other products were isolated.

Dehydration Using p-Tosylchloride

General Procedure: One part of urea was mixed with two parts of triethylamine in methylene chloride, then two parts of freshly recrystallized p-tosylchloride in methylene chloride were added with the temperature of the reaction mixture being kept below 5° by external cooling with an ice bath. The mixture was allowed to slowly warm to room temperature and was maintained at reflux for three hours. The mixture was allowed to cool to room temperature and 40% aqueous potassium carbonate solution was added in three equal portions to the mixture, with the organic phase being separated from the solids and aqueous phase. The combined organic layers were combined, stripped of solvent at the aspirator, the residue extracted with diethyl ether, the extracts stripped of solvent at the aspirator and the residue distilled under high vacuum.

Reaction 1. The above reaction procedure was carried out on N^1 -tert.-butyl- N^2 -(N,N-dimethylamino)urea, 17.3 g. (0.1 moles), using 20.2 g. (0.2 moles) of triethylamine and 38.2 g. (0.2 moles) of p-tosyl chloride. The only material isolated from the ether extract was some p-tosyl chloride.

Reaction 2. The above reaction procedure was carried out on di-tert.-butyl-bis-urea, 23.04 g. (0.1 moles), using 40.4 g. (0.4 moles) of triethylamine and 76.4 g. (0.4 moles) of p-tosyl chloride. As the ir spectrum of the methylene chloride layer contained no absorptions in the 2100 cm^{-1} region for $N=C=N$ group, the mixture was not worked with further.

Preparation of Iminocarbodiimides and bis-Carbodiimides from the Respective Thioureas

General Procedure: One part of thiourea, or one part of bis-thiourea was mixed with one part, or two parts, respectively, of yellow mercury (II) oxide in dry benzene, and the mixture maintained at reflux for six hours with the water being azeotroped off. The mixture was filtered and the filtrate mixed with a second portion of mercury(II)-oxide. The mixture was maintained at reflux for an additional six hours, filtered, the filtrate stripped of solvent at the aspirator, and the residue distilled.

Reaction 1. The above procedure was carried out with N^1 -phenyl- N^2 -isopropyliminothiourea, 20.73 g. (0.1 moles), using 21.7 g. (0.1 mole)

of yellow mercury(II)oxide. No product was isolated upon distillation.

Reaction 2. The above procedure was carried out with di-tert.-butyl-bis-thiourea, 26.25 g. (0.1 moles), using 43.4 g. (0.2 moles) of yellow mercury(II)oxide. One drop of distillate was collected. The ir spectrum of the distillate contained an absorption band at 2200 cm^{-1} , indicative of the presence of an N=C=O group, but positive identification could not be made.

Reaction 3. The above reaction procedure was carried out with di-tert.-octyl-bis-thiourea, 37.47 g. (0.1 moles), using 43.4 g. (0.2 moles) of yellow mercury(II)oxide. The small amount of distillate collected proved to be tert.-octylisothiocyanate based on spectral data.

Reaction of Phenylisocyanate with 21a

Sodium hydride (50% in oil), 4.8 g. (0.1 moles), was slowly added to 21a, 19.52 g. (0.1 moles), dissolved in 100 ml. of dry benzene under a dry nitrogen atmosphere. The mixture was stirred for a six hour period until gas evolution had ceased. Phenylisocyanate, 11.91 g. (0.1 moles), was slowly added to the reaction mixture, which was stirred until the magnetic stir bar "froze" in the residue. The flask was sealed under a dry nitrogen atmosphere and set aside. After one week, the mixture was filtered and the filtrate stripped of solvent at the aspirator. Distillation of the residue gave no products. No identifiable products were extracted from the reaction mixture residue.

Reaction of Methylisocyanate with 21a

Sodium hydride (50% in oil), 4.8 g. (0.1 moles), was slowly added to 21a, 19.52 g. (0.1 moles), dissolved in dry benzene under a dry nitrogen atmosphere. The mixture was stirred for six hours until gas evolution had ceased. Methylisocyanate, 5.71 g. (0.1 moles), was added to the reaction mixture, which was stirred until the stir bar "froze" in the reaction mixture. The flask was sealed under a dry nitrogen atmosphere and set aside. After one week, the mixture was filtered and the filtrate reduced in volume at the aspirator, yielding a small amount of white solid, m.p. 182-4°. The ir spectrum of the solid was identical with that of authentic trimethylisocyanurate.

Dehydrosulfurization of N¹-Phenyl-N²-(N,N-dimethylamino)thiourea

N¹-Phenyl-N²-(N,N-dimethylamino)thiourea, 5.0 g. (0.027 moles), was mixed with 10 g. of yellow mercury(II)oxide in benzene and the mixture maintained at reflux for six hours. The mixture was filtered and stripped of solvent at the aspirator giving 2.85 g. of solid material. Upon washing the solid with ethanol, part of the residue dissolved and part did not. Both the ethanol-soluble and ethanol-insoluble solids were recrystallized from acetone. The ethanol-soluble solid decomposed at 175-6°, and the ethanol-insoluble solid decomposed at 208-9°. The spectral data of the ethanol-soluble solid indicated that the sample was not pure, but the spectral data of the ethanol-insoluble solid indicated that it was pure. Analysis for N¹-phenyl-N²-(N,N-dimethylamino)carbodiimide - Calculated: C, 67.04; H, 6.89; N, 26.07. Found

for ethanol-insoluble solid: C, 66.86; H, 6.87; N, 25.85. The initial spectral data for the ethanol-insoluble solid supported its identification as the carbodiimide, but subsequent attempts to duplicate this reaction gave no product.

LITERATURE CITED

1. a. Lengfeld, F., and J. Stieglitz, Chem. Ber., 27, 926 (1894).
b. Khorana, H. G., Can. J. Chem., 32, 227 (1954).
c. Op. cit., 261.
2. Schlack, P., and G. Keil, Ann., 661, 164 (1963); German Patent #1,173,460 (1964); Chem. Abstr., 62, 1605 (1965).
3. Schmidt, E., and W. Carl, Ann., 639, 24 (1961).
4. a. Khorana, H. G., Chem. Rev., 53, 145 (1953).
b. MacHoldt-Erdniss, J., Chem. Ber., 91, 1992 (1958).
c. Kurzer, F., and P. M. Sanderson, J. Chem. Soc., 3240 (1960).
5. Kurzer, F., and K. Douraghi-Zadeh, Chem. Rev., 67, 107 (1967);
private communication from Adcock to Kurzer - see ref. 1.
6. Adcock, B., and A. Lawson, J. Chem. Soc., 474 (1965).
7. Adcock, B., A. Lawson, and D. H. Miles, J. Chem. Soc., 5120 (1961).
8. Busch, M., and T. Ulmer, Chem. Ber., 35, 1721 (1902).
9. Stolle, R., Chem. Ber., 55, 1289 (1922).
10. Smith, M., J. G. Moffatt, and H. G. Khorana, J. Am. Chem. Soc., 80, 6204 (1958).
11. Bose, A. K., and S. Garrat, J. Am. Chem. Soc., 84, 1310 (1962).
12. Detar, D. F., and L. A. Carpino, J. Am. Chem. Soc., 77, 6370 (1955).
13. Sheehan, J. C., and G. P. Hess, J. Am. Chem. Soc., 77, 1067 (1955).
14. Sheehan, J. C., P. A. Cruickshank, and G. L. Boshart, J. Org. Chem., 26, 2525 (1961).
15. Weith, W., Chem. Ber., 6, 1398 (1873).
16. Hinterberger, Jahresber. Fortsch. Chem., 629 (1852); cited from ref. 27.

17. Zinin, N., Jahresber. Fortsch. Chem., 628 (1852); cited from ref. 27.
18. a. Biziro, J., Jahresber. Fortsch. Chem., 497 (1861).
b. Biziro, J., Nuovo Cimento, 14, 139 (1862).
c. Biziro, J., J. Prakt. Chem., 86, 292 (1862).
d. Biziro, J., Chem. Zentr., 7, 846 (1862).
All are cited from ref. 27.
19. Schall, C., and S. Paschkowestzky, Chem. Ber., 25, 2880 (1892).
20. Busch, M., G. Blume, and E. Pungs, J. Prakt. Chem., 79, 513 (1909);
Chem. Abstr., 4, 898 (1910).
21. Zetzsche, F., and A. Fredrich, Chem. Ber., 73, 1114 (1940).
22. Brown, C. J., J. Chem. Soc., 2931 (1955).
23. Richter, R., Chem. Ber., 101, 174 (1968).
24. Hartke, K., and F. Rossbach, Angew. Chem., Int. Ed., Engl., 7, 72 (1968).
25. a. Wadsworth, Jr., W. S., and W. D. Emmons, J. Am. Chem. Soc., 84, 1316 (1962).
b. Wadsworth, Jr., W. S., and W. D. Emmons, J. Org. Chem., 29, 2816, (1964).
26. Atherton, F., H. Openshaw, and A. Todd, J. Chem. Soc., 660 (1945).
27. Kurzer, F., and K. Douraghi-Zadeh, Chem. Rev., 67, 107 (1967).
28. Sheehan, J. C., and J. J. Hlavka, J. Org. Chem., 21, 439 (1956).
29. Bellamy, L. J., The Infra-red Spectra of Complex Molecules, John Wiley and Sons, Inc., New York (1964) p. 267.
30. Silverstein, R. M., and G. C. Bassler, Spectrophotometric Identification of Organic Compounds, 2nd, ed., John Wiley and Sons, Inc., New York (1968) p. 136.

31. Nelson, D. A., and R. L. Atkins, Tetra.Let., 5197 (1967).
32. Gould, E. S., Mechanism and Structure in Organic Chemistry, Holt, Rinehart and Winston, New York (1959) pp. 200-9.
33. Ulrich, H., B. Tucker, and A. A. R. Sayigh, Angew. Chem., Int. Ed., Engl., 7, 291 (1968).
34. Neumann, W., and P. Fischer, Angew. Chem., Int. Ed., Engl., 1, 621 (1962).
35. Farrisey, Jr., W. J., R. J. Ricciardi, and A. A. R. Sayigh, J. Org. Chem., 33, 1913 (1968).
36. Brady, W. T., and E. D. Dorsey, J. Org. Chem., 35, 2732 (1970).
37. Schmidt, E., and F. Moosmuller, Ann., 597, 235 (1955).
38. Kurzer, F., and K. Douraghi-Zadeh, Chem. Rev., 67, 107 (1967).
39. Farr, F.; Dr. Farr obtained and interpreted the esr spectrum while at the University of Texas, Austin. We extend our gratitude to him for this service.
40. Gilchrist, T. L., and C. W. Rees, Carbenes, Nitrenes and Arynes, Thomas Nelson and Sons Ltd., London (1969).
41. Boyer, J. H., and P. J. A. Frints, Tetra. Let., 3211 (1968).
42. Silverstein and Bassler, op. cit., pp. 148-69.
43. Woodward, R. B., and R. Hoffman, The Conservation of Orbital Symmetry, Verlag Chemie Academic Press, Germany (1970).
44. Ibid., pp. 5-20.
45. Ibid., pp. 65-9.
46. Brady, W. T., F. H. Parry, III, R. Roe, Jr., and E. F. Hoff, Jr., Tetra. Let., 819 (1970).
47. Woodward and Hoffman, op. cit., pp. 164-5.

48. Hoffman, R., Chem. Comm., 240 (1969).
49. a. Wadsworth, Jr., W. S., J. Org. Chem., 32, 1279 (1967).
b. Wadsworth, Jr., W. S., and W. J. Bruxvoort, Chem. Comm., 542 (1968).
50. Field, L., and J. W. McFarland, Organic Synthesis, Col.Vol. 4, John Wiley and Sons, Inc., New York (1963) pp. 940-2.
51. Krynitsky, J. A., and H. W. Carhart, ibid., pp. 436-7.
52. Mitsunobu, O., K. Kato, and M. Tomari, Tetrahedron, 26, 5731 (1970).
53. Smith, P. A. S., Open-chain Nitrogen Compounds, Vol. 2, W. A. Benjamin, Inc., New York (1966) pp. 127-8.
54. Cignarella, G., Chim. Ind., 42 145 (1966); Chem. Abstr., 64, 15791g (1966).
55. Hinman, R. L., and D. Fulton, J. Am. Chem. Soc., 80, 1895 (1958).
56. Pedersen, C. T., Acta. Chem. Scand., 18, 2199 (1964).
57. Cram, D. J., and G. S. Hammond, Organic Chemistry, 2nd ed., McGraw-Hill Book Company, New York (1964) p. 491.
58. Dimroth, O., and W. Wislicenus, Chem. Ber., 38, 1573 (1905).
59. Kosolapoff, G. M., Organophosphorus Compounds, John Wiley and Sons, Inc., New York (1950) p. 350.
60. Ibid., p. 258.
61. Ibid., p. 226.
62. Ibid., pp.336-41.
63. Schaeffer, J. R., Organic Chemical Bulletin, 33 (2) Research Laboratories of the Eastman Kodak Company, Rochester, New York (1961).
64. Fukui, K., F. Tanimoto, and H. Kitano, Bull. Chem. Soc. Japan, 38, 1586 (1965).

65. Zimmerman, D. M., and R. A. Olofson, Tetra. Let., 3453 (1970).
66. Weast, R. C., ed., Handbook of Chemistry and Physics, 46th ed.,
The Chemical Rubber Co., Cleveland, Ohio (1965) p. C-181.
67. Hinman, R. L., J. Am. Chem. Soc., 78, 2463 (1956).
68. _____, The Sadtler Standard Spectra, Sadtler Research Labor-
atories, Philadelphia, (1967) Spectrum #15671.
69. Jackman, L. M., and S. Sternhill, International Series of Monographs
in Organic Chemistry, Vol. 5, Applications of Nuclear Magnetic
Resonance Spectroscopy in Organic Chemistry, 2nd ed., Pergamon
Press, New York (1969) p. 353.
70. _____, Sadtler, op. cit., Spectrum #5959.