Oxygen-, Nitrogen-, and Sulfur-Substituted Heteroallenes

WERNER REICHEN

Joseph Muller Corporation Zurich, Scheuchzerstrasse 7, 8006 Zurich, Switzerland

Received June 8, 1978

Contents

I. Introduction

Heteroallenes, compounds containing a three-center moiety connected by two orthogonal, nonconjugated double bonds in which at least one carbon atom is replaced by a heteroatom, belong to one of the most important classes of synthons and intermediates in organic chemistry to date. Even though a few of the theoretically possible combinations—if only the elements carbon, nitrogen, oxygen, phosphorus, and sulfur are considered—have escaped synthesis thus far, the chemical behavior of most of them has been well established.

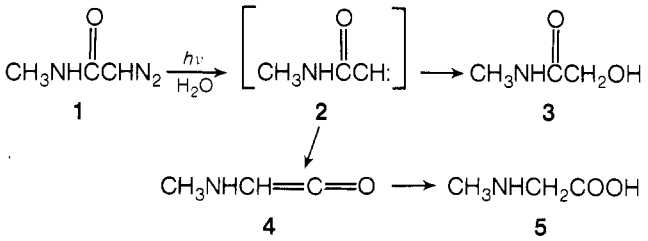
$$X{=}Y{=}Z$$
$$X = C, N, P, S$$
$$Y = C, P, S$$
$$Z = C, N, O, P, S$$

It is known that the reactivity (and so the electronic character of the three involved atoms) of heteroallenes can be strongly influenced and even inverted if more or less electron-withdrawing or -donating substituents are attached to one (or more) of the functional atoms. Many reviews have appeared on the former subject in which an electron-withdrawing group such as sulfonyl,[1,2] chlorosulfonyl,[3] phosphorus,[4] and carbonyl[5,6] is attached to an isocyanate function. The opposite case, in which an electron-donating atom such as oxygen, nitrogen, or sulfur alters the chemical behavior of a heteroallenic system from its usual behavior in a particular compound, has received considerable attention in the past 10 years owing to the variety of important synthetic possibilities that several of these molecules have created. In this article we shall deal with their synthesis and reactions, hoping to stimulate further work in this most promising field. The literature has been covered from the beginning up to the early spring 1978 issues and nearly 200 references are cited.

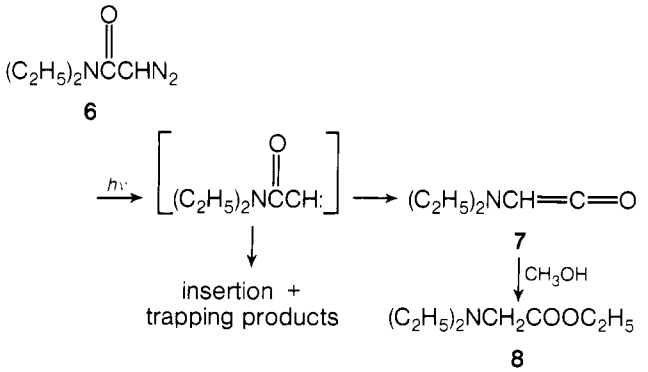
II. Ketenes

A. N-Substituted Ketenes

Intermediate aminoketenes are always formed when α-diazoamides are photolytically or thermally decomposed; however, the reaction of the carbene, probably formed first, with a substrate in the reaction medium competes effectively. Thus, *N*-methyldiazoacetamide)**1**), upon photolysis in water, gives hydroxymethylacetamide (**3**) and *N*-methylglycine (**5**) in a ratio 2:1.[7] The intermediate carbene **2** can be trapped by the solvent but undergoes, in part, a Wolff rearrangement to methylaminoketene (**4**) which is hydrolyzed to the amino acid derivative.



Similarly, small amounts (18%) of methyl *N,N*-diethylglycinate (**8**) have been isolated when *N,N*-diethyldiazoacetamide (**6**) was photolytically decomposed in methanol, its formation involving a ketene intermediate **7** also.[8]



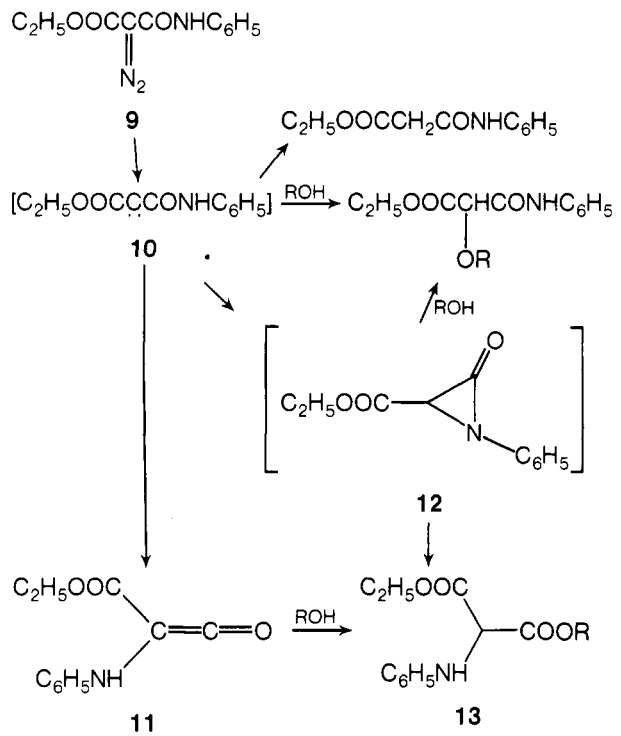
Photolysis and thermolysis of ethyl diazomalonanilate (**9**) in various alcohols yield considerable amounts of α-*N*-phenylaminomalonic esters **13**.[9] A possible mechanism could involve migration of the phenylamino group to give a ketene intermediate **11**. Since no ketene species could be trapped (e.g., with styrene), an alternative mechanism could involve formation of an α-lactam intermediate **12** by carbene **10** N–H insertion.

Anhydro-5-hydroxo-3-methyl-2,4-diphenyloxazoline hydroxide inner salt (**14**) reacts with imines by a [2 + 2] cycloaddition to give four-membered lactam **16** (see Table I). This contrasts with its usual behavior toward other double and triple bonds where

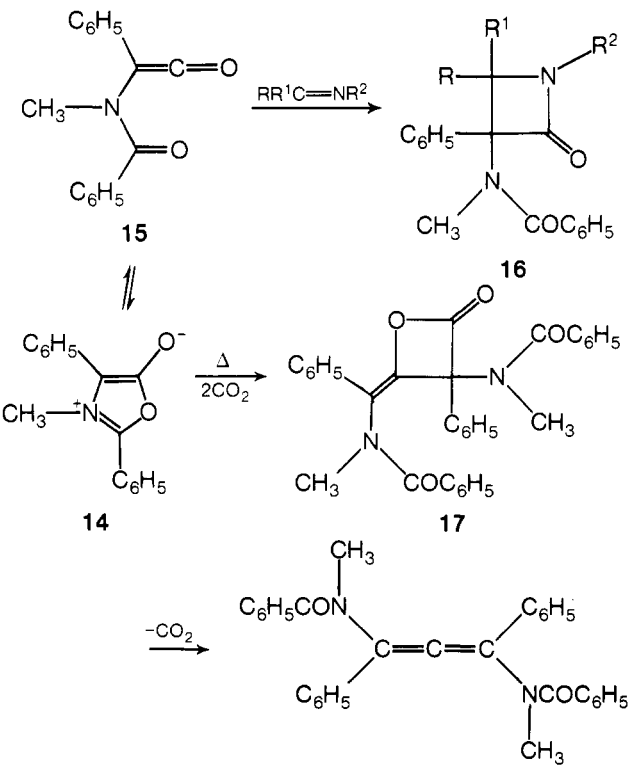
0009-2665/78/0778-0569$05.00/0

TABLE I. Formation of β-Lactams 16[15]

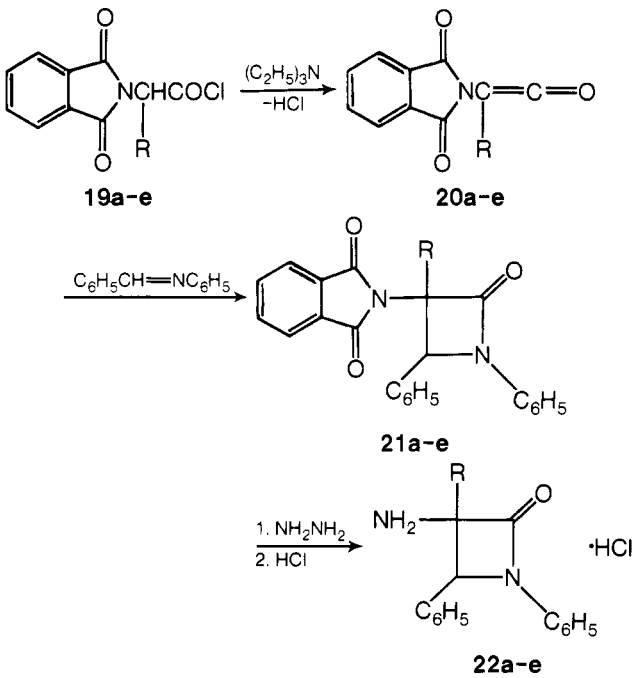
16	R	R^1	R^2	yield, %	mp, °C
a	H	C_6H_5	CH_3	62	158–159
b	H	C_6H_5	$CH_2C_6H_5$	47	156–157
c	H	C_6H_5	C_6H_5	33	162.5–163
d	C_6H_5	C_6H_5	C_6H_5	25	170.5–171
e	fluorenylidene		C_6H_5	56	208.5–209



a [3 + 2] addition takes place.[10,11] A ring open-chain tautomerism which leads to an acylaminoketene **15** could explain the difference; carbon–nitrogen double bonds are known to be very powerful ketene trapping agents and the formation of β-lactams from ketenes and azomethines[12,13] as well as their cycloaddition to carbodiimides[14] are known. The result obtained by thermolyzing **14** in boiling xylene further supports the hypothesis of the tautomerism: dimerization of the ketene **15** to β-lactone **17** followed by carbon dioxide elimination gives 1,3-diphenyl-1,3-bis(benzoylmethylamino)allene (**18**) in 86% yield.[15] Analogous photoinduced ring openings have been observed with mesoionic thiadiazoles[16–19] (see below).



Attempts to generate aminoketenes by dehydrohalogenation of amino acid chlorides are limited to such cases in which the nitrogen atom carries an electron-withdrawing substituent such as succinoyl, maleyl, or phthaloyl[13,20–30] or an N_2^+ group.[31] Thus, addition of a benzene solution of phthaloylglycyl chloride **19** to an equimolar amount of triethylamine and an excess of benzalaniline gives instantaneous formation of β-lactam **21**.[13]



The reaction can be visualized by proceeding through an aminoketene intermediate **20** which adds to benzalaniline in a [2 + 2] cycloaddition (yield 50%). The base **22** can be set free by treating the phthalimido derivative with hot alcoholic hydrazine.

Aminoketenes **20** also add to carbon–nitrogen double bonds which make part of a ring system. With this method it was possible to synthesize a 5-phenylpenicillin derivative **24** which had the complete structure of natural penicillin. The key step is the condensation of the aminoketene with methyl 2-phenyl-5,5-dimethyl-2-thiazoline-4-carboxylate (**23**).[21] The corresponding

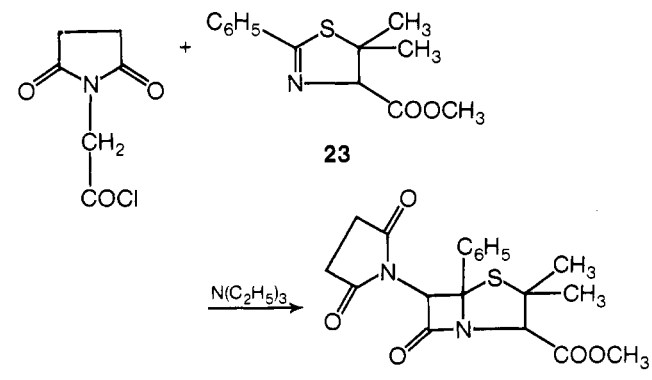
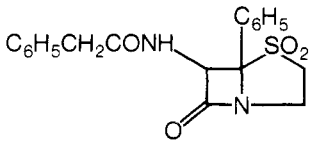


TABLE II. β-Lactams 31[30]

31	R	R^1	R^2	yield, %	mp, °C
a	C_6H_5	CH_3	H	18	219.5–221
b	C_6H_5	C_2H_5	H	46	203.5–205
c	C_6H_5	CH_3	CH_3	29	213–213.5
d	C_6H_5	C_2H_5	CH_3	32	235–238
e	C_6H_5	CH_3	Cl	17	225.5–229
f	C_6H_5	C_2H_5	Cl	28	223–225
g	C_6H_5	CH_3	Br	22	222.5–224
h	C_6H_5	C_2H_5	Br	27	223–224
i	C_6H_5	CH_3	OCH_3	36	206–207
k	C_6H_5	C_2H_5	OCH_3	40	241.5–243
l	CH_3	C_2H_5	H	24	174–174.5

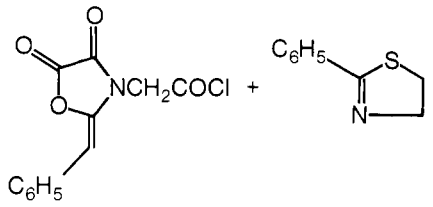
derivatives were obtained when 2-phenyl-2-thiazoline was caused to react under various conditions with phthaloylglycyl chloride[24,29] or succinoylglycyl chloride.[25] Analogously, the reaction of these substituted glycyl chlorides with 2-phenyl-Δ^2-dihydro-1,3-thiazines in presence of triethylamine gave compounds with the cephalosporin skeleton.[26,27]

Application of the 5-phenyloxazoline-2,4-dione instead of the phthalimido precursor leads to the α-(phenylacetylamino) derivative; however, it was only possible to obtain the sulfone **25** since hydrogenolysis of the unoxidized lactam failed.[22] This

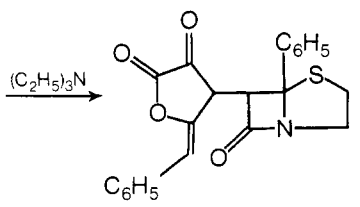


25

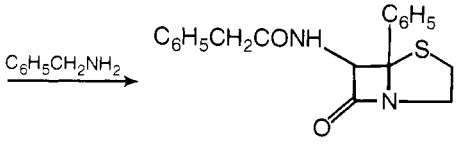
difficulty was overcome by starting with 2-benzylidene-4,5-diketo-3-oxazolidineacetyl chloride (**26**); treating the β-lactam **27** with 2 equiv of benzylamine produced the two alternative cleavage products **28** and **29** in 32 and 21% yield,[25] respectively.



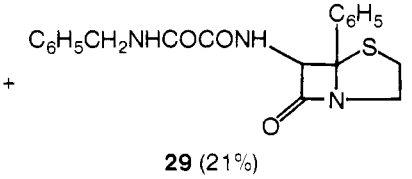
26



27



28 (32%)

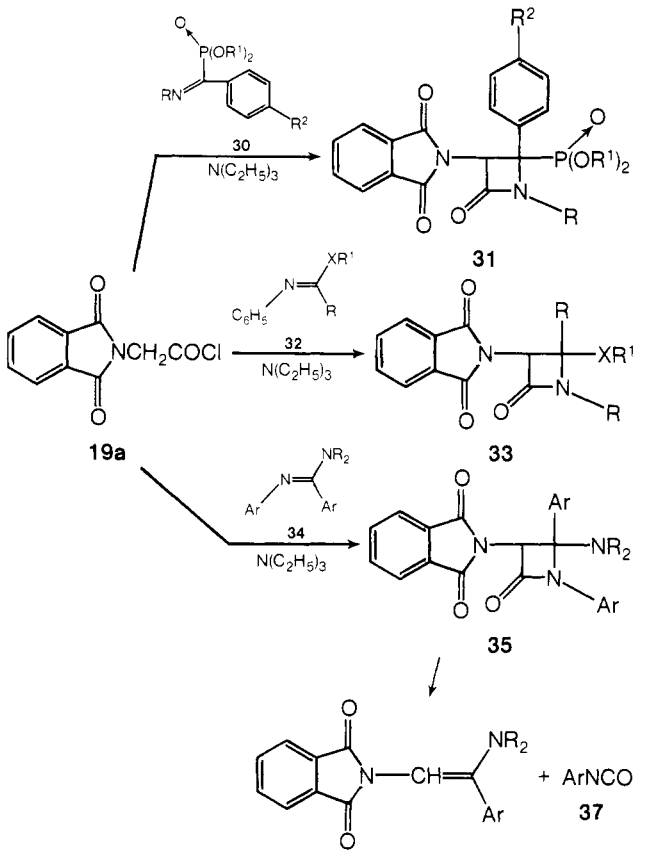


29 (21%)

TABLE III. β-Lactams 33[29]

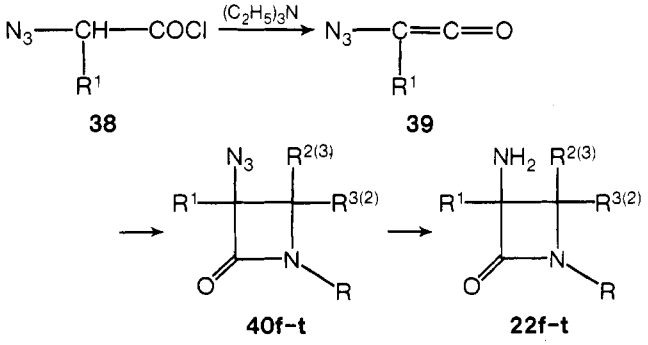
33	R	XR^1	yield, %	mp, °C
a	C_6H_5	OCH_3	50	190
b	C_6H_5	OC_2H_5	55	191
c	C_6H_5	$OCH(CH_3)_2$	51	218
d	C_6H_5	SCH_3	70	203
e	H	OC_2H_5	31	165
f	H	SC_2H_5	33	138

Azomethines containing a phosphonoester group, **30,** give the stable phosphorus-containing azetidinones **31**[30] (Table II). Imidates **32** behave in the same way[29] (Table III); however, when amidines **34** are used as trapping agents for the aminoketene, β-lactams **35** are formed as intermediates only; a cycloreversion takes place forming an enamine **36** and an isocyanate **37.**[28]



19a **31** **33** **35** **36** **37**

A convenient synthesis of α-amino-β-lactams **22f–t** (see Table IV) is based on the facile reduction of corresponding α-azido-β-lactams **40f–t** which in turn are obtained by cycloaddition of α-azidoketene **39.** Thus, when a methylene chloride solution



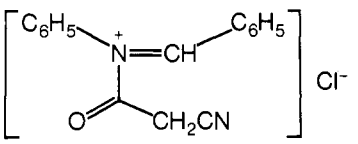
38 **39** **40f-t** **22f-t**

TABLE IV. Monocylic β-Lactams 40[31]

40	R	R^1	R^2	R^3	stereo chemistry	yield, %	mp, °C
f	C_6H_5	H	H	C_6H_5	cis	35–45	132–134
					trans	50	81–83
g	C_6H_5	H	H	4-$NO_2C_6H_4$	cis	35	135
h	C_6H_5	H	H	4-$CH_3OC_6H_5$	cis	25–30	125
					trans	53	96–97
i	4-BrC_6H_4	H	H	C_6H_5	cis	30	153–154
					trans	65	108
k	4-BrC_6H_4	H	H	3,4-$OCH_2OC_6H_3$	cis	30–35	165–167
					trans	31	123–124
l	C_6H_5	H	H	OC_2H_5	trans	*a*	
m	4-FC_6H_4	H	H	C_6H_5	cis	23	113–114
n	C_6H_5	H	H	4-BrC_6H_4	cis	30	141–143
o	C_6H_5	H	H	4-FC_6H_4	cis	19	142–143
p	C_6H_5	H	CH_3	C_6H_5	*a*	30	
q	C_6H_5	H	C_6H_5	C_6H_5	*a*	60	121–122
r	C_6H_5	CH_3	H	C_6H_5	*a*	10	130–132
s	C_6H_5	C_2H_5	H	C_6H_5	*a*	9	115–117
t	C_6H_5	C_6H_5	H	C_6H_5	*a*	5,7	160–161

[a] Not indicated.

of azidoacetyl chloride **38**[32] was added dropwise to a solution of benzalaniline and triethylamine in the same solvent at room temperature or below, a mixture of the cis and trans β-lactam **40** (ratio 3:1) was obtained. When triethylamine was added to a solution of the Schiff base and the acid chloride **38,** the relative proportions of cis and trans isomers were reversed and were found to be about 1:3. This indicates that different mechanisms may be involved in the cyclization step,[31] an alternative pathway being the formation of a salt with a structure like **41** which has been proposed as intermediate in the lactam-formation using cyanoacetyl chloride.[39]



41

When the dehydrochlorination is performed on substituted phthalyl amino acid chlorides **19b–e**[34,35] in carbon tetrachloride without added trapping agent, the formation of the ketenes **20b–e** can be evidenced by IR absorptions between 2100 and 2150 cm^{-1}. As in the case of β-phenylalanine (**20b**), phenylglycine (**20c**), and valine (**20d**), these absorptions disappeared rather quickly; phthalimido-*tert*-butylketene (**20e**) was isolated.[20]

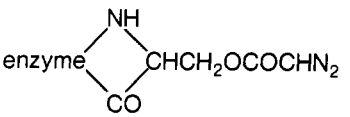
When optically active *N*-phthalyl-α-amino acid chlorides are esterified by base catalysis with an optically active base (e.g., brucine), the reaction products show (at least partial) optical inversion.[36] However, from the data given it cannot be conclusively determined to what extent an asymetric synthesis of an alcohol to an aminoketene is involved.

N-(α-Diazoacyl)phthalimides undergo Wolff rearrangement upon photolysis giving the corresponding aminoketenes which react as shown above, i.e,, methanolysis or β-lactam formation with benzalaniline.[37,38]

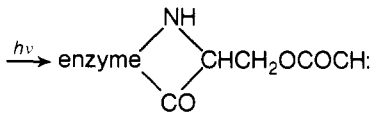
Evidence for the existence of aminoketene fragments, formed by the decomposition of cyclodepsipeptides,[39] methyl and ethyl picolinate[40] in the mass spectrometer, has been reported.

B. O-Substituted Ketenes

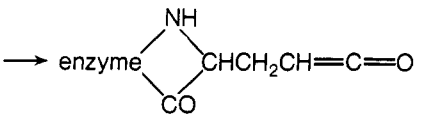
Ketenes connected by an oxygen cannot be isolated; however, there is a large amount of evidence showing their intermediacy in reactions. Westheimer[41] observed, for the first time, Wolff rearrangement of a diazo ester on photolysis of diazoacetylchymotrypsin (**42**). The formation of *O*-carboxymethylserine (**45**) presumably involves elimination of nitrogen and rearrangement of the carbene **43** followed by hydrolysis of the resulting alkoxyketene **44.** Subsequent hydrolysis of the protein yields **45.** This reaction had not been previously observed with diazo esters.[42–44] A similar reaction has been observed with azaserine.[41]



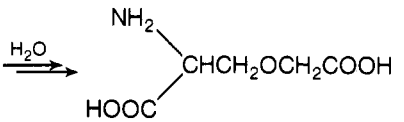
42



43



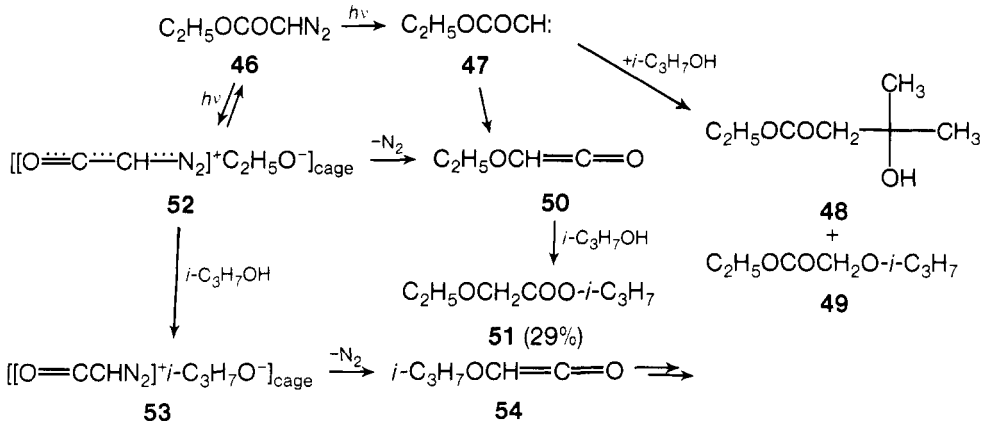
44



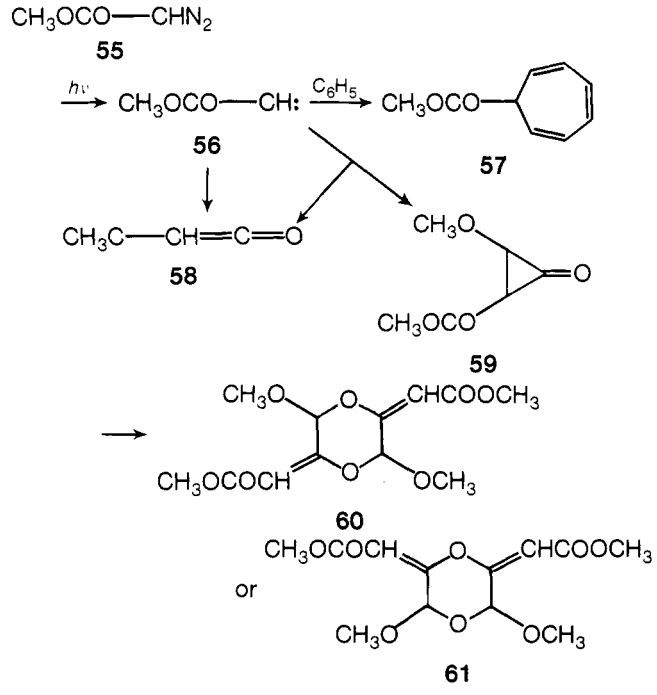
45

The first step in the photolysis of ethyl diazoacetate (**46**) in 2-propanol is the formation of the carbenic carbethoxymethylene **47.** This inserts into the tertiary carbon–hydrogen bond of the solvent **48,** undergoes polar addition with the hydroxy function **49,** and rearranges to a certain extent (29%) to ethoxyketene (**50**) which reacts with the solvent to give the corresponding ethoxyacetate **51.**[45] Similar results have been obtained with ethyl and phenyl diazoacetate in methanol, the former yielding 20–25%, the latter 45–60%, of rearrangement products.[7]

An interesting alkoxy exchange has been observed in this type of reaction by Strausz and his co-workers.[46] He interprets it as a light-induced heterolysis in which ion pairs are produced. The resonance-stabilized ketenediazonium ion **52** may live long enough to undergo anion exchange to **53** and eventually form the ketene **54.** Stable aliphatic diazonium ions of similar structure have been synthesized,[47] and diazo compounds with a good leaving group may be expected to undergo heterolysis.[48]

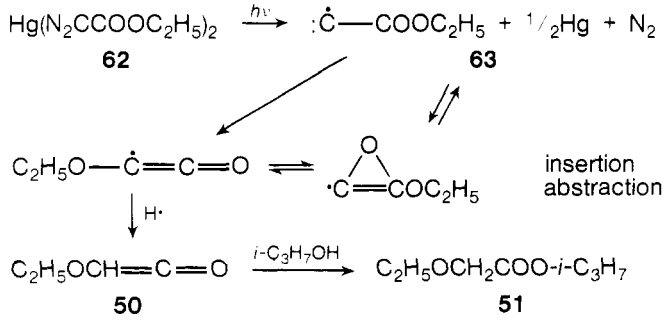


Carbomethoxycarbene (**56**) generated by photolysis of the corresponding diazo precursor **55** in benzene gives, besides cycloheptatrienecarboxylic ester **57**, a tetramer of carbomethoxymethylene (**60**) consisting of four stereoisomers of the dioxanes **60** or **61**. Their formation can only be rationalized by



assuming a Wolff-type rearrangement of two moieties of **56** to the methoxyketene **58**.[49] Dimerization of the probably formed cyclopropanone **59** may lead to either one of the dioxanes.

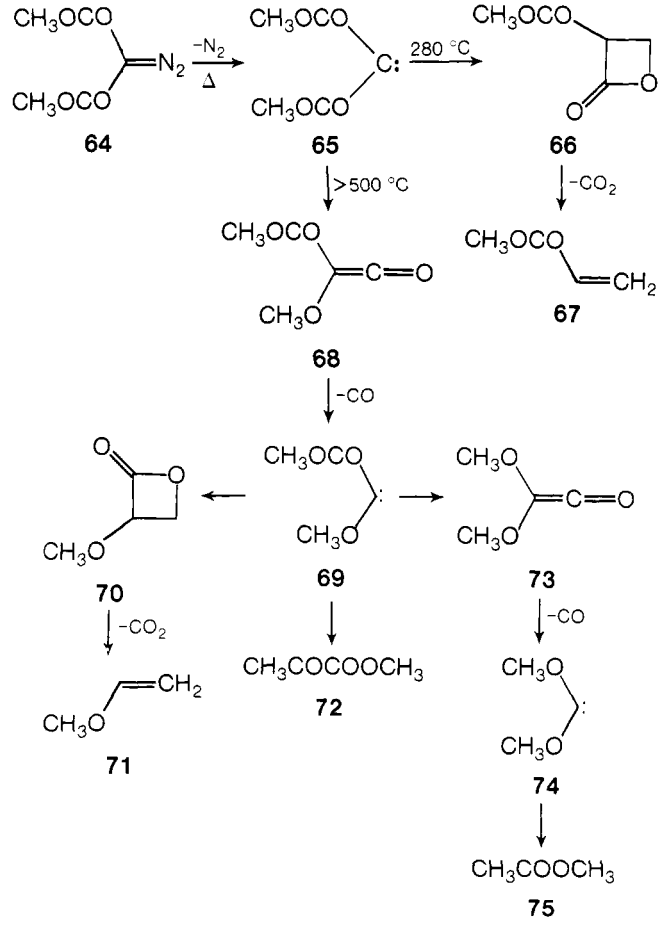
A similar but somewhat modified method of generating ethoxyketene (**50**) is the photolysis of mercury salts of diazo compounds. Under these conditions mercury bis(ethyl diazoacetate) (**62**) cleaves off nitrogen and mercury leading to a ketene-type radical intermediate **63**. Ethoxyketene (**50**) is then formed by either an oxygen shift or an ethoxy migration followed



by hydrogen abstraction.[50] As in the former cases the ketene adds to the solvent yielding an ester **51**.

The suggested oxacyclopropene mechanism has been shown to occur to a certain extent (30%) along with the Wolff rearrangement: thermolysis of [1-C^{13}]ethyl diazoacetate yields ethoxyketene labeled in both the C-1 or the C-2 positions.[51] The same reaction path was observed in the decomposition of other diazo compounds;[52-55] however, in other cases it has been excluded.[56-58] Ethoxyketyl radicals and subsequently the ketene may also be formed in nonpolar solvents.[59]

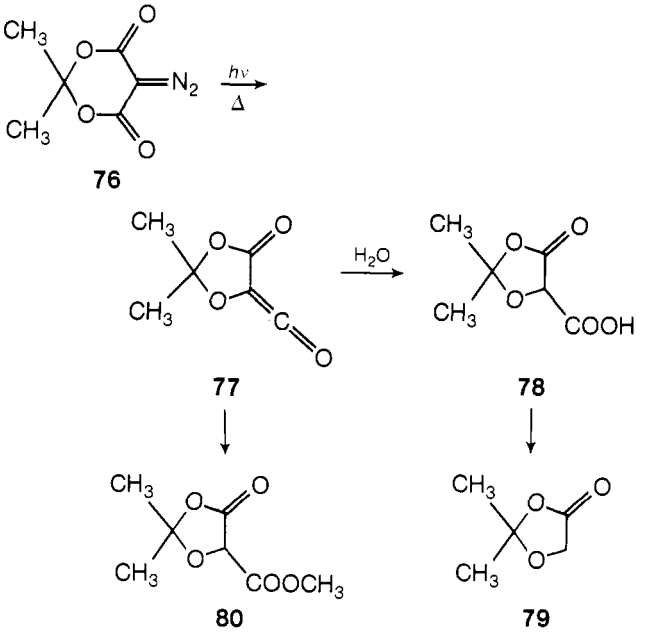
Gas-phase thermolysis of methyl diazomalonate (**64**) at 280 °C gave mainly methyl acrylate (**67**, 92%). At this temperature, presumably the dimethyl dicarboxycarbene (**65**), initially formed, undergoes only intramolecular insertion to the four-membered lactone **66** which is thermolyzed further by loss of carbon dioxide to methyl acrylate (**67**), a known reaction.[60] At 500 °C the yield of **67** was found to be only 30% while other reaction products appeared. The formation of methyl vinyl ether (**71**) may be attributed to a Wolff rearrangement of **65** to carbomethoxy-



methoxyketone (**68**), followed by loss of carbon monoxide, intra-molecular insertion, and cleavage of the β-lactone **70.** A further Wolff rearrangement of carbomethoxy methoxycarbene (**69**) gives methyl pyruvate (**72,** 8%) and dimethoxymethylketene (**67**) and leads to the formation of methyl acetate (**75**)[67] via dimethoxycarbene (**74**).

A polymer which was formed in the temperature range of 280–360 °C and isolated showed only methoxy signals in the NMR spectrum; its structure has tentatively been attributed to a polymer of the carbomethoxymethoxyketene (**68**). In view of the results obtained by Schenck and Ritter[49] (see above), this polymer could correspond to their carbene–ketene tetramer **60** or **61.**

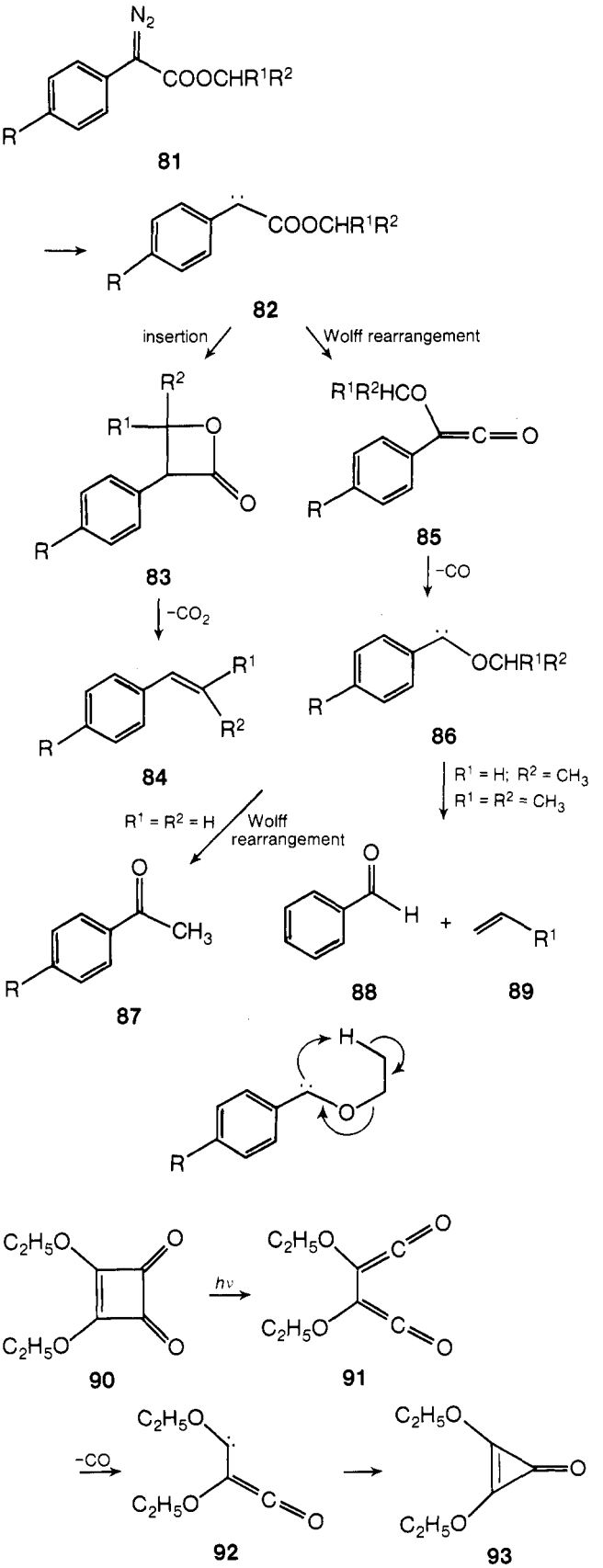
An analogous behavior has been observed in the thermolysis of 2,2-dimethyl-4,6-diketo-5-diazo-1,3-dioxane (Meldrum's Diazo, **76**). Wolff rearrangement leads to the ketene **77** which can be trapped by water and isolated as the known dioxolanone **79** after decarboxylation of **78.** Photolysis in benzene/methanol results in the formation of the ester **80.**[62]



A similar reaction scheme was found for the thermal decomposition of alkyl diazophenylacetates (**81**). The first formed carbenes **82** undergo both intramolecular insertion and Wolff rearrangement. In the former case the β-lactones **83** eliminate carbon dioxide and the styrenes **84** can be isolated. In the latter case an alkoxy phenylketene **85** is formed which loses carbon monoxide (as do the other alkoxycarbenes **68** and **73**[61,68]) to give the corresponding carbene **86.** The methoxyphenylcarbene undergoes a Wolff rearrangement as expected to form acetophenone **87.** However, if instead of a methoxy group ethoxy or isopropoxy substituents are present, the Wolff rearrangement fails to take place. An intramolecular 1,4 hydrogen transfer gives benzaldehyde (**88**) and an alkene **89.**[63] This alkoxycarbene–formyl rearrangement has its analogy in the rearrangement of cyclic aminimides as will be seen later.[122,125]

The bis-ketene **91** can be generated by photolysis from 1,2-diethoxycyclobutene-3,4-dione (**90**) in ether. It eliminates carbon monoxide to give the intermediate carbene–ketene **92** which collapses to 1,2-diethoxycyclopropenone (**93**). The yield, however, was only about 10%.[64]

The most effective method for generating ethoxyketene **50** is that of Strausz and his co-workers, who use the classical method of dehydrochlorination of ethoxyacetyl chloride (**94**).[65] The 1,2-elimination can be effected with triethylamine at temperatures as low as −78 °C. While the ketene appears to be relatively stable at this temperature, it slowly dimerizes and

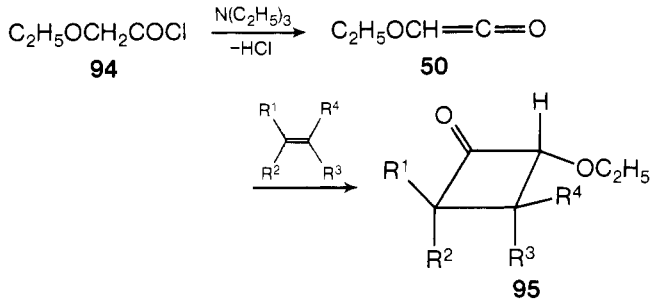


polymerizes at room temperature. Generated in situ in the presence of an olefinic compound, it undergoes a cycloaddition reaction to form cyclobutanones **95** in fairly good yields (see Table V). Temperatures between 80 and 100 °C are needed. As expected according to the Woodward–Hoffmann rules of orbital symmetry conservation, these cycloadditions proceed with high stereoselectivity.

The cycloaddition can also be effected by photolysis; how-

TABLE V. Preparation of Ethoxycyclobutanones 95[65]

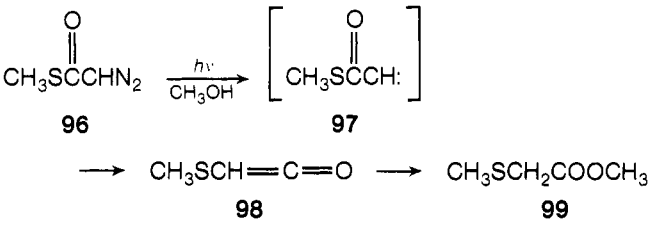
95	R^1	R^2	R^3	R^4	yield, %
a	H	CH_3	CH_3	H	45
b	CH_3	H	CH_3	H	31
c	H	H	CH_3	CH_3	30
d	CH_3	CH_3	CH_3	CH_3	43
e	H	H	OC_2H_5	H	55
f	H		$(CH_2)_3$	H	56
g	H		$(CH_2)_4$	H	46



ever, yields are considerably lower. Stereospecific addition of ketoketenes to double bonds are well known[67-70] and also seem to occur with monohalo- and monomethylketene.[71]

C. S-Substituted Ketenes

Only two reports dealing with sulfur-substituted ketenes exist in the literature: photolysis of methyldiazothioacetate (**96**) generates a singlet carbene **97** which must then undergo a very rapid Wolff rearrangement; carbene insertion products are found to a very small extent only. The thiomethoxyketene **98** adds to the solvent to give methyl methylthioacetate (**99**) in 86% yield.[72]



Another successful approach to the synthesis of sulfenylketenes has recently been reported.[72] Derivatives of Meldrum's acid (2,2-dimethyl-1,3-dioxan-4,6-dione) are known to fragment thermally into carbon dioxide, acetone, and ketene. Thus, pyrolysis of the 5-methyl-5-methylthio compound **100a** at 410 °C generated the ketene **101a** which could be trapped with aniline vapor to give 2-methylthiopropananilide (**102**, 35%). On pyrolysis at 600 °C the corresponding 5-phenylthio compound **100b** gave a mixture of 2-methylbenzo[*b*]thiophen-3(2*H*)-one (**103**) and phenyl vinyl sulfide (**105**), the latter being formed by thermal carbon dioxide elimination from **101b** and rearrangement of the resulting thiophenylmethylcarbene (**104**).[73]

III. Carbodiimides

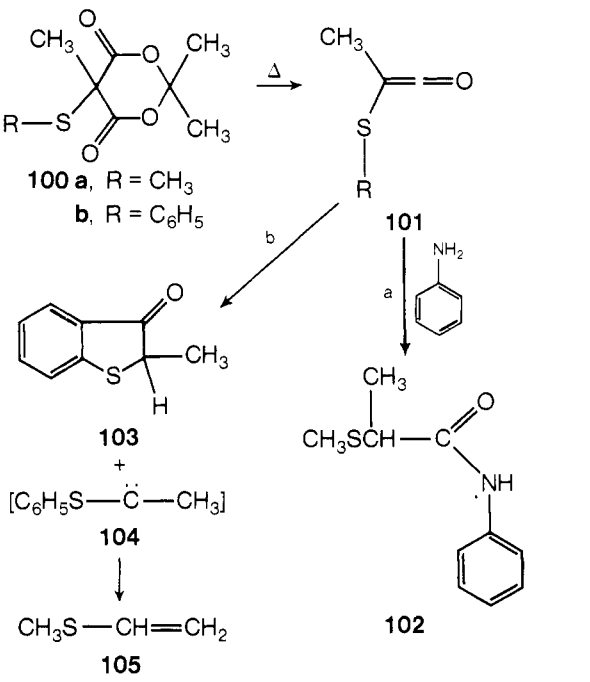
A. N-Substituted Carbodiimides

The reaction of phosphoramidate anions with carbon dioxide leading to isocyanates[74] can be modified by replacing the amidate by hydrazidate **106** and the carbon dioxide by an isocyanate molecule. Under these circumstances aminocarbodiimides **107** are formed (method A).[75] They show a rather interesting behavior: while distillable liquids, on standing they crystallize to dimers whose structures have been interpreted as 1,3-bis(di-

TABLE VI. Monomeric and Dimeric Aminocarbodiimides 107 and 108

		107		108	
R	R^1	bp, °C torr	yield, %	mp, °C	method
CH_3	$C(CH_3)_3$	65-67 (11)	83.4	142-143	A, B
CH_3	*t*-Oct	59-60 (0,45)	51.3	*a*	A, B
$-(CH_2)_5-$	$C(CH_3)_3$	70-72 (0,4)	30.0	125-126	B
C_2H_5	CH_3	*b*			C

[a] No dimer obtained.[76] [b] Unstable.[78]



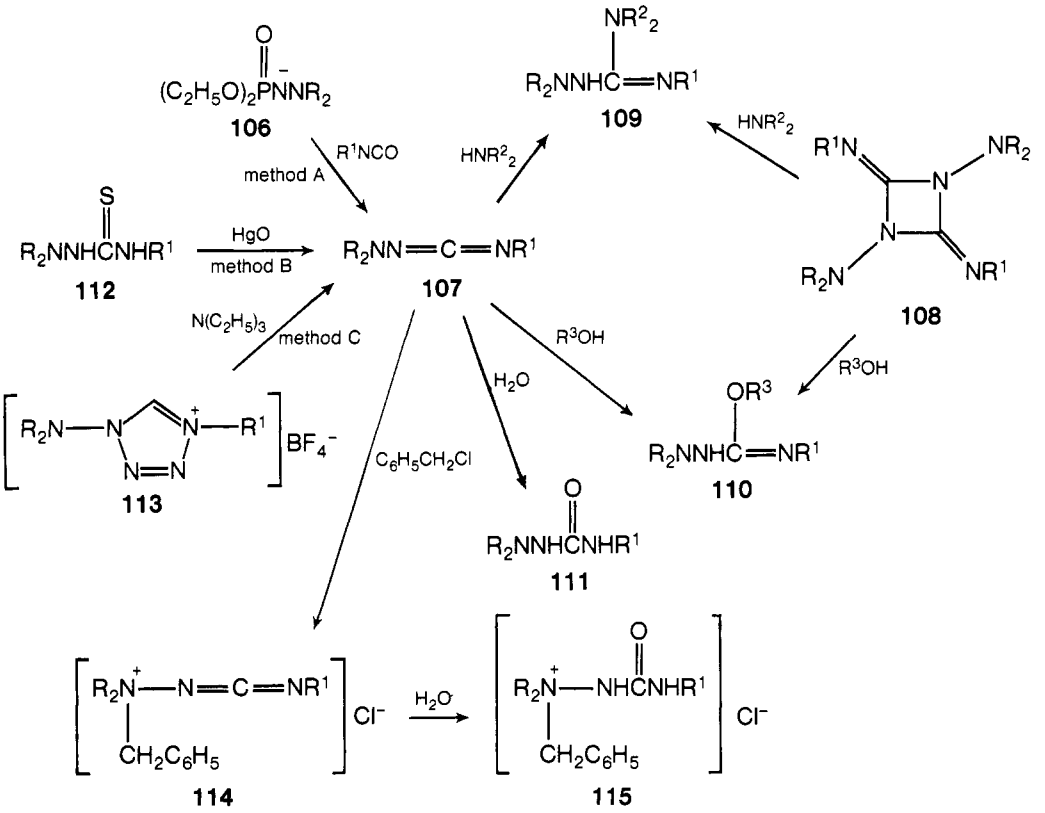
alkylamino)-2,4-bis(alkylimino)-1,2-diazetidines (**108**).[76] This dimerization process is reversible: upon heating the monomer reappears. The chemistry of both the monomeric **107** and the dimeric species **108** has not been explored extensively; see Table VI. Treatment with amines gave the corresponding aminoguanidine derivatives **109.** Hydrogenation failed to take place; even when it was carried out in the presence of platinum oxide catalyst at 1000 psi and 50 °C, only ethoxyisoureas **110** were obtained,[76] while hydrolysis formed the semicarbazides **111.**

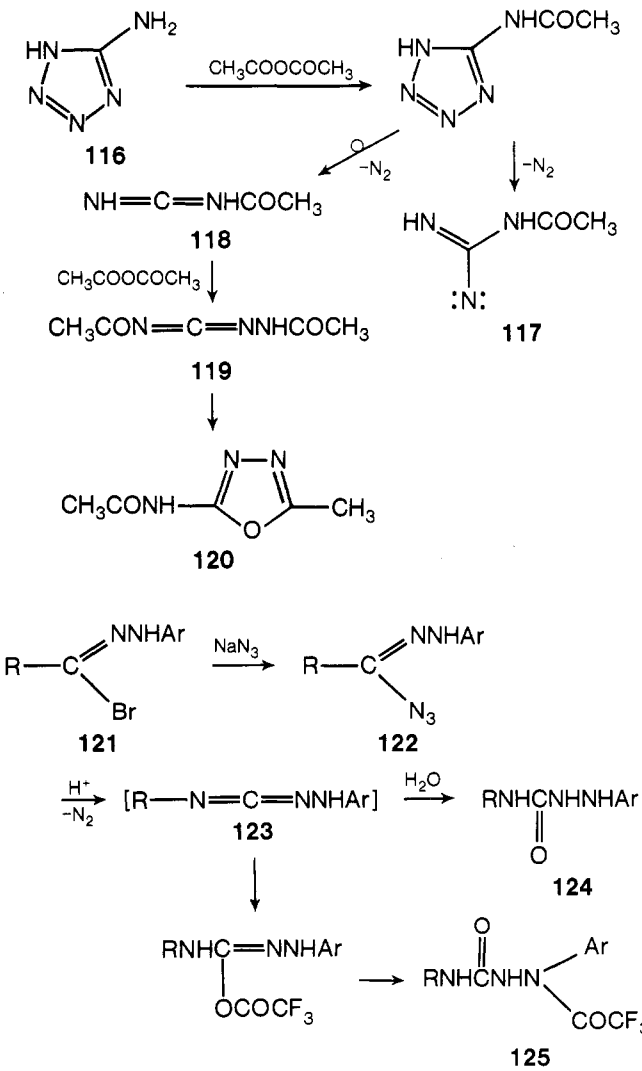
Two other methods lead also to aminocarbodiimides **107:** dehydrosulfurization of the aminothioureas **112** (method B) with yellow mercuric oxide[77] and treatment of the dialkylaminotetrazolium fluoroborates **113** with triethylamine (method C).[78]

The monomer can also be benzylated with benzyl chloride to give a water-soluble, stable carbodiimide salt **114** which, on standing in water for several hours, is converted to a quaternary semicarbazide **115.** Attempts to desulfurize 1-(1,3,4,6-*O*-tetraacetyl-β-D-glucos-2-yl)-4-phenyl-3-thiosemicarbazide with mercuric oxide to the aminocarbodiimide failed.[79]

An interesting ring conversion which could involve an aminocarbodiimide intermediate has been reported by Stolle.[80] Thus, 5-aminotetrazole (**116**), when treated with boiling acetic anhydride, eliminated nitrogen; the isolated product was found to be 2-acetylamino-5-methyl-1,3,4-oxadiazole (**120**). Even though a nitrene intermediate **117** has been suggested, it seems to be more reasonable to assume a concerted rearrangement–elimination-type mechanism leading to the unsymmetrically substituted carbodiimide **118** which is then acylated to **119.** Other tetrazoles[81,82] and triazoles[83,84] are known to behave in the same way upon pyrolysis.

N-Arylaminocarbodiimides (**123**) have been obtained as



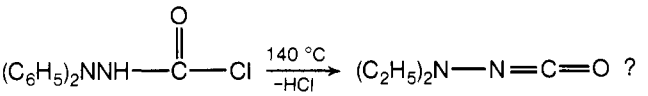


transient species only by acid-induced rearrangement of the hydrazidic azides **122.** They exist in open-chain form when synthesized by nucleophilic substitution of bromide with azide ion from the hydrazidic bromides **121.**[85] (Treatment of hydrazidines with nitrite leads only to the cyclized products (tetrazoles).[81,82]) The diimides are hydrolyzed to the semicarbazides **124** in aqueous medium or trapped by trifluoroacetic acid to give the acetylated semicarbazides **125** after rearrangement.

IV. Isocyanates

A. N-Substituted Isocyanates

The first approach to the synthesis of amino isocyanates was based on the ease of hydrogen chloride elimination from *N,N*-diphenylhydrazidic acid chloride (**126**).[88] There is, however, no convincing evidence (besides the odor) given for the existence of a free amino isocyanate **127.**



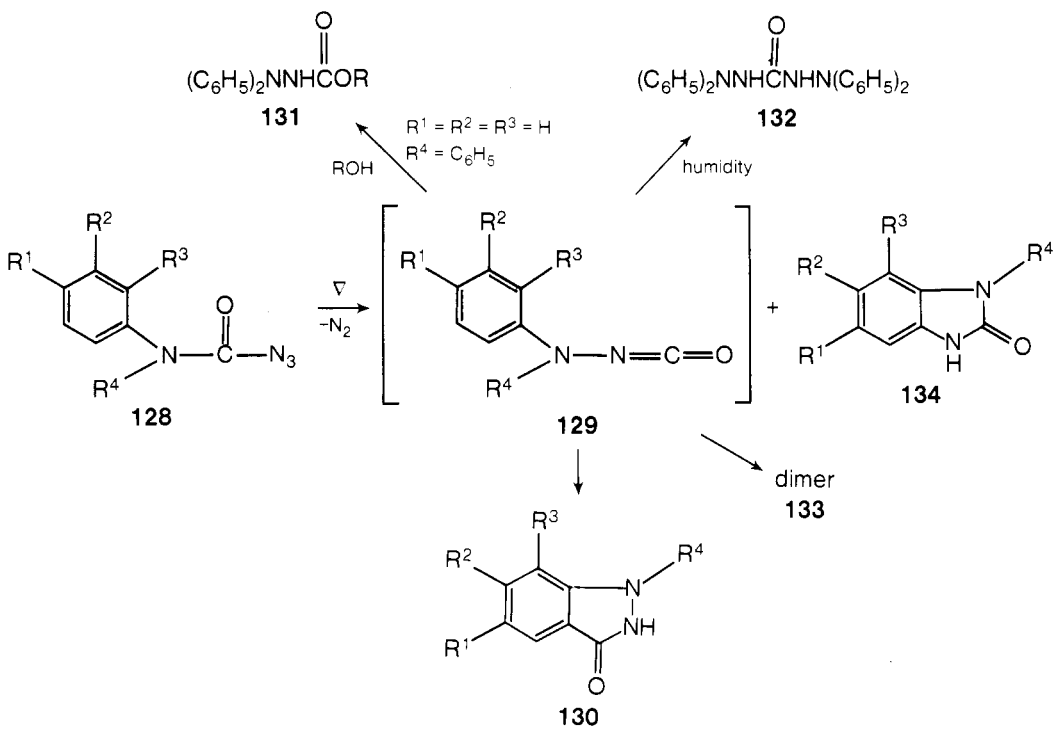
Already in the early 20s Stolle recognized that diphenylcarbamoyl azide (**128a**) rearranges readily upon heating with the elimination of nitrogen (Curtius rearrangement[89]) and subsequent intramolecular condensation to 1-phenylindazolone (**130a**) (see Table VII). He proposed diphenylamino isocyanate (**129a**) as an intermediate. On thermolysis in ethanol the isocyanate was intercepted by the solvent giving the carbazic ester **131**;[90-92] when humidity was present it was hydrolyzed and decarboxylated to the hydrazine which trapped another isocyanate moiety to give 1,1,4,4-tetraphenylcarbazide (**132a**).[91,92] He investigated a number of cases of diaryl- and alkylarylcarbamoyl azides **128b–e** and found the ring closure to be general. In some instances a dimer of **129** has been found.[93,94]

In a later examination of this thermal Curtius rearrangement Baiocchi[95,96] failed to find any dimeric products. Instead he isolated various amounts of N-substituted benzimidazolones **134**

TABLE VII. Thermal Decomposition of Carbomoylazides 128, Formation of Indazolones 130, Benzimidazolones 134, and Dimeric Amino Isocyanates 133

					indazolones **130**		benzimidazolones **134**		dimers **133**	
128	R^1	R^2	R^3	R^4	yield, %	mp, °C	yield, %	mp, °C	yield, %	mp, °C
a	H	H	H	C_6H_5	97,[a] 90[b]	209,[a] 206–207[b]			*g*	*g*
b	H	H	H	$CH_2C_6H_5$	99,[c] 66.9[d]	167[c,d]	6.7[d]	197–198[d]		
c	H	H	H	CH_3	*g*	154[e]				
d	H	H	H	C_2H_5	68[e]	134[e]				
e	H	H	CH_3	CH_3	31[e]	240[e]			11[e]	160[e]
f	H	H	CH_3	C_2H_5	10[e]	175[e]			28[e]	149[e]
g	H	H	Cl	$CH_2C_6H_5$		201[f]		190[f]		
h	H	Cl	H	$CH_2C_6H_5$		229[f]				
i	H	$-(CH)_4-$		C_2H_5	50[c]	195[c]				
k	H	$-(CH)_4-$		C_6H_5	58[c]	267[c]				
l	CH_3	H	H	p-$CH_3C_6H_4$	31,[c] 51[d]	202[c,d]	5.1[d]	223–224[d]	11[c]	202[c]
m	CH_3	H	H	$CH_2C_6H_4$	63.1[d]	180–181[d]	9.5[d]	185–186[d]		
n	CH_3	H	H	C_2H_5	*g*	156[c]				
o	OCH_3	H	H	$CH_2C_6H_5$	15.2[d]	189–190,[d] 187[f]	35.6[d]	178–179,[d] 189[f]		
p	OCH_2CH_3	H	H	$CH_2C_6H_5$	12.3[d]	196–197[d]	43.1[d]	178–179[d]		
q	$O(CH_2)_3CH_3$	H	H	$CH_2C_6H_5$	7.5[d]	148–149[d]	48.3[d]	142–143[d]		
r	Cl	H	H	$CH_2C_6H_5$	46.4[d]	206–207,[d] 213[f]	5.3[d]	179–180[d] 176[f]		
s	NO_2	H	H	$CH_2C_6H_5$	37[d]	250[d,f]	1.6[d]	234[d,f]		
t	$CO(CH_2)_2CH_3$	H	H	$CH_2C_6H_5$		206[f]				
u	$CO(CH_2)_3CH_3$	H	H	$CH_2C_6H_5$		177[f]				
v	$-(CH)_4-$[h]		H[h]	C_6H_5	96[c]	234[c]				
w	$-(CH)_4-$[h]		H[h]	$-C_{10}H_7$	94[c]	254[c]				
x	4-chlorophenyl			$CH_2C_6H_5$		223[f]				

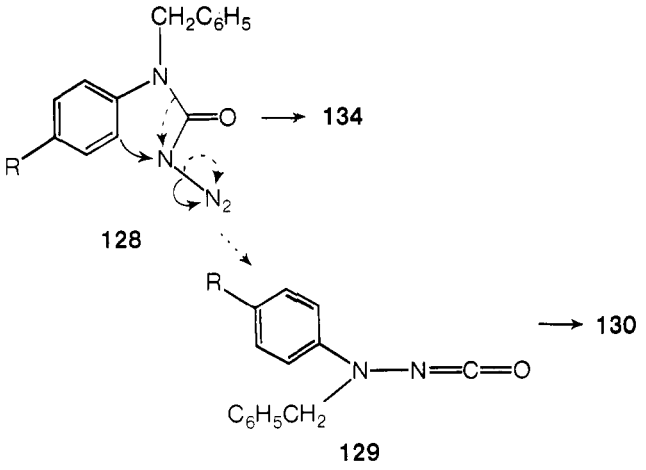
[a] Reference 92. [b] Reference 97. [c] Reference 94. [d] Reference 98. [e] Reference 93. [f] Reference 95. [g] Not indicated. [h] Not sure whether 4,5-benzindazolone or 5,6 isomer.



along with the indazolones **130.** This observation has been confirmed by two Japanese groups.[97-99] The thermal decomposition of all these azides does not seem to involve a nitrene intermediate. Typical nitrene products (insertion or addition) have never been observed. Apparent exceptions have been dealt with by Lwowski.[100] Most likely the reaction proceeds by a concerted S_N2 displacement on the azide β-nitrogen in **128** either by the aromatic ring to give the benzimidazolones **124** or by the "amide" nitrogen to give the amino isocyanate **129** which subsequently undergoes intramolecular electrophilic substitution to the indazolone derivative **130.** It seems that the nucleophilic displacement of nitrogen by the aromatic rings is strongly favored when the R^1 position of the aromatic ring carries an electron-donating substituent. The direct cyclization (without Curtius rearrangement) is further enhanced by the size of the aliphatic chain attached to the oxygen in this position, as Table VIII shows.

TABLE VIII. Yield Ratios of Indazolones 130 to Benzimidazolones 134

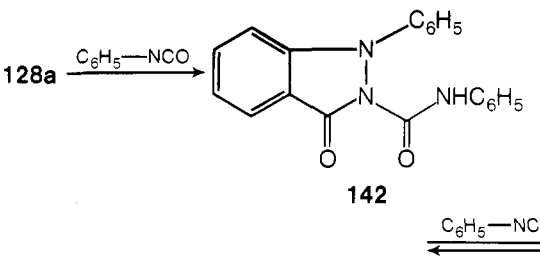
128		% indazolones **130**
R^1	R^2	% benzimidazolones **134**
NO_2	$CH_2C_6H_5$	0.04
H	$CH_2C_6H_5$	0.10
Cl	$CH_2C_6H_5$	0.11
CH_3	$CH_2C_6H_5$	0.15
OCH_3	$CH_2C_6H_5$	2.34
OCH_2CH_3	$CH_2C_6H_5$	3.50
$O(CH_2)_3CH_3$	$CH_2C_6H_5$	6.44



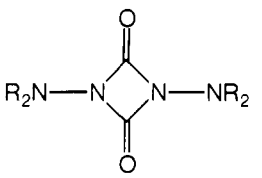
Thorough analysis of some of these reaction mixtures led to the isolation of several other products.[98,99] It was found that once formed, benzimidazolone **134a–c** could trap another amino isocyanate moiety to form the corresponding hydrazinocarbonyl substituted benzimidazolones **135a–c** from which the original benzimidazolones **134a–c** could be set free by heating the adducts **135a–c** with sodium ethoxide in ethanol in a sealed tube.[98] A similar addition–elimination can be effected by treating benzimidazolones **134** with isocyanates or urethanes to give the aminocarbonylbenzimidazolones **136.** Formation of the 1,2,4-oxadiazole **137c** probably arises from a 1,3-dipolar cycloaddition involving the carbon–nitrogen double bond of the amino isocyanate and a formal carbamoylnitrene (or the initial azide with concerted nitrogen elimination).

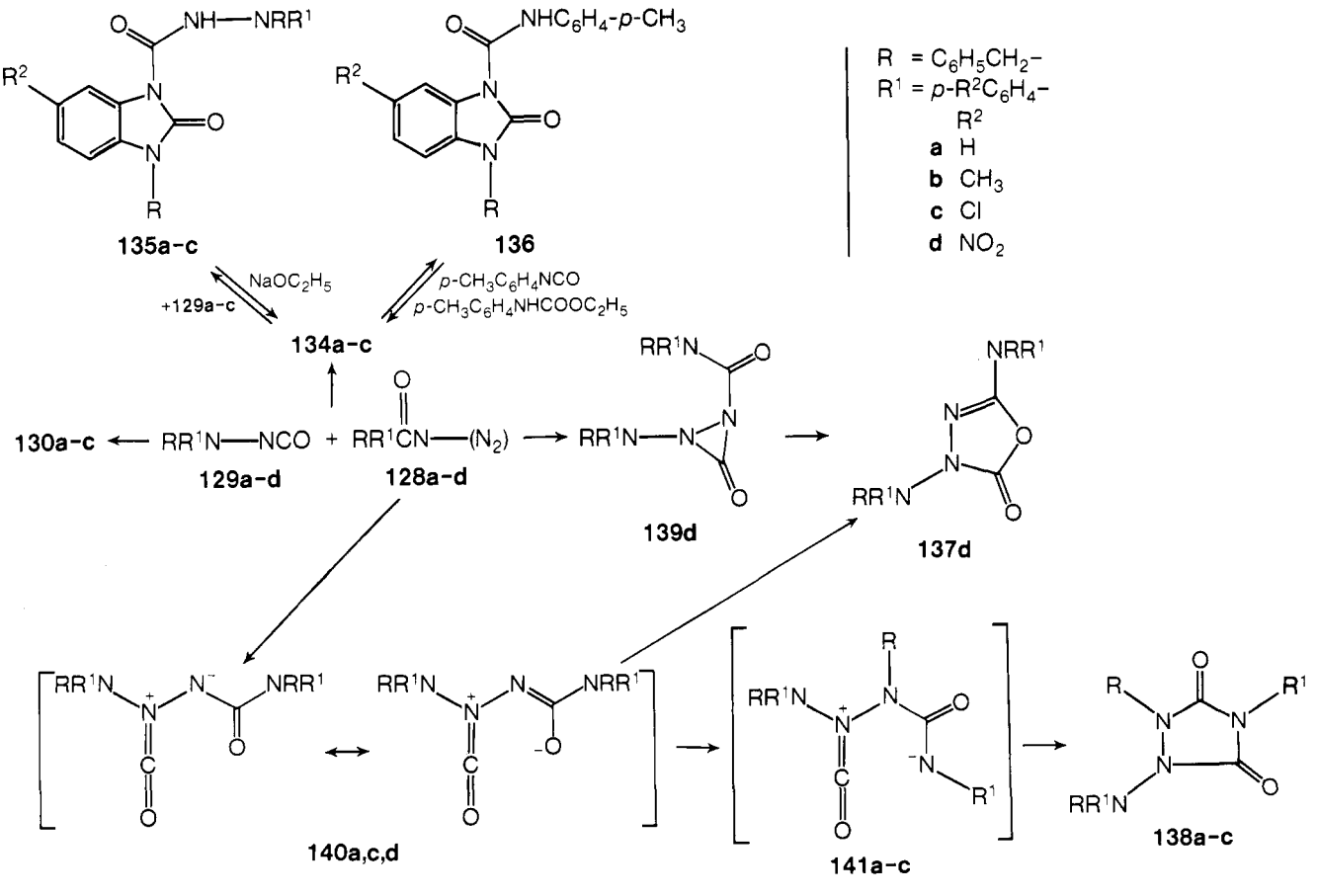
Similar reactions of ethoxycarbonylnitrene with allenes,[101] alkynes,[102,103] and nitriles[104–107] are known. However, as the transformation of *N*-acylaziridines to oxazolines by ring expansion[108–112] and the formation of 1,3,4-oxadiazoles by cyclization of nitrilimines[104] are known reactions, formation of diaziridinone **139d** or an intermediate betaine **140a,c** could also be responsible for the formation of 1,2,4-triazolidinediones **138a,c.**[99]

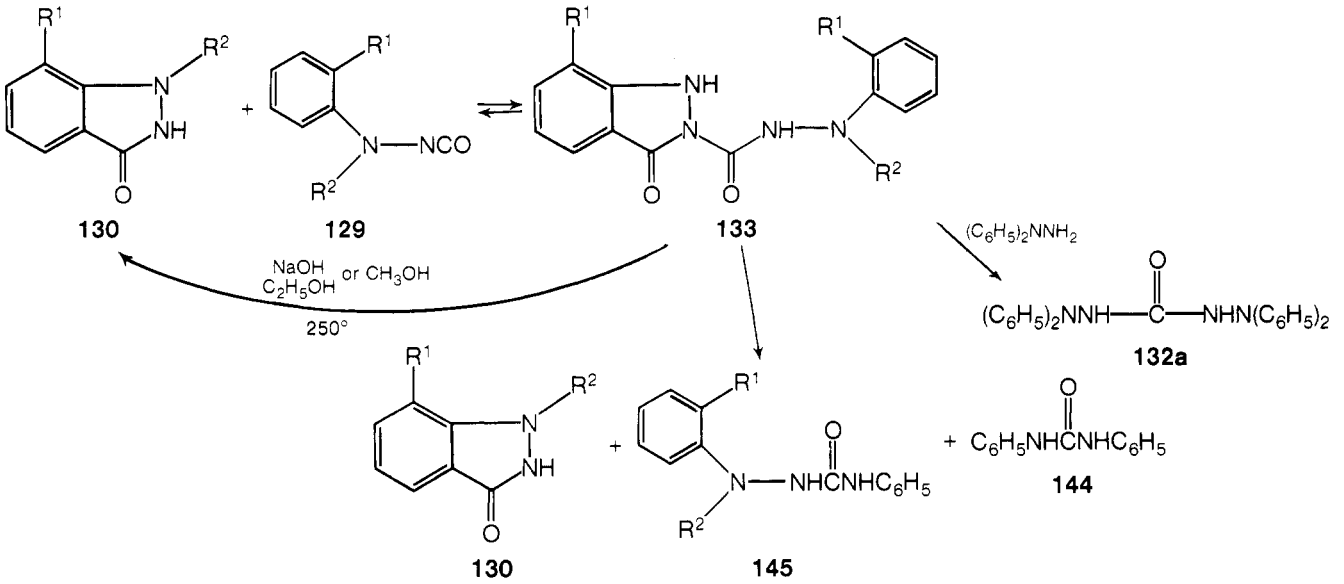
The addition of isocyanates to benzimidazolones mentioned above[98] has its analogy as has been shown recently. Thus, thermolysis of diphenylcarbamoyl azide **128** in boiling phenyl isocyanate gave a quantitative yield of 1-phenyl-2-(*N*-phenylcarbamoyl)indazolone (**142**) which, upon heating, released the phenyl isocyanate moiety re-forming the indazolone **130a.** When



this was boiled with excess phenyl isocyanate the adduct **142** was formed again.[113] This common behavior of benzimidazolones **134** and indazolones **130** suggests that the structure of yet another dimeric species of certain diaryl- and alkylarylamino isocyanates **129** which were obtained by Stolle[93,94] probably do not correspond to the symmetrical diazetidinedione **143,** the



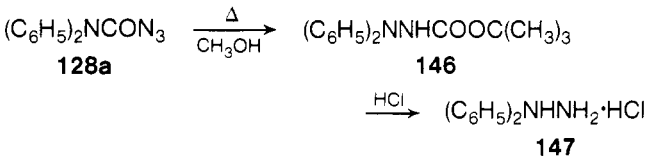




well-known dimer of isocyanates,[114] proposed by Lieber.[115] Heating the dimer **133** with sodium hydroxide, methanol, or ethanol in a steel bomb at 250 °C yielded the corresponding indazolone **130,** while boiling it in aniline gave diphenylurea (**144**), indazolone **130,** and the semicarbazide **145.** Such a scheme may be expected by assuming an indazolone–isocyanate adduct **133** as a dimeric form of **129.** It would also explain the fact that an unspecified amount of tetraphenylsemicarbazide **132a** was found when the "free diphenylamino isocyanate" [88] was reacted with diphenylhydrazine (see above).

When diphenylcarbamoyl azide **128** is boiled with various alcohols the azide-displacement reaction competes with the Curtius rearrangement yielding urethanes in the former and carbazates in the latter case.

A useful synthetic application of this azide thermolysis in alcohols has been reported.[115] Asymmetrical diphenylhydrazine (**147**) can be made in high purity (difficult to get in other ways[117-121]) by performing the thermolysis in *tert*-butyl alcohol; the resulting carbazate **146** is easily hydrolyzed and decarboxylated.



Dialkylcarbamoyl azides **148** also undergo a Curtius rearrangement upon photolysis[122-124] and flash vacuum thermolysis.[125] Isolation of the products and analysis showed them to be derivative of a transient amino isocyanates **149.** In methanolic solution they are trapped to give carbazates **150,**[123] while in aprotic solvents the amino isocyanates **149** dimerize[122] or add to other heterocumulenes such as isocyanates[122] or carbodiimides[124] present in the photolysis mixture. The compounds formed have been identified as 1,2,4-triazolidine-3,5-dione-1,2-aminimides (**151**) or **152,** respectively, based on chemical behavior and spectroscopic data[126] (see Tables IX and X).

Thermolysis of **148** under high vacuum affords only the dimers **151** in yields as high as 93%. The relatively low yields of **151b,c** are explained by a subsequent thermal rearrangement which takes place under these particular conditions.[125] Thus, one of the substituents on N^1 in the aminimide **151** is eliminated as alkene; the corresponding 2*H*-triazolidines **157b,c** have been isolated.[122,125]

Treatment of phosphorohydrazidate anion **153** with carbon dioxide resulted in carboxylation to **154** which then rearranges to a phosphoric acid derivative and the dialkylamino isocyanate **149b** which was isolated as its dimer as in the fomer case.[126,129]

TABLE IX. Dimeric Amino Isocyanates 151

151	R_2	mp, °C	yield, %
a	$(CH_3)_2$	178,[a] 168[b]	37,[a] 61[b]
b	$(CH_3CH_2)_2$	112–115,[c] 93[b]	69[b]
c	$((CH_3)_2CH)_2$	95[b]	66[b]
d	$-(CH_2)_5-$	269[b]	93[b]
e	$-(CH_2)_2O(CH_2)_2-$	249[b]	91[b]

[a] Reference 126. [b] Reference 125. [c] Reference 122.

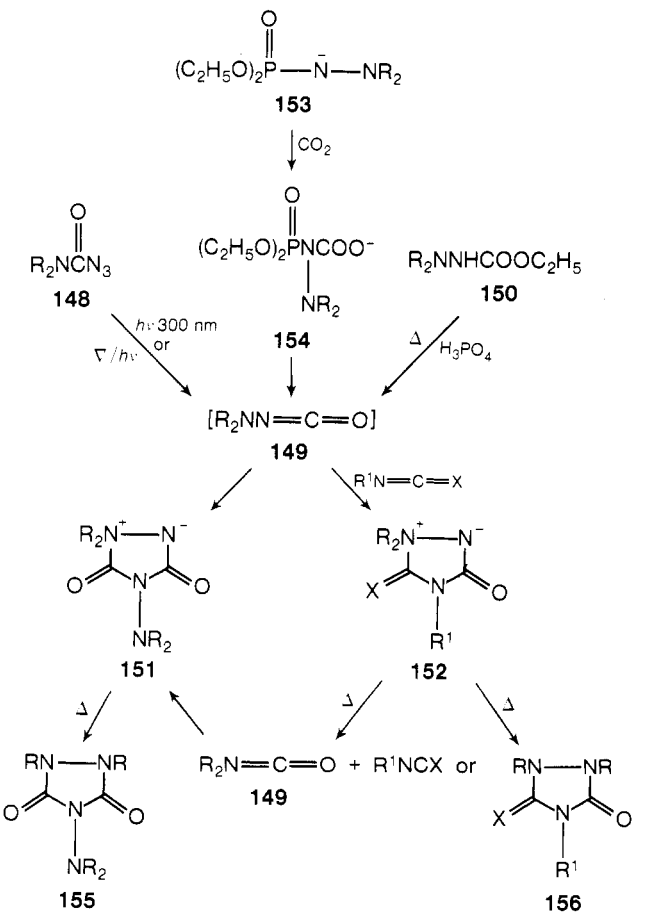


TABLE X. Adducts of Amino Isocyanates and R^1–N=C=X (152)

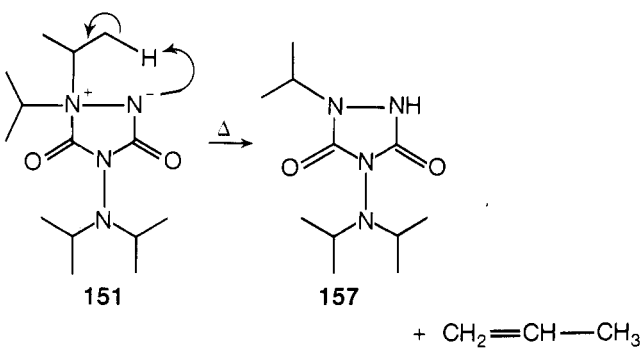
152	R	R^1	X	mp, °C	yield, %	ref
a	CH_3	t-C_4H_9	O	185	27	124, 131
b	CH_3	n-C_4H_9	O	99	62	126
c	CH_3	t-C_8H_{17}	O	97	71	126
d	CH_3	C_6H_5	O	179	40	126, 131
e	CH_3	1-$C_{10}H_7$	O	164	*a*	124, 131
f	C_2H_5	CH_3	O	81–83	*a*	122
g	C_2H_5	C_2H_5	O	131–133	*a*	122
h	C_2H_5	t-C_4H_9	O	99	42	124,131
i	C_2H_5	C_6H_5	O	135	55	124,131
k	C_2H_5	1-$C_{10}H_7$	O	144	*a*	124,131
l	$-(CH_2)_5-$	n-C_4H_9	O	164–165	*a*	129
m	$-(CH_2)_6-$	n-C_4H_9	O	124–125	*a*	129
n	CH_3	CH_3	S	146–148	86	130
o	CH_3	n-C_4H_9	S	*b*	*b*	126
p	CH_3	$CH_2C_6H_5$	S	125–127	89	130, 131
q	C_2H_5	CH_3	S	121–123	80	130, 131
r	C_2H_5	$CH_2C_6H_5$	S	143–145	65	130, 131

[a] Not indicated. [b] Only Stevens rearrangement product **156** obtained.

TABLE XI. Adducts of Amino Isocyanates and Acetylenes 163[131,137]

163	R	R^1	R^2	mp, °C	yield, %
a	CH_3	H	$COOCH_3$	192–193	67
b	CH_3	C_2H_5	$C{\equiv}CC_2H_5$	78	40*a*
c	CH_3	C_6H_5	H	207	83
d	CH_3	C_6H_5	CH_3	202	67
e	CH_3	C_6H_5	$COCH_3$	176	68
f	CH_3	C_6H_5	$COOCH_3$	158	40
g	CH_3	$COOCH_3$	$COOCH_3$	128	76
h	CH_3	1-C_5NH_4	H	220	69

[a] Exact structure not chemically established.



Again, the monomeric species can be trapped when the reaction is quenched with another isocyanate.

Another route leading to amino isocyanates **149** is the pyrolysis of 1,1-dialkylcarbazates **150** in the presence of phosphoric acid catalyst at 200 °C.[126] Under these conditions the initially formed aminimides **151** or **152** respectively convert to 1,2-dimethyl-4-substituted-triazolidinediones **155** or **156** (R^1 = O), or the 1,2,4-triazolidin-3-one-5-thiones **156** (R^1 = S) when an isothiocyanate is present in the pyrolysis mixture.[126] This Stevens-type rearrangement[132] is known to occur in other molecules containing a similar betaine-type moiety[133,134] and has been realized for other amino isocyanate adducts as well.[126,127,129]

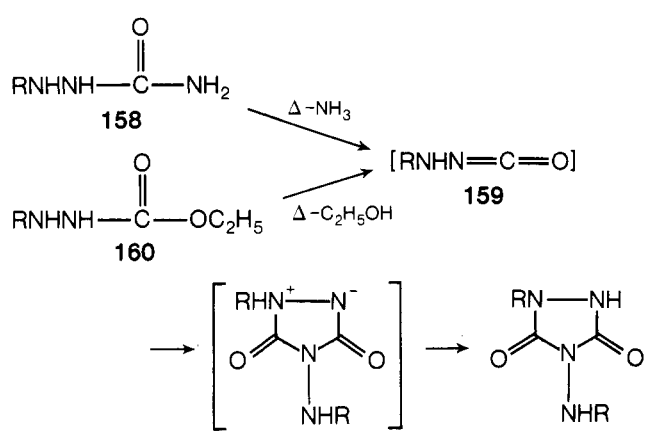
A closely related reaction is the pyrolysis of 1-alkylsemicarbazides (**158**); the products obtained were believed to be the triazolidinediones **161.**[135] This could involve an intermediate monosubstituted alkylamino isocyanate **159.** Finally, 1-phenylcarbazate **160** eliminates ethanol upon heating and the same type of compound, **161,** has been isolated.[136]

A very elegant method of generating amino isocyanates **149** is based on the facile thermal reversibility of the cycloaddition product of amino isocyanates **149** and bulky isocyanates, i.e., when a bulky substituent is attached to position 4 of the triazolidine derivative **152** such as R′ = *tert*-butyl[124] or *tert*-octyl.[126] Thus, when **152a** or **h** are heated to above 60° they dissociate to their parent compounds. The amino isocyanates **149a,h** dimerize to the aminimides **151a,h** when no other reactive substrate is present, although, in the presence of other isocyanates, isothiocyanates (as seen above[124,125,130]), carbodiimides,[124] acetylenes[137] or cyanates,[138] cycloaddition with these partners can compete effectively with dimerization. A great variety of new heterocyclic compounds have been prepared in this manner as Scheme I shows (see also Tables XI and XII).

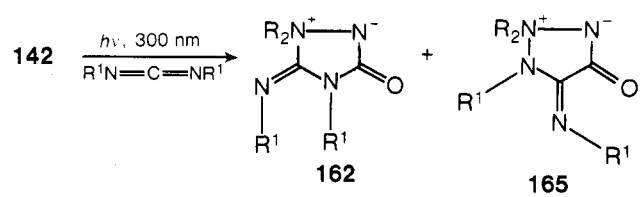
TABLE XII. Adducts of Amino Isocyanates and Cyanates 164[138]

164	R	R^1	mp, °C	yield, %
a	CH_3	Cl_3CCH_2	184	82
b	CH_3	C_6H_5	140	60[a]
c	CH_3	2,6-$(CH_3)_2C_6H_3$	194	68
d	CH_3	1-$C_{10}H_7$	182	58
e	CH_3	2-CN-C_6H_4	160	25[a]
f	C_2H_5	C_6H_5	157	55[a]

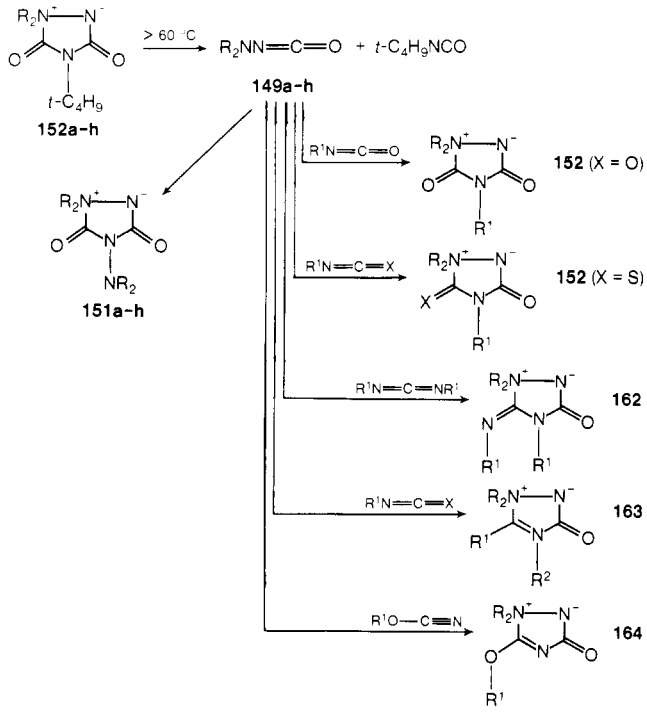
[a] Containing minor impurities.



It should be noted that in contrast to the photolytically generated dimethylamino isocyanate **149,** the thermally generated species affords only one adduct **162** with carbodiimides. When



SCHEME I



carbodiimide was present in the photolysis mixture, two different adducts **162** and **165** were formed in almost quantitative yield in a 3:1 ratio[122] (see Table XIII). If one considers the amino isocyanate as acting like an allylic anion, an addition in two directions is possible since relative orientations of the reacting partners in such cases are not governed by the "1,3-dipole" having a negative and a positive end.[139,140] However, there seems to be some uncertainty about the structure of the minor product.[131]

The generality of the thermal dissociation of aminimides of types **152** and **162** is further illustrated by the behavior of compounds **162b** and **152n.**[124] They are both sources of dimethylamino isocyanate **149a,** but the diisopropylcarbodiimide cannot be removed as easily as *tert*-butyl isocyanate. Furthermore, it competes with other addends for the dimethylamino isocyanate **149a,** for example, in the preparation of the isocyanate adduct **152;** thus refuxing **162b** in benzene with an excess of methyl isothiocyanate yields a mixture of **162b** and **152n.** Irradiation of

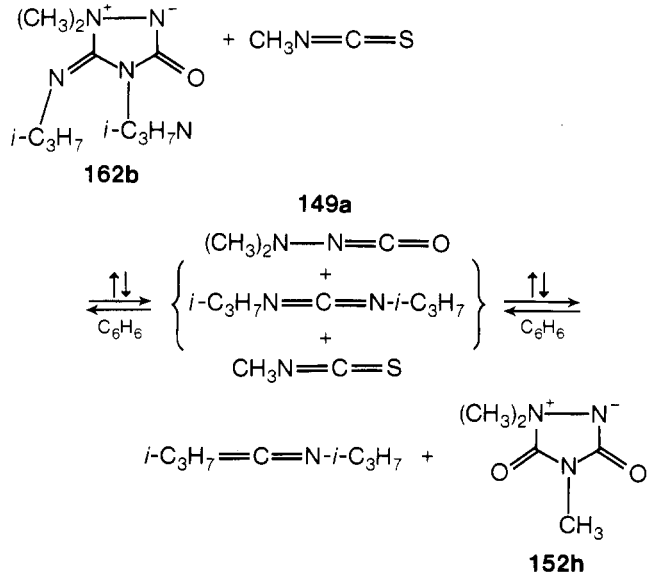


TABLE XIII. Adducts of Amino Isocyanates and Carbodiimides 162 and 165[121]

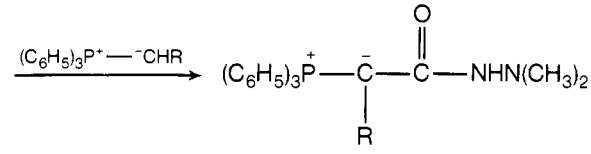
162 / 165	R	R¹	mp, °C 162	mp, °C 165	ratio	total yield, %
a	CH_3	C_2H_5	100–102	oil	3:1	95
b	CH_3	i-C_3H_7	141–143	163–165	3:2	95
c	C_2H_5	C_2H_5	88–89	*a*		95

[a] Not observed.

151b reverts the dimer to the monomer **149** which can be trapped with a protic solvent, e.g., methanol, to the carbazate **150** in 83% yield.[122]

When dimethylamino isocyanate **149a** is generated in the presence of phosphonium ylides, such as ethoxycarbonyl- and cyanomethylenetriphenylphosphorane, 1:1 adduct **166** results.

152a ⟶ **149a**

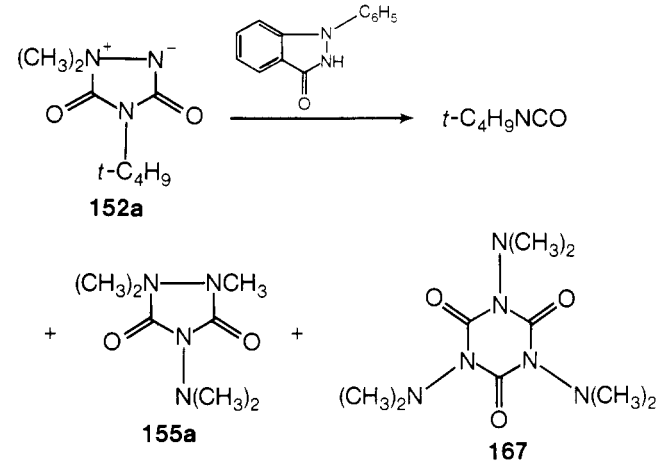


166a, R = $COOC_2H_5$

b, R = CN

It also reacts with less reactive phosphoranes as well as with phosphorus(III) compounds, but reversibly, and this leads to the complete irreversible dimerization of the amino isocyanate.[128] The well-known reaction of iminophosphoranes with isocyanates which give carbodiimides could not be extended to the amino isocyanates.

Recently a trimeric species of dimethylamino isocyanate has been found. When the *tert*-butyl adduct **152a** is well mixed with various amounts of 1-phenylindazolone and dry-thermolyzed for a few minutes at 170 °C, a mixture is obtained which contains, as main products, unchanged 1-phenylindazolone, the Stevens rearrangement product **155a** and up to 50% of 1,3,5-tris(dimethylamino)-1,3,5-triazidinetrione (**167**).[113]



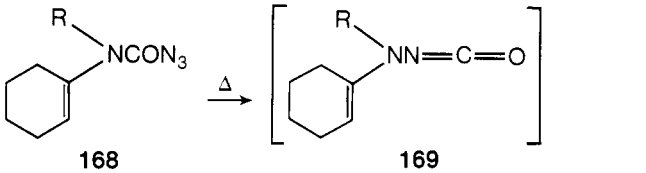
A versatile synthesis of 1-substituted 4,5,6,7-tetrahydroindazol-3-ones adapted from Stolle's method[92] has been reported. When cyclohexenylcarbamoyl azides **168,** readily available from the corresponding cyclohexenimine[141] by reaction with phosgene[142,143] and treatment of the acid chloride with sodium azide, are thermolyzed in boiling chlorobenzene, the intermediate amino isocyanates cyclize to the indazolines **170** (see Table XIV). The enhanced nucleophilicity of the β carbon in **169** appears to be responsible for the fact that ring closure takes place in the cyclohexene ring only, the alternative indazolone not being formed.[144] The reaction fails when the

TABLE XIV. Preparation of Indazolines 170[145]

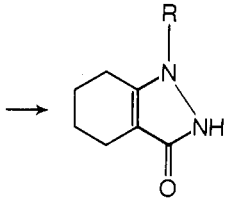
170	R	mp, °C	yield, %
a	CH_3	178–181	76
b	$(CH_3)_2CH$	225–227	32
c	$CH_3(CH_2)_3$	139–140	34
d	$(CH_3)_2CHCH_2$	165–166	73
e	$C_6H_5CH_2$	188–188.5	57
f	C_6H_5	213–214	45
g	$3,4\text{-}Cl_2C_6H_3$	208–218	62

TABLE XV. Preparation of Imidazolones 172[146]

172	R	R^1	mp, °C	yield, %
a	H	1-cyclohexenyl	156–161	50
b	H	4-methyl-1-cyclohexenyl	128–135	55
c	H	C_6H_5	170	65
d	H	$3,4\text{-}Cl_2C_6H_3$	176–178	
e	H	$C_6H_5CH_2$	162–165	70
f	H	$CH_2{=}CH\text{-}CH_2$	100–105	75
g	C_6H_5	CH_3	159–160	35

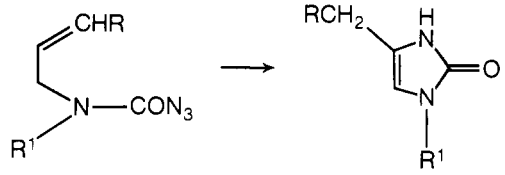


168 169



170

carbamoyl azide bears an *N*-allyl or terminally substituted propenyl group as in **171,** imidazolones **172** being mainly formed in this case[145,146] (see Table XV)



171 172

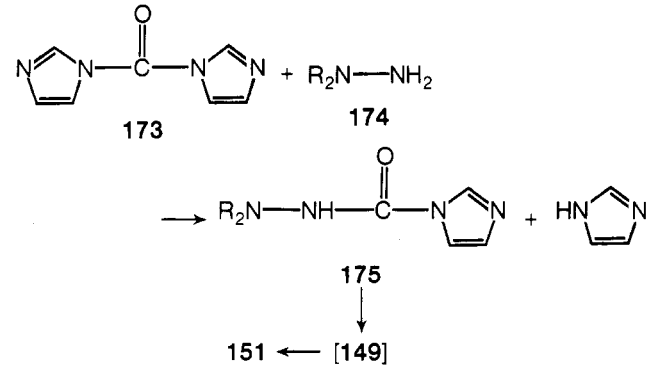
Again, a nitrene mechanism representing a high-energy pathway seems unlikely[149] while olefinic azides containing a double bond three carbon atoms removed from the azido group add intramolecularly to give stable triazolines which lose nitrogen forming cyclic imines and 1-azabicyclo[3.1.0]hexane.[148]

Thermolysis of imidazolidides **175,** easily prepared by reacting carbonyldiimidazole **173** and the appropriate disubstituted hydrazine **174,** results in elimination of imidazole and, as in previous cases,[122,125,127] dimerization of the amino isocyanate **149.**[149] A possible indication that **149** is a true intermediate is that if the hydrogen atom at the carbonyl nitrogen is replaced by an alkyl substituent, the reaction rate of **175** with amines is considerably lowered. This type of reaction is commonly applicable to the synthesis of isocyanates from amines[150] as well as of other heterocumulenes.[151,152]

Another useful method of making amino isocyanates lies in the ease of the [2 + 2] cycloreversion of diazetidinones of type **177.** Thus *N,N*-dimethyl-*N'*-dimethylaminoformamidine (**176**) cycloadds to isocyanates forming the four-membered ring which

TABLE XVI. Preparation of 1,1-Dimethyl-4-aryl-1,2,4-triazolidine-3,5-dione-1,2-aminimides 152[153]

152	R	mp, °C	yield, %
a	C_6H_5	179–181	81
b	$4\text{-}ClC_6H_5$	180–182	76
c	$4\text{-}FC_6H_4$	156–158	66
d	$4\text{-}BrC_6H_4$	177–179	74
e	$4\text{-}CH_3C_6H_4$	153–155	47
f	$4\text{-}OCH_3C_6H_4$	175–177	64
g	$3\text{-}OCH_3C_6H_4$	140–146	24
h	$3\text{-}SCH_3C_6H_4$	145–148	76
i	$3\text{-}COOCH_3C_6H_4$	159–162	65
j	$3\text{-}ClC_6H_4$	168–169	33
k	$3\text{-}CF_3C_6H_4$	143–145	50
l	$2\text{-}OCH_3C_6H_4$	166–173	20
m	$3,4\text{-}Cl_2C_6H_3$	163–165	22
n	$3\text{-}Cl\text{-}4\text{-}OCH_3C_6H_3$	170–175	25
o	$3,5\text{-}(CH_3)_2C_6H_3$	158–161	32
p	$3,5\text{-}(OCH_3)_2C_6H_3$	134–136	54

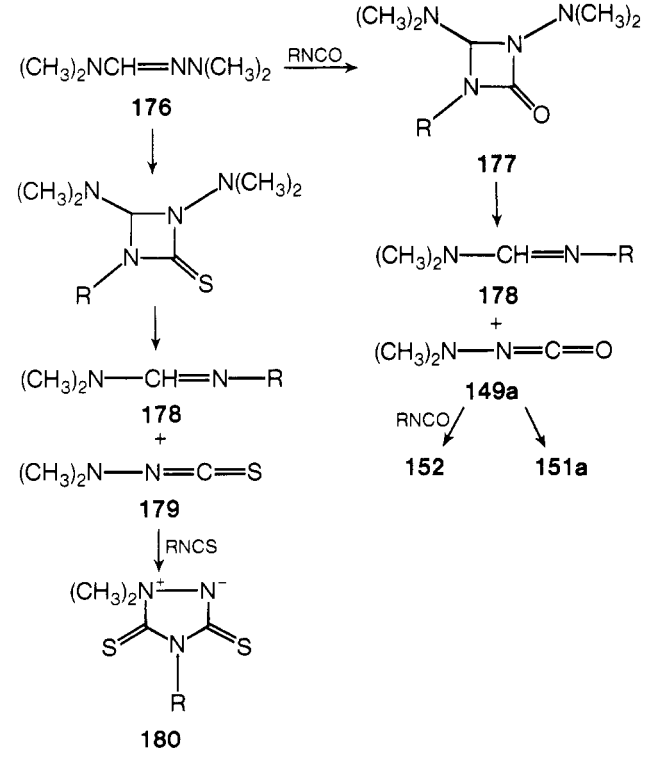


173 174

175

151 ← [149]

reverts orthogonal to the addition direction to another formamidine **178** and dimethylamino isocyanate **149a.**[153] The latter



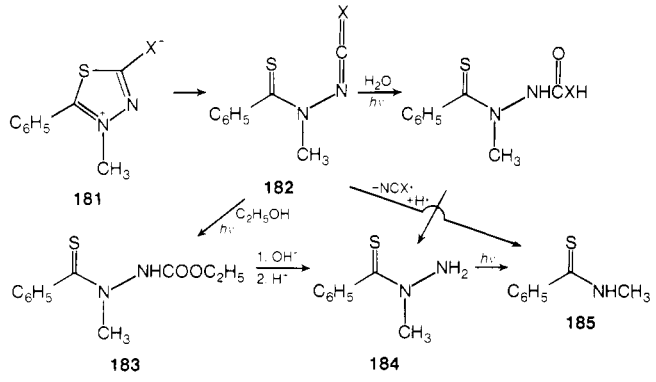
176 177

178 + 179

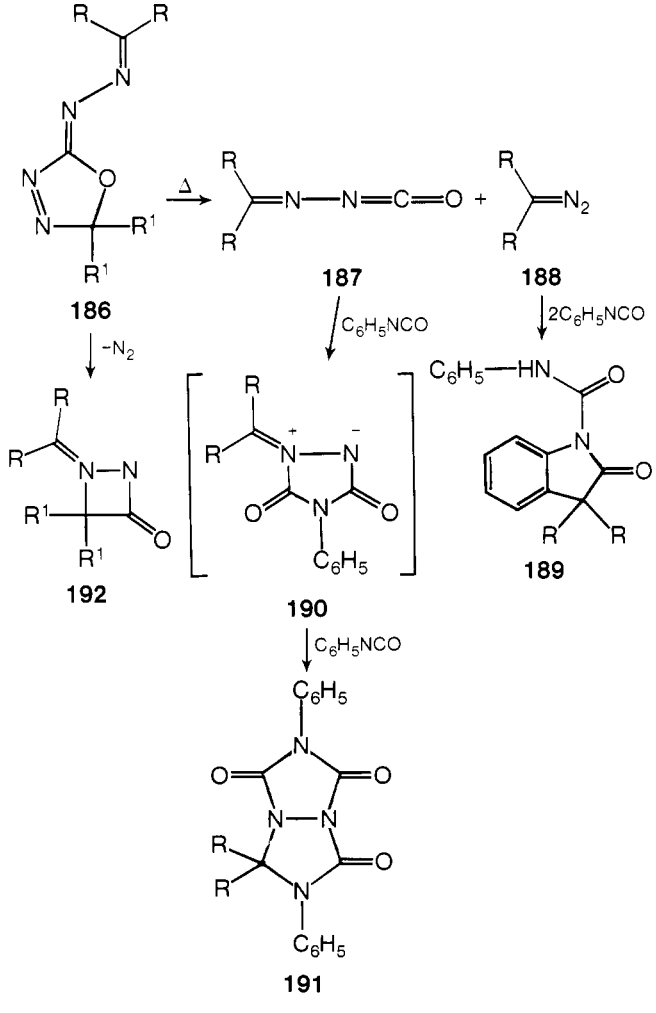
180

dimerizes or reacts with excess isocyanate in the usual manner to form aminimides **151a** and **152**[122,124,126,130] (see Table XVI). When phenyl isothiocyanate is used, the corresponding dithioneaminimides **180** result via dimethylamino isothiocyanate **179.**

Mesoionic thiadiazoles of type **181** can undergo a ring-opening reaction (light-induced) to the thiobenzoylmethylamino isocyanate and **182.**[154-157]



The intermediates can eliminate isocyanato or isothiocyanato radical, respectively; and methylthiobenzamide **183** is isolated in both cases.[155] When the reaction was monitored in acetonitrile and Nujol by means of IR spectroscopy, absorptions at 2260 and 2060 cm^{-1}, were observed and interpreted as NCO and NCS stretching,[156] respectively. In a later reexamination, however, these interpretations were considered dubious owing to observation of a new product.[154] Thus, when the photolysis was carried out in moist acetonitrile, formation of *N*-methyl-*N*-thiobenzoylhydrazine (**184**) was observed, again, in both cases. Furthermore the intermediate amino isocyanate **182** could be trapped with ethanol to the hydrazidic ester **185** which can be hydrolyzed to **184.** The two IR bonds most probably were due to the solvent (acetonitrile (2260 cm^{-1})) and carbonyl sulfide (2060 cm^{-1}).



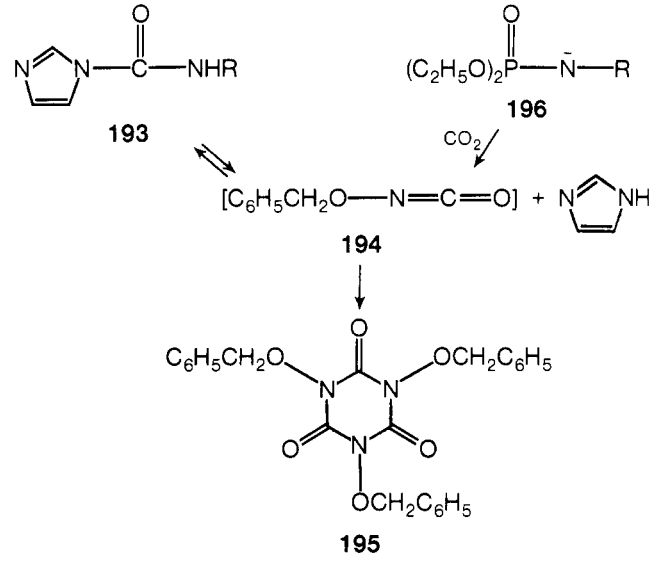
Evidence for the existence of diarylmethylenimino isocyanate (**187**) comes from trapping of both intermediates formed in the thermolysis of 2-hydrazono-Δ^3-1,3,1-oxadiazolines (**186**) in the presence of aryl isocyanates.[158] The diazo derivative **188** adds to 2 equiv of aryl isocyanate to the oxindole **189.** The imino isocyanate **187** reacts with two molecules of the trapping agent to the tetraazabicyclooctanetrione **191** by means of two subsequent [2 + 3] cycloadditions via aminimide **190** which closely resembles that found in reactions of dialkylamino isocyanates with isocyanates.[124,126,127,130,133]

Furthermore, the proposed decomposition mechanism parallels that of 2-arylimido-Δ^3-1,3,4-oxadiazolines which also proceeds through a 1,3-dipolar cycloreversion forming an isocyanate moiety and the corresponding diazomethane.[159,160] In the absence of reactive scavengers the 1,2-diazetidin-3-one-1,2-aminimides **192** are formed.[161]

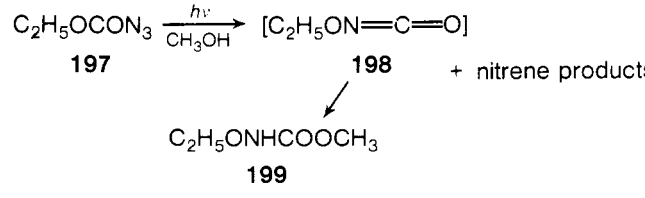
B. O-Substituted Isocyanates

Several unsuccessful attempts to prepare the monoxime of carbon dioxide or its *O*-alkyl derivative were made[162,163] before Staab tried to apply his general method of making isocyanates.[150] Imidazolidides of the type **193,** which are easily accessible by reacting the appropriate amine with carbonyl diimidazole, decompose on heating, setting free imidazole and an isocyanate **194.**

In the case of **193** (R = benzyloxy) 1,3,5-tribenzyloxy-2,4,6-trioxahexahydrotriazine-1,3,5-trione (**195**) was isolated in high yield.[164] Presumably the intermediate benzyloxy isocyanate **161** trimerized. In view of the results obtained by Reichen[113] (see above), it may well be that the imidazolidine catalyzes this trimerization. Analogous trimers were isolated when *N*-alkoxyphosphoramidates **196** were treated with carbon dioxide.[165] This is a modification of Wadsworth's isocyanate synthesis.[74]

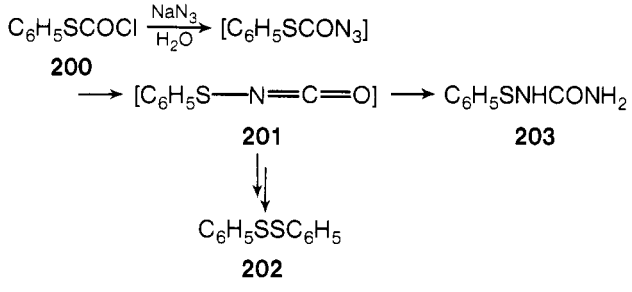


Ethoxy isocyanate **198** can be formed, as an intermediate on photolysis of ethoxycarbonyl azide **197,** in protic solvents only, however, with which it reacts immediately. Thus a 13% yield of ethoxymethyl carbamate **199** has been isolated when the photolysis is performed in methanol.[166] Flash photolysis of **197** failed to give the rearranged isocyanate.[167]

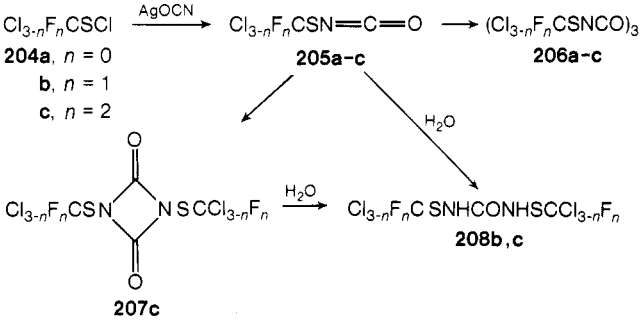


C. S-Substituted Isocyanates

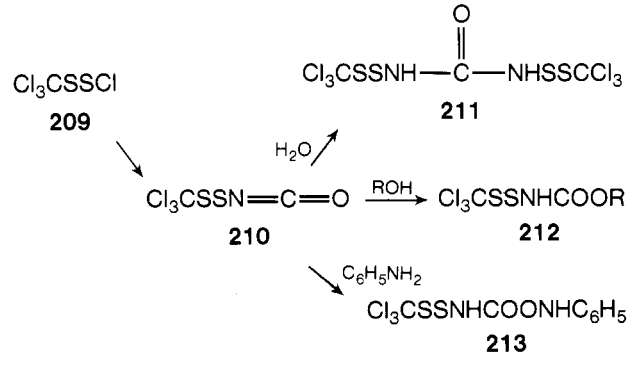
Phenylchlorothioformate (**200**) reacts vigorously with sodium azide in water with gas evolution (nitrogen and carbon dioxide). The two main products isolated, diphenyl disulfide (**202**) and *N*-benzenesulfenylurea (**203**), suggest a thiophenyl carbon-to-nitrogen migration. Whether or not intermediate phenyl thioisocyanate (**201**) appears along the reaction paths is not clear.[168]



Mercaptans of type **204** react with silver cyanate to form the corresponding thiaisocyanates **205.** While the trichloro species **205a** trimerizes instantaneously to the isocyanurate **206a,** the two other can be isolated as monomers. **205c** di- or trimerizes slowly at room temperature to the corresponding diazetidinedione **207c** or the isocyanurate **206.**[169,170] Hydrolysis of the free thiaisocyanates **205b,c** yields the ureas **208b,c** eliminating carbon dioxide as does **207c.**[170]

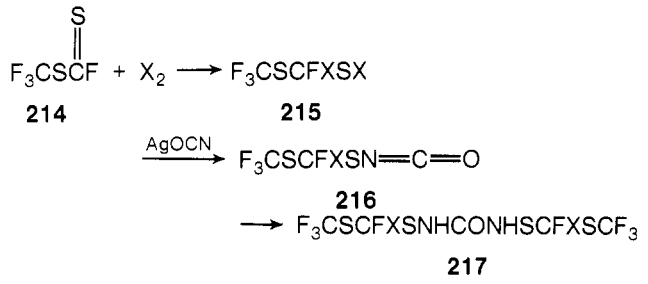


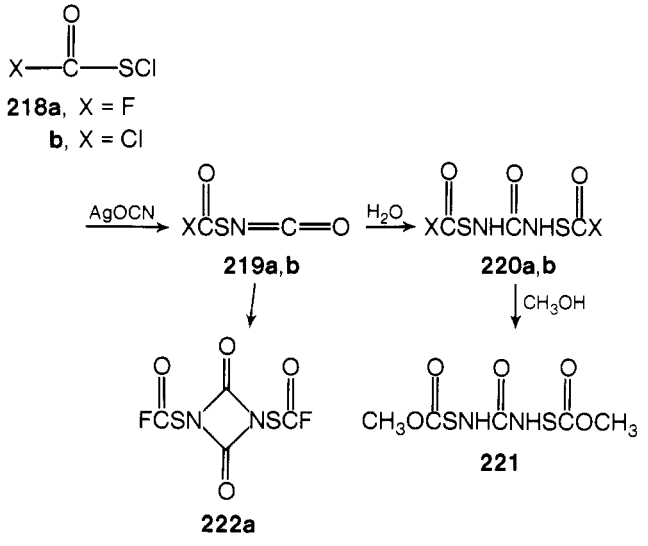
Similarly, trichloromethylthiosulfenyl chloride (**209**) gives isocyanate **210** upon treating with silver cyanate. It is a stable, distillable liquid (bp 60 °C (0.1 Torr)) and can be hydrolyzed to the urea **211,** alcoholyzed to the urethane **212,** and aminolyzed to unsymmetrical ureas **213** as normal isocyanates can.[171]



When trifluoromethyl dithiofluoroformate (**214**) is treated with chlorine and resulting trifluoromethylmercaptochlorofluoromethanesulfenyl chloride (**215**) reacted with silver cyanate at −20 °C, the isocyanate **216** can be isolated. In the presence of humidity it forms the urea **217.**[172]

Fluorocarbonylsulfenyl chloride (**218a**)[173,174] and the chloro compound **218b** both exchange first the sulfenyl halide ion in the presence of silver cyanate to form the isocyanates **219a,b.**



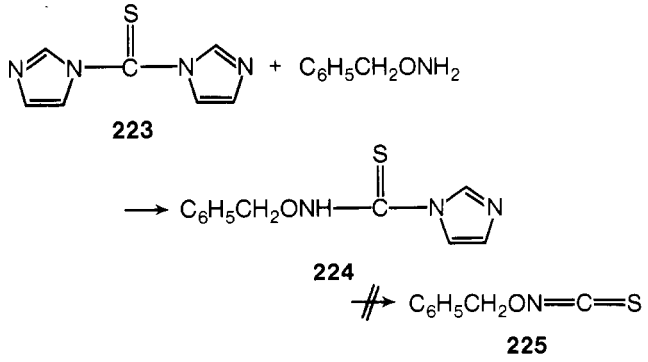


Careful hydrolysis gives the ureas **220.** The second carbonyl halide can be substituted by a methoxy group on methanolysis to give the methoxycarbonylsulfenylurea **221.** Again, **219a** dimerizes slowly to the diazetidinedione **222a** if no trapping agent is present.[175]

V. Isothiocyanates

A. O-Substituted Isothiocyanates

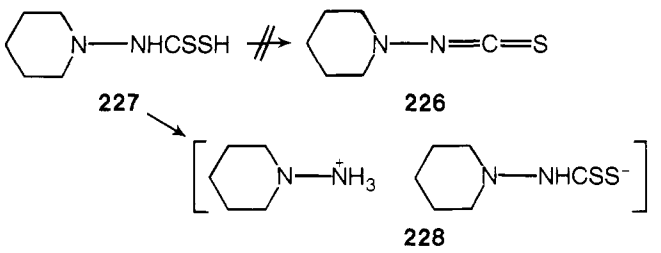
Reaction of thiocarbonyldiimidazole (**223**) with *O*-benzylhydroxylamine gave the imidazolidine **224** as did the corresponding oxo homolog **194.** However, in this case the thermal elimination of imidazole and formation of the benzyloxy isothiocyanate (**225**) could not be effected.



Even prolonged heating in cyclohexylamine did not afford *N*-cyclohexyl-*N'*-benzyloxythiourea, a compound whose analysis indicated a cyclohexylammonium salt of **224** was isolated in quantitative yield.[176]

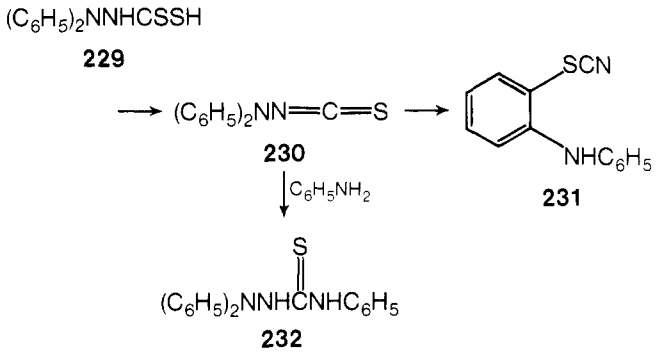
B. N-Substituted Isothiocyanates

A Russian group[177] reported formation of pentamethyl eneamino isothiocyanate (**226**) by elimination of hydrogen sulfide from *N*-piperidinodithiocarbamic acid (**227**). A later

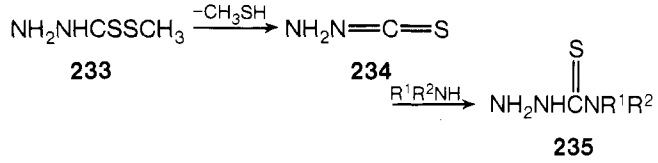


reexamination showed the product to be the *N,N*-pentamethylenehydrazinium salt **228.**[178]

While the thermal hydrogen sulfide elimination did not work, the chemical elimination succeeded. Thus, treatment of *N,N*-diphenyldithiocarbazic acid (**229**) at −80 °C with dicyclohexylcarbodiimide gave an intermediate diphenylamino isothiocyanate (**230**) which upon warming rearranged spontaneously to 2-thiocyanatophenylphenylamine (**231**).[179] Evidence for the existence of **230** was based on its IR absorption at 1956 cm^{-1} and the trapping experiment with aniline to form 1,1,4-triphenylthiosemicarbazide (**232**).



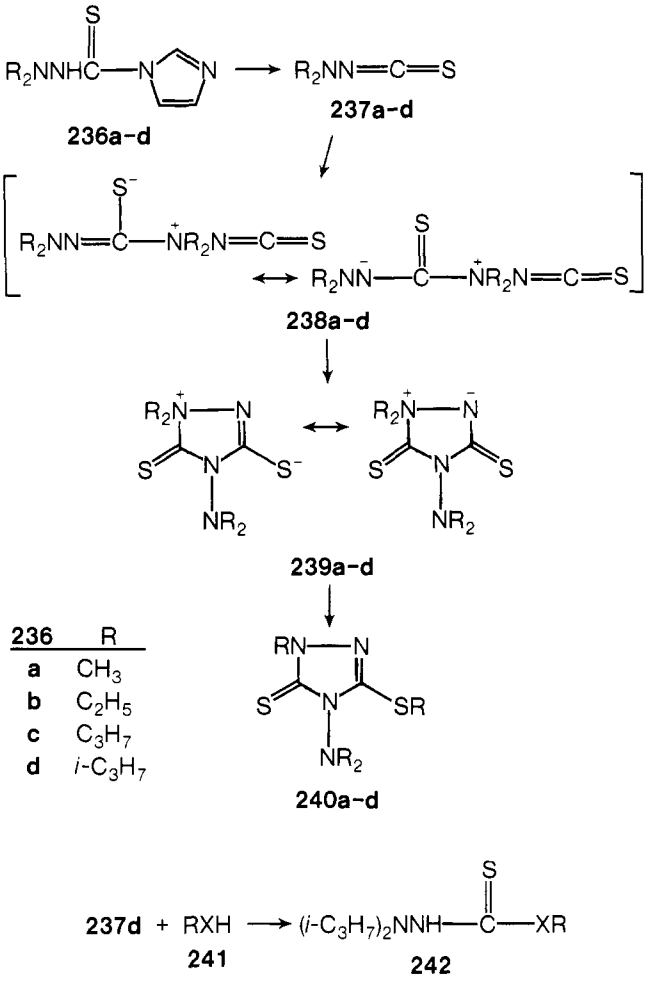
The reaction of primary and secondary amines with thiocarbazate ester **233** to give the thiosemicarbazides **235** may proceed through the intermediate amino isothiocyanate **234.**[180] This is supported by the fact that monosubstituted dithiocarbamates easily afford the corresponding isothiocyanates which subsequently react with an amine; on the other hand, the fairly great stability of N,N-disubstituted dithiocarbamates toward amines is well established.[181-185]



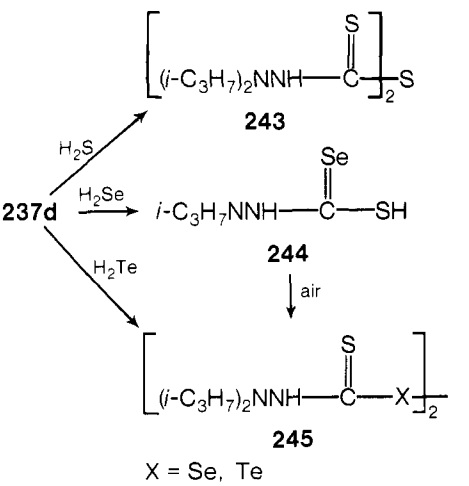
Another way of preparing amino isothiocyanates is by heating *N,N*-dialkythiocarbazoylimidazoles (**236**) in vacuo.[178,186,187] Again, this is a variation of Staab's method[150,152,164] (see above).

As in the case of the corresponding dialkylamino isocyanates **149**[122,125,126,133] compounds of type **237** dimerize, even though they show an enhanced stability compared with **149;**[178] dimerization of **237** proceeds at a negligible rate at −80 °C while the diisopropyl derivative needed several hours at room temperature. It has been suggested that this isomerization passes again through the open-chain intermediate **238,** but experimental proof is still lacking.[187] A linear intermediate **238** has been observed in solution which yields two types of isomers **239** and **240** of which the former, **239,** is converted to **240** at room temperature.[186] A variety of addition reactions with amines, hydrazines, and thiols has been performed with **237**[186,188] (see Table XVII).

The formation of 1,1-diisopropyl-4-arylthiosemicarbazides **242s-u,x,y** was not influenced by the presence of hydroxy, hydroxymethylene, hydroxycarbonyl, and amido groups, while in the case of **241v,w** the attack occurred at the thiol function to give the corresponding aminophenyl *N,N*-diisopropyldithiocarbazates **242v,w.**[188] In the aliphatic series, **237d** invariably reacted with both the amino and the thiol function even when the reacant was present in excess.



Reaction with hydrogen sulfide gave the thiocarbazoyl sulfide **243;**[189] with hydrogen selenide the corresponding selenothiocarbazic acid **244** resulted, which on exposure to air converted to the bisthiocarbazoyldiselenide **245** (X = Se). Similar treatment of **237d** with hydrogen telluride resulted directly in the formation of ditelluride **245** (X = Te).[190]

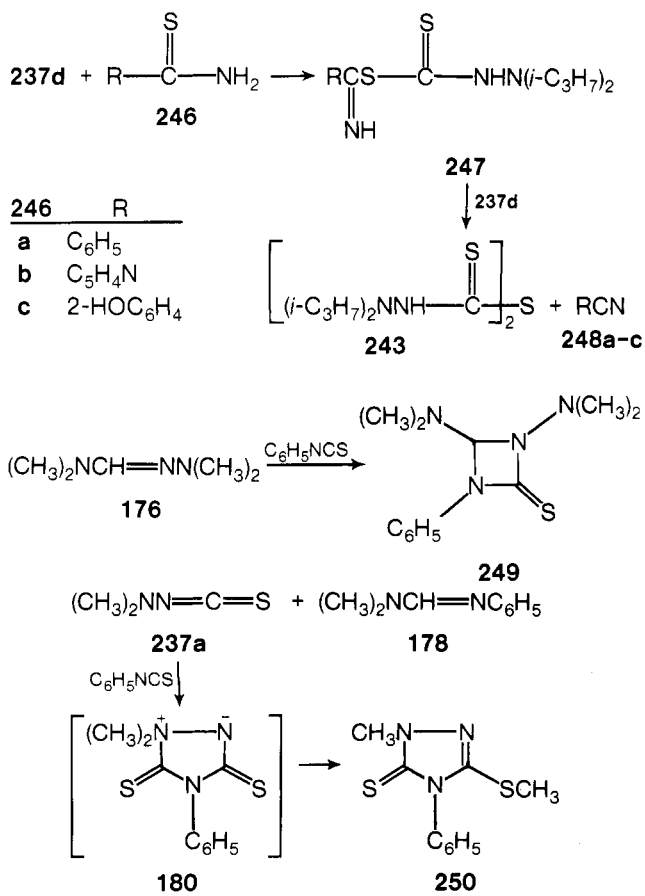


Thioureas as well as secondary or tertiary thioamides failed to undergo addition, while thiobenzamide (**246a**), 4-pyridi-

TABLE XVII. Reactions of Diisopropylamino Isothiocyanate 237d with Various Amines 241

	241	242	yield, %	mp, °C
a	methylamine	1,1-diisopropyl-4-methylthiosemicarbazide	10	121–122
b	hydrazine	4,4′-bis(1,1-diisopropylthiosemicarbazide)	85	240–241
c	phenylhydrazine	1,1-diisopropyl-5-phenylthiocarbohydrazide	55	147–149
d	benzoylhydrazine	5-benzoyl-1,1-diisopropylthiocarbohydrazide	58	164–166
e	tosylhydrazine	1,1-diisopropyl-5-(*p*-toluenesulfonyl)thiocarbohydrazide	73	186–187
f	1,2-diphenylguanidine	1,1-diisopropyl-4-(*N,N′*-diphenylamidino)thiosemicarbazide		169–170
g	ethylenediamine	ethylene-4,4′-bis(1,1-diisopropylthiosemicarbazide)	50	236
h	aniline	1,1-diisopropyl-4-phenylthiosemicarbazide	75	99–101
i	piperidine	1,1-diisopropyl-4,4-pentamethylenethiosemicarbazide	42	61–62
k	methylhydrazine	1,2-bis(*N,N*-diisopropylthiocarbazoyl)-1-methylhydrazine	28	180
l	1,2-phenylenediamine	1,1-diisopropyl-4-(*o*-aminophenyl)thiosemicarbazide	55[a]	194–195
m	1,3-phenylenediamine	1,1,1′,1′-tetraisopropyl-4,4′-*m*-phenylenebisthiosemicarbazide	20[b]	175–176
n	1,4-phenylenediamine	1,1-diisopropyl-4-(*p*-aminophenyl)thiosemicarbazide	69[a]	201–203
o	3-aminopyridine	1,1-diisopropyl-4-(3-pyridyl)thiosemicarbazide	40[b]	168–169
p	4-aminopyridine	1,1-diisopropyl-4-(4-pyridyl)thiosemicarbazide	46[b]	127–128
q	3-aminoquinoline	1,1-diisopropyl-4-(3-quinolyl)thiosemicarbazide	73[a]	177–178
r	8-aminoquinoline	1,1-diisopropyl-4-(8-quinolyl)thiosemicarbazide	52[a]	159–160
s	2-aminophenol	1,1-diisopropyl-4-(*o*-hydroxyphenyl)thiosemicarbazide	61[b]	152–153
t	3-aminophenol	1,1-diisopropyl-4-(*m*-hydroxyphenyl)thiosemicarbazide	60[b]	119–120
u	4-aminophenol	1,1-diisopropyl-4-(*p*-hydroxyphenyl)thiosemicarbazide	55[b]	161–162
v	2-aminothiophenol	2-aminophenyl-*N,N*-diisopropyldithiocarbazate	39[a]	134–135
w	4-aminothiophenol	4-aminophenyl-*N,N*-diisopropyldithiocarbazate	90[a]	169–170
x	2-aminobenzyl alcohol	1,1-diisopropyl-4-(*o*-hydroxymethylphenyl)thiosemicarbazide	72	160–161
y	2-aminobenzoic acid	1,1-diisopropyl-4-(*o*-carboxyphenyl)thiosemicarbazide	86	207–208
z	methyl 2-aminobenzoate	1,1-diisopropyl-4-(*o*-methoxycarbonylphenyl)thiosemicarbazide	82	154–155
aa	2-aminobenzamide	1,1-diisopropyl-4-(*o*-carbamoylphenyl)thiosemicarbazide	52[a]	197–198
bb	4-nitrobenzhydrazide	1,1-diisopropyl-5-(*p*-nitrobenzoyl)thiocarbonohydrazide	65	198–199
cc	2-aminoethanol	1,1-diisopropyl-4-(*p*-hydroxyethyl)thiosemicarbazide	65	80–81
dd	ethyl 2-methyldithiocarbazate	ethyl 2-methyl-3-(*N,N*-diisopropylthiocarbazoyl)dithiocarbazate	66	182–183
ee	methoxyamine	1,1-diisopropyl-4-methoxythiosemicarbazide	70[c]	95–96
ff	2-aminoethanethiol	*N,S*-bis(3,3-diisopropylthiocarbazoyl)amino-4-thiazolidone	70[a]	185–186
gg	3-aminorhodanine	2-thioxo-3-(*N,N*-diisopropylthiocarbazoyl)amino-4-thiazolidone	40[a]	164–165
hh	3-amino-2-oxazolidine	3-(*N,N*-diisopropylthiocarbazoyl)amino-2-oxazolidone	48[a]	163–164
ii	*N*-phenyl-1,2-phenylenediamine	1,1-diisopropyl-4-(2-anilinophenyl)thiosemicarbazide	56[a]	134–135

Solvents used for recrystallization: [a] Ethanol. [b] Ethanol–water. [c] Cyclohexane.



nethiocarboxamide (**246b**), and 2-hydroxythiobenzamide (**246c**) afforded the sulfide **243** and the corresponding nitriles **248a–c.**[189]

An intermediate thioimino ether **247** may be formed, by attack of the sulfur at the isothiocyanato carbon instead of the nitrogen, which then reacts with a second molecule of **237d** through one of the sulfur atoms, again.

As in the case of aryl isocyanates (see above), phenyl isothiocyanate adds to *N,N*-dimethyl-*N′*-dimethylaminoformamidine (**176**) to a diazetidinethione (**249**) which then dissociates into dimethylamino isothiocyanate (**237a**) and formamidine **178.** The former dimerizes to the aminimide **180** and rearranges to 1-methyl-3-methylthio-4-phenyl-Δ^2-1,2,4-triazoline-5-thione (**250**) as in the case of amino isothiocyanate dimers **239.**[187]

VI. References

(1) H. Ulrich, *Chem. Rev.*, **65,** 369 (1965).
(2) N. Onodera, *Kagaku (Kyoto)*, **19,** 1240 (1964).
(3) R. Graf, *Angew. Chem. Int. Ed. Engl.*, **7,** 172 (1968).
(4) G. I. Derkatsch, *Angew. Chem., Int. Ed. Engl.*, **8,** 421 (1969).
(5) O. Tsuge, *Kagaku To Kogyo (Tokyo)*, **22,** 770 (1969).
(6) K. A. Nuridzhanyan, *Usp. Khim.*, **39,** 259 (1970).
(7) H. Chaimovich, R. J. Vaughan, and F. H. Westheimer, *J. Am. Chem. Soc.*, **90,** 4088 (1968).
(8) R. R. Rando, *J. Am. Chem. Soc.*, **92,** 6706 (1970).
(9) N. T. Buu and J. T. Edward, *Can. J. Chem.*, **50,** 3719 (1972).
(10) R. Husigen and E. Funke, *Angew. Chem.*, **79,** 320 (1967).
(11) H. Gotthardt, R. Huisgen, and F. C. Schäfer, *Tetrahedron Lett.*, 487 (1963).
(12) H. Staudinger, *Justus Liebigs Ann. Chem.*, **356,** 51 (1907).
(13) J. C. Sheehan and J. J. Ryan, *J. Am. Chem. Soc.*, **73,** 1204 (1951).
(14) E. Schmidt et al., German Patent 960458 (Bayer); *Chem. Zentralbl.*, **129,** 6967 (1958).
(15) R. Huisgen, E. Funke, F. C. Schäfer, and R. Knorr, *Angew. Chem.*, **79,** 321 (1967).
(16) A. Holm, N. H. Toubro, and H. Harrit, *Tetrahedron Lett.*, 1909 (1976).

(17) R. M. Moriarty and R. Mukherjee, *Tetrahedron Lett.*, 4627 (1969).
(18) R. M. Moriarty, R. Mukherjee, O. L. Chapman, and D. Eckroth, *Tetrahedron Lett.*, 397 (1971).
(19) R. Mukherjee and R. M. Moriarty, *Tetrahedron*, **32**, 661 (1976).
(20) S. Winter and G. Pracejus, *Chem. Ber.*, **99**, 151 (1966).
(21) J. C. Sheehan et al., *J. Am. Chem. Soc.*, **72**, 3828 (1950).
(22) J. C. Sheehan and G. D. Laubach, *J. Am. Chem. Soc.*, **73**, 4752 (1951).
(23) J. C. Sheehan and J. J. Ryan, *J. Am. Chem. Soc.*, **73**, 4367 (1951).
(24) J. C. Sheehan, H. W. Hill, and E. L. Buhle, *J. Am. Chem. Soc.*, **73**, 4373 (1951).
(25) J. C. Sheehan and E. J. Corey, *J. Am. Chem. Soc.*, **73**, 4756 (1951).
(26) L. Paul, P. Polczynski, and G. Hilgetag, *Chem. Ber.*, **100**, 2761 (1967).
(27) S. M. Deshpande and A. K. Mukherjee, *J. Chem. Soc. C*, 1241 (1966).
(28) G. Hilgetag, L. Paul, and A. Draeger, *Chem. Ber.* **96**, 1697 (1963).
(29) L. Paul, A. Draeger, and G. Hilgetag, *Chem. Ber.*, **99**, 1957 (1966).
(30) L. Paul and K. Zieloff, *Chem. Ber.* **99**, 1431 (1966).
(31) A. K. Bose, B. Anjyneyulu, S. K. Bhattacharya, and M. S. Manhas, *Tetrahedron*, **23**, 4769 (1967).
(32) A. Bertho and J. Maier, *Justus Liebigs Ann. Chem.*, **498**, 52 (1932).
(33) H. Böhme, S. Ebel, and K. Hartke, *Chem. Ber.*, **98**, 1463 (1965).
(34) H. Pracejus and G. Winter, *Chem. Ber.*, **97**, 1373 (1964).
(35) J. C. Sheehan, D. W. Chapman, and R. W. Roth, *J. Am. Chem. Soc.*, **74**, 3822 (1952).
(36) G. Pracejus, *Justus Liebigs Ann. Chem.*, **622**, 10 (1959).
(37) E. Müller and P. Heinrich, *Chem. Ztg.*, **95**, 567 (1971).
(38) E. Müller and P. Heinrich, *Chem. Ztg.*, **96**, 112 (1972).
(39) N. S. Wulfson et al. *Tetrahedron Lett.*, 951 (1964).
(40) P. H. Chen, *J. Org. Chem.*, **41**, 2973 (1976).
(41) F. H. Westheimer et al., *J. Biol. Chem.*, **241**, 421 (1965).
(42) W. v. Kirmse and L. Horner, *Justus Liebigs Ann. Chem.*, **625**, 34 (1959).
(43) K. v. Möller and O. Süss, *Justus Liebigs Ann. Chem.*, **612**, 153 (1957).
(44) W. v. Kirmse, "Carbene Chemistry", Academic Press, New York and London, 1971, and references cited therein.
(45) O. P. Strausz, T. DoMinh, and H. E. Gunning, *J. Am. Chem. Soc.*, **90**, 1660 (1968).
(46) T. DoMinh, O. P. Strausz, and H. E. Gunning, *J. Am. Chem. Soc.*, **91**, 1261 (1969).
(47) K. Bott, *Angew. Chem., Int. Ed. Engl.*, **3**, 804 (1964).
(48) A. C. Day and M. C. Whiting, *J. Chem. Soc. B*, 991 (1967), and references cited therein.
(49) G. O. Schenck and A. Ritter, *Tetrahedron Lett.*, 3189 (1968).
(50) T. DoMinh, H. E. Gunning, and O. P. Strausz, *J. Am. Chem. Soc.*, **89**, 6785 (1967).
(51) D. E. Thornton, R. K. Gosavi, and O. P. Strausz, *J. Am. Chem. Soc.*, **92**, 1768 (1970).
(52) J. G. Csizmadia, J. Font, and O. P. Strausz, *J. Am. Chem. Soc.*, **90**, 7360 (1968).
(53) G. Frater and O. P. Strausz, *J. Am. Chem. Soc.*, **92**, 6654 (1970).
(54) K.-P. Zeller, H. Meier, H. Kolshorn, and E. Müller, *Chem. Ber.*, **105**, 1875 (1972).
(55) S. A. Martin and P. G. Sammes, *J. Chem. Soc., Chem. Commun.*, 11 (1972).
(56) K.-P. Zeller, *Chem. Ber.*, **108**, 3566 (1975).
(57) Z. Majerski and C. S. Redvanly, *J. Chem. Soc., Chem. Commun.* 694 (1972).
(58) K.-P. Zeller, *Z. Naturforsch., Teil B*, **31**, 586 (1976).
(59) O. P. Strausz et al., *J. Am. Chem. Soc.*, **96**, 5723 (1974), and references cited therein.
(60) R. Wheland and P. D. Bartlett, *J. Am. Chem. Soc.*, **92**, 6057 (1970).
(61) D. C. Richardson, M. E. Hendrick, and M/ Jones, Jr., *J. Am. Chem. Soc.*, **93**, 3790 (1971).
(62) S. L. Kammula, H. L. Tracer, P. B. Shevlin, and M. Jones, Jr., *J. Org. Chem.*, **42**, 2931 (1977).
(63) W. Reichen and B. v. Wartburg, *Helv. Chim. Acta*, to be submitted for publication.
(64) E. V. Dehmlow, *Tetrahedron Lett.*, 1271 (1972).
(65) T. DoMinh and O. P. Strausz, *J. Am. Chem. Soc.*, **92**, 1766 (1970).
(66) R. Montaigne and L. Ghosez, *Angew. Chem.*, **80**, 194 (1968).
(67) R. Huisgen, L. A. Feiler, and P. Otto, *Tetrahedron Lett.*, 4485 (1969).
(68) R. Huisgen and P. Otto, *Tetrahedron Lett.*, 4491 (1968).
(69) W. T. Brady and H. R. O'Neal, *J. Org. Chem.*, **32**, 612 (1967).
(70) W. T. Brady and E. F. Hoff, *J. Am. Chem. Soc.*, **90**, 6256 (1968).
(71) W. T. Brady, E. F. Hoff, R. Roe, Jr., and F. H. Harry, *J. Am. Chem. Soc.*, **91**, 5679 (1969).
(72) S. S. Hixson and S. H. Hixson, *J. Org. Chem.*, **37**, 1279 (1972).
(73) R. F. C. Brown, F. W. Eastwood, and G. L. McMullen, *Aust. J. Chem.*, **30**, 179 (1977).
(74) W. S. Wadsworth, Jr., and W. D. Emmons, *J. Am. Chem. Soc.*, **84**, 1316 (1962).
(75) W. S. Wadsworth, Jr., and W. D. Emmons, *J. Org. Chem.*, **29**, 2816 (1964).
(76) D. M. Plautz, Thesis, South Dakota State University, 1971.
(77) W. Weith, *Ber.*, **6**, 1395 (1873); **7**, 10, 1306 (1874).
(78) D. M. Zimmermann, Thesis, Pennsylvania State University, 1970.
(79) J. C. Jochims, *Angew. Chem.*, **77**, 454 (1965).
(80) R. Stolle, E. Schick, F. Henke-Stark, and L. Krauss, *Ber.*, **62**, 1118 (1929).
(81) P. A. S. Smith and E. Leon, *J. Am. Chem. Soc.*, **80**, 4647 (1958).
(82) P. A. S. Smith and J. Vaughan, *J. Org. Chem.*, **23**, 1909 (1958).
(83) T. L. Gilchrist, G. E. Gymer, and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1 (1975).
(84) T. L. Gilchrist, C. W. Rees, and C. Thomas, *J. Chem. Soc., Perkin Trans. 1*, (1975).
(85) A. F. Hergarthy, J. B. Aylward, and F. L. Scott, *J. Chem. Soc. C*, 1967, 2587.
(86) A. F. Hergarthy, J. B. Aylward, and F. L. Scott, *Tetrahedron Lett.*, 1259 (1967).
(87) J. M. Burgess and M. S. Gibson, *Tetrahedron*, **18**, 1001 (1962).
(88) S. F. Acree, *Ber.*, **36**, 3154 (1903).
(89) T. Curtius, *Z. Angew. Chem.*, **27**, 111, 213 (1914).
(90) F. L. Scott and M. T. Scott, *J. Am. Chem. Soc.*, **79**, 6077 (1957).
(91) R. Stolle and M. Merkle, *J. Prakt. Chem.*, **227**, 275 (1928).
(92) R. Stolle, *Ber.*, **57**, 1063 (1924).
(93) R. Stolle, N. Nieland, and M. Merkle, *J. Prakt. Chem.*, **116**, 192 (1927).
(94) R. Stolle, N. Nieland, and M. Merkle, *J. Prakt. Chem.*, **117**, 185 (1928).
(95) I. Baiocchi, G. Corsi, and G. Palazzo, *Ann. Chim. (Rome)*, **55**, 116 (1965).
(96) G. Palazzo and G. Corsi, *Ann. Chim. (Rome)*, **55**, 126 (1965).
(97) N. Koga, G. Koga, and J.-P. Anselme, *Tetrahedron*, **28**, 4515 (1972).
(98) T. Kametani, K. Sota, and M. Shio, *J. Heterocycl. Chem.*, **7**, 807 (1970).
(99) T. Kametani, Shibuya, and M. Shio, *J. Heterocycl. Chem.*, **8**, 889 (1971).
(100) S. Patai, "The Chemistry of the Azido Group", W. Lwowski, Ed. Interscience, New York, N.Y., 1971, p 425 ff.
(101) R. F. Bleiholder and H. Schechter, *J. Am. Chem. Soc.*, **90**, 2131 (1968).
(102) R. Huisgen and H. Blaschke, *Chem. Ber.*, **98**, 2985 (1965).
(103) R. Huisgen and H. Blaschke, *Tetrahedron Lett.*, 1409 (1964).
(104) T. Bachetti, *Gazz. Chim. Ital.*, **91**, 866 (1961).
(105) R. Putner and K. Hafner, *Tetrahedron Lett.*, 3119 (1964).
(106) R. Huisgen and H. Blaschke, *Justus Liebigs Ann. Chem.*, **586**, 145 (1965).
(107) M. Bush, *Ber.*, **35**, 1562 (1902).
(108) H. Heine, *Angew. Chem.*, **74**, 712 (1962).
(109) R. Huisgen, J. Sauer, H. J. Sturm, and J. H. Markgraf, *Chem. Ber.*, **93**, 2106 (1960).
(110) R. Huisgen, *Angew. Chem.*, **72**, 359 (1960).
(111) W. Lwowski, and T. Maricich, *J. Am. Chem. Soc.*, **86**, 3164 (1964).
(112) A. Mishra, S. N. Rice, and W. Lwowski, *J. Org. Chem.*, **33**, 481 (1968).
(113) W. Reichen, *Tetrahedron Lett.*, 1433 (1978).
(114) C. J. Brown, *J. Chem. Soc.*, 2931 (1955).
(115) E. Lieber and R. L. Minnis, *Chem. Rev.*, **65**, 377 (1965).
(116) N. Koga and J.-P. Anselme, *J. Org. Chem.*, **33**, 3963 (1968).
(117) E. Fischer, *Justus Liebigs Ann. Chem.*, **190**, 175 (1878).
(118) R. Stahel, *Justus Liebigs Ann. Chem.*, **258**, 243 (1890).
(119) C. Hanna and F. W. Schneler, *J. Am. Chem. Soc.*, **73**, 4996 (1951).
(120) R. H. Poirier and F. Bennington, *J. Am. Chem. Soc.*, **74**, 3192 (1952).
(121) A. T. Balaban et al., *Tetrahedron*, **13**, 258 (1961).
(122) W. Lwowski, R. A. DeMauriac, R. A. Murray, and L. Lünow, *Tetrahedron Lett.*, 425 (1971); R. A. DeMauriac, Thesis, Yale University, 1966.
(123) W. Lwowski, R. A. DeMauriac, T. W. Mattingly, Jr., and E. Scheiffele, *Tetrahedron Lett.*, 3285 (1964).
(124) W. J. S. Lockley, V. T. Ramakrishnan, and W. Lwowski, *Tetrahedron Lett.*, 2621 (1974).
(125) W. Reichen, *Helv. Chim. Acta*, **59**, 2601 (1976).
(126) W. S. Wadsworth, Jr., and W. D. Emmons, *J. Org. Chem.*, **32**, 1279 (1967).
(127) W. Lwowski and R. A. DeMauriac, 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968, Abstract P-056.
(128) W. Lwowski and B. Walker, *J. Chem. Soc., Perkin Trans. 1*, 1975, 1309
(129) W. S. Wadsworth, Jr., and W. Bruxvoort, *J. Chem. Soc., Chem. Commun.*, 542 (1968).
(130) V. T. Ramakrishnan and W. Lwowski, *Tetrahedron Lett.*, 3249 (1974).
(131) W. Lwowski, private communication.
(132) T. S. Stevens, E. M. Creighton, A. B. Gordon, and M. McNiol, *J. Chem. Soc.*, 3193 (1928).
(133) S. Wawzonek and E. Yeakey, *J. Am. Chem. Soc.*, **82**, 5718 (1960).
(134) H. P. Benecke and J. H. Winkel, *Tetrahedron Lett.*, 3479 (1971).
(135) G. Pinner, *Ber.*, **21**, 1225 (1808).
(136) G. Heller, *Justus Liebigs Ann. Chem.*, **263**, 282 (1881).
(137) W. J. S. Lockley and W. Lwowski, *Tetrahedron Lett.*, 4263 (1974).
(138) W. Lwowski and W. Reichen, unpublished results.
(139) R. Huisgen, *J. Org. Chem.*, **33**, 2291 (1968).
(140) R. Huisgen, H. Seidl, and I. Brühning, *Chem. Ber.*, **102**, 1102 (1969).
(141) H. Weingarten, J. P. Chupp, and W. A. White, *J. Org. Chem.*, **32**, 3246 (1967).
(142) H. Breederveld, *Recl. Trav. Chim. Pays-Bas*, **79**, 401 (1960).
(143) J. P. Chupp and E. R. Weiss, *J. Org. Chem.*, **33**, 2357 (1968).
(144) G. H. Alt and J. P. Chupp, *Tetrahedron Lett.*, 3155 (1970).
(145) J. P. Chupp, *J. Heterocycl. Chem.*, **8**, 557 (1971).
(146) J. P. Chupp, U.S. Patent 3,723,455; *Chem. Abstr.*, **78**, 159 599j (1973).
(147) G. L'Abbe, *Chem. Rev.*, **69**, 347 (1969).
(148) A. L. Logothetis, *J. Am. Chem. Soc.*, **87**, 749 (1965).
(150) H. A. Staab and W. Benz, *Justus Liebigs Ann. Chem.*, **648**, 72 (1961).
(151) H. A. Staab and D. W. Müller, unpublished results.
(152) H. A. Staab and G. Walther, *Justus Liebigs Ann. Chem.*, **657**, 104 (1962).
(153) K. Seckinger, *Helv. Chim. Acta*, **56**, 2061 (1973).
(154) A. Holm, N. H. Toubro, and N. Harrit, *Tetrahedron Lett.*, 1909 (1976).
(155) R. M. Moriarty and R. Mukherjee, *Tetrahedron Lett.*, 4627 (1969).
(156) R. M. Moriarty, R. Mukherjee, O. L. Chapman, and D. R. Eckroth, *Tetrahedron Lett.*, 397 (1975).
(157) R. Mukherjee and R. M. Moriarty, *Tetrahedron*, **32**, 661 (1976).
(158) K. Ramakrishnan, J. B. Fulton, and J. Warkentin, *Tetrahedron*, **32**, 2685 (1976).
(159) S. L. Lee, A. M. Camerson, and J. Warkentin, *Can. J. Chem.*, **50**, 2326 (1972).

(160) P. R. West and J. Warkentin, *J. Org. Chem.*, **34,** 3233 (1969).
(161) P. C. Ip, K. Ramakrishnan, and J. Warkentin, *Can. J. Chem.*, **52,** 3671 (1974).
(162) A. F. McKay, D. L. Garmaise, G. Y. Paris, and S. Gelblum, *Can. J. Chem.*, **31,** 343 (1960).
(163) L. W. Jones and L. Neuffer, *J. Am. Chem. Soc.*, **39,** 652 (1917), and references cited therein.
(164) H. Staab and W. Benz, *Angew. Chem.*, **73,** 657 (1961).
(165) R. T. Major and R. J. Hedrick, *J. Org. Chem.*, **30,** 1268 (1965).
(166) See ref 123.
(167) R. S. Berry, D. Cornell, and W. Lwowski, *J. Am. Chem. Soc.*, **85,** 1200 (1963).
(168) M. Prince and C. M. Orlando, Jr., *J. Chem. Soc., Chem. Commun.*, 818 (1967).
(169) A. Haas and D. Y. Oh, *Chem. Ber.* **98,** 3353 (1965).
(170) A. Haas and D. Y. Oh, *Chem. Ber.*, **100,** 480 (1967).
(171) H. Bayreuther and A. Haas, *Chem. Ber.*, **104,** 2588 (1971).
(172) A. Haas and W. Klug, *Chem. Ber.* **101,** 2609 (1968).
(173) California Research Corp., F. Freedman, French Patent U 372911; *Chem. Abstr.*, **62,** 1366 (1965).
(174) Farbenfabrik Bayer, German Patent 1224720; *Chem. Abstr.*, **65,** 12112 (1966).
(175) A. Haas and H. Reinke, *Chem. Ber.* **102,** 2718 (1969).
(176) H. A. Staab and G. Walther, *Justus Liebigs Ann. Chem.*, **657,** 104 (1962).
(177) I. V. Podgornaya, N. N. Tayusheva, and I. Y. Postovskii, *Zh. Obshch. Khim.*, **34,** 2521 (1964).
(178) U. Anthoni, C. Larsen, and P. H. Nielsen, *Acta Chem. Scand.*, **20,** 1714 (1966).
(179) U. Anthoni, C. Larsen, and P. H. Nielson, *Acta Chem. Scand.*, **21,** 1201 (1967).
(180) R. S. McElhinney, J. Chem. Soc. C, 950 (1966).
(181) Z. El-Hewehi, E. Taeger, and F. Runge, *J. Prakt. Chem.*, **18,** 275 (1962).
(182) M. Delépine, *Bull. Soc. Chim. Fr.*, **27,** 587, 816 (1902).
(183) M. Delépine and P. Schving, *Bull. Soc. Chim. Fr.*, **7,** 896 (1910).
(184) P. Aubert, E. B. Knott, and L. A. Williams, *J. Chem. Soc.*, 2188 (1951).
(185) E. B. Knott, *J. Chem. Soc.*, 1644 (1956).
(186) U. Anthoni, C. Larsen, and P. Nielsen, *Acta Chem. Scand.*, **21,** 2061 (1967).
(187) U. Anthoni, C. Larsen, and P. Nielsen, *Acta Chem. Scand.*, **22,** 309 (1968).
(188) U. Anthoni, C. Larsen, and P. Nielsen, *Acta Chem. Scand.*, **22,** 1898 (1968).
(189) U. Anthoni, C. Larsen, and P. Nielsen, *Acta Chem. Scand.*, **21,** 2580 (1967).
(190) U. Anthoni, C. Larsen, and P. Nielsen, *Acta Chem. Scand.*, **21,** 2571 (1967).