RECENT ADVANCES IN ISOCYANATE CHEMISTRY

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Contents

- I. Introduction 457
- II. Synthetic Methods 457
  - A. Phosgenation of Amines 457
  - B. Amides with Oxalyl Chloride 460
  - C. Amines with Oxalyl Chloride 460
  - D. Olefins with Isocyanic Acid 460
  - E. Olefins with Iodo Isocyanate 461
  - F. Carbonyl Compounds with Isocyanic Acid 462
  - G. Halides with Isocyanic Acid 462
  - H. Organometal Oxides with Isocyanic Acid or Urea 462
  - I. Acid Anhydrides with Isocyanic Acid 462
  - J. Chlorides with Alkali Cyanates 463
  - K. Nitro Compounds with Carbon Monoxide 463
  - L. Oxidation of Isocyanides 464
  - M. Dissociation of an Isocyanate Adduct 464
  - N. Curtius Rearrangement 465
  - O. Thermolysis of Nitrile Sulfites and Carbonates 465
  - P. Rearrangement of β-Lactams 466
  - Q. Thermal Decomposition of 1,2-Diazetidinones 466
  - R. Electrolysis of Cyanates 466
  - S. Reactions of Amines with Diethylthiocarbamoyl Chloride 466
  - T. Pyrolysis of Isocyanurates 466
  - U. Sulfinylamines with Phosgene 466
  - V. Lossen Rearrangement (and Modifications) 466
  - W. Other Recent Methods 467
  - X. Synthesis of Certain Isocyanates 467
- III. New Reactions of Isocyanates 469
  - A. Addition Reactions of Isocyanates 469
  - B. Addition Reactions to Double Bonds 474
  - C. Polymerizations and Copolymerizations of Isocyanates 476
  - D. Ring Formation Reactions 478
  - E. Insertion Reactions 484
  - F. Deoxy Reactions 485
  - G. Carbodiimide Formation Reactions 486
  - H. Reactions with Cyclic Compounds 486
  - I. Reactions with Hydrogen Peroxide and Olefins 486
  - J. Reaction with *N*-Hydroxy Ureas 487
- IV. Reactions of Certain Isocyanates 487
  - A. Reactions of Isocyanic Acid 487
  - B. Reactions of Acyl Isocyanates 491
  - C. Sulfonyl Isocyanates 493
- V. Conclusion 495

I. Introduction

This review covers the new contributions to the chemistry of isocyanates which have been reported in recent years. An isocyanate was first made[1] in 1849 by the double decomposition of a dialkyl sulfate with potassium cyanate. Significant progress was slow until the discovery of polyurethanes in 1937. Innumerable reports including patents, reviews,[2–4] and one book[5] were published on the work before 1960. Since 1960, many isocyanates have been investigated. Sulfonyl,[6,7] chlorosulfonyl,[8] phosphorus,[9] and acyl isocyanates[10–11] have been reviewed, and a new book[12] on polyurethanes has been published. A review[13] in Japanese, "Recent Advances in Isocyanate Chemistry," covered the literature published from 1960 to April 1969; it is now offered in English translation and enlarged to cover the literature to Sept 1971 as it is found in primary journals, *Chemical Titles*, and *Chemical Abstracts*.

II. Synthetic Methods

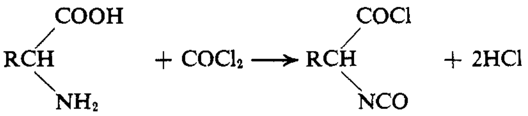
There are more than 25 methods for the preparation of isocyanates. Phosgenation of an amine or its salt is one of great importance. Even though more economical methods may have appeared, *e.g.*, the reaction of a nitro compound with carbon monoxide and the reaction of isocyanic acid with an olefin, none have replaced the amine–phosgene reaction.

A. PHOSGENATION OF AMINES

$$RNH_2 + COCl_2 \longrightarrow RNCO + 2HCl$$

This popular synthesis has been adapted to technical manufacturing methods. The following applications have been developed.

1. 2-Isocyanatoacyl Chlorides (1)



$$\mathrm{RCH}\begin{matrix}\nearrow \mathrm{COOH}\\ \searrow \mathrm{NH_2}\end{matrix} + \mathrm{COCl_2} \longrightarrow \mathrm{RCH}\begin{matrix}\nearrow \mathrm{COCl}\\ \searrow \mathrm{NCO}\end{matrix} + 2\mathrm{HCl}$$

1

The reaction of an amino acid, *e.g.*, glycine and alanine, with phosgene gives a 2-isocyanatoacyl chloride[14] (**1**). By a similar reaction, ω-isocyanatoalkanecarboxylic acid chlorides and isocyanatobenzoyl chloride have been prepared.[15] The

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(1) A. Wurtz, *Justus Liebigs Ann. Chem.*, **71**, 326 (1849).

(2) J. H. Saunders and R. J. Slocombe, *Chem. Rev.*, **43**, 203 (1948).

(3) R. J. Arnold, J. A. Nelson, and J. J. Verbanc, *ibid.*, **57**, 47 (1957).

(4) T. Mukaiyama, *Yuki Gosei Kagaku Kyokai Shi*, **19**, 775 (1961).

(5) J. H. Saunders and K. C. Frisch, "Polyurethanes, Chemistry and Technology. Part I. Chemistry," Interscience, New York, N. Y., 1962.

(6) H. Ulrich, *Chem. Rev.*, **65**, 369 (1965).

(7) N. Onodera, *Kagaku (Kyoto)*, **19**, 1240 (1964).

(8) R. Graf, *Angew. Chem., Int. Ed. Engl.*, **7**, 172 (1968).

(9) G. I. Derkatsch, *ibid.*, **8**, 421 (1969).

(10) O. Tsuge, *Kagaku To Kogyo (Tokyo)*, **22**, 770 (1969).

(11) K. A. Nuridzhanyan, *Usp. Khim.*, **39**, 259 (1970).

(12) R. Vieweg and A. Hochtlen, "Kunststoff Handbuch. Band VII. Polyurethane," Carl Hanser Verlag, München, 1966.

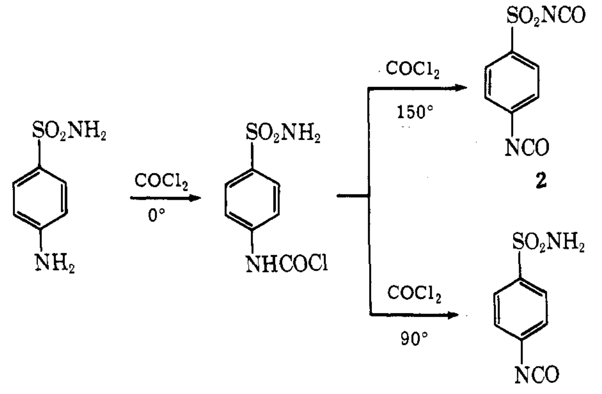
(13) S. Ozaki, *Yuki Gosei Kagaku Kyokai Shi*, **28**, 17 (1970).

(14) Y. Iwakura and K. Uno, *J. Org. Chem.*, **30**, 1158 (1965).

(15) Y. Iwakura, K. Uno, and S. Kang, *ibid.*, **31**, 142 (1966).

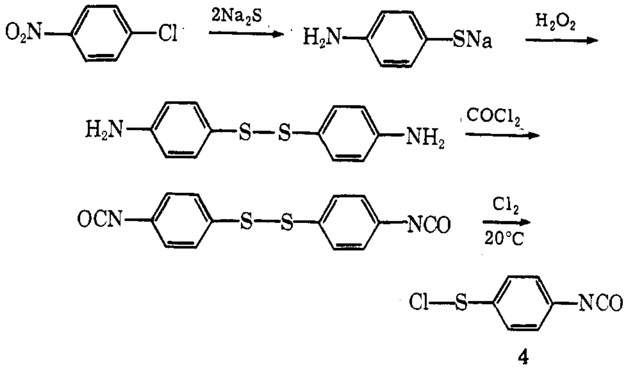
preparation of polyamidourethanes[16] and polyester urethanes[17] from these isocyanates has been reported.

2. *Isocyanatobenzenesulfonyl Isocyanates* (**2** *and* **3**)[18]



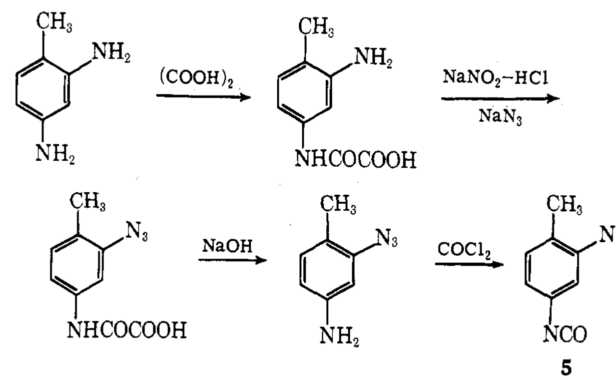
Starting with *p*-aminobenzenesulfonamide, **2** and **3** have been obtained.

3. *4-Isocyanatobenzenesulfenyl Chloride* (**4**)[19,20]



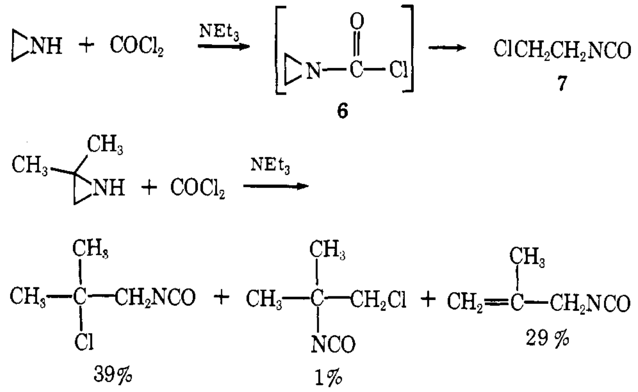
The isocyanate **4** has been produced from the related disulfide and chlorine.

4. *2-Azidotolyl Isocyanate* (**5**)[19,20]



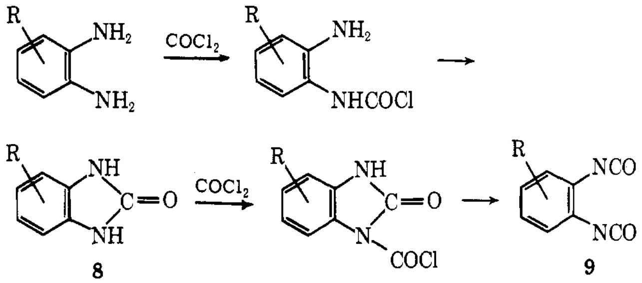
The azido function is not destroyed in transforming the amino group into an isocyanato group by phosgene.

5. *2-Chloroethyl Isocyanate* (**7**)[21]



The reaction between an aziridine and phosgene in the presence of triethylamine gives 1-(aziridino)carbonyl chloride (**6**), which rearranges into 2-chloroethyl isocyanate (**7**). Substituted aziridines react similarly.[22]

6. *Aromatic Ortho Diisocyanates* (**9**)

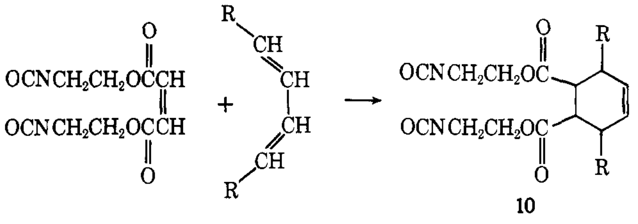


The phosgenation of an ortho diaminoarene gives benzimidazolones (**8**), but prolonged phosgenation of an *o*-tolylenediamine at elevated temperature afforded the corresponding *o*-tolylene diisocyanate (**9**).[23]

7. *Phosgenation of a Urea*

The mechanism for the formation of an isocyanate from phosgene and a urea has been studied;[24] *cf.*, **8** → **9**.

8. *β-Isocyanatoethyl Esters*[25]



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(16) K. Hayashi and Y. Iwakura, *Makromol. Chem.*, **90**, 198 (1966).

(17) Y. Iwakura, K. Hayashi, S. Kang, and K. Inagaki, *ibid.*, **95**, 205 (1966).

(18) J. Smith, Jr., T. K. Brotherton, and J. W. Lynn, *J. Org. Chem.*, **30**, 1260 (1965).

(19) H. Holtschmidt, *Makromol. Chem.*, **101**, 271 (1967).

(20) G. Oertel and H. Holtschmidt, *Polym. Prepr., Amer. Chem. Soc., Div. Polym. Chem.*, **9**, 1520 (1968).

(21) D. A. Tomalia, *J. Heterocycl. Chem.*, **4**, 178 (1967).

(22) C. K. Johnson, *J. Org. Chem.*, **32**, 1508 (1967).

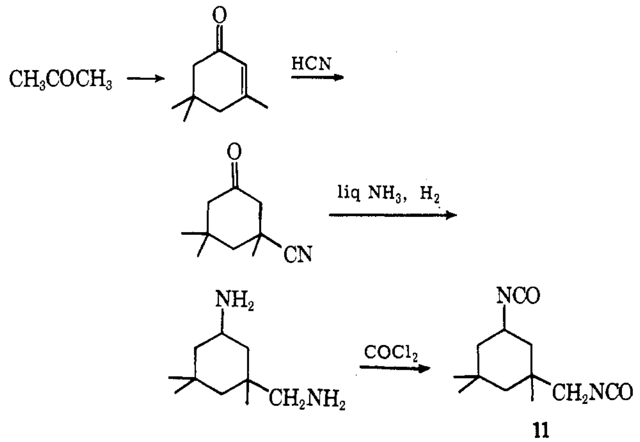
(23) W. J. Schnabel and E. Kober, *ibid.*, **34**, 1162 (1969).

(24) A. A. R. Sayigh, N. J. Jilley, and H. Ulrich, *ibid.*, **29**, 3344 (1964); **31**, 2658 (1966).

(25) Union Carbide Corp., Japanese Patent 41-1854 (1966); U. S. Patent 256496 (1963); U. S. Patent 212480 (1962).

From ethanolamine, maleic anhydride, and a diene, diisocyanate **10** may be prepared.

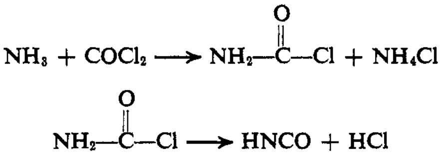
9. 3-Isocyanatomethyl-3,5,5-trimethylcyclohexyl Isocyanate (11)



11

In Scholven-Chemie, **11** is technically obtained from acetone.[26] It is used in the manufacture of nonyellowing polyurethanes.

10. Isocyanic Acid[27]



$$\mathrm{NH_3 + COCl_2 \longrightarrow NH_2{-}\overset{O}{\overset{\|}{C}}{-}Cl + NH_4Cl}$$

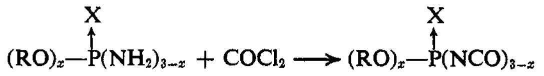
$$\mathrm{NH_2{-}\overset{O}{\overset{\|}{C}}{-}Cl \longrightarrow HNCO + HCl}$$

1,2-Dimethoxyethane is a good solvent for the dehydrochlorination of carbamoyl chloride, an assumed intermediate in the reaction between ammonia and phosgene, and it stabilizes isocyanic acid by forming a complex with it.

11. Miscellaneous Isocyanates

The treatment of a primary amino function with phosgene has been extended to various types of molecules:

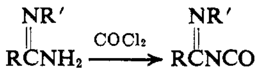
Phosphoryl isocyanates (**12**) and thiophosphoryl isocyanates (**13**)[28]



$$\mathrm{(RO)_x{-}\overset{X}{\overset{\uparrow}{P}}(NH_2)_{3-x} + COCl_2 \longrightarrow (RO)_x{-}\overset{X}{\overset{\uparrow}{P}}(NCO)_{3-x}}$$

12, X = O
13, X = S

Iminoacyl isocyanates (**14**)[29]

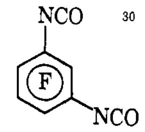


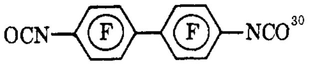
$$\mathrm{R\overset{NR'}{\overset{\|}{C}}NH_2 \xrightarrow{COCl_2} R\overset{NR'}{\overset{\|}{C}}NCO}$$

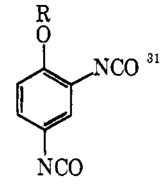
14

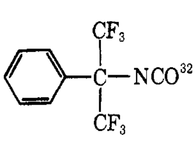
Fluoroaryl isocyanates

$OCN(CF_2)_3NCO$[30] $OCNCO(CF_2)_3CONCO$[30]



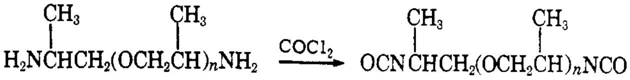






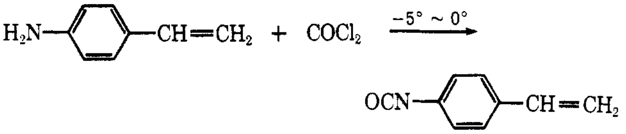
(R = perfluoroalkyl)

Isocyanato derivatives of aliphatic ethers[33]

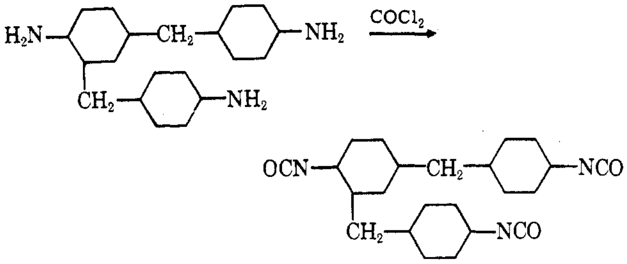


$$\mathrm{H_2N\overset{CH_3}{\overset{|}{C}}HCH_2(OCH_2\overset{CH_3}{\overset{|}{C}}H)_nNH_2 \xrightarrow{COCl_2} OCN\overset{CH_3}{\overset{|}{C}}HCH_2(OCH_2\overset{CH_3}{\overset{|}{C}}H)_nNCO}$$

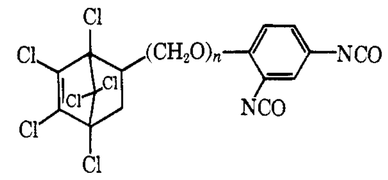
p-Styryl isocyanate[34]



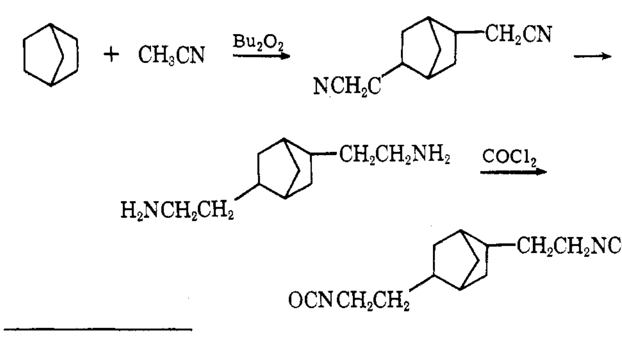
2,4-Bis(4-isocyanatocyclohexylmethyl)cyclohexyl isocyanate[35]



Hexahalobicyclo diisocyanatophenyl ethers[36]



Norbornane diisocyanate[37]



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(26) Scholven-Chemie, British Patent 1036980 (1966); *Chem. Abstr.*, **65**, 17933d (1965).

(27) Stauffer Chemical Co., Japanese Patent 42-2225 (1967).

(28) Union Carbide Corp., U. S. Patent 3470271 (1969).

(29) L. I. Samarai, V. A. Bondar, and G. I. Derkach, *Zh. Org. Khim.*, **5**, 119 (1969).

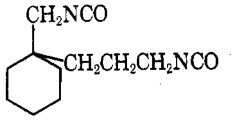
(30) F. D. Trischler and J. Hollander, *J. Polym. Sci., Part A-1*, **5**, 2343 (1967); *Polym. Prepr. Amer. Chem. Soc., Div. Polym. Chem.*, **8**, 1149 (1967).

(31) B. F. Malichenko and A. V. Yaslovitskii, USSR Patent 241428 (1969); *Chem. Abstr.*, **71**, 80913d (1969).

(32) E. I. du Pont de Nemours & Co., U. S. Patent 3468924 (1969); *Chem. Abstr.*, **71**, 112604x (1969).

(33) Mitsui Toatsu Chemicals, Japanese Patent 44-27365 (1969); *Chem. Abstr.*, **72**, 31220n (1970).

Isocyanatomethyl(3-isocyanatopropyl)cyclohexane (15), 2-isocyanatomethyl-2-(3-isocyanatopropyl)-bicyclo[2.2.1]heptane (16)[38]



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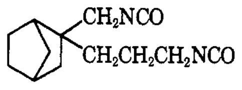

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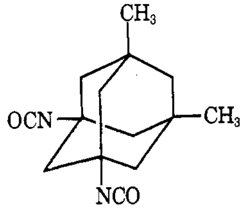
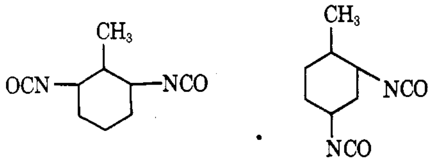
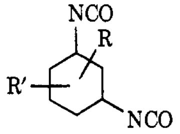
1,3-Diisocyanato-5,7-dimethyladamantane[39,40]



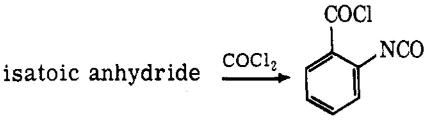
2,4- and 2,6-Hexahydrotoluene diisocyanate[41]



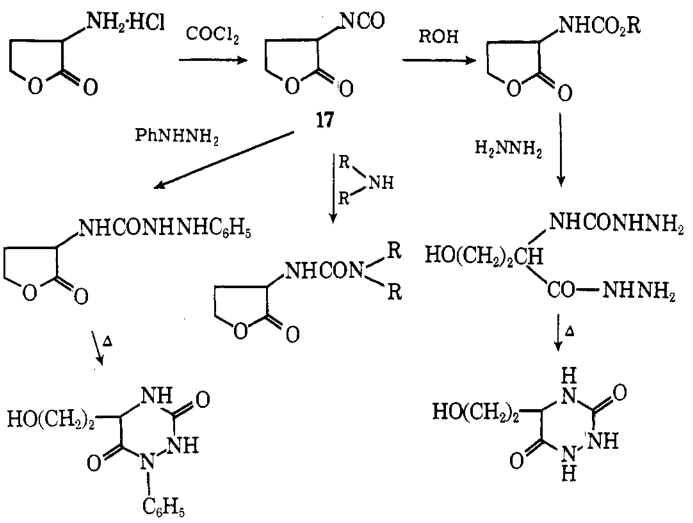
1,3-Diisocyanatocyclohexane[42,43]



o-Isocyanatobenzoyl chloride[44]



α-Isocyanato-γ-butyrolactone (17)[45]



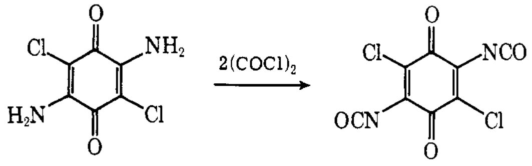
α-Isocyanato-γ-butyrolactone (**17**) was obtained by the phosgenation of α-amino-γ-butyrolactone. With alcohols, amines, and phenylhydrazine, **17** gives corresponding urethanes, ureas, and semicarbazides.

B. AMIDES WITH OXALYL CHLORIDE

$$RCONH_2 + (COCl)_2 \longrightarrow RCONCO$$

Speziale, *et al.*,[46,47] and Goerdeler, *et al.*,[48–50] independently found preparations of acyl or thioacyl isocyanates in high yields by the reaction of amides with oxalyl chloride. Trichloroacetamide and oxalyl chloride gave trichloroacetyl isocyanate.[51] Terephthalamide and dialkyl phosphoramidates react similarly with oxalyl chloride.[52]

C. AMINES WITH OXALYL CHLORIDE



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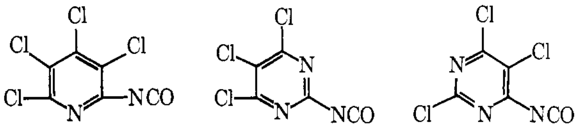
Isocyanatoquinones, such as 2,5-dichloro-3,6-diisocyanato-1,4-benzoquinone (**18**), were obtained by the reactions of corresponding amines with oxalyl chloride.[53] Pyridine, pyrimidine and pyrazine derivatives with an isocyanato substituent vicinal to nitrogen,[54] and isocyanato-*s*-triazines (**19**)[55] have also been prepared.



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(34) V. G. Sinyavskii and V. F. Kovalova, *Zh. Org. Khim.*, **5**, 1888 (1969); *Chem. Abstr.* **72**, 21454o (1970).

(35) E. I. du Pont de Nemours & Co., German Patent 1932832 (1970); *Chem. Abstr.*, **72**, 89891y (1970).

(36) Velsicol Chemical Corp., U. S. Patent 3509199 (1970); *Chem. Abstr.*, **73**, 3652g (1970).

(37) Union Carbide Corp., U. S. Patent 3492330 (1970); *Chem. Abstr.*, **72**, 101631y (1970).

(38) National Distillers, German Patent 1814303 (1969); *Chem. Abstr.*, **71**, 82093k (1969).

(39) Sun Oil Co., French Patent 1541359 (1968); *Chem. Abstr.*, **71**, 13799h (1969).

(40) Sun Oil Co., Netherlands Patent 6809872 (1969).

(41) Mobay Chemical Co., U. S. Patent 3351650 (1967).

(42) Wyandotte Chemicals Corp., German Patent 2005297 (1970); *Chem. Abstr.*, **73**, 98475p (1970).

(43) Wyandotte Chemicals Corp., Netherlands Patent 7001474 (1970).

(44) Upjohn Co., U. S. Patent 3531509 (1970).

(45) U. Kraatz, H. Wamhoff, and F. Korte, *Justus Liebig Ann. Chem.*, **744**, 33 (1971).

(46) A. J. Speziale and L. R. Smith, *J. Org. Chem.*, **27**, 4361 (1962).

(47) A. J. Speziale and L. R. Smith, *ibid.*, **28**, 1805 (1963).

(48) J. Goerdeler and H. Schenk, *Angew. Chem.*, **75**, 675 (1963).

(49) J. Goerdeler and H. Schenk, *Chem. Ber.*, **98**, 2954 (1965).

(50) J. Goerdeler and K. Jones, *ibid.*, **99**, 3572 (1966).

(51) L. I. Samaray, USSR Patent 210140 (1965).

(52) L. I. Samaray and G. I. Derkatsch, *Zh. Obshch. Khim.*, **35**, 755 (1965); **36**, 1433 (1966).

(53) U. von Gizychi, *Angew. Chem., Int. Ed. Engl.*, **10**, 403 (1971).

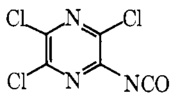
(54) U. von Gizychi, *ibid.*, **10**, 402 (1971).

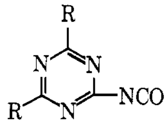
(55) U. von Gizychi, *ibid.*, **10**, 403 (1971).

Table I

Synthesis of Isocyanates from Olefins and Isocyanic Acid

Olefins	*Isocyanate*	*Yields, %*
$(CH_3)_2C{=}CH_2$	$(CH_3)_3CNCO$	10
$C_6H_5C(CH_3){=}CH_2$	$C_6H_5C(CH_3)_2NCO$	41
$C_6H_5CH{=}CH_2$	$C_6H_5C(CH_3)HNCO$	5
$C_6H_4(C(CH_3){=}CH_2)_2$-(m)	$CH_2{=}C(CH_3)C_6H_4C(CH_3)_2NCO$	30
	$OCNC(CH_3)_2C_6H_4C(CH_3)_2NCO$	35
$C_2H_5OCH{=}CH_2$	$C_2H_5OC(CH_3)HNCO$	50
$C_4H_9OCH{=}CH_2$	$C_4H_9OC(CH_3)HNCO$	64
$C_6H_5OCH{=}CH_2$	$C_6H_5OC(CH_3)HNCO$	80





19, R = Cl, F, CCl_3

D. OLEFINS WITH ISOCYANIC ACID

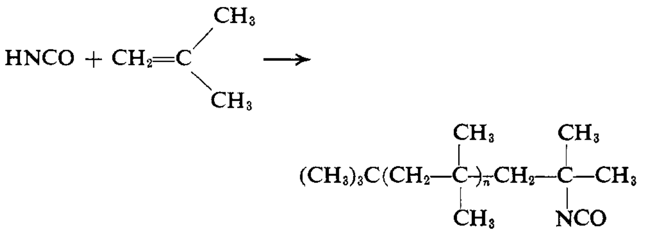
In general an olefin reacts with isocyanic acid with difficulty, but certain olefins with electron-releasing substituents react readily. These include vinyl ethers,[56,57] isobutylene, α-methylstyrene,[58,59] and other olefins which are also polymerized by cationic catalysts (Table I).

In our hands the reaction of ethylene, propylene, butene-1, or butadiene with isocyanic acid at 200–600° in the gas phase in the presence of a catalyst such as H_3PO_4, polyphosphoric acid, $PdCl_2$, $ZnCl_2$, or Pd, on supports such as Cellite, silica, or silica–alumina, gave isocyanates in trace amounts. Ethyl isocyanate was detected by gas chromatography.[60]

Thermodynamic calculations[61] supported an equilibrium conversion of 1.6% at 300° and a pressure of 100 kg/cm², 0.23% at 400° and a pressure of 100 kg/cm², and 50% conversion at 400° and a pressure of 62,500 kg/cm², for the reaction between ethylene and isocyanic acid.

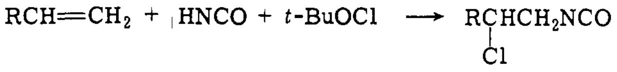
$$CH_2{=}CH_2 + HNCO \rightleftharpoons CH_3CH_2NCO$$

Apparently bulky alkyl substituents in the olefin favor isocyanate formation (Table I). There is a patent[62] for the preparation of hexadecyl isocyanate, but a yield is not given. Telomeric isocyanates[63] are prepared by cationic reaction of olefins such as isobutylene, with isocyanic acid at <20° in the presence of Lewis acids.

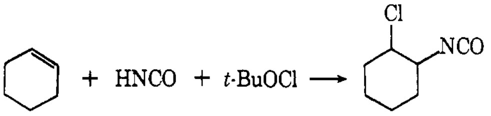


$$HNCO + CH_2{=}C(CH_3)_2 \longrightarrow (CH_3)_3C(CH_2-\underset{CH_3}{\overset{CH_3}{C}})_n-CH_2-\underset{NCO}{\overset{CH_3}{C}}-CH_3$$

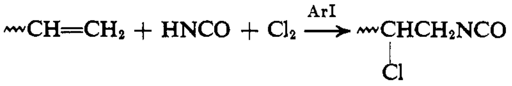
The reaction of olefins with isocyanic acid in the presence of a *tert*-butyl hypohalite gives β-halo isocyanates.[64,65]



$$RCH{=}CH_2 + HNCO + t\text{-}BuOCl \longrightarrow R\underset{Cl}{C}HCH_2NCO$$

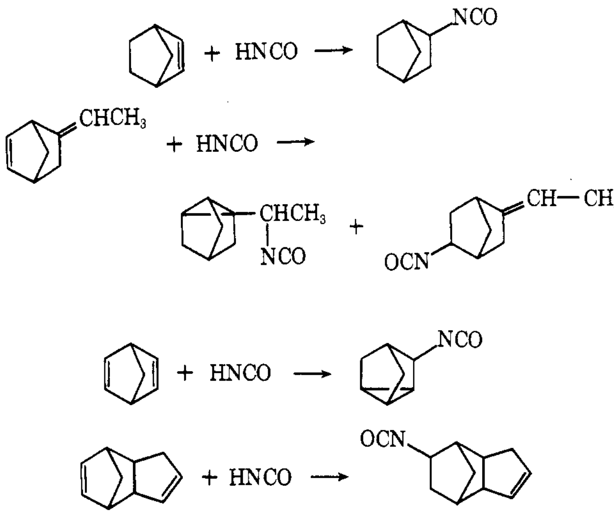


β-Chloro isocyanates are obtained by the reaction of olefins, isocyanic acid, and chlorine in the presence of an iodoaryl compound.[66]

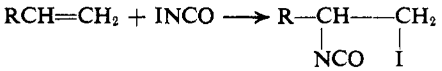


$$\sim CH{=}CH_2 + HNCO + Cl_2 \xrightarrow{ArI} \sim\underset{Cl}{C}HCH_2NCO$$

Certain bicyclic olefins such as 2-norbornene, 2-ethylidenenorbornene, norbornadiene, and dicyclopentadiene react with isocyanic acid to give the corresponding isocyanates.[67]



E. OLEFINS WITH IODO ISOCYANATE



$$RCH{=}CH_2 + INCO \longrightarrow R-\underset{NCO}{CH}-\underset{I}{CH_2}$$

The addition of iodo isocyanate to many olefins proceeds smoothly at room temperature.[68,69] It is useful for converting an olefin into an isocyanate, carbamate, or aziridine, and its success in reacting with steroid olefins is significant. Iodo isocyanate adds to polyisoprene, and each unit in the polymeric adduct may be converted into a methyl carbamate, aziridine urea, oxazolidone, and oxazole[70] (Scheme I).

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(56) F. W. Hoover and H. S. Rothrock, *J. Org. Chem.*, **28**, 2082 (1963).

(57) J. L. McClanahan, *Chem. Ind. (London)*, 1280 (1965).

(58) F. W. Hoover and H. S. Rothrock, *J. Org. Chem.*, **29**, 143 (1964).

(59) E. I. du Pont de Nemours & Co., Japanese Patent 38-8967; British Patent 991110; *Chem. Abstr.*, **63**, 5864h (1965).

(60) S. Ozaki, unpublished work.

(61) S. Ozaki, unpublished work.

(62) E. I. du Pont de Nemours & Co., U. S. Patent 3471542 (1969); *Chem. Abstr.*, **71**, 123533z (1969).

(63) Instytut Tworzyw Sztucznych, German Offen. 1944343 (1970).

(64) W. R. Grace & Co., U. S. Patent 3483175 (1968); *Chem. Abstr.*, **72**, 56770e (1970).

(65) W. R. Grace & Co., U. S. Patent 3483243 (1968); *Chem. Abstr.*, **66**, 28446m (1967).

(66) W. R. Grace & Co., U. S. Patent 3574694 (1971).

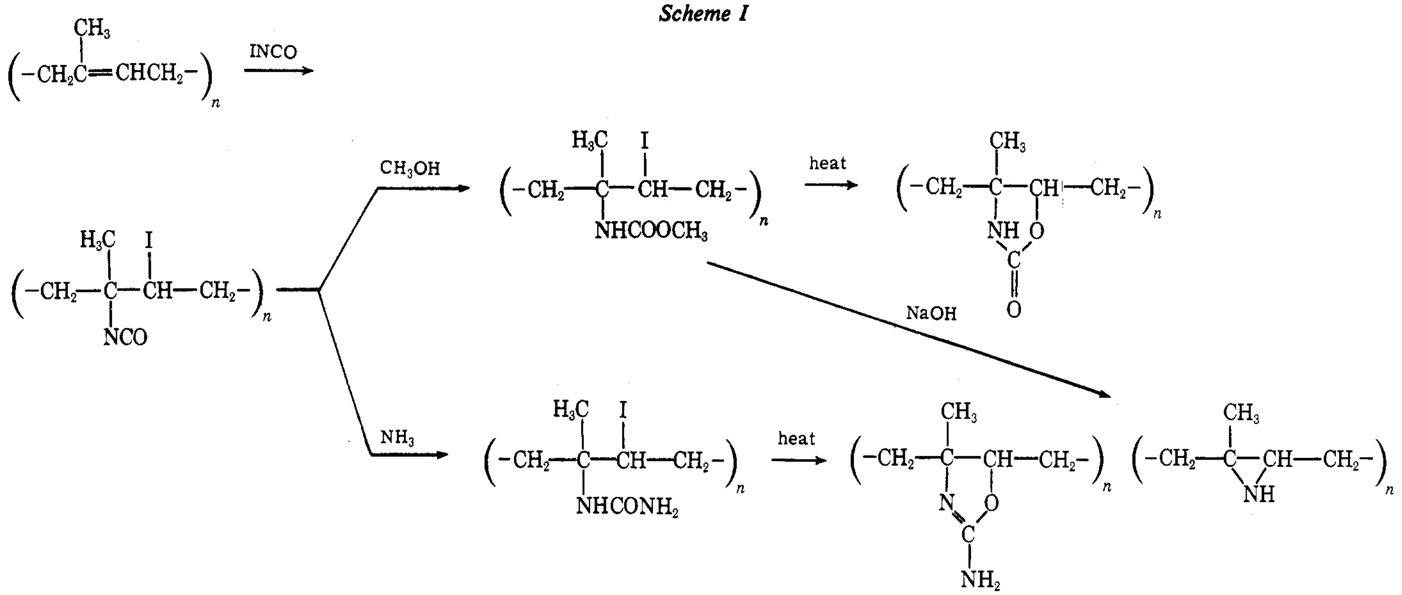
(67) S. Ozaki, unpublished work.

(68) A. Hassner and C. Heathrock, *J. Org. Chem.*, **30**, 1748 (1965); **32**, 540 (1967).

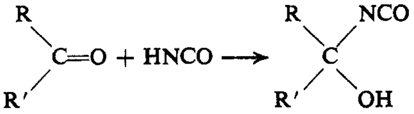
(69) A. Hassner, *Angew. Chem.*, **77**, 355 (1965).

(70) C. G. Gebelein, *J. Macromol. Sci., Chem.*, **5**, 433 (1971).

Scheme I

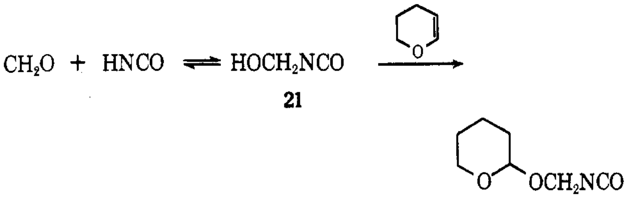


F. CARBONYL COMPOUNDS WITH ISOCYANIC ACID[71]



20

This addition proceeds readily at lower temperatures and gives isocyanatohydrins (**20**). For example, formaldehyde and isocyanic acid react at −78° to give hydroxymethyl isocyanate (**21**) which may be isolated as an adduct, **22**, with an unsaturated ether.



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22

G. HALIDES WITH ISOCYANIC ACID

$$\mathrm{RCOCl + HNCO \longrightarrow RCONCO}$$

$\mathrm{R} = n\text{-}\mathrm{C_{17}H_{35}}$, 87%
$\mathrm{R} = \mathrm{OCNCO(CH_2)_8}$–, 90%

$$\mathrm{Cl(CH_2)_6Cl + HNCO \xrightarrow[\text{NiO}]{100\text{–}150^\circ} OCN(CH_2)_6NCO}$$

Acyl chlorides react with isocyanic acid at −10° in the presence of pyridine to give acyl isocyanates.[72,73] Alkyl isocyanates are obtained in a similar reaction under more rigorous conditions.[74]

Chlorosilanes and isocyanic acid react from −10° to room temperature to give isocyanatosilanes.[72] In a similar way chlorine attached to phosphorus may be displaced.[72,75]

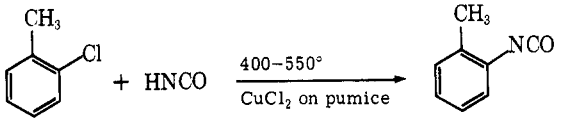
Starting materials	Isocyanato-silanes	Yields, %
$\mathrm{SiCl_4}$	$\mathrm{Si(NCO)_4}$	60
$\mathrm{(CH_3)_2SiCl_2}$	$\mathrm{(CH_3)_2Si(NCO)_2}$	58
$\mathrm{(CH_3)_3SiCl}$	$\mathrm{(CH_3)_3SiNCO}$	57

$$\mathrm{RPCl_2 + HNCO \xrightarrow[\text{pyridine}]{} RP(NCO)_2}$$

R	Yields, %
$\mathrm{CH_3}$	64.3
$\mathrm{C_2H_5}$	51.5
$\mathrm{C_6H_5}$	61.0

$$\mathrm{PCl_3 + HNCO \xrightarrow[\text{bases}]{-74^\circ} P(NCO)_3}$$

Our attempts to reproduce the patent claim[76] for an interaction between an aryl chloride and isocyanic acid were unsuccessful.



H. ORGANOMETAL OXIDES WITH ISOCYANIC ACID OR UREA[77]

$$\mathrm{(R_3Sn)_2O + 2HNCO \xrightarrow{70\text{–}80^\circ} 2R_3SnNCO + H_2O}$$

$$\mathrm{(R_3Sn)_2O + 2H_2NCONH_2 \xrightarrow{130^\circ} 2R_3SnNCO + 2NH_3 + H_2O}$$

Organotin, -antimony, and -arsenic isocyanates were prepared by the reaction of oxides with isocyanic acid or urea. The organotin isocyanate was stable enough to be isolated.

I. ACID ANHYDRIDES WITH ISOCYANIC ACID[78]

Perfluoroacyl isocyanates (**23**) were prepared from perfluorinated carboxylic acid anhydrides and isocyanic acid.

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(71) F. W. Hoover, H. B. Stevenson, and H. S. Rothrock, *J. Org. Chem.*, **28**, 1825 (1963).

(72) P. R. Steyermark, *ibid.*, **28**, 586 (1963).

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(74) Mobay Chemical Co., Canadian Patent 805181 (1969).

(75) Olin Mathieson Chemical Corp., Japanese Patent 39-11359 (1964).

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(77) W. Stamm, *J. Org. Chem.*, **30**, 693 (1965).

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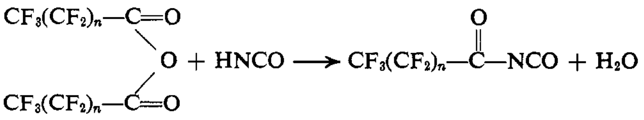


23

J. CHLORIDES WITH ALKALI CYANATES

In aprotic polar solvents, such as dimethylformamide, an isocyanate produced by the reaction between an alkyl chloride and an alkali cyanate trimerizes so readily that the isocyanate is isolated with difficulty.

In a mixture of xylene and dimethylformamide, methoxymethyl chloride gave methoxymethyl isocyanate.[79,80]

$$CH_3OCH_2Cl + NaOCN \longrightarrow CH_3OCH_2NCO + NaCl$$

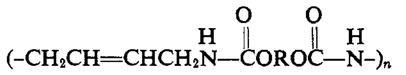
Patents[81,82] have reported that tetramethylene diisocyanate was synthesized but not isolated from 1,4-dichlorobutane and sodium cyanate. Other patents claim that an alkyl isocyanate[83] from an alkyl bromide, methylene diisocyanate[84] from methylene dibromide, allyl isocyanate[85] from allyl chloride, an α,β-alkenyl isocyanate[86] from the corresponding alkenyl chloride, and 2-butenyl isocyanate from crotyl bromide[87] have been similarly obtained.

$$BrCH_2Br + KOCN \longrightarrow OCNCH_2NCO$$

Isocyanurates are sometimes easier to isolate than isocyanates.[88] If the reaction is carried out in alcohol, carbamates[89-92] may be obtained.

Polyurethanes (**24**) have been obtained by treating 1,4-dichloro-2-butene with sodium cyanate in glycol.[93,94]

$$ClCH_2CH{=}CHCH_2Cl + NaOCN + HOROH \longrightarrow$$



$$(-CH_2CH{=}CHCH_2\overset{H}{N}-\overset{O}{\overset{\|}{C}}OR O\overset{O}{\overset{\|}{C}}-\overset{H}{N}-)_n$$

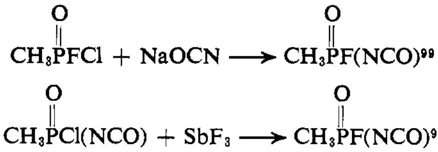
24

Halides of phosphorus, sulfur, silicon, and germanium give similar reactions with cyanates.

$$PCl_3 + NaOCN \xrightarrow{\text{in liq } SO_2} P(NCO)_3$$ [95]

$$PhPCl_2 + NaOCN \longrightarrow PhP(NCO)_2$$ [96]

$$PhPCl_2 + NaOCN \longrightarrow PhPCl(NCO)$$ [97,98]



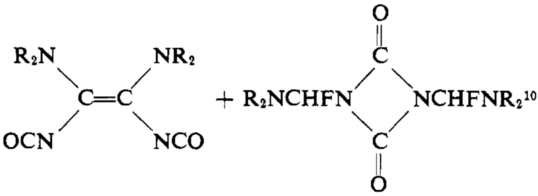
$$CH_3\overset{O}{\overset{\|}{P}}FCl + NaOCN \longrightarrow CH_3\overset{O}{\overset{\|}{P}}F(NCO)$$ [99]

$$CH_3\overset{O}{\overset{\|}{P}}Cl(NCO) + SbF_3 \longrightarrow CH_3\overset{O}{\overset{\|}{P}}F(NCO)$$ [99]

$$PCl_5 + HCHO \longrightarrow P(OCH_2Cl)_3 \xrightarrow{AgOCN} P(OCH_2NCO)_3$$ [100]

$$SiCl_4 + HCHO \longrightarrow Si(OCH_2Cl)_3 \xrightarrow{AgOCN} Si(OCH_2NCO)_4$$ [100]

$$HF_2CNR_2 + KOCN \longrightarrow$$



$$RSO_2Cl + NaOCN \longrightarrow RSO_2NCO$$ [102]

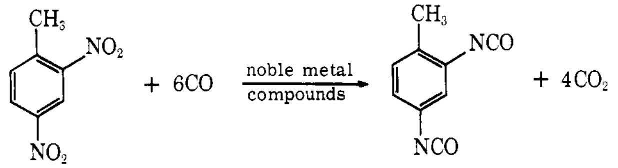
$$SnCl_4 + NaOCN \longrightarrow Sn(NCO)_4$$ [77]

$$p\text{-}CH_3C_6H_4SOCl + AgNCO \longrightarrow p\text{-}CH_3C_6H_4SONCO$$ [103]

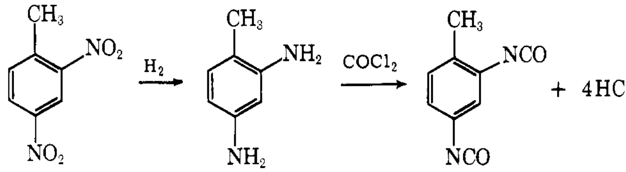
$$CH_2{=}CHC(CH_3)HBr + AgOCN \longrightarrow CH_2{=}CHC(CH_3)HNCO$$ [104]

$$GeH_3I + AgOCN \longrightarrow GeH_3NCO$$ [105]

K. NITRO COMPOUNDS WITH CARBON MONOXIDE



A nitro compound and carbon monoxide give an isocyanate in one step. In contrast, the present technical process for the production of tolylene diisocyanate is a two-step process



which employs carbonyl chloride, a hazardous reagent. The former method may become a major process for the production of tolylene diisocyanate in few years. An 18% reduction

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(79) G. Oertel and H. Holtschmidt, *Polym. Prepr., Amer. Chem. Soc., Div. Polym. Chem.*, **9**, 1520 (1968).

(80) Farbenfabriken Bayer A.-G., German Patent 1205087; *Chem. Abstr.*, **64**, 19413g (1966).

(81) G. M. Himel and L. M. Richards (Ethyl Corp.), U. S. Patent 2866801 (1958).

(82) B. Gramam (Ethyl Corp.), U. S. Patent 2866802 (1958).

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(84) Hokko Chemical Industry Co., Ltd., Japanese Patent 026894 (1970).

(85) Casella Farbwerke Mainkur A.-G., French Patent 1550942 (1968).

(86) Cassella Farbwerke Mainkur A.-G., U. S. Patent 3558684 (1970).

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(88) K. Fukui and H. Kitano, U. S. Patent 3037979 (1962).

(89) D. W. Kaiser (American Cyanamid Co.), U. S. Patent 2697720 (1954).

(90) A. Nagasawa, H. Kitano, and K. Fukui, *Bull. Jap. Petrol. Inst.*, **6**, 72 (1964).

(91) P. A. Argabright, H. D. Rider, and R. Sieck, *J. Org. Chem.*, **30**, 3317 (1965).

(92) Marathon Oil Co., French Patent 1516417; *Chem. Abstr.*, **70**, 79251j (1969).

(93) S. Ozaki, *J. Polym. Sci., Part B*, **5**, 1053 (1967).

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(95) Imperial Chemical Industries, U. S. Patent 3145077; *Chem. Abstr.*, **55**, 14491g (1961).

(96) J. J. Pilts, M. A. Robinson, and S. I. Troty, *Inorg. Nucl. Chem. Lett.*, **4**, 483 (1968).

(97) Imperial Chemical Industries, British Patent 907029 (1962); *Chem. Abstr.*, **58**, 279d (1963).

(98) *U. S. Govt. Res. Develop. Rep.*, **67**, 50 (1967); *Chem. Abstr.*, **68**, 87349w (1968).

(99) V. A. Shokol, V. F. Gamaleya, and G. I. Derkach, *Zh. Obshch. Khim.*, **38**, 1104 (1968); *Chem. Abstr.*, **69**, 59336s (1968).

(100) Imperial Chemical Industries, British Patent 968109 (1962); *Chem. Abstr.*, **61**, 14864e (1964).

(101) E. I. du Pont de Nemours & Co., U. S. Patent 3214412 (1966); *Chem. Abstr.*, **64**, 3542h (1966).

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(103) W. Guenter, *Z. Chem.*, **9**, 305 (1969).

(104) C. Carston and H. Arne, *Acta Chem. Scand.*, **24**, 1852 (1970).

(105) K. R. Ramaparsad, R. Verma, and R. Nelson, *J. Amer. Chem. Soc.*, **90**, 6247 (1968).

in capital cost (for a plant producing 100 million lb per year) and an 83% improvement in profit over the current process can be estimated;[106] however, other technical problems such as recovery and recycling the catalyst must be solved.

The production of tolylene diisocyanate has been dealt with in many patents.[107–131]

L. OXIDATIONS OF ISOCYANIDES

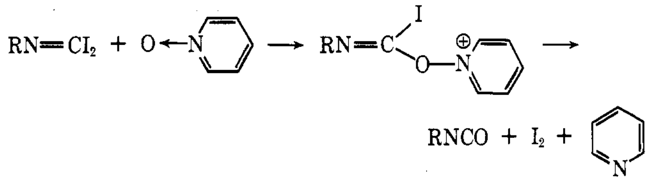
Several methods have been developed. In the first, oxidation of an isocyanide with DMSO in the presence of a catalytic amount of bromine[132] presumably involves the initial formation of an isocyano dibromide.[132]

$$RNC + X_2 \longrightarrow RN{=}CX_2$$

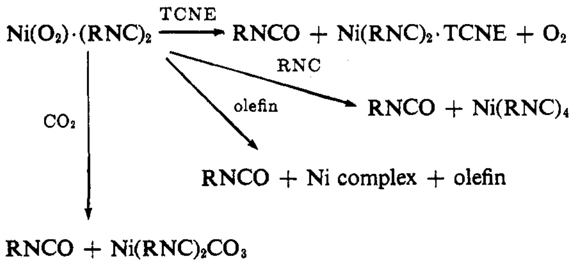
$$RN{=}CX_2 + (CH_3)_2SO \longrightarrow RNCO + (CH_3)_2S + X_2$$

Another oxidation by pyridine *N*-oxide has been reported.[133]

$$RNC + I_2 \rightleftharpoons R{-}N{=}CI_2$$



Oxidation by oxygen apparently requires an oxygen complex,[134] mercury, or a mercury oxide.[135]

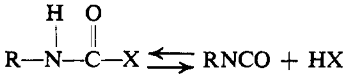


Further investigation may show that oxidation by a nitrile oxide[136] or nitric oxide[137] may have generality.

$$RNC + C_6H_5CNO \longrightarrow RNCO + C_6H_5CN$$

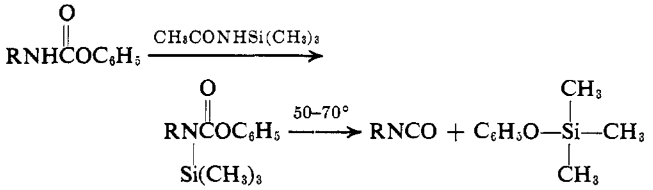
$$RNC + NO \longrightarrow RNCO + {}^1\!/\!_2N_2$$

M. DISSOCIATION OF AN ISOCYANATE ADDUCT

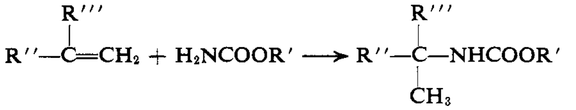


$$R{-}\overset{H}{\overset{|}{N}}{-}\overset{O}{\overset{\|}{C}}{-}X \rightleftharpoons RNCO + HX$$

The isolation of an isocyanate from a carbamic acid derivative is complicated by the tendency of HX and RNCO to recombine easily. In the dissociation of an *N*-silyl derivative,[138] the absence of a reverse addition affords an easy isolation of an isocyanate.



An ester exchange method[139,140] depends upon the availability of the N-substituted carbamate. A straightforward preparation is provided by an addition of an olefin to an N-unsubstituted carbamate.



$$RNHCOOR' + \text{high boiling isocyanate} \xrightarrow{140\text{–}270°} RNCO + \text{high-boiling carbamate}$$

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(106) M. S. Sherwin and P. H. Spitz, *Chem. Eng. News*, 51 (Sept 13, 1971).

(107) American Cyanamid Co., Belgian Patent 651876; Japanese Patent 41-7941 (1966).

(108) W. B. Hardy, *Tetrahedron Lett.*, 961 (1967).

(109) Olin Mathieson Chemical Corp., Netherlands Patent Appl. 6802765 (1968).

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(111) E. W. Stern and M. L. Spector, *J. Org. Chem.*, **31**, 596 (1966).

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(119) Olin Mathieson Chemical Corp., French Patent 1567321 (1969); U. S. Patent 3523962 (1970); *Chem. Abstr.*, **72**, 111015q (1970).

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(123) Olin Mathieson Chemical Corp., French Patent 1558899 (1969); *Chem. Abstr.*, **72**, 66597t (1970).

(124) Olin Mathieson Chemical Corp., German Patent 1944747 (1970); *Chem. Abstr.*, **72**, 132289x (1970).

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(126) Olin Mathieson Chemical Corp., U. S. Patent 3481067 (1969).

(127) Olin Mathieson Chemical Corp., German Patent 1931211 (1970); *Chem. Abstr.*, **72**, 78650t (1970).

(128) Olin Mathieson Chemical Corp., German Patent 1815517 (1969); *Chem. Abstr.*, **71**, 80911b (1969).

(129) Olin Mathieson Chemical Corp., German Patent 1907595 (1969); *Chem. Abstr.*, **72**, 31474y (1970).

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(133) H. W. Johnson, Jr., and H. Krutzch, *ibid.*, **32**, 1939 (1967).

(134) S. Ohtsuka and A. Nakamura, 22nd Meeting of the Chemical Society of Japan, No. 17306, Tokyo, 1969.

(135) Universal Oil Products Co., U. S. Patent 3493596 (1970).

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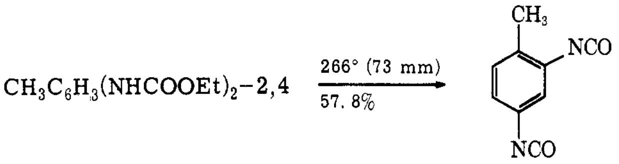
(138) G. Greber and H. R. Kricheldovf, *Angew. Chem.*, **80**, 1028 (1968).

(139) Imperial Chemical Industries, British Patent 1001330; *Chem. Abstr.*, **62**, 11687c (1965).

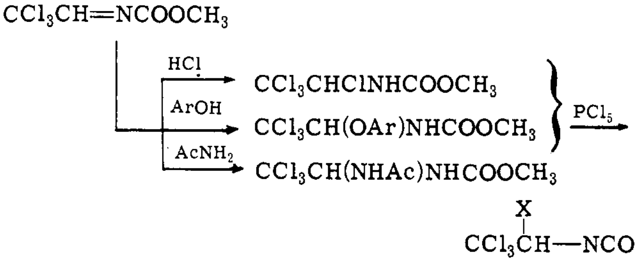
(140) G. Müller and R. Merten, *Chem. Ber.*, **98**, 1097 (1965).

Isocyanates have been dissociated from carbamates thermally[141,142] and by phosphorus pentachloride.[143]

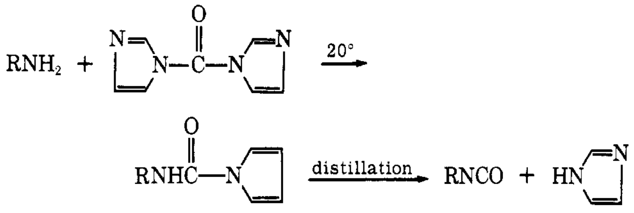


$$\mathrm{RNH\overset{O}{\overset{\|}{C}}SR'} \xrightarrow{160\text{–}260°} \mathrm{RNCO} + \mathrm{R'SH}$$

(89%, $R = C_2H_5OCH_2CH_2$–)



A convenient laboratory method for the transformation of amines into isocyanates employs *N,N'*-carbonyldiimidazole.[144]



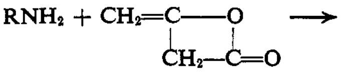
Urea or a substituted urea decomposes in the presence of sulfuric or phosphoric acid to give isocyanic acid or an isocyanate.[145] Certain ureas are transformed into isocyanates by phosgene[146] and by nitrogen dioxide.[147]

$$p\text{-}\mathrm{CH_3C_6H_4SO_2NHCONHR} \xrightarrow[>80°]{\mathrm{COCl_2}} p\text{-}\mathrm{CH_3C_6H_4SO_2NCO} + \mathrm{RNCO}$$

$$\mathrm{C_6H_5NHCONH_2} + \mathrm{NO_2} \xrightarrow{-10°} \underset{71\%}{\mathrm{C_6H_5NCO}}$$

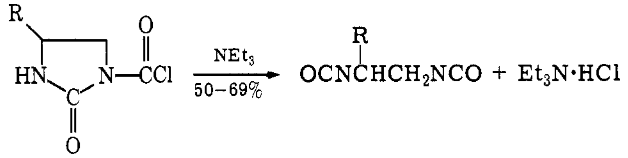
A molecular rearrangement is required for the formation of an isocyanate by the dehydration of a hydroxamic acid by an acetylene ether.[148] An inability of the by-product, an acetate ester, to combine with an isocyanate undoubtedly facilitates the formation of the isocyanate. This principle is shared with the dissociation of acetylacetanilides[149] and trichloroacetanilide[150] and in the dehydrochlorination of an allophanoyl chloride.[151]

$$\mathrm{RCONHOH} + \mathrm{HC{\equiv}COR'} \longrightarrow \mathrm{RNCO} + \mathrm{CH_3COOR'}$$



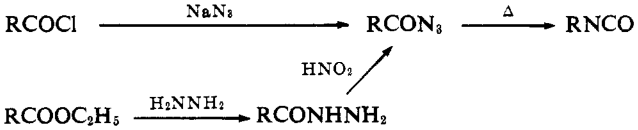
$$\mathrm{CH_3COCH_2CONHR} \xrightarrow{350\text{–}740°} \mathrm{RNCO} + \mathrm{CH_3COCH_3}$$

$$\mathrm{C_6H_5NHCOCCl_3} \longrightarrow \mathrm{C_6H_5NCO} + \mathrm{C_6H_5CN} + \mathrm{HCl} + \mathrm{COCl_2} + \mathrm{Cl_2}$$



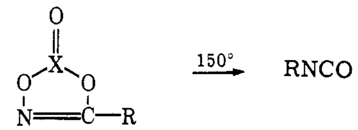
N. CURTIUS REARRANGEMENT

This method is often recommended when an isocyanate is to be prepared from a carboxylic acid chloride or ester. Vinyl isocyanate,[152,153] 3-isocyanatopyridine, and 2,6-diisocyanatopyridine have been prepared by this method.[154]

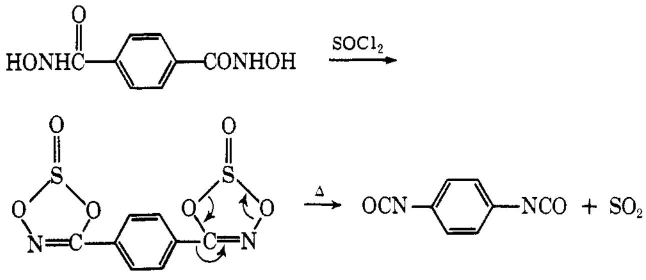


O. THERMOLYSIS OF NITRILE SULFITES AND CARBONATES[155]

A new synthesis of aromatic isocyanates from hydroxamic acids involves pyrolysis of 1,3,2,4-dioxathiazole *S*-oxides.[156]



X = S, nitrile sulfite
X = C, nitrile carbonate



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(141) American Cyanamid Co., Japanese Patent 46-17773 (1971).

(142) Farbenfabriken Bayer A.-G., German Patents 1176127, 1171421 (1964); *Chem. Abstr.*, **61**, 6919g (1964).

(143) B. S. Drach, A. D. Sinitsa, and A. V. Kirsanov, *Zh. Org. Khim.*, **5**, 2117 (1969).

(144) H. A. Staab and W. Benz, *Angew. Chem.*, **73**, 66 (1961).

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(148) T. Mukaiyama, H. Nohira, and S. Asano, *Bull. Chem. Soc. Jap.*, **35**, 72 (1962).

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(153) R. Hart, *Bull. Soc. Chim. Belg.*, **65**, 291 (1956).

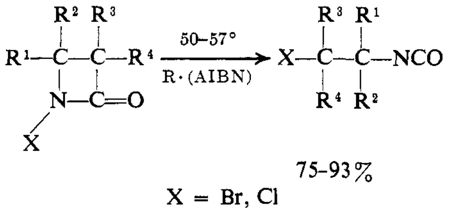
(154) S. Heyden and G. Wilbert, *Chem. Ind.* (*London*), **33**, 1406 (1967).

(155) Sinclair Research, Inc., Netherlands Patent Appl. 6615003 (1968); *Chem. Abstr.*, **70**, 57383b (1969).

(156) E. H. Burk and D. Dcarlos, *J. Heterocycl. Chem.*, **7**, 177 (1970).

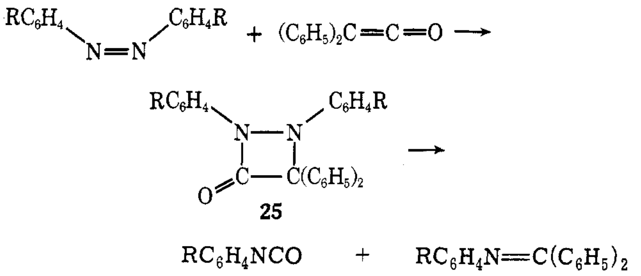
P. REARRANGEMENT OF β-LACTAMS

When a β-lactam is heated with a radical initiator, a β-haloalkyl isocyanate is obtained.[157]



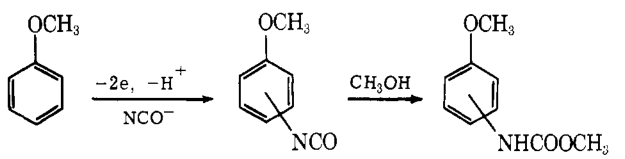
Q. THERMAL DECOMPOSITION OF 1,2-DIAZETIDINONES[158]

Addition of azobenzene to diphenylketene gives a 1,2-diazetidinone (25). This four-membered ring fragments when heated to give an isocyanate and an anil.

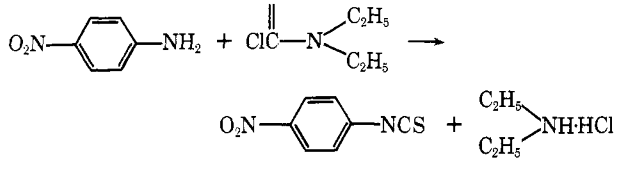


R. ELECTROLYSIS OF CYANATES

Olefins or aromatic hydrocarbons are bubbled through a melt obtained by fusing sodium cyanate and urea at 135° while treated with an electrical current. Carbamates are produced when alcohols are present, and ureas are produced when amines are present.[159] When a methanol solution of potassium cyanate and anisole is electrically treated with a cathode potential of 1.8 V, methyl *N*-anisylcarbamate is produced.[160] Intermediate isocyanate formation has been postulated but not established.

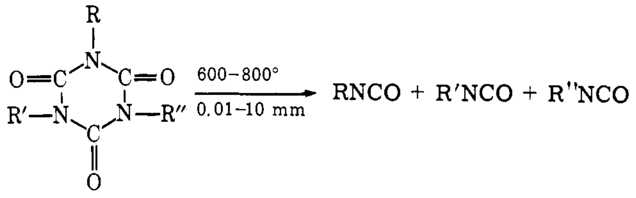


S. REACTIONS OF AMINES WITH DIETHYLTHIOCARBAMOYL CHLORIDE[161]

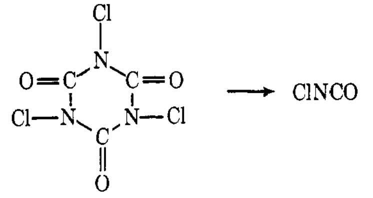


A facile dissociation of *p*-nitrophenyl isothiocyanate from an intermediate urea is assumed.

T. PYROLYSIS OF ISOCYANURATES[162]



Chloroisocyanate was obtained for the first time by pyrolysis of trichloroisocyanuric acid under low pressure.[163–165]



U. SULFINYLAMINES WITH PHOSGENE[166]

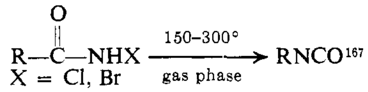
$$RNH_2 + SOCl_2 \longrightarrow RN{=}S{=}O + 2HCl$$

$$RN{=}S{=}O + COCl_2 \longrightarrow RN{=}C{=}O + SOCl_2$$

overall yield 65–78%

Phosgenation of an amine takes a long time if the amine hydrochloride does not dissolve. Heating to 80° generally speeds the reaction to completion in a short period of time. Since thionyl chloride can be recycled, this offers an elegant way to transform an amine into an isocyanate.

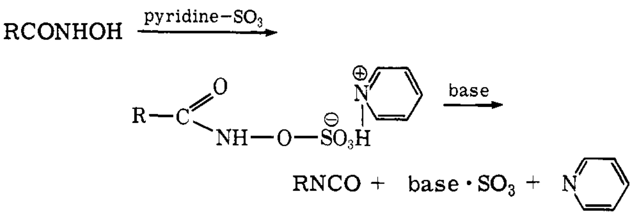
V. LOSSEN REARRANGEMENT (AND MODIFICATIONS)



$$R-\overset{\overset{O}{\|}}{C}-NHX \xrightarrow[\text{gas phase}]{150-300^\circ} RNCO^{167}$$

X = Cl, Br

The reaction of a hydroxamic acid with an equimolar complex of sulfur trioxide and a tertiary amine proceeds by O-sulfonation to give a crystalline water-soluble trisubstituted-ammonium *N*-acylhydroxylamine-*O*-sulfonate. Aliphatic isocyanates have been prepared in good yield by treating these salts with a tertiary amine.[168]



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(157) K. D. Kampe, *Tetrahedron Lett.*, 177 (1969).

(158) J. H. Hall and R. Kellogg, *J. Org. Chem.*, **31**, 1079 (1966).

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(168) F. A. Daniher, *J. Org. Chem.*, **34**, 2908 (1969).

W. OTHER RECENT METHODS

In the presence of palladium dichloride, an olefin may combine with an alkali cyanate.[169]

$$C_7H_{15}CH{=}CH_2 + NaOCN + PdCl_2 \xrightarrow[2\ hr]{90°} \text{organic isocyanate}$$

With the evolution of nitrogen, an azide combines with carbon monoxide to give an isocyanate.[170]

$$RC_6H_4N_3 + CO \xrightarrow[150\ atm]{160°} RC_6H_4NCO + RC_6H_4N{=}NC_6H_4R$$

$$R = o\text{-}CH_3,\ 67.5\%;\ m\text{-}CH_3,\ 40\%$$

Isocyanide dihalides may be hydrolyzed.[171,172]

$$RN{=}CCl_2 \xrightarrow[\text{strong acid}]{H_2O} \underset{94\%}{RNCO}$$

Condensation between a primary amine and a carbonate may produce an isocyanate.[173]

$$H_2N(CH_2)_6NH_2 + (C_6H_5O)_2CO \xrightarrow{94°C} OCN(CH_2)_6NCO$$

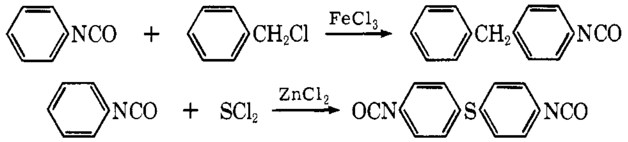
$$C_6H_5NH_2 + (C_6H_5O)_2CO \longrightarrow C_6H_5NCO$$

An interesting thermal exchange of radicals between an isocyanate and an imine gives a new isocyanate and new imine.[174]

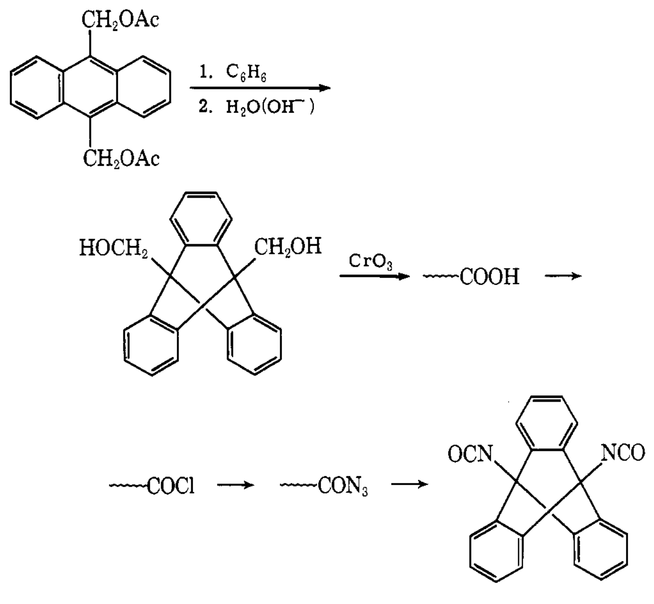
$$R^1NCO + R^2N{=}CR^3R^4 \xrightarrow{160\text{–}300°} R^2NCO + R^1N{=}CR^3R^4$$

X. SYNTHESIS OF CERTAIN ISOCYANATES

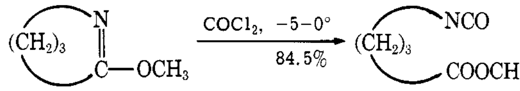
Di- and trichlorotolylene diisocyanates are obtained by chlorination of TDI with I_2 and $FeCl_3$.[175,176] Perchloroaryl isocyanates[177] and brominated diphenylmethane and diphenyl sulfide diisocyanates[178–180] have been reported.



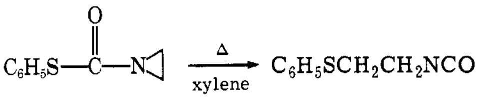
Triptycene diisocyanate[181] has resulted from a Curtius rearrangement after a lengthy synthesis.



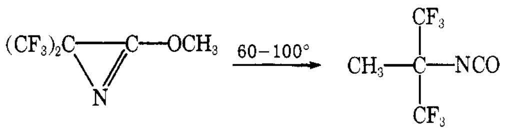
Difunctional compounds such as methyl γ-isocyanatobutyrate are obtained by the phosgenation of lactam ethers.[182]



2-Thioarylalkyl isocyanates are produced by heating 1-(thioarylcarbonyl)aziridines.[183]



Fluorinated isocyanates may be obtained by a new rearrangement.[184]



Hydrazine reacts with cyclopentadienyliron tricarbonyl cation to form a carbazoyl intermediate which loses NH_3 to give an isocyanate complex.[185]

$$C_5H_5Fe(CO)_3^+ + 2H_2NNH_2 \xrightarrow[-N_2H_5]{}$$

$$C_5H_5Fe(CO)_2(CONHNH_2) \xrightarrow[-NH_3]{} C_5H_5Fe(CO)_2(NCO)$$

From 1,4-dinitro-2,3-dialkyl-2-butene the intermediate formation of *N*-hydroxy isocyanate (**26**) is indicated by the products obtained in the sequence of Scheme II.[186]

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(172) Farbenfabriken Bayer A.-G., British Patent 1192900 (1970); *Chem. Abstr.*, **73**, 14177g (1970).

(173) Olin Mathieson Chemical Corp., U. S. Patent 3366662 (1968); *Chem. Abstr.*, **69**, 26764b (1968).

(174) Farbenfabriken Bayer A.-G., German Patent 1222042; *Chem. Abstr.*, **65**, 13604 (1966).

(175) Farbenfabriken Bayer A.-G., French Patent 1375412 (1964).

(176) FMC Corp., U. S. Patent 2915545 (1959).

(177) Farbenfabriken Bayer A.-G., German Patent 1157601 (1963); *Chem. Abstr.*, **60**, 5394e (1964).

(178) F. W. Berk & Co., Ltd., British Patent 971168 (1964); *Chem. Abstr.*, **61**, 14582d (1964).

(179) E. I. du Pont de Nemours & Co., British Patent 1013710 (1962); French Patent 1377888 (1964); *Chem. Abstr.*, **62**, 9082*f* (1965).

(180) E. I. du Pont de Nemours & Co., U. S. Patent 3041364 (1970).

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(182) Farbenfabriken Bayer A.-G., Japanese Patent 46-23371 (1971); German Patent 1913273 (1970).

(183) D. A. Tomalia, D. R. Sheetz, and G. E. Ham, *J. Org. Chem.*, **35**, 47 (1970).

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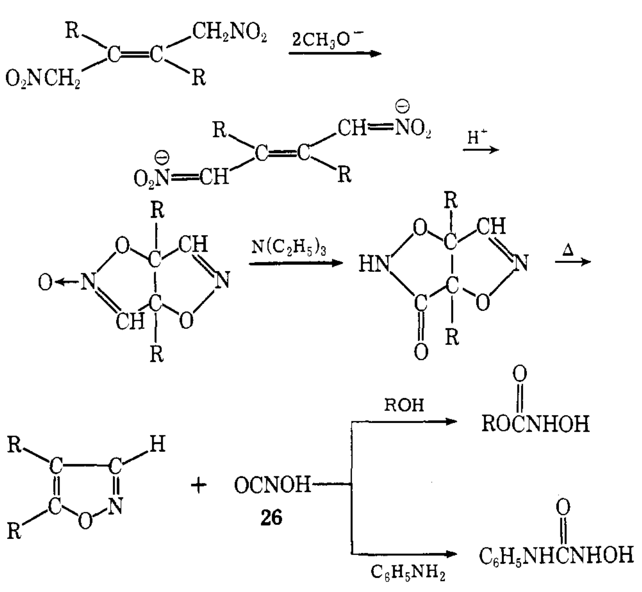
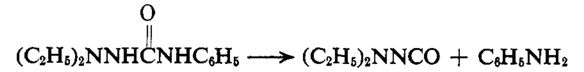
(185) R. J. Angelici and L. Busetto, *J. Amer. Chem. Soc.*, **91**, 3197 (1969).

(186) A. Berndt, *Tetrahedron Lett.*, 173 (1970).

Scheme II

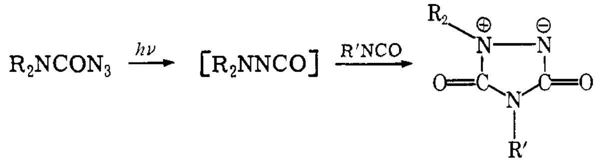


When 1,1-diethylphenylsemicarbazide is heated in a gas chromatographic–mass spectrometric apparatus diethylamino isocyanate, *m/e* 114, is detected.[187]

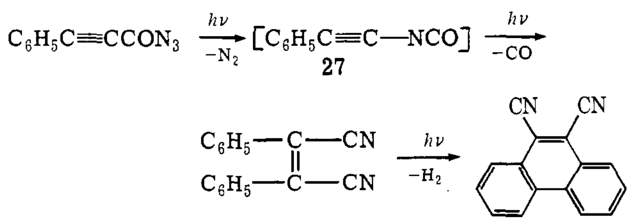


$$(C_2H_5)_2NNH\overset{O}{\overset{\|}{C}}NHC_6H_5 \longrightarrow (C_2H_5)_2NNCO + C_6H_5NH_2$$

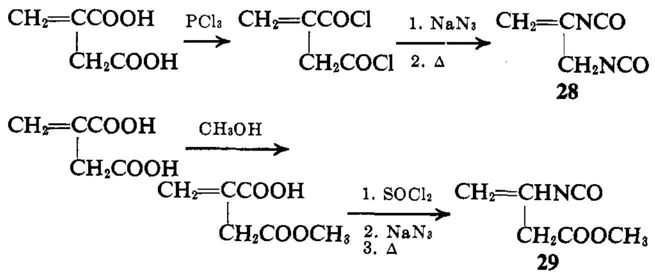
The photolysis of a dialkylcarbamoyl azide gives a transient *N*-isocyanatoamine. The aminoisocyanate may add to another isocyanate to give a 1,2,4-triazolidine-3,5-dione-1,2-ylide.[188]



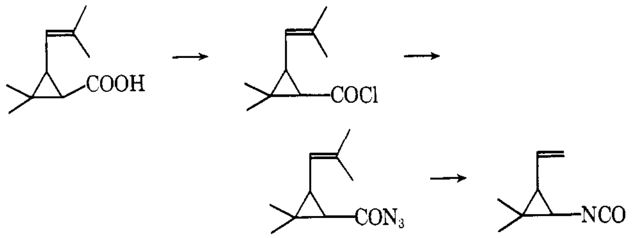
When phenylethynyl azide is decomposed photochemically, phenylethynyl isocyanate (**27**) is obtained as an intermediate.[189]



2,3-Diisocyanato-1-propene (**28**) and 3-isocyanato-3-butenoic ester (**29**) have been prepared by standard reactions.[190,191]



Chrysanthemyl isocyanate (**30**) is prepared from chrysanthemic acid *via* the corresponding acid azide.[192]



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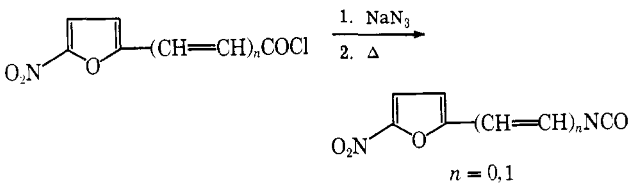
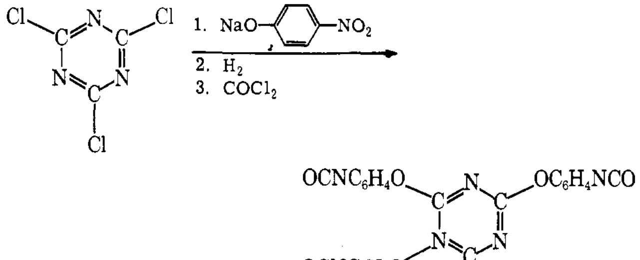
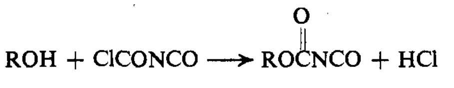
5-Nitro-2-furyl isocyanate and (5-nitro-2-furyl)vinyl isocyanate[193] are interesting unsaturated isocyanates.

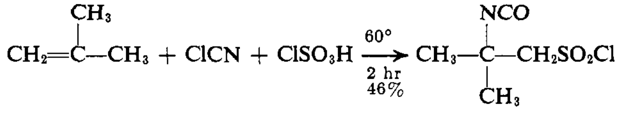


Tris(*p*-isocyanatophenyl) cyanurate,[194] isocyanatoformates,[195] 2-isocyanato-2-methylpropanesulfonyl chloride,[196] chlorosulfonylvinyl isocyanates,[197] and cyanogen isocyanate[198] are readily available and serve to demonstrate the versatility of preparative methods.





$$ROH + ClCONCO \longrightarrow RO\overset{O}{\overset{\|}{C}}NCO + HCl$$



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(190) R. Harada, *Nippon Kagaku Zasshi*, **90**, 1044 (1969).

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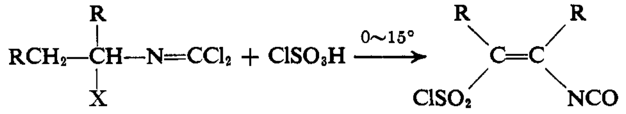
(195) Farbenfabriken Bayer A.-G., French Patent 2014805 (1970).

(196) Farbenfabriken Bayer A.-G., French Patent 1570995 (1969); *Chem. Abstr.*, **72**, 89781n (1970).

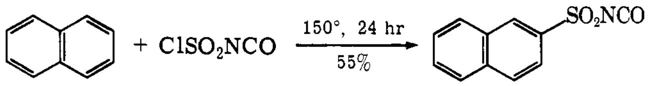
(197) Farbenfabriken Bayer A.-G., French Patent 2010305 (1970); *Chem. Abstr.*, **73**, 55637a (1970).

(198) M. Erwin, *Monatsh. Chem.*, **101**, 834 (1970).



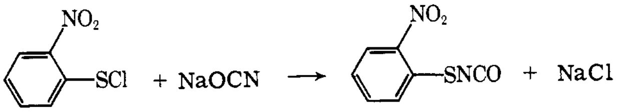
$$AgOCN + ClCN \xrightarrow{>140°} NCNCO$$

Aromatic sulfonyl isocyanates are prepared by treating an aromatic hydrocarbon with chlorosulfonyl isocyanate.[199]



Normally isocyanic acid can be prepared by the pyrolysis of cyanuric acid. It has also been obtained by the pyrolysis of urea in molten cyanates[200] and by treating sodium cyanate with hydrochloric acid in an inert solvent[201] or in a glass tube.[202]

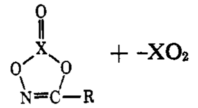
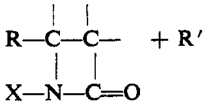
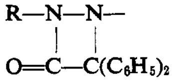
o-Nitrophenylsulfuryl isocyanate is prepared from *o*-nitrophenylsulfuryl chloride and sodium cyanate.[203]



The synthetic methods of isocyanates are outlined in Table II.

Table II

Synthetic Methods of Isocyanates (RNCO)[a]

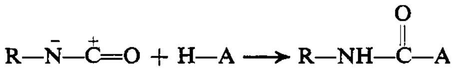
Starting materials	*Sub-section*
$RNH_2 + COCl_2$	A
$RCONH_2 + (COCl)_2$[b]	B
$RNH_2 + (COCl)_2$	C
$>C=C< + HNCO$	D
$>C=C< + INCO$	E
$-CO- + HNCO$	F
$R-Cl + HNCO$	G
$(R_mMetal)_nO + HNCO$ or urea	H
$(R'CO)_2O + HNCO$[c]	I
$RCl + NaOCN$	J
$RNO_2 + CO$	K
$RNC + O$	L
$RNHCOX - HX$	M
$RCON_3 + \Delta, -N_2$	N
 $+ -XO_2$	O
 $+ R'$	P
	Q
$C_6H_6 - H^+ + NCO^- - 2e$	R
$RNH_2 + ClCSNR_2$[d]	S
Trisubstituted isocyanuric acid $+ \Delta$	T
$RNSO + COCl_2$	U
$R-CONHX$	V
$>C=C< + NaOCN + PdCl_2$	W
$RN_3 + CO$	W
$RN=CCl_2 + H_2O$	W
$RNH_2 + (C_6H_5O)_2CO$	W
$R'NCO + RN=C(R^2)_2$	W

[a] All products RNCO except where noted. [b] Product, RCONCO. [c] Product, R'CONCO. [d] Product, RNCS.

III. New Reactions of Isocyanates

An ionic nucleophilic reagent adds in the predicted manner to the polarized azomethine linkage of the isocyanate group

$$R-N=C=O \rightleftharpoons R-\bar{N}-\overset{+}{C}=O$$



$$R-\bar{N}-\overset{+}{C}=O + H-A \longrightarrow R-NH-\overset{\overset{\displaystyle O}{\|}}{C}-A$$

where HA = NH_3, RNH_2, RRNH, H_2NOH, H_2NNH_2, H_2O, H_2S, H_2O_2, $RNHCONH_2$, RNHCOOR, $RC(=NH)NH_2$, H_2NCN, ROH, ArOH, RSH, ArSH, PH_3, HF, HCl, HBr, HCN, RCOOH, $CH_2(COOR)_2$, $CH_2(COCH_3)COOR$, RCH_2NO_2, ArH, $NaHSO_3$, R_2NOH, R_3SiOH, ROOH.

An electron-attracting group may enhance the reactivity of the isocyanate group and leads to a reactivity classification in the following order: $ClSO_2NCO > RSO_2NCO > O=P(NCO)_3 >$ arylNCO (aryl = p-$NO_2C_6H_4$– $>$ p-ClC_6H_4– $>$ p-tolyl $>$ p-anisyl) $>$ alkyl NCO.

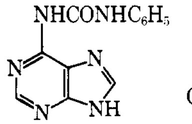
A. ADDITION REACTIONS OF ISOCYANATES

Nucleophilic addition to an isocyanate is a popular and widely used reaction.

1. Reaction with Primary or Secondary Amines and Amides

Many primary and secondary amines and amides react with isocyanates, but the more basic compounds are the more reactive. Several new reactions, each leading to a urea, have been reported.

The reaction of phenyl isocyanate with adenine, cytosine, and guanine gave 4-*N*-phenylcarbamyladenine (**31**), 6-*N*-phenylcarbamylcytosine (**32**), and 2-*N*-phenylcarbamylguanine (**33**), respectively.[204] Uracil did not react.



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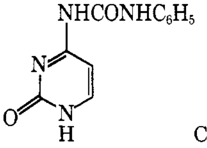

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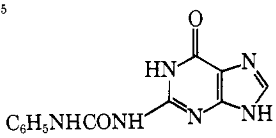

33

The reaction of 3,6-diphenyl-1,2,4,6-tetraaza-3,6-diborinane with methyl isocyanate has been shown to give probably a 1,4-bis-addition product (**34**).[205]

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(199) B. Herbert, B. Werner, and G. Dierter, German Patent 1289526 (1969); *Chem. Abstr.*, **70**, 87312v (1969)

(200) Carbogen Corp., German Patent 1159411 (1963); *Chem. Abstr.*, **60**, 10254a (1964).

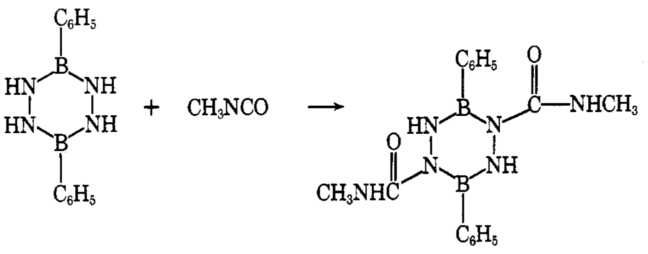
(201) Farbenfabriken Bayer A.-G., Japanese Patent 42-77260 (1967).

(202) N. Groving and A. Holm, *Acta Chem. Scand.*, **19**, 1769 (1965).

(203) S. Ozaki and A. Tamaki, unpublished work.

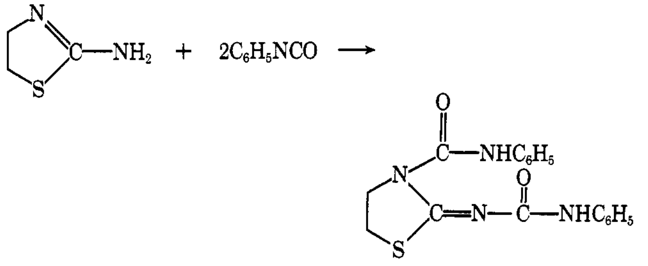
(204) A. S. Jones and J. H. Warren, *Tetrahedron*, **26**, 791 (1970).

(205) J. J. Miller, *J. Organometal. Chem.*, **24**, 595 (1970).



34

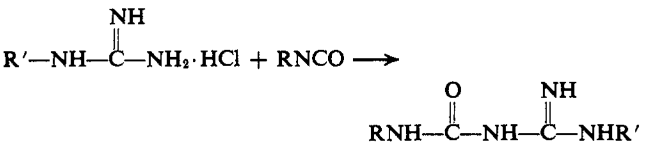
The reaction of 2-aminothiazoline with phenyl isocyanate has been shown to give a bis-addition product (35).[206]



35

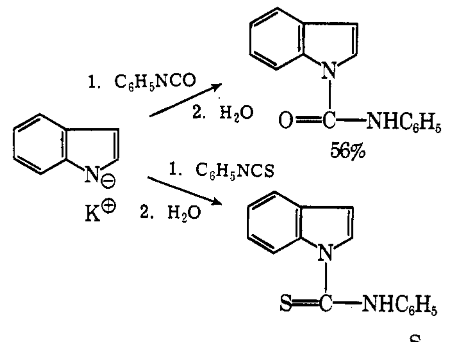
In DMF the isocyanato group can be measured by titration against *n*-butylamine at room temperature in 5 min with Methyl Red as the indicator.[207]

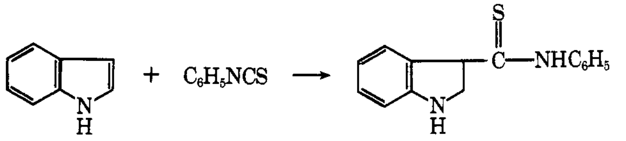
Guanylurea derivatives are obtained by the addition reactions of substituted guanidine hydrochloride with isocyanates.[208]



$$R'{-}NH{-}\overset{NH}{\overset{\|}{C}}{-}NH_2\cdot HCl + RNCO \longrightarrow RNH{-}\overset{O}{\overset{\|}{C}}{-}NH{-}\overset{NH}{\overset{\|}{C}}{-}NHR'$$

Indole metal salts react with either an isocyanate or isothiocyanate at indole nitrogen,[209] but definite products were not obtained from indole treated with phenyl isocyanate.

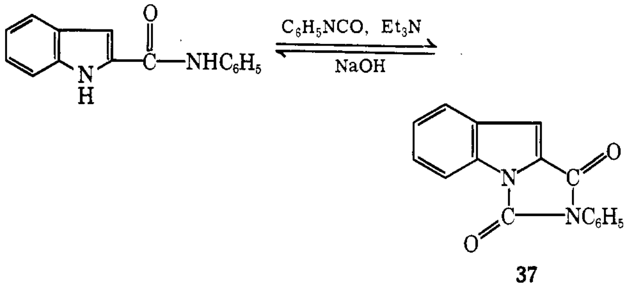




36

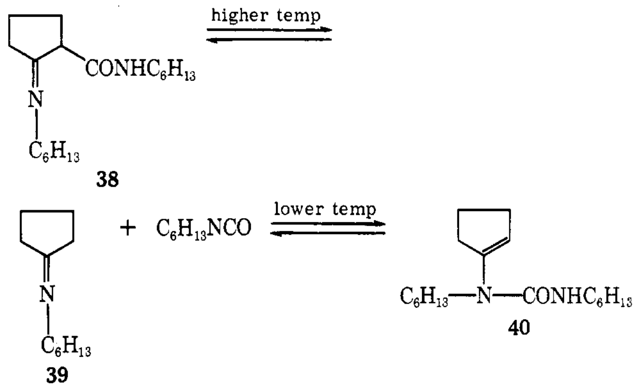
In contrast, 3-indolethiocarbanilide (36) was obtained from the treatment of indole with phenyl isothiocyanate.

2-Phenylindole[1,2-*c*]hydantoin (37) was obtained from indolecarboxanilide and phenyl isocyanate.



37

At higher temperature *N*-*n*-hexyl-2-(*n*-hexylimino)cyclopentane-1-carboxamide (38) decomposes in an equilibrium reaction to form cyclohexylidene-*n*-hexylamine (39) and *n*-hexyl isocyanate. At lower temperatures the latter compounds reversibly react with each other to form ureas (40).[210]

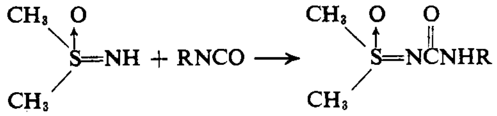


38

39

40

Addition of dimethylsulfoxime to an isocyanate gives *N*-dimethylsulfoxylidene-*N*′-alkylurea (41).[211]



$$(CH_3)_2\overset{O}{\overset{\uparrow}{S}}{=}NH + RNCO \longrightarrow (CH_3)_2\overset{O}{\overset{\uparrow}{S}}{=}N\overset{O}{\overset{\|}{C}}NHR$$

41

2. *Reactions with Alcohols and Phenols*

The formation of carbamates from isocyanates is fundamentally important to polyurethane industries. Procedures have been known for some time, but intensive studies are still going on.

A catalyst–isocyanate complex and a catalyst–alcohol complex formation are important. At one time a dibutyltin dilaurate–alcohol complex was considered to be a source of catalytic action.[212] The absence of initial interaction between a catalyst and an isocyanate was in agreement with no shift in the nmr absorption when the isocyanate was mixed with catalyst, and no change in uv absorption when an equimolar amount of catalyst was mixed with the isocyanate.

A three-component (alcohol, isocyanate, catalyst) com-

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(206) D. L. Klayman and J. J. Maul, *J. Heterocycl. Chem.*, **3**, 517 (1968).

(207) J. A. Vinson, *Anal. Chem.*, **41**, 1661 (1969).

(208) D. D. Diana, 155th National Meeting of the American Chemical Society, San Francisco, Calif., 1968.

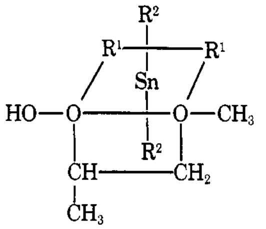
(209) E. P. Papadopoulos and S. B. Bedrosian, *J. Org. Chem.*, **33**, 4551 (1968).

(210) F. Wiloth and E. Schindler, *Chem. Ber.*, **103**, 757 (1970).

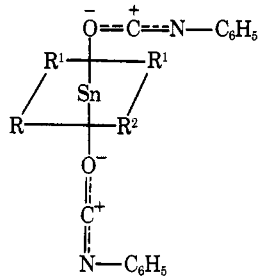
(211) R. Wehr, *J. Chem. Soc. (London)*, 3004 (1965).

(212) K. C. Frisch, *J. Polym. Sci., Part A*, **5**, 35 (1967).

plex[213–215] was based on the molecular weight determination by freezing point depression of a benzene solution. In benzene, complex formation was observed for 1-methoxy-2-propanol and dibutyltin dilaurate (**42**), 1-methoxy-2-propanol and triethylamine, and an isocyanate and dibutyltin dilaurate (**43**).



42



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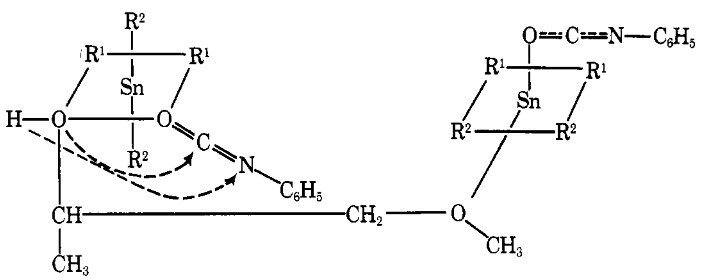
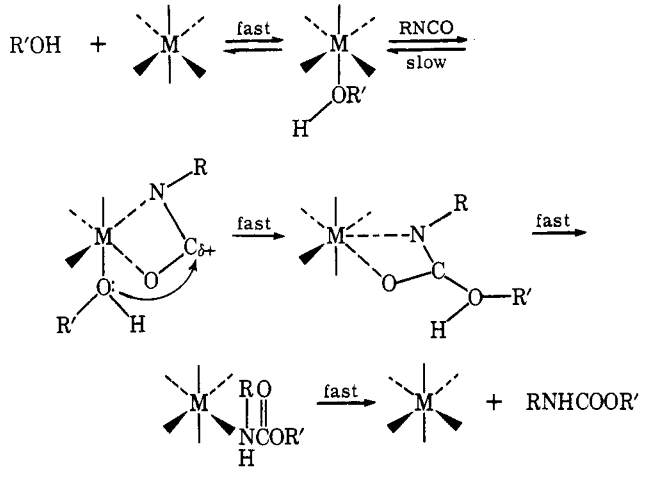


The mechanism of Scheme III was based on the kinetic study of the disappearance of absorption for the isocyanate group in the infrared.[216]

Scheme III



Catalysis by metallorganic acetates decreases in the following order: RHgOAc > R_3SnOAc > RPbOAc (R = aryl > alkyl).

Partial alcoholysis of ferric acetylacetonate provides activation for an alcohol in its reaction with an isocyanate.[217]

$$2ROH + Fe(AA)_3 \rightleftharpoons [Fe(AA)_2(OR)_2]H + HAA$$

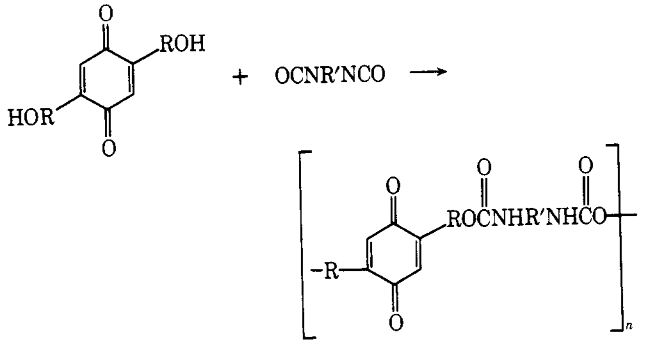
$$[Fe(AA)_2(OR)_2]H + RNCO \rightleftharpoons [Fe(AA)_2(OR)_2]H\cdot RNCO$$

$$[Fe(AA)_2(OR)_2]H\cdot RNCO \rightleftharpoons RNHCOOR + Fe(AA)_2OR$$

Catalysis by urethanes in the reaction of an isocyanate with alcohols has been studied.[218]

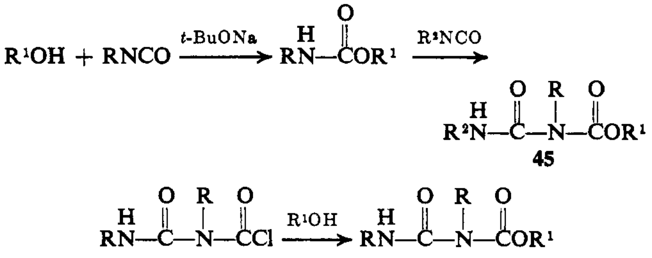
Kinetic and mechanistic investigations of metal catalysts have been carried out.[219] From a study of the kinetics of the reaction between poly(ether)polyols and tolylene diisocyanate, it was found that the reactivity of the alcohol is independent of the chain length and the numbers of polyol functional groups, and a primary alcohol group is more reactive than a secondary alcohol group.[220]

It is possible to prepare new redox polymers (**44**) from *p*-benzoquinonediols and diisocyanates by using a dibutyltin diacetate catalyst at room temperature or below.[221]



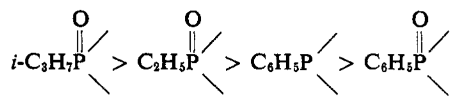
44

Detailed studies for the formation of an allophanate from a carbamate and an isocyanate, and from a mixture which is 1 *M* in phenol and 2 *M* in an isocyanate, have been carried out.[222]



45

Isocyanato groups attached to phosphorus which is also attached to electron-releasing substituents are more reactive toward alcohols:[223,224]



The dehydrating action of an isocyanate may be illustrated in the preparation of α-methylstyrene and cumene containing ^{14}C.[225]

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(213) S. L. Reegen and K. C. Frisch, *J. Polym. Sci., Part A-1*, **8**, 2883 (1970).

(214) L. Rand, B. Thir, S. L. Reegen, and K. C. Frisch, *J. Appl. Polym. Sci.*, **9**, 1787 (1965).

(215) L. Rand, *J. Polym. Sci., Part A-1*, **5**, 35 (1967).

(216) F. William, F. W. Abbate, and H. Ulrich, *J. Appl. Polym. Sci.*, **13**, 1929 (1969).

(217) A. E. Overth and R. S. Bruenner, *Ind. Eng. Chem. Fundam.*, **8**, 383 (1969).

(218) H. A. Smith, *J. Polym. Sci., Part A*, **6**, 1299 (1968).

(219) J. Robins, *J. Appl. Polym. Sci.*, **9**, 821 (1965).

(220) H. G. Wissman, L. Rand, and K. C. Frisch, *J. Appl. Polym. Sci.*, **8**, 2971 (1964).

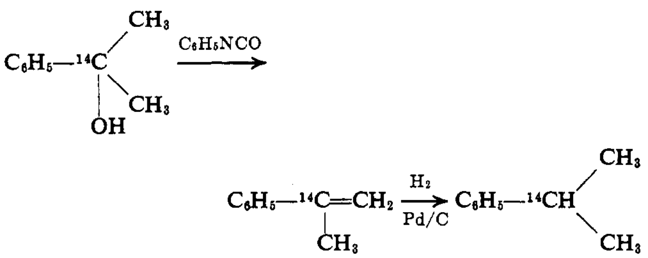
(221) G. Wenger, N. Nakabayashi, and H. G. Cassidy, *J. Polym. Sci., Part A-1*, **6**, 3151 (1968).

(222) H. Ulrich, B. Tucker, and A. A. R, Sayigh, *J. Org. Chem.*, **32**, 3938 (1967).

(223) M. Yokoyama, E. Akagi, and K. Mimami, *Kogyo Kagaku Zasshi*, **68**, 460 (1965); *Chem. Abstr.*, **63**, 7037e (1965).

(224) P. R. Steyermark, *J. Org. Chem.*, **28**, 3570 (1963).

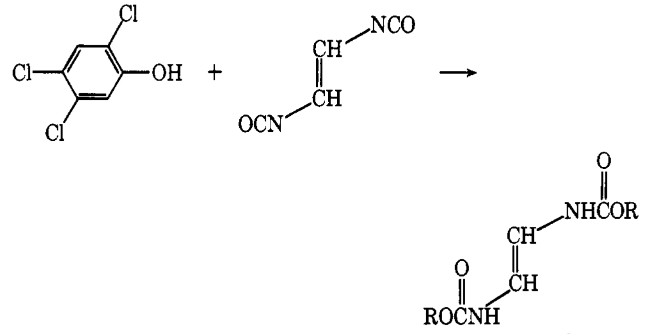
(225) H. Pines and M. Abramovici, *ibid.*, **34**, 472 (1969).



Trichloroacetyl isocyanate reacts quickly and quantitatively with primary, secondary, and tertiary alcohols. A quantitative analysis is based upon following the reaction by nmr.[226] A terpene alcohol can be regenerated from its carbamate by refluxing the derivative with 10% potassium hydroxide.[227]

Acetate and triacetate fibers were treated with tolyene diisocyanate in the vapor phase at 150°.[228] The treated fibers showed the same strength, decreased elongation, and increased Yang modulus.

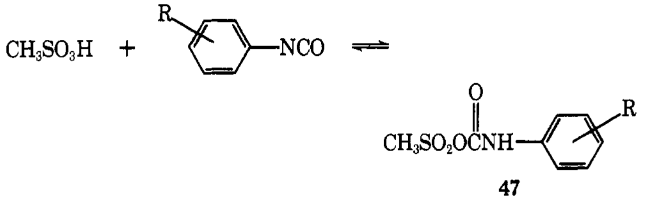
trans-Diisocyanatoethylene gives products (**46**) with abnormally high melting points when treated with alcohols and amines. This diisocyanate is very reactive at room temperature. With a carboxylic acid it gives a stable addition product; however, normal isocyanates and carboxylic acids do not give stable addition products.



46, mp 244°

3. Reaction with Sulfonic Acids

Detailed studies of reactions between sulfonic acids and isocyanates have not been published. Mixed carbamic and sulfonic acid anhydrides (CSA) (**47**) have been obtained quantitatively by mixing methane sulfonic acid and an aryl isocyanate at room temperature.[230]

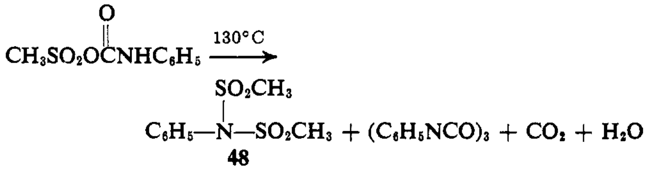


47

R = H	mp 40–50°
R = p-CH$_3$	mp 30–32°
R = p-Cl	mp 56°
R = m-NO$_2$	mp 50–52°

CSA dissociates readily. Crystalline *N*-phenylcarbamic acid–methanesulfonic acid anhydride and *N*-anisylcarbamic acid–methanesulfonic acid anhydride dissociate when mixed with benzene or toluene, and two layers are formed. The upper layer contains a benzene (or toluene) solution of phenyl isocyanate and the lower layer contains methanesulfonic acid. The CSA from *m*-chloro- or *m*-nitrophenyl isocyanate and methanesulfonic acid are more stable.

When a CSA is heated at 130–140°, a disulfonimide (**48**) is obtained.

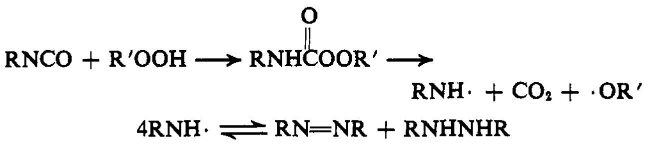


$$CH_3SO_2OC(=O)NHC_6H_5 \xrightarrow{130°C} C_6H_5-N(SO_2CH_3)-SO_2CH_3 + (C_6H_5NCO)_3 + CO_2 + H_2O$$

48

4. Reaction with Peroxy Compounds[231,232]

A new colorimetric method for the determination of aromatic isocyanates and peroxy compounds has been reported. The method is based on the intense color formed when an aromatic isocyanate and a peroxy compound are mixed in a dry solvent and the solution is made alkaline.

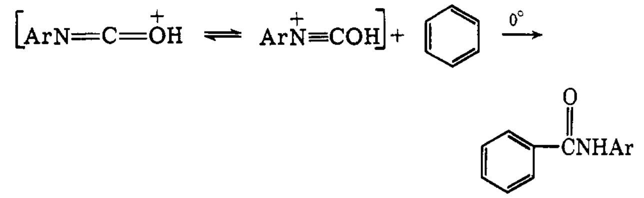


$$RNCO + R'OOH \longrightarrow RNH\overset{O}{\overset{\|}{C}}OOR' \longrightarrow RNH\cdot + CO_2 + \cdot OR'$$

$$4RNH\cdot \rightleftharpoons RN{=}NR + RNHNHR$$

5. Friedel–Crafts Reaction

Phenyl isocyanate, protonated with HBF$_4$, HPF$_6$ in sulfolane, reacted with benzene or toluene at 0°. A similar reaction in the presence of aluminum chloride requires 60°.[233]



Sulfonyl isocyanate and anisole reacted without a catalyst.[234]

6. Reactions with Orthoformates

Ethyl orthoformate and phenyl isocyanate gave a hydantoin derivative (**50**) when refluxed without catalyst.[235] Apparently an amide **49** was an intermediate.

In the presence of boron trifluoride, ethyl orthoformate adds ionically to phenyl isocyanate to produce **51**.[236,237]

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(226) V. W. Goodlett, *Anal. Chem.*, **37**, 431 (1965).

(227) P. A. Hedin, R. C. Gueldner, and A. C, Thompson, *ibid.*, **42**, 403 (1970).

(228) K. Suzuki, I. Kido, and S. Inoue, *Sen-i Gakkaishi*, **25**, 278 (1970).

(229) D. A. Scola, J. S. Adams, and D. D. Lopiekes, *J. Chem. Eng. Data*, **14**, 490 (1969).

(230) S. Ozaki, *Nippon Kagaku Zasshi*, **80**, 440 (1959); *Chem. Abstr.* **55**, 4397a (1961).

(231) R. F. Layton and L. A. Knecht, *Anal. Chem.*, **43**, 794 (1971).

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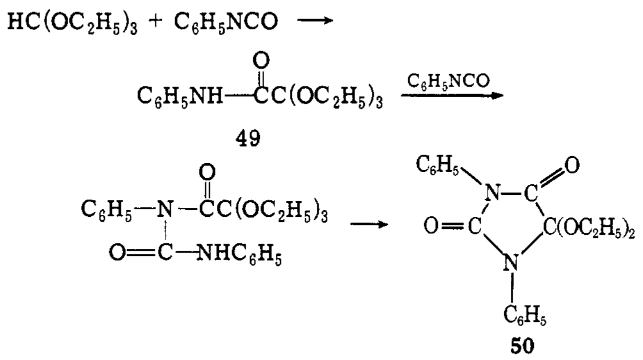
(233) R. W. Alder, G. R. Chalkley, and M. C. Whiting, *J. Chem. Soc. C*, 52 (1966).

(234) F. Effenberger, R. Gleiter, L. Heider, and R. Niess, *Chem. Ber.*, **101**, 502 (1968).

(235) C. W. Whitehead and J. Traverso, *J. Amer. Chem. Soc.*, **80**, 962 (1958).

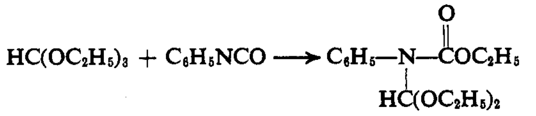
(236) H. Brechel and R. Merten, *Angew. Chem.*, **74**, 872 (1962).

(237) Farbenfabriken Bayer A.-G., German Patent 1156780 (1964); *Chem. Abstr.*, **60**, 5344b (1964).



49

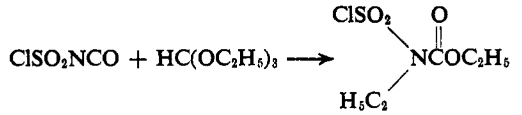
50



$$HC(OC_2H_5)_3 + C_6H_5NCO \longrightarrow C_6H_5\text{—}\underset{HC(OC_2H_5)_2}{N}\text{—}\overset{O}{\overset{\|}{C}}OC_2H_5$$

51

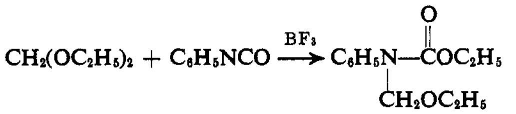
Chlorosulfonyl isocyanate and ethyl orthoformate react without catalyst to give *N*-chlorosulfonyl-*N*-ethylurethane (**52**).[238,239]



52

7. *Reaction with Acetals*[236]

Formaldehyde diacetal and phenyl isocyanate react in the presence of BF_3 to give **53**. This reaction is similar to the formation of **51**.

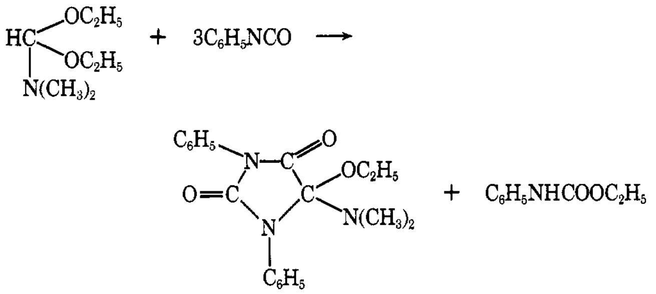


$$CH_2(OC_2H_5)_2 + C_6H_5NCO \xrightarrow{BF_3} C_6H_5\underset{CH_2OC_2H_5}{N}\text{—}\overset{O}{\overset{\|}{C}}OC_2H_5$$

53

8. *Reaction with Amine Acetals*[240]

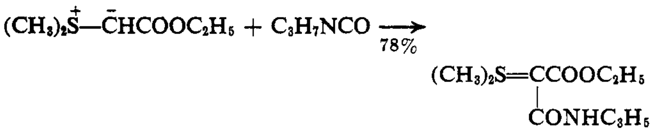
Parabanic acid *O,N*-acetal (**54**) is obtained from 1 mol of dimethylformamide diethyl acetal and 3 mol of phenyl isocyanate. This reaction is similar to the formation of **50**.



54

9. *Reaction with Ylides*

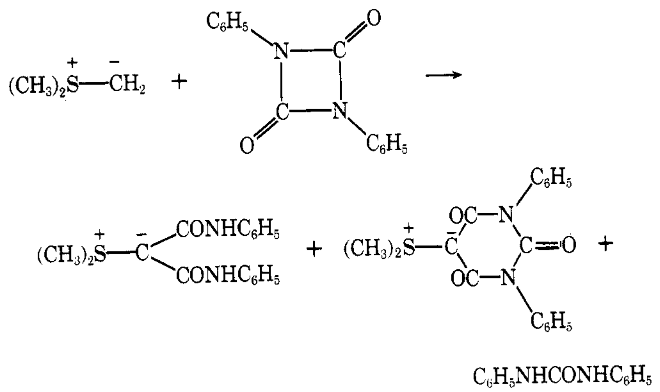
Addition of allyl isocyanate to ethyl dimethylsulfuranylidene acetate gives **55**.[241]



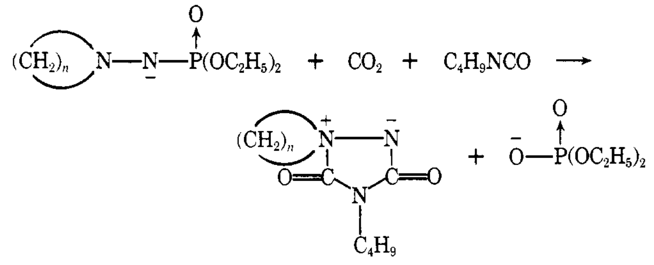
$$(CH_3)_2\overset{+}{S}\text{—}\overset{-}{C}HCOOC_2H_5 + C_3H_7NCO \xrightarrow[78\%]{} (CH_3)_2S{=}\underset{CONHC_3H_5}{C}COOC_2H_5$$

55

Phenyl isocyanate dimer and dimethylsulfonium methylide give a 1:1 adduct and a pyrimidine derivative.[242]

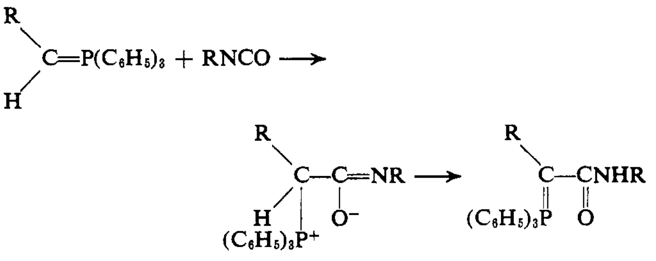


The reaction between *N*-alkylaminophosphoramidate, carbon dioxide, and *n*-butyl isocyanate gives a spiroylide (**56**).[243]



56

An adduct from a Wittig reagent and an isocyanate may rearrange into an amide.[244]



10. *Reaction with Dimethyl Sulfoxide and Dimethyl Sulfone*[245]

Addition of phenyl isocyanate to dimethyl sulfoxide gives two compounds, **57a** and **57b**, which are easily separated. In contrast dimethyl sulfone gives only a 2:1 adduct, a β-diamido sulfone (**58**).

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[238] H. Biener, *Justus Liebigs Ann. Chem.*, **686**, 102 (1965).

[239] Farbwerke Hoechst A.-G., German Patent 1186044 (1965); *Chem. Abstr.*, **62**, 9060e (1965).

[240] H. Bredereck, G. Simchen, and E. Goknel, *Angew. Chem.*, **76**, 861 (1964).

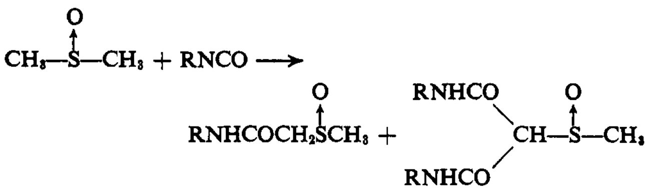
[241] G. B. Payne, *J. Org. Chem.*, **33**, 3517 (1968).

[242] T. Mukaiyama, M. Higo, and H. Takei, *Bull. Chem. Soc. Jap.*, **43**, 2566 (1970).

[243] W. S. Wadsworth, Jr., and W. Bruxvoort, *Chem. Commun.*, 542 (1968).

[244] H. Saikachi and K. Takei, *Yakugaku Zasshi*, **89**, 1401 (1969); *Chem. Abstr.*, **72**, 12452y (1970).

[245] M. von Strandmann, S. Klutchko, D. Conner, and J. Shavel, Jr., *J. Org. Chem.*, **36**, 1742 (1971).

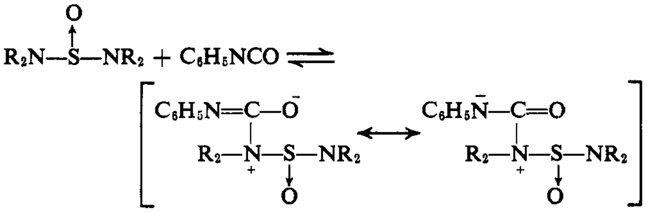


57a **57b**

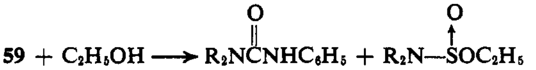
$$CH_3SO_2CH_3 + RNCO \longrightarrow \underset{\mathbf{58}}{(RNHCO)_2CHSO_2CH_3}$$

11. Reactions with Bis(dialkylamino)sulfoxides[246]

The sulfoxides combine with phenyl isocyanate to give a 1:1 adduct (**59**) which reacts with protic reagents such as alcohols and carboxylic acids.



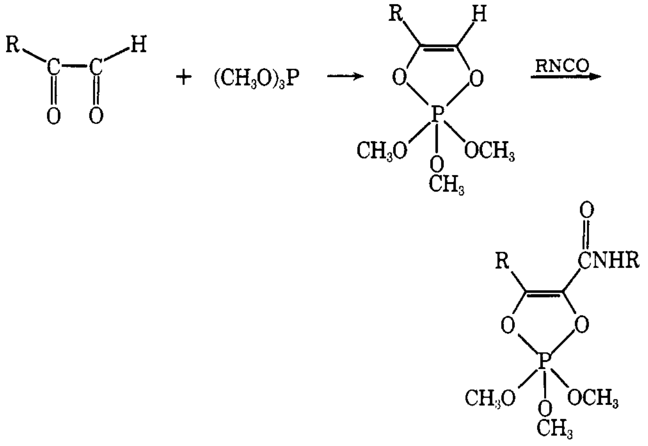
59



$$\mathbf{59} + C_2H_5OH \longrightarrow R_2N\overset{O}{\overset{\|}{C}}NHC_6H_5 + R_2N-\overset{O}{\overset{\uparrow}{S}}OC_2H_5$$

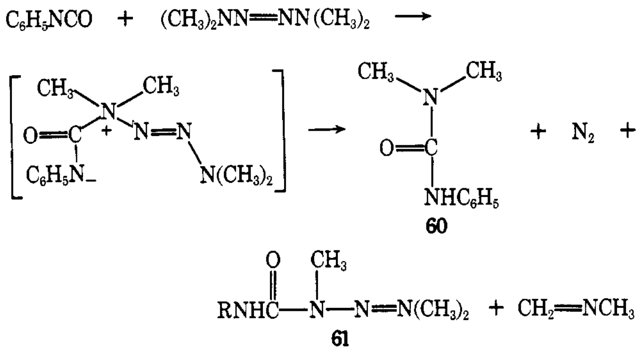
12. Reactions with 1,3,2-Dioxaphospholenes[247]

Carbamyl-1,3,2-dioxaphospholenes with pentavalent phosphorus were synthesized from α-ketoaldehydes, isocyanates, and trialkyl phosphites. Apparently lability of hydrogen attached to C-4 in a dioxaphospholene accounts for the reaction with an isocyanate.



13. Reaction with Tetrazene[248]

Phenyl isocyanate and tetramethyltetrazene-2 give *N*-phenyl-*N'*,*N'*-dimethylurea (**60**, 94–100%), a molar equivalent of nitrogen, and **61**.



60

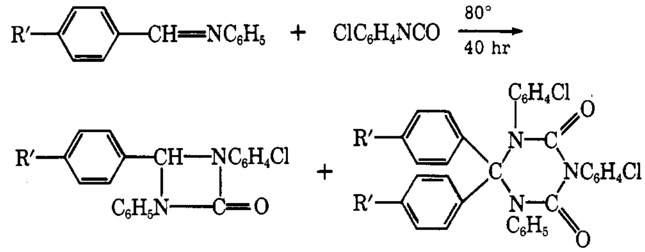
61

B. ADDITION REACTIONS TO DOUBLE BONDS

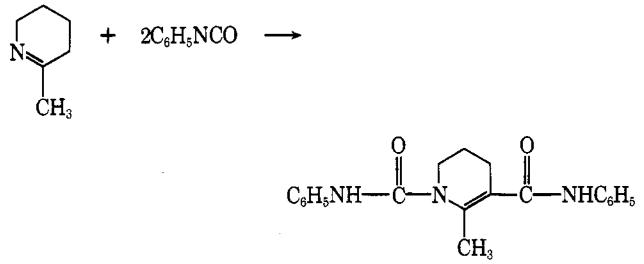
Both (2 + 2) additions to form four-membered rings and (2 + 2 + 2) additions to form six-membered rings are known.

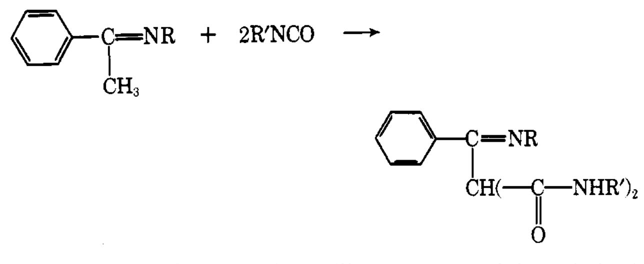
1. Reaction with Schiff's Bases

The presence of an electron donor in the para position of benzaldehyde anil and benzophenone anil facilitated the addition of an aryl isocyanate to give cyclic 1:1 and 1:2 adducts.[249]



2-Methyl-Δ¹-piperideine reacts with 2 mol of phenyl isocyanate.[250] An open-chain Schiff's base also reacts with 2 mol of isocyanate but in a different way.





The product from tolylene diisocyanate and 2-methyl-Δ'-piperideine started to decompose at 250°. Polyamide ureas or polyamides can be produced in similar reactions.

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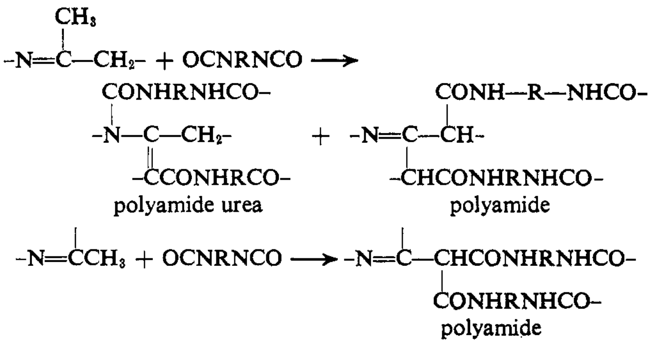
(246) T. Mukaiyama, H. Shimizu, and H. Takei, *J. Org. Chem.*, **32**, 3475 (1967).

(247) F. Ramireg, J. Bauer, and C. D. Telefus, *J. Amer. Chem. Soc.*, **92**, 6935 (1970).

(248) R. C. Kerber and T. J. Ryan, *J. Org. Chem.*, **36**, 1566 (1971).

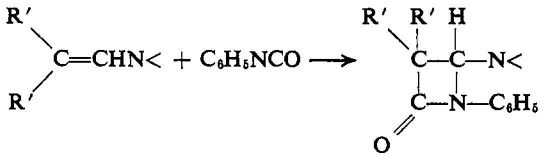
(249) R. Richter, *Chem. Ber.*, **102**, 938 (1969).

(250) K. Harada, Y. Mizoe, J. Furukawa, and S. Yamashita, *Makromol. Chem.*, **132**, 295 (1970).

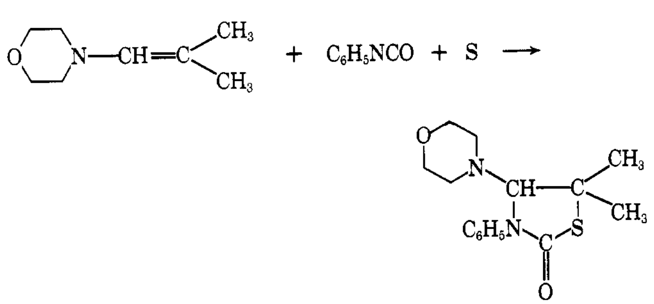


2. *Reaction with Enamines*

Enamines combine with isocyanates to give β-lactams.

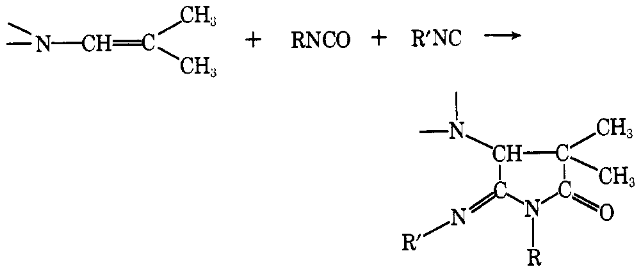


However, an enamine, an isocyanate, and sulfur give a 1,3-thiazolidin-2-one (**62**).[251]



62

In a similar reaction an enamine, an isocyanate, and an isonitrile give an iminopyrrolidone (**63**).[252]



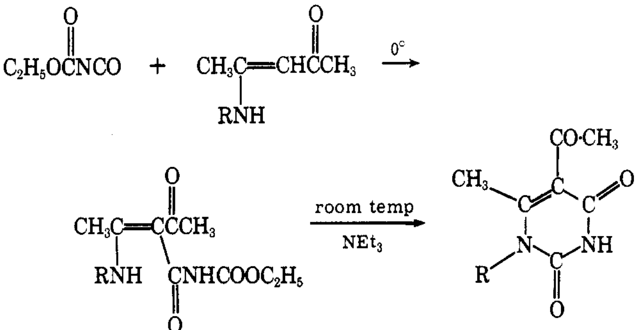
63

R′ = piperidino, morpholino.

Lability of a β hydrogen in an enamine may lead to another addition reaction with an isocyanate.

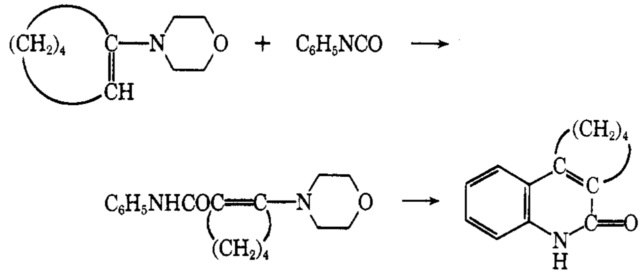
$$R'{-}CH{=}CHN< + RNCO \longrightarrow R'\underset{\underset{O=CNHR}{|}}{C}{=}CHN<$$

In this way an ethoxycarbonyl isocyanate and an enamine give a uracil derivative (**64**)[253]

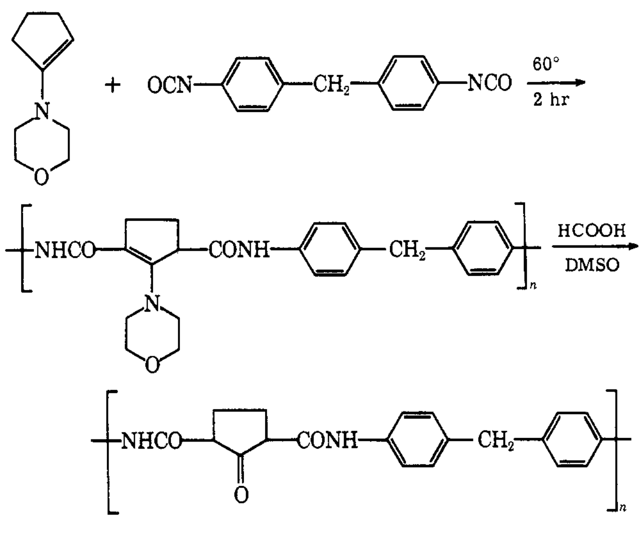


64

A cycloalkenylamine and an isocyanate give a quinoline derivative.[254]



The following two polyamides were obtained from diisocyanates.[255]



1,1-Di(1-piperidinyl)ethylene reacts with one or two molecules of phenyl isocyanate to give a mono- or a diamide (eq 1).[256]

Alkyl and aryl isocyanates generally do not add to unactivated olefinic double bonds; however, when heated (Δ^2-diphenylcyclopropenyl)methyl isocyanate (**65**) in refluxing ethanol reacts intramolecularly to give diphenyl-α-pyrolidone (**66**) as the main product along with a small amount of ethyl carbamate (eq 2).[257]

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[251] K. Ley and R. Nast, *Angew. Chem.*, **77**, 544 (1965).

[252] K. Ley, U. Eholzer, and R. Nast, *ibid.*, **77**, 544 (1965).

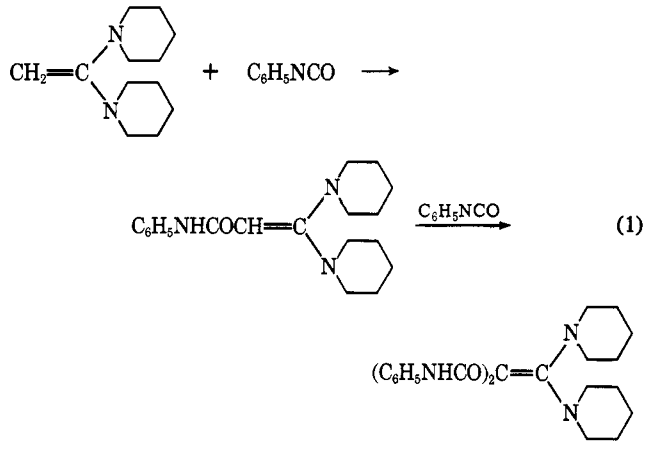
[253] R. W. Lamon, *J. Heterocycl. Chem.*, **6**, 261 (1969).

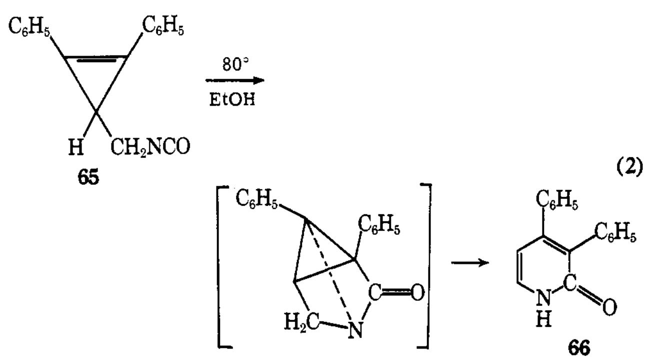
[254] W. Reid and W. Kappeler, *Justus Liebigs Ann. Chem.*, **688**, 177 (1965).

[255] W. H. Daly and W. Kern, *Makromol. Chem.*, **108**, 1 (1967).

[256] D. H. Clemens, A. J. Bell, and J. L. O'Brien, *J. Org. Chem.*, **29**, 2932 (1964).

[257] S. Masamune and K. Fukumoto, *Tetrahedron Lett.*, 4652 (1965).


(1)

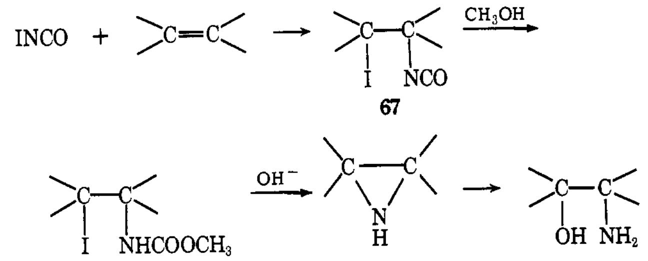

65

(2)

66

3. *Addition of Iodo Isocyanate to Olefins*

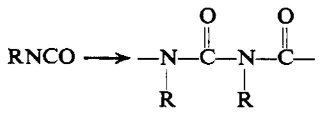
The formation of 1:1 adducts (**67**) between iodo isocyanate and an olefin have been reported.[68]


67

Adduct **67** may react with methanol to give a carbamate and then be converted to an aziridine by hydrolysis with alkali. This is a convenient route from an olefin to aziridine. The aziridine may be hydrolyzed into an amino alcohol, often difficult to obtain by other methods.

C. POLYMERIZATIONS AND COPOLYMERIZATIONS OF ISOCYANATES

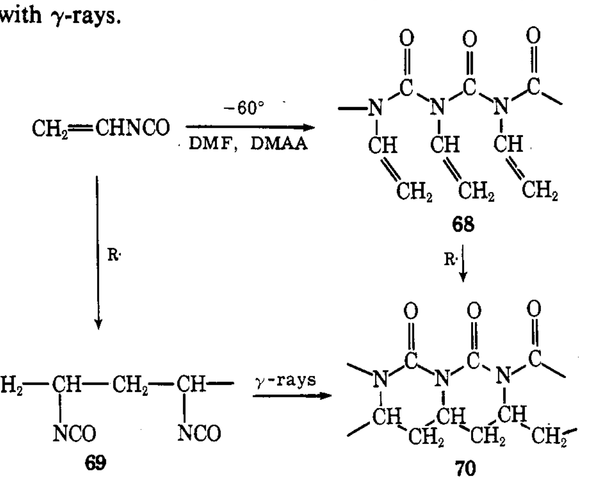
Following the discovery in 1959 by Shashoua[258,259] of the formation of 1-nylon, many investigations have been carried out.


1-nylon

1. *Polymerization of Vinyl Isocyanate*

Without a catalyst vinyl isocyanate polymerizes in DMF below −40° to give *N*-vinyl-1-nylon (**68**).

In the presence of radicals, **68** is converted into the ladder polymer **70**, also obtained by treating polyvinyl isocyanate (**69**) with γ-rays.

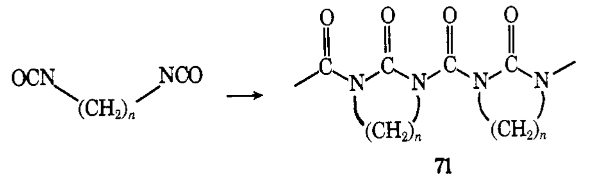

68

69

70

2. *Cyclopolymerizations*

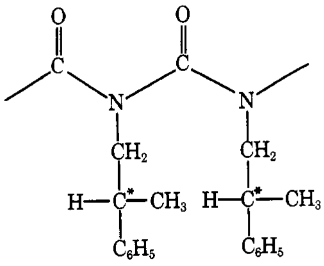
Cyclopolymerizations of diisocyanates such as trimethylene diisocyanate have been carried out at three laboratories at about the same time.[260-263]


71

1,3-Diisocyanatocyclohexane was cyclopolymerized using sodium cyanide as an initiator to give soluble polymers which contained little or no residual isocyanato groups.[264] Cyclopolymerizations of *cis*- and *trans*-1,3,5-triisocyanatocyclohexane were reported recently.[265]

3. *Optically Active Polyisocyanates*[266]

The circular dichroism of poly(*d*-β-phenylpropyl isocyanate) has been studied.


$[\alpha]^{25}{}_D$ −468.8° (in CHCl$_3$)

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[258] V. E. Shashoua, *J. Amer. Chem. Soc.*, **81**, 3156 (1959).

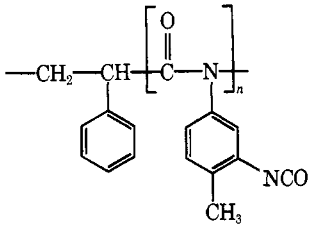
[259] V . E. Shashoua, *ibid.*, **82**, 866 (1960).

[260] Y. Iwakura, K. Uno, and K. Ichikawa, *J. Polym. Sci., Part A*, **2**, 3387 (1964).

[261] W. L. Miller and W. B. Black, *Polym. Prepr., Amer. Chem. Soc., Div. Polym. Chem.*, **3**, 345 (1962).

4. *Block Copolymers*

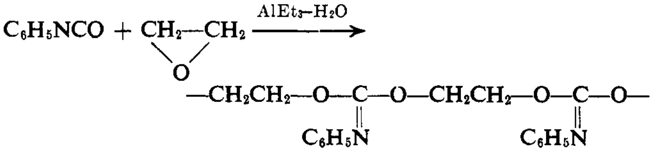
By copolymerization isocyanates have been attached to the living end of vinyl polymers obtained by anionic catalysis.[267] The block copolymer (**72**) with a free isocyanato group was prepared from tolylene diisocyanate.[268]



72

5. *Alternating Copolymers*

An alternating copolymer was obtained from the copolymerization of phenyl isocyanate and ethylene oxide with triethylaluminum by itself or combined with water as catalysts.[269]

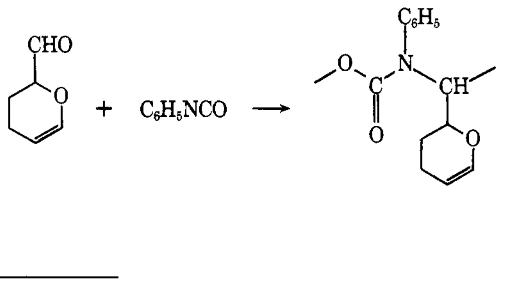


$$C_6H_5NCO + \underset{\diagdown O \diagup}{CH_2{-}CH_2} \xrightarrow{AlEt_3{-}H_2O} -CH_2CH_2{-}O{-}\underset{\underset{C_6H_5N}{\|}}{C}{-}O{-}CH_2CH_2{-}O{-}\underset{\underset{C_6H_5N}{\|}}{C}{-}O-$$

73

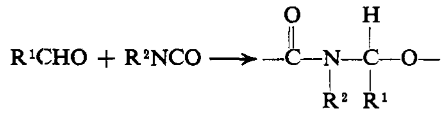
The polymer **73** is unique in requiring combination with CO rather than CN linkages in the isocyanate. The mechanism of this alternating copolymerization has been studied.[270,271] It appears to be limited to aromatic isocyanates since aliphatic and alicyclic isocyanate do not give copolymers. Ortho-substituted aromatic isocyanates give copolymers in high yields. It has been suggested that aluminum triethyl coordinates with both the isocyanato group and the ortho substituent.

An alternating copolymer was obtained from the copolymerization of phenyl isocyanate with acrolein dimer in the presence of an anionic catalyst such as butyllithium at room temperature. Changes in the monomer ratio had no effect.[272]



6. *Copolymerizations*

Aldehydes and isocyanates copolymerize anionically at low temperature to give polycarbamates.[273,274] Chloral and a monoisocyanate give a copolymer.[275-280] Anionic polymerization of styrene followed by copolymerization with acetaldehyde and phenyl isocyanate gives a polymer which melts at 201° and decomposes to the extent of 5% at 100° in 2 hr.[281] Diphenylketene and an isocyanate may undergo anionic polymerization at low temperatures.[282]



$$R^1CHO + R^2NCO \longrightarrow -\overset{\overset{O}{\|}}{C}{-}\underset{R^2}{\underset{|}{N}}{-}\overset{\overset{H}{|}}{\underset{\underset{R^1}{|}}{C}}{-}O-$$

7. *Thermal Decomposition of Polyisocyanates*[283]

Poly(cyclohexyl isocyanate) gives cyclohexyl isocyanate upon heating. Poly(*n*-butyl isocyanate) at 190° turns to a liquid in few minutes. Distillation gives *n*-butyl isocyanate and a trimer in the residue.

8. *Trimerization*

Even though trimerization is well known, numerous new patents and reports on the trimerization of isocyanate have been published.

Two moles of an aromatic diisocyanate may be polymerized, and the product may copolymerize with 1 mol of an aliphatic diisocyanate when Bu_3P, Et_3P, or $(C_6H_5)_3P$ is the catalyst.[284] Diethyldipyridylnickel is also a catalyst.[285] Tertiary amines have functioned as catalysts, with a cocatalyst selected from benzoyl peroxide or 2,3-butanedione. This combined catalyst acts at room temperature in 1 or 2 min.[286] Fire-retardant polyurethane foams have been obtained by trimerization of an excess of isocyanates in the presence of catalysts,[287,288] such as acetylacetonate,[289] followed by a reaction between the remaining isocyanates with alcohols or amines.

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(262) Monsanto Chemicals, Japanese Patent 39-15533 (1964).

(263) C. King, *J. Amer. Chem. Soc.*, **86**, 437 (1964).

(264) G. C. Corfield and A. Crawshaw, *J. Macromol. Sci., Chem.*, **5**, 3 (1971).

(265) G. B. Butler and G. C. Corfield, *ibid.*, **5**, 37 (1971).

(266) M. Goodman and S. Chen, *Macromolecules*, **3**, 398 (1970).

(267) E. I. du Pont de Nemours & Co., British Patent 987741 (1965); Japanese Patent 40-12304 (1965); *Chem. Abstr.*, **62**, 1818a (1965).

(268) R. A. Godfrey and G. W. Miller, *Polym. Prepr., Amer. Chem. Soc., Div. Polym. Chem.*, **10**, 218 (1969).

(269) J. Furukawa, S. Yamashita, M. Murahashi, and K. Harada, *Makromol. Chem.*, **85**, 80 (1965).

(270) K. Harada, A. Deguchi, and J. Furukawa, *ibid.*, **132**, 281 (1970).

(271) K. Harada, J. Furukawa, and S. Yamashita, *ibid.*, **131**, 185 (1970).

(272) Y. Kitayama, H. Ohama, and H. Kobayashi, *J. Polym. Sci., Part A-1*, **7**, 935 (1969).

(273) H. Takida and T. Noro, *Kobunshi Kagaku*, **22**, 463 (1965); *Chem. Abstr.*, **64**, 2174b (1966).

(274) Spencer Chemical Co., British Patent 959527 (1964).

(275) G. Odian and L. S. Huraoka, *J. Polym. Sci., Part A-1*, **8**, 1309 (1970).

(276) Y. P. Getmanchuk, Y. L. Spirin, and R. I. Dryagileva, *Dokl. Akad. Nauk SSSR*, **171**, 1173 (1966).

(277) M. C. Raes, J. Kavabinos, and H. J. Dietrich, *J. Polym. Sci., Part A-1*, **6**, 1067 (1968).

(278) H. Takida and K. Noro, *Kobunshi Kagaku*, **22**, 243 (1965).

(279) Y. P. Getmarchuk, Y. L. Spirin, R. I. Dryagileva, and N. P. Doroshenko, *Sin. Fiz.-Khim. Polim.*, 8 (1968).

(280) E. I. du Pont de Nemours & Co., Japanese Patent 46-10184 (1971).

(281) Japan Synthetic Chemical Industry Co., Japanese Patent 43-18155 (1968).

(282) Chisso Corp., Japanese Patent 44-11140 (1969).

(283) Y. Iwakura, K. Uno, and N. Kobayashi, *J. Polym. Sci., Part A-1*, **6**, 2611 (1968).

(284) Farbenfabriken Bayer A.-G., French Patent 1510342 (1968); *Chem. Abstr.*, **70**, 37845 (1969).

(285) T. Kashiwagi, M. Hidai, Y. Uchida, and A. Misono, *J. Polym. Sci., Part B*, **3**, 173 (1970).

(286) Atlas Chemical Industries, Inc., Japanese Patent 46-13257 (1971).

(287) Farbenfabriken Bayer A.-G., Belgian Patents 723152, 723153, 726333 (1971).

(288) L. Nicholas and G. T. Gmitter, *J. Cell. Plast.*, **1**, 85 (1965).

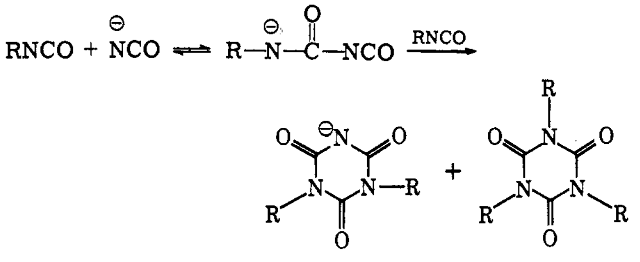
(289) Nisshin Boseki, Japanese Patent 46-28424 (1971).

D. RING FORMATION REACTIONS

There are many recent publications on ring formation reactions.

1. *Disubstituted Diisocyanurates*[290]

An isocyanate and an alkali cyanate kept at 75° in DMF give disubstituted isocyanurates (**74**) and trisubstituted isocyanurates (**75**).

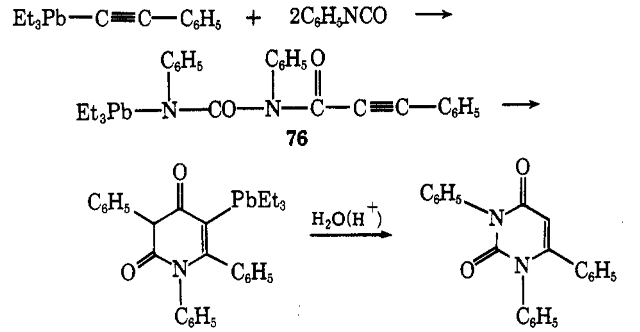


74 **75**

Selectivity indexes for **74** are 0.93 (R = C_6H_5), 0.33 (*n*-Bu), 0.60 ($C_6H_5CH_2$), 0.87 (*o*-$CH_3C_6H_4$–).

2. *Reaction with an Ethynyllead Derivative*[291]

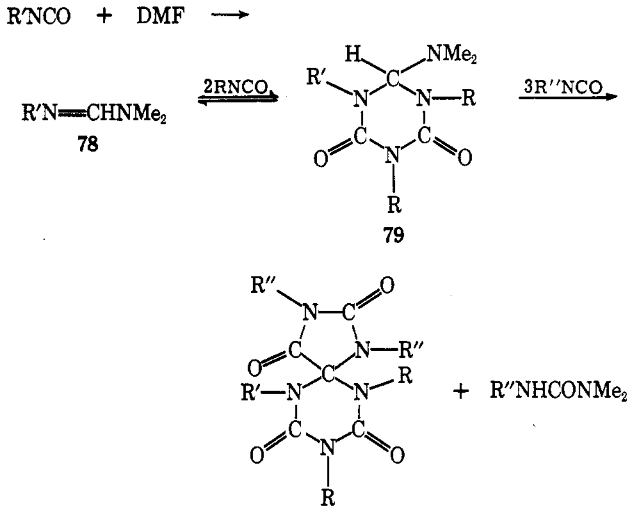
An insertion of two isocyanate groups between lead and the ethynyl group gives **76**, in a new route to *N*,*N'*-diaryluracil (**77**).



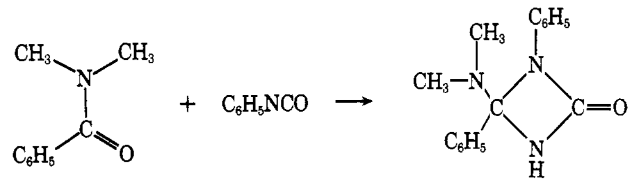
76 **77**

3. *Reaction with DMF and with an Amidine*

It is known that *N*-phenyl-*N'*,*N'*-dimethylformamidine (**78**) is produced by the reaction of phenyl isocyanate with DMF.[292] Amidine **78** reacts with phenyl isocyanate to give a 1:2 adduct (**79**)[293,294] along with a high-melting spiro derivative (**80**).[295–297] *N*,*N*-Dimethylbenzamidine reacts with phenyl isocyanate to give a 1:1 cyclic adduct (**81**).[298]

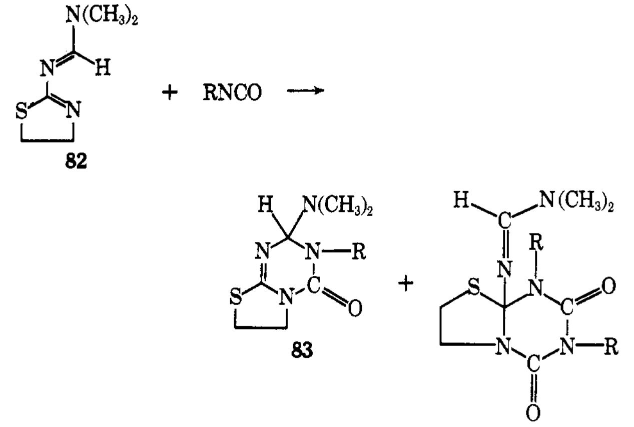


78 **79** **80**

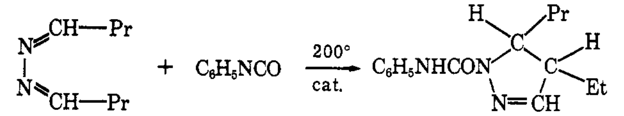


81

N,*N*-Dimethyl-*N'*-[Δ^2-thiazolinyl-(2)]formamidine (**82**) and phenyl isocyanate give a 1:1 adduct (**83**) and a 1:2 adduct (**84**).[299] Butyraldazine and phenyl isocyanate give a 1:1 adduct (**85**).[300]



82 **83** **84**



85

4. *Reaction with Substituted Guanidines*

Substituted guanidines and isocyanates give 1:2 adducts (**86**).[301]

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[290] P. A. Argabright, B. L. Phillips, and C. H. De Puy, *Tetrahedron Lett.*, 5033 (1968).

[291] A. G. Davies and R. J. Puddephatt, *ibid.*, 2265 (1967).

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[293] R. Richter, *Chem. Ber.*, **101**, 3002 (1968).

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[296] E. Dyer, T. E. Majewski, and J. D. Travis, *ibid.*, **33**, 3932 (1968).

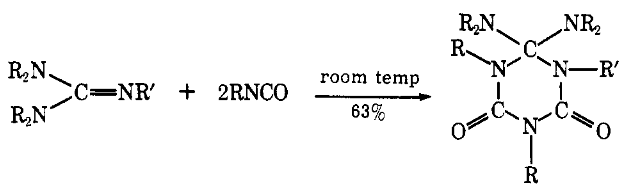
[297] R. Richter and H. Ulrich, *ibid.*, **36**, 2003 (1971).

[298] G. Schwenker and R. Kolb, *Tetrahedron*, **25**, 5437 (1969).

[299] R. Richter and H. Ulrich, *Chem. Ber.*, **103**, 3525 (1970).

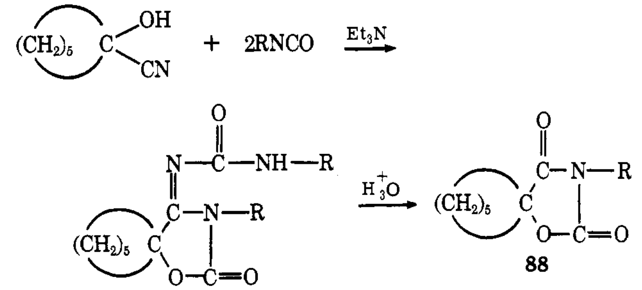
[300] L. Zirngibl, *Helv. Chim. Acta*, **53**, 1927 (1970).

[301] R. Richter, *Tetrahedron Lett.*, 5037 (1968).



86

5. *Reaction with a Cyanohydrin*[302]



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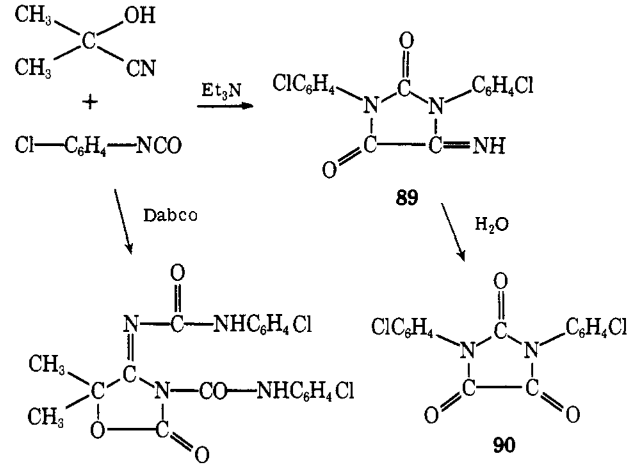
88

Hydrolysis of 4-imino-2-oxazolidinone (**87**), produced by the reaction between a cyanohydrin and an isocyanate in the presence of a tertiary amine, gives 2,4-oxazolidindione (**88**). From acetone–cyanohydrin 4-imino-2,5-imidazolidione (**89**) was obtained. Parabanic acids (**90**) result from the hydrolysis of **89**.



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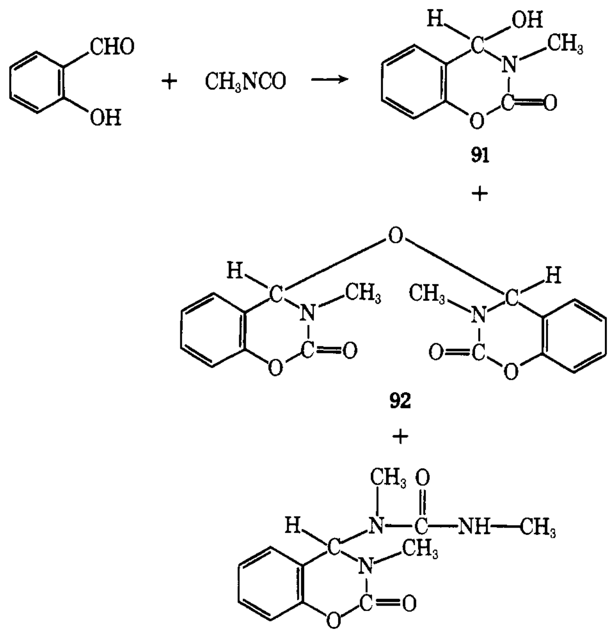
90

6. *Reaction with o-Hydroxy Aromatic Aldehydes*[303]

Salicylaldehyde and methyl isocyanate in benzene react exothermically. In this way three compounds, 3,4-dihydro-4-hydroxy-3-methyl-2*H*-1,3-benzoxazin-2-one (**91**), 4,4′-oxobis-(3,4-dihydro-3-methyl-2*H*-benzoxazin-2-one) (**92**), and 1-(3,4-dihydro-3-methyl-2-oxo-2*H*-1,3-benzoxazin-4-yl)-1,3-dimethylurea (**93**) were obtained.



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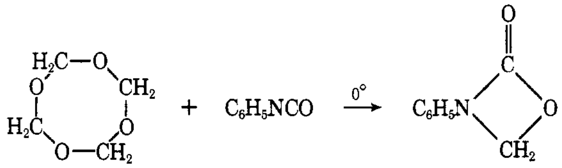
93

7. *Reaction with Tetraoxane*[304]

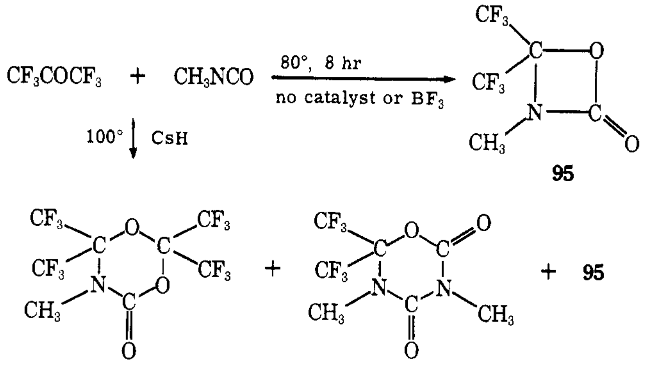
When tetraoxane reacted with phenyl isocyanate at 0° in the presence of boron trifluoride etherate for 24 hr, 2-oxo-3-phenyl-1,3-oxazetidine (**94**) was produced. The product is a new four-membered ring system containing oxygen and nitrogen at the 1,3 positions.



94

8. *Reaction with Hexafluoroacetone*[305]

Hexafluoroacetone reacts with methyl isocyanate to give a 1,3-oxazetidine (**95**). Neither acetone nor trifluoroacetone gives a four-membered ring with an isocyanate.



95

9. *Reaction with β-Propiolactone*[306]

Phenyl isocyanate and β-propiolactone in the presence of boron trifluoride etherate produced 2,4-dioxo-3-phenyl-3,4,5,6-tetrahydro-2*H*-1,3-oxazine (**96**).

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(302) T. L. Patton, *J. Org. Chem.*, **32**, 383 (1967).

(303) G. Bobowski and J. Shavel, Jr., *ibid.*, **32**, 953 (1967).

(304) S. Ozaki, *Tetrahedron Lett.*, 3637 (1967).

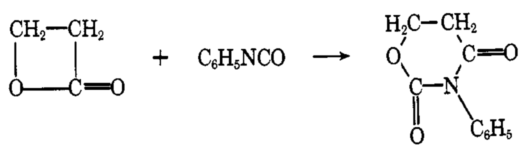
(305) R. J. Shozda, *J. Org. Chem.*, **32**, 2960 (1967).

(306) S. Ozaki and T. Kato, *J. Polym. Sci., Part C*, **23**, 695 (1968).

Table III

Synthesis of Oxazines (93) and Pyrones (99)

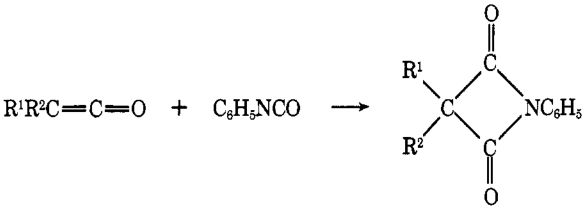
		98		99	
R	*Catalyst*	*Yield, %*	*Mp, °C*	*Yield, %*	*Mp, °C*
C_6H_5	*p*-TSA	41	160	20	143
2-ClC_6H_4	*p*-TSA	0		35.4	200
3-ClC_6H_4	*p*-TSA	38.2	149.5	Trace	
4-ClC_6H_4	*p*-TSA	69.4	209	0	
2-$NO_2C_6H_4$	*p*-TSA	26.0	166	7.3	182
3-$NO_2C_6H_4$	*p*-TSA	11.9	157	51.2	183
4-$NO_2C_6H_4$	*p*-TSA	93.9	218	0	
2-$CH_3C_6H_4$	$BF_3 \cdot Et_2O$	0		59.9	159
4-$CH_3C_6H_4$	*p*-TSA	54.5	211	6.7	190
	$BF_3 \cdot Et_2O$	0		9.9	190
2,5-$Cl_2C_6H_3$	*p*-TSA	82.1	195	0	
	$BF_3 \cdot Et_2O$	16.4	195	13.6	171
n-C_6H_{13}	*p*-TSA	37.9	78	0	



96

10. *Reactions with Ketenes*[307]

Dialkylketenes and isocyanates give malonimides (**97**).



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11. *Reactions with Diketene*[308]

The reactions of isocyanates with diketene give different products according to reaction conditions. In the presence of acids,[309] 3-aryl-2,4-dioxo-3,4-dihydro-6-methyl-2*H*-1,3-oxazines (**98**) and 3-arylcarbamoyl-2,6-dimethyl-4-pyrones (**99**) are obtained (see Table III). In the presence of base,[310] 3-acetyl-1-aryl-4-hydroxy-6-methyl-2-oxo-1,3-dihydropyridines (**100**) are obtained (Table IV).

12. *Reaction with Carbodiimide*

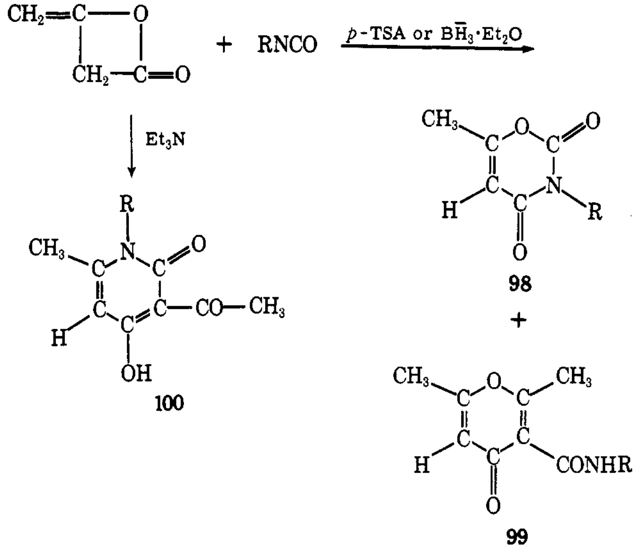
In a 1:1 ratio a carbodiimide and an isocyanate give an iminouretidinone (**101**).[311] Because **101** dissociates in two ways, it is possible to generate a new isocyanate. An iminouretidinone also gives the reactions shown in Scheme IV.[312]

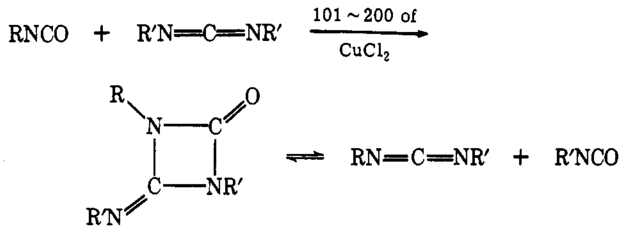
Table IV

Synthesis of Pyridines (100)[a]

	100	
R	*Yield %*	*Mp, °C*
2-ClC_6H_4	65.0	221
3-ClC_6H_4	34.0	200
2-$NO_2C_6H_4$	53.1	179
4-$NO_2C_6H_4$	60.0	264
2-$CH_3C_6H_4$	0	
4-$CH_3C_6H_4$	52.3	205
2,5-$Cl_2C_6H_3$	65.5	185
$C_{10}H_7$	38.9	194

[a] The catalyst in each case was Et_3N.





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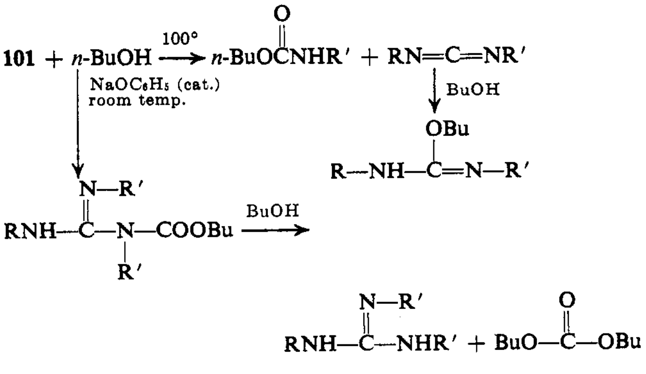
Scheme IV



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(307) J. C. Martin, R. D. Burpitt, P. G. Gott, M. Harris, and R. H. Meen, *J. Org. Chem.*, **36**, 2205 (1971).

(308) S. Ozaki and T. Kato, Meeting on Organic Reaction Mechanism Chemical Society of Japan, Yamagata, Nov 10, 1968.

(309) Mitsui Toatsu Chemicals Co., Japanese Patent 604712 (1971).

(310) Mistui Toatsu Chemicals Co., Japanese Patent 602368 (1971).

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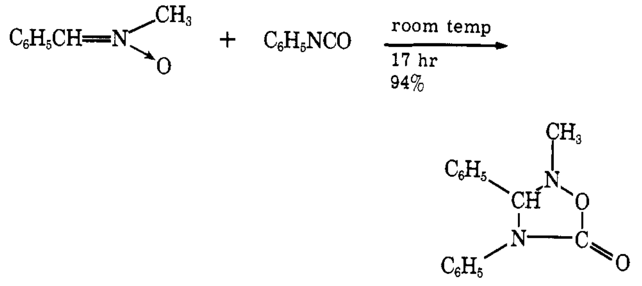
13. Reaction with Nitrones[313]

A 1,2-oxadiazolidone-5 (**102**) was obtained by the reaction of the *N*-oxide of the *N*-methylimine of benzaldehyde and phenyl isocyanate.



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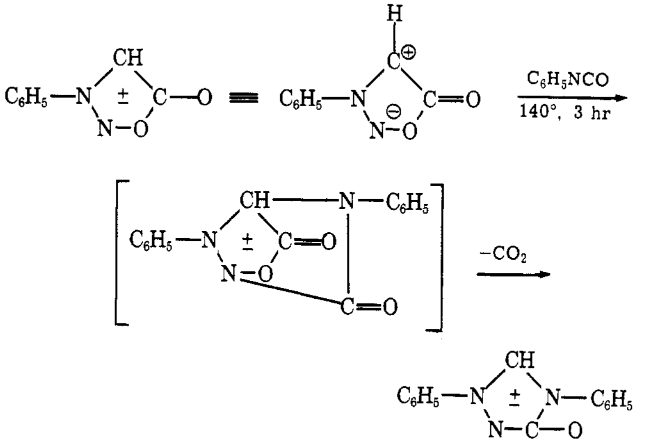
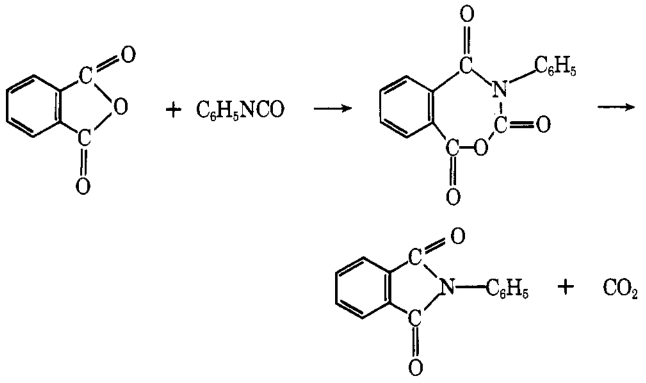
14. Reaction with Sydnone[314]

A reaction between 3-phenylsydnone and phenyl isocyanate gives 1,4-diphenyl-1,3,4-triazolone (**103**).



103

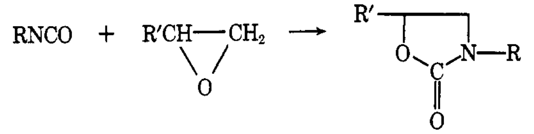
15. Reaction with Acid Anhydrides[315]



Diisocyanates and bis anhydrides give cellular polymides.[316]

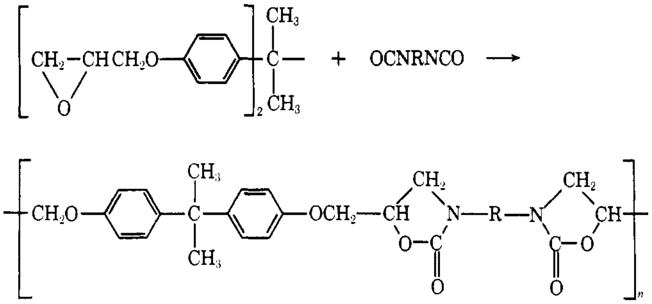
16. Reactions with Epoxides

A 2-oxazolidone may be prepared from an isocyanate and an epoxide.



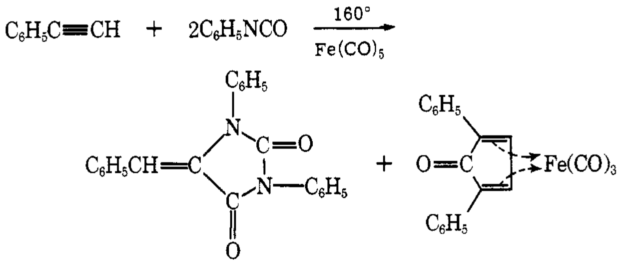
The reaction proceeds rapidly and in high yield in the presence of a soluble lithium bromide–phosphine oxide adduct.[317]

Polyoxazolidones are obtained from diisocyanates and bis epoxides.[318] *n*-Butyllithium is a good catalyst.[319]



17. Reaction with Phenylacetylene[320]

A reaction between phenyl isocyanate and phenylacetylene in the presence of $Fe(CO)_5$ leads to 4-benzylidene-1,3-diphenylhydantoin (**104**) in 85% yield. Relocation of hydrogen appears to follow a 1,2 shift.



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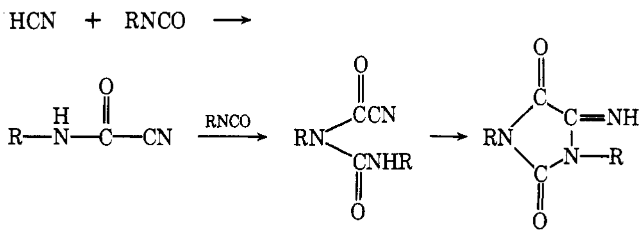
18. Reaction with Hydrogen Cyanide

Hydrogen cyanide and an isocyanate in a 1:2 molar ratio give an iminohydantoin (**105**). This reaction has been extended to diisocyanates[321] and to vinyl isocyanate.[322]



105

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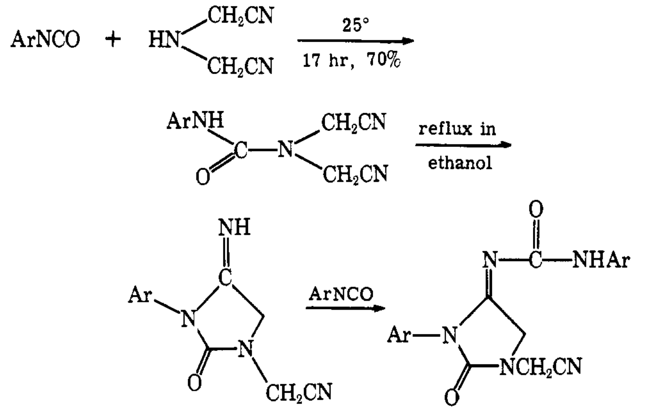
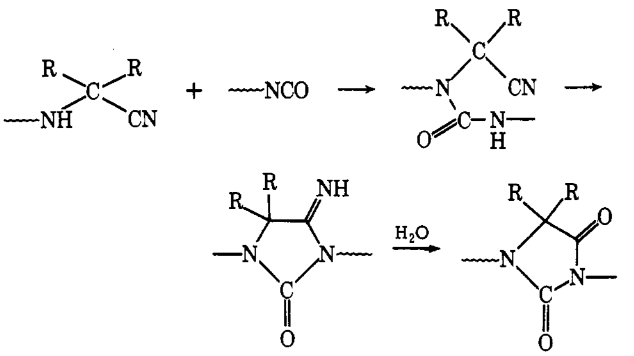
19. Reaction with Iminodiacetonitrile

This reaction gives an iminoimidazolidinone (**106**) and its derivative (**107**).[323]



106 **107**

The reaction between a glycine nitrile and an isocyanate gives a urea, which may cyclize into an iminohydantoin (**108**).[324]



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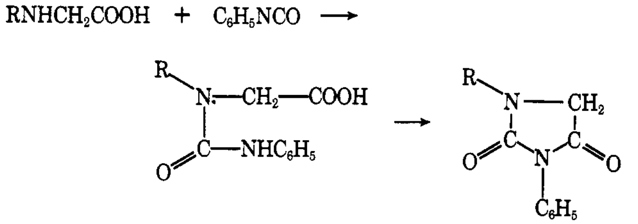
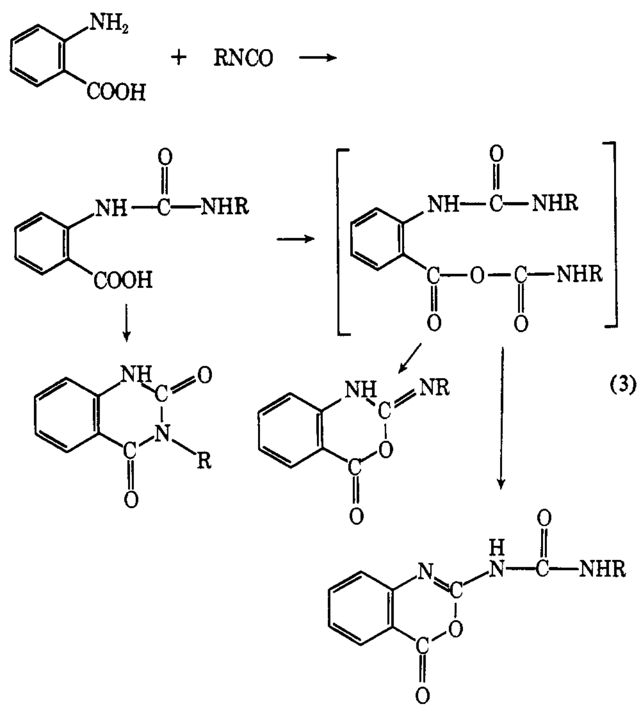
20. Reaction with Amino Acid



109

An α-amino acid or its ester and an isocyanate give a hydantoin (**109**). This reaction can be extended to diisocyanates to give polyhydantoins.[325,326] Anthranilic acid and isocyanate react as shown in eq 3.[327]

The reaction between a diaminodicarboxylic acid and a diisocyanate gives a high temperature resistant polymer (eq 4).[328]



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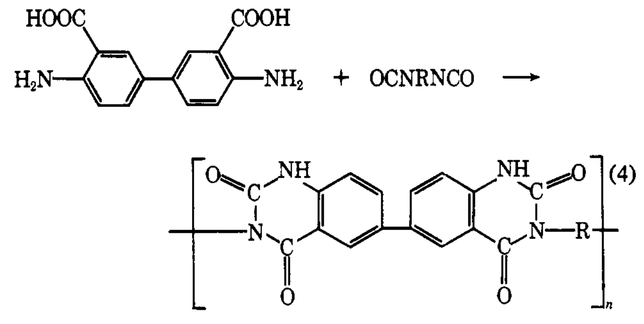
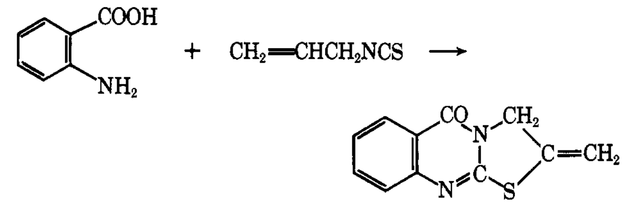


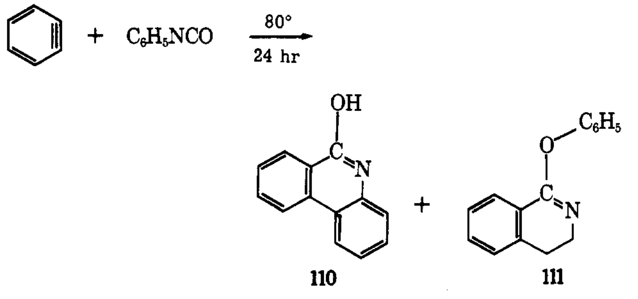
(4)

Anthranilic acid and allyl isothiocyanate react as follows.[329]



21. Reaction with Benzyne[330]

Benzyne and phenyl isocyanate give phenanthridone (**110**) and 9-phenoxyphenanthridine (**111**).



110 **111**

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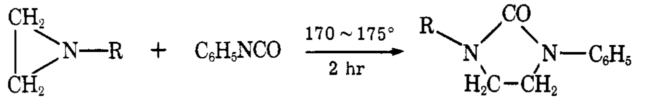
22. Reaction with Aziridines[331]

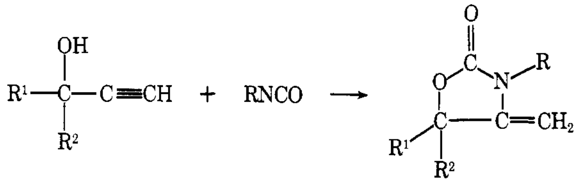
A non-N-substituted aziridine and an isocyanate give addition products whereas an N-substituted aziridine gives imidazolidines (**112**).



112

23. Reaction with Propargyl Alcohols and Propargylamines[332]

By the following reactions propargyl alcohols give 4-methylene-4-oxazolidinones (**113**), and propargylamines give 4-methylene-2-imidazolones (**114**).



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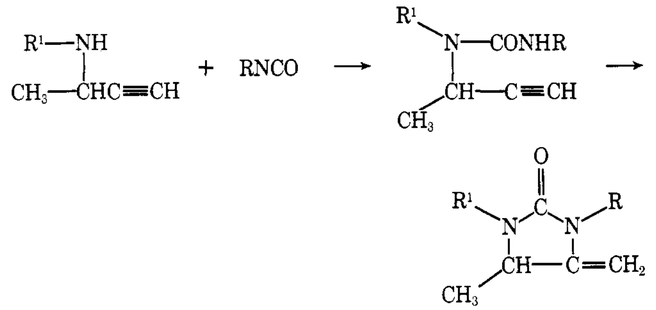
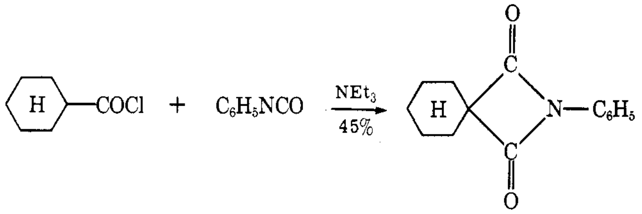


114

24. Reaction with Cyclohexanecarbonyl Chloride[333]

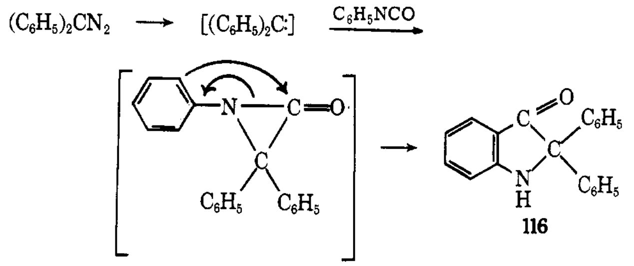
N-Phenylpentamethylenemalonimide (**115**) is produced when phenyl isocyanate reacts with cyclohexanecarboxylic acid chloride in the presence of a tertiary amine



115

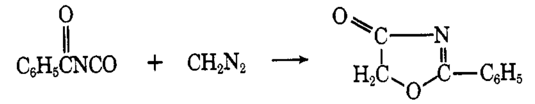
25. Reaction with Diazomethanes[334]

When diphenyldiazomethane and phenyl isocyanate are irradiated, 2,2-diphenylindoxyl (**116**) is produced.



116

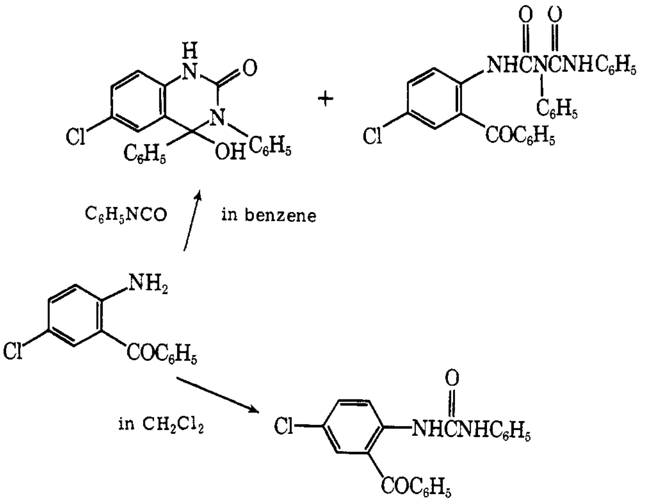
The reaction of benzoyl isocyanate with diazomethane gives oxazolones (**117**).[335]



117

26. Reaction with 2-Amino-5-chlorobenzophenone[336]

In different solvents 2-aminobenzophenones and phenyl isocyanate give various products.



27. Reaction with Phthalic Acid Monoamide[337]

This reaction also depends upon the solvent (see eq 5).

28. Reaction with Phthalaldehyde[338]

When an equimolar mixture of phenyl isocyanate and phthaldehyde was heated at 170° for 4 hr, *N*-phenylphthalimidine (**121**) and carbon dioxide were obtained quantitatively (see eq 6).

29. Reaction with Tartaric Acid[339]

The reaction between a tartrate ester and a diisocyanate produces a polyoxazolidinedione (**123**) *via* the urethane intermediate (**122**) (eq 7).

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[331] E. Gulbins, R. Morlock, and K. Hamann, *Justus Liebigs Ann. Chem.*, **698**, 180 (1966).

[332] N. Shachat and J. J. Bagnell, Jr., *J. Org. Chem.*, **28**, 991 (1963).

[333] A. C. Poshkus and J. E. Herweh, *ibid.*, **30**, 2466 (1965).

[334] J. C. Sheehan and I. Lengyel, *ibid.*, **28**, 3254 (1963).

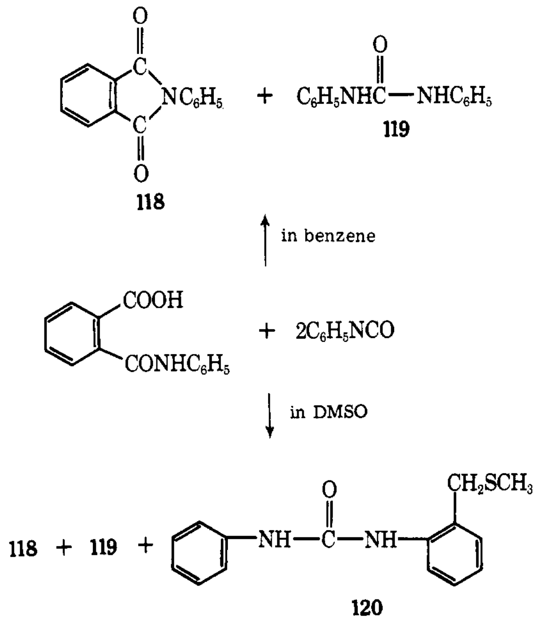
[335] J. C. Sheehan, *J. Amer. Chem. Soc.*, **71**, 4059 (1949).

[336] T. Ishiwaka, N. Ojima, K. Isagawa, and Y. Fushigaki, *Nippon Kagaku Zasshi*, **90**, 917 (1969).

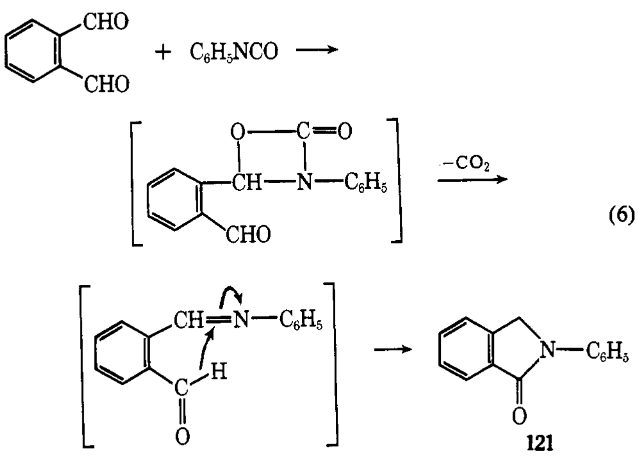
[337] P. S. Carleton and W. J. Farrissey, *Tetrahedron Lett.*, 3485 (1969).

[338] I. Yamamoto, Y. Tobo, H. Gotoh, T. Minami, Y. Ohshiro, and T. Agawa, *ibid.*, 2295 (1971).

[339] E. I. du Pont de Nemours & Co., U. S. Patent 3244675 (1966); Farbenfabriken Bayer A.-G., Netherlands Patent 6705983 (1967).



(5)



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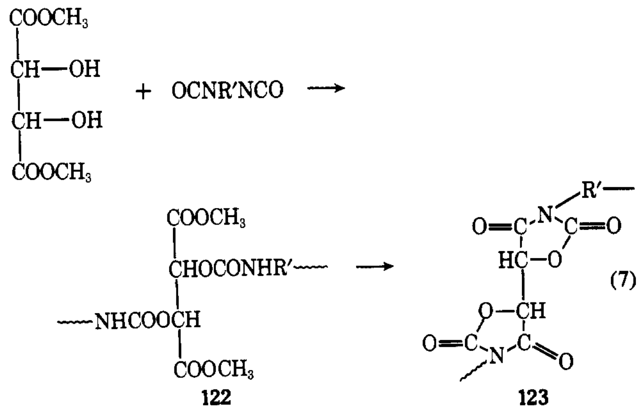
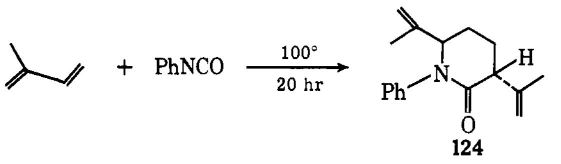


(7)

30. Reactions with Conjugated Dienes[340]

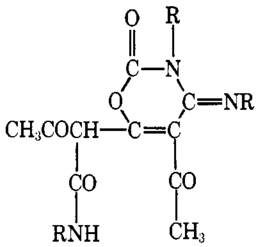
Conjugated dienes, such as isoprene and butadiene, react with isocyanates to form divinylpiperidones (**124**) in high yields when catalytic amounts of palladium–triphenylphosphine complexes are present.



31. Reactions with Diacetylacetone[341]

Phenyl isocyanate and diacetylacetone react to give 5-acetyl-4-phenylimino-2-oxo-3-phenyl-6-(α-phenylcarbamoyl)acetonyl-3,4-dihydro-2H-1,3-oxazine in the presence of triethylamine.

$$RNCO + CH_3COCH_2COCH_2COCH_3 \xrightarrow{Et_3N}$$

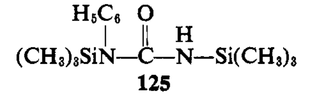


E. INSERTION REACTIONS

1. Insertion of Isocyanate Group into a Si–N Bond[342,343]

Phenyl isocyanate inserts into the Si–N bond of hexamethyldisilazane to give 1,3-bistrimethylsilyl-1-phenylurea (**125**).[344]

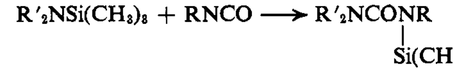
$$(CH_3)_3SiNHSi(CH_3)_3 + C_6H_5NCO \longrightarrow$$



$$(CH_3)_3Si\overset{H_5C_6}{\overset{|}{N}}-\overset{O}{\overset{\|}{C}}-\overset{H}{N}-Si(CH_3)_3$$

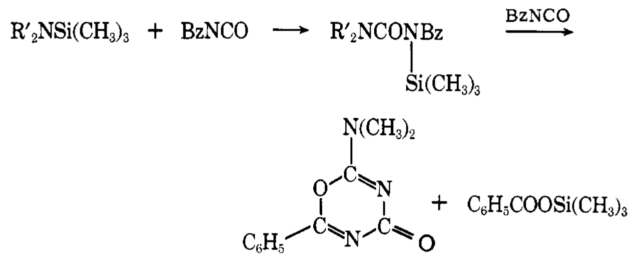
125

Trimethylsilazane and an alkyl isocyanate[345] or an arylsulfonyl isocyanate[346] react as follows.



$$R'_2NSi(CH_3)_3 + RNCO \longrightarrow R'_2NCO\underset{Si(CH_3)_3}{\underset{|}{N}}R$$

Benzoyl isocyanate and trimethylsilazane react in a similar way. The product then combines with another mole of benzoyl isocyanate.[347]



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(340) K. Ohno and J. Tsuji, *Chem. Commun.*, 247 (1971).

(341) S. Ozaki, unpublished work.

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(343) K. Itoh, S. Sakai, and Y. Ishii, *Yuki Gosei Kagaku Kyokai Shi*, **24**, 729 (1966).

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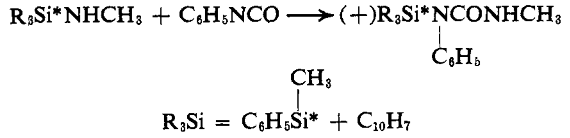
(347) I. Matsuda, K. Itoh, and Y. Ishii, *J. Chem. Soc., C*, 1870 (1971).

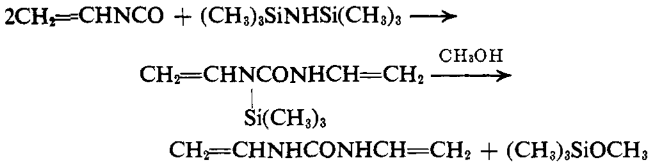
Optically active aminosilanes react with phenyl isocyanate to form silylureas with retention of configuration at the Si atom.[348]



$$R_3Si^*NHCH_3 + C_6H_5NCO \longrightarrow (+)R_3Si^*\underset{C_6H_5}{N}CONHCH_3$$

$$R_3Si = C_6H_5\overset{CH_3}{Si^*} + C_{10}H_7$$

The reaction has been extended to a synthesis of 1,3-divinylurea (**126**), for which other attempts to prepare were unsuccessful.[349]

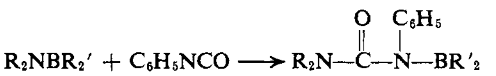


$$2CH_2{=}CHNCO + (CH_3)_3SiNHSi(CH_3)_3 \longrightarrow CH_2{=}CH\underset{Si(CH_3)_3}{N}CONHCH{=}CH_2 \xrightarrow{CH_3OH} CH_2{=}CHNHCONHCH{=}CH_2 + (CH_3)_3SiOCH_3$$

126

2. *Insertion Reaction between N-B Bond*

Isocyanates come into the N-B bond of aminoborane to give *N*-dialkylboron ureas (**127**).[350]

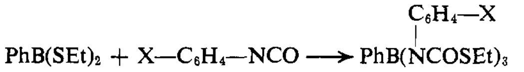


$$R_2NBR_2' + C_6H_5NCO \longrightarrow R_2N-\overset{O}{\overset{\|}{C}}-\overset{C_6H_5}{\overset{|}{N}}-BR'_2$$

127

3. *Thioboration of Isocyanates*[351]

Bis(ethylthio)phenylborane and an aryl isocyanate give bis(*N*-aryl-*N*-ethylthiocarbonylamino)phenylboranes (**128**).

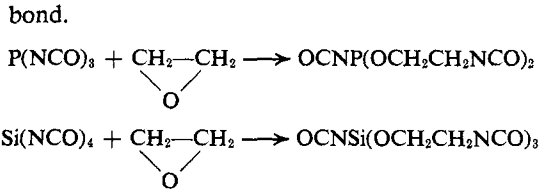


$$PhB(SEt)_2 + X-C_6H_4-NCO \longrightarrow PhB(\overset{C_6H_4-X}{\overset{|}{N}}COSEt)_3$$

128

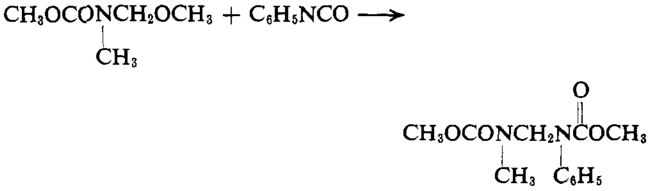
4. *Reaction of Phosphorus Isocyanate or a Silyl Isocyanate with Ethylene Oxide*[352]

Opening of the epoxide ring by either reagent permits sandwiching of the ring-opened species into either a P-N or an Si-N bond.



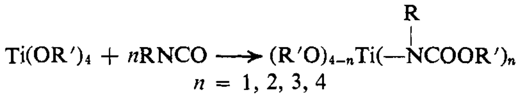
5. *Reaction with Labile Methoxy Derivatives*[353]

An isocyanate may insert between CH_2 and OCH_3 in a reaction with a labile methyl ether.



$$CH_3OCO\underset{CH_3}{N}CH_2OCH_3 + C_6H_5NCO \longrightarrow CH_3OCO\underset{CH_3}{N}CH_2\underset{C_6H_5}{N}\overset{O}{\overset{\|}{C}}OCH_3$$

6. *Insertion Reactions of Titanium Alkoxides with Isocyanates*[354]

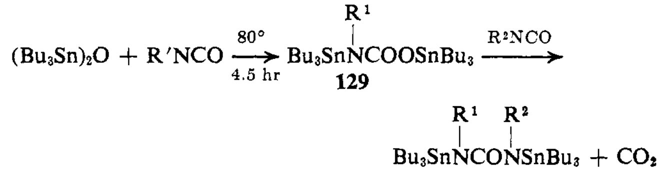


$$Ti(OR')_4 + nRNCO \longrightarrow (R'O)_{4-n}Ti(-\overset{R}{\overset{|}{N}}COOR')_n$$

$$n = 1, 2, 3, 4$$

7. *Reactions with Organotin Oxides*

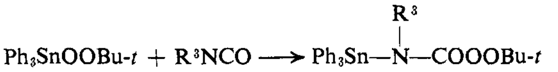
Organotin oxides and isocyanates give trialkyltin carbamates (**129**) and *N,N'*-dibutylbis(tributylstannyl)ureas (**130**).[355]



$$(Bu_3Sn)_2O + R'NCO \xrightarrow[4.5\ hr]{80^\circ} Bu_3Sn\overset{R^1}{\overset{|}{N}}COOSnBu_3 \xrightarrow{R^2NCO} Bu_3Sn\overset{R^1}{\overset{|}{N}}CO\overset{R^2}{\overset{|}{N}}SnBu_3 + CO_2$$

129 **130**

Triphenyltin *tert*-butyl peroxide adds to an alkyl isocyanate to yield crystalline *tert*-butyl *N*-alkyl-*N*-triphenylstannyl peroxycarbamates (**131**), a new family of organic peroxides.[356]

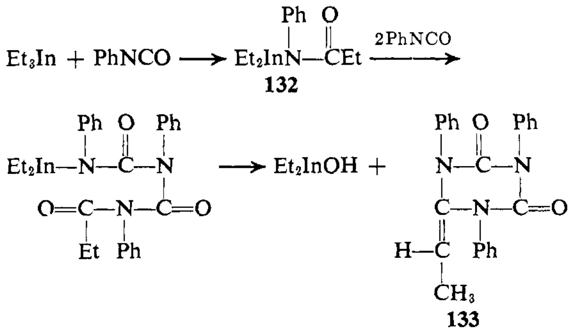


$$Ph_3SnOOBu\text{-}t + R^3NCO \longrightarrow Ph_3Sn-\overset{R^3}{\overset{|}{N}}-COOOBu\text{-}t$$

131

8. *Reaction with Triethylindium*

In a molar ratio of 1:1, phenyl isocyanate and triethylindium give an adduct **132**,[357] and when an excess of phenyl isocyanate is used, **133** is produced.[358]



132 **133**

F. DEOXY REACTIONS[359]

In the previous section (II.L), the preparations of isocyanates by oxidation of isonitriles are described. The reverse reaction is also known. Reaction of phenylphosphorus dichloride with

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[348] K. D. Kaufmann, H. Bormann, K. Ruhlmann, G. Engelhardt, and H. Kriegsmann, *J. Organometal. Chem.*, **23**, 385 (1970).

[349] C. G. Overberger and S. Ishida, *J. Polym. Sci., Part B*, **3**, 789 (1965).

[350] H. Beyer, J. W. Dawson, H. Jenner, and K. Niedenzo, *J. Chem. Soc.* (*London*), 2115 (1964).

[351] R. H. Gragg, *J. Chem. Soc., A*, 2962 (1968).

[352] Imperial Chemical Industries, British Patent 923581 (1963).

[353] Farbenfabriken Bayer A.-G., Japanese Patent 40-26812 (1965).

[354] O. M. Cohn, D. Thorpe, and H. J. Twitchett, *J. Chem. Soc. C*, 132 (1970).

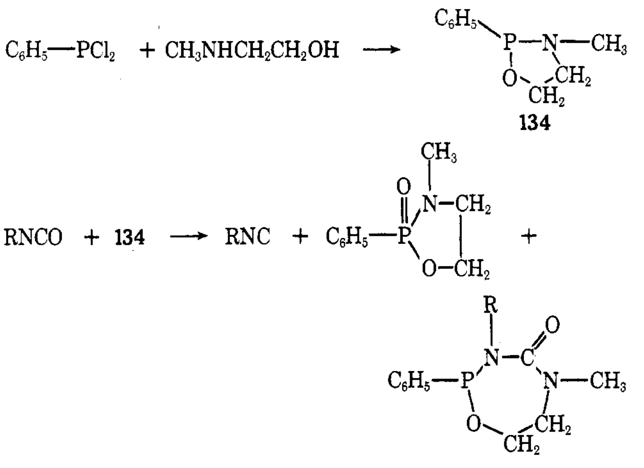
[355] A. J. Bloodworth, A. G. Davies, and S. C. Vasishtha, *ibid.*, 2640 (1968).

[356] A. J. Bloodworth and W. Ramsay, *ibid.*, 2380 (1968).

[357] H. Tada, K. Yasuda, and R. Okawara, *J. Organometal. Chem.*, **16**, 215 (1967).

[358] H. Tada and R. Okawara, *J. Org. Chem.*, **35**, 1666 (1970).

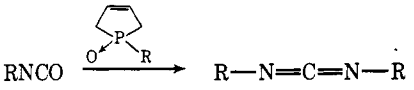
[359] T. Mukaiyama and Y. Yokota, *Bull. Chem. Soc. Jap.*, **38**, 858 (1965).



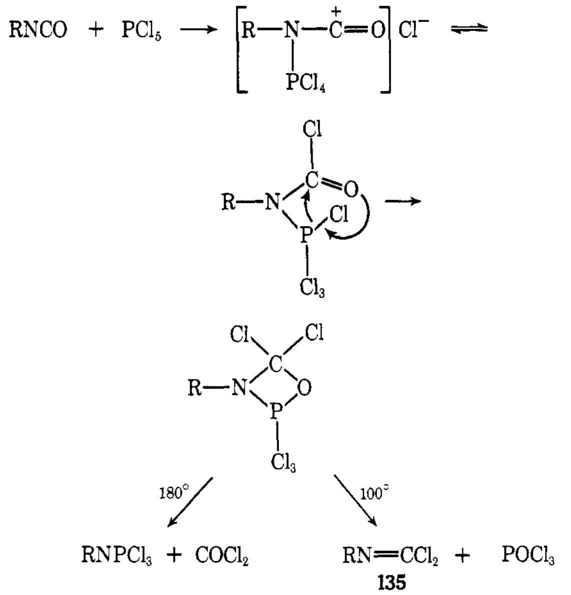
2-methylaminoethanol gives 2-phenyl-3-methyl-1,3,2-oxazophospholidine (**134**). Phenyl isocyanate is deoxygenated by **134** when both compounds are left standing at room temperature for 1 day, to yield phenyl isonitrile.

G. CARBODIIMIDE FORMATION REACTIONS

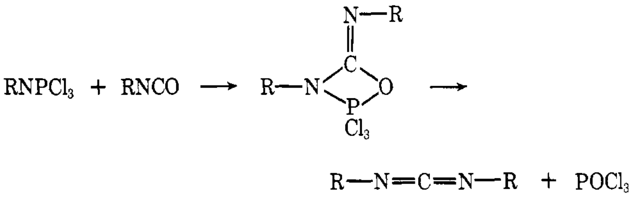
Preparations of carbodiimides from isocyanates with 1-ethyl-3-phospholine 1-oxide as catalyst are known.[360–362] Iron carbonyl compounds such as $Fe(CO)_5$ or $Fe(CO)_4C_6H_5NC$ are also good catalysts for the formation of carbodiimides from isocyanates.[363]



When phosphorus pentachloride and *o*-tolyl isocyanate are heated at 100°, *N*-dichloromethylene-*o*-toluidine (**135**) is produced. When the same starting materials or **135** and an isocyanate are heated at 180°, di-*o*-tolylcarbodiimide (**136**) is produced.[364]



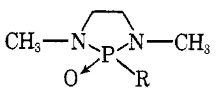
135



136

Steric hindrance may account for certain carbodiimides which are obtained when the corresponding isocyanates are heated with potassium hydroxide.[311]

1,3,2-Diazaphosphorizine 2-oxides (**137**) has also catalyzed the formation of carbodiimides from isocyanates.[365]



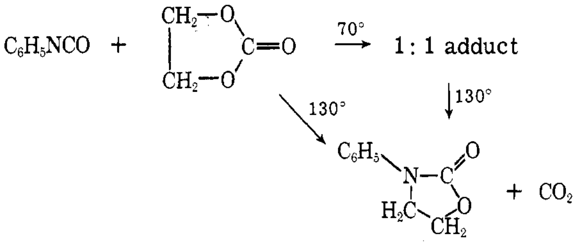
137

Polycarbodiimides have been prepared from diisocyanates.[366, 367]

H. REACTIONS WITH CYCLIC COMPOUNDS

1. *Reaction with Alkylene Carbonates*[368]

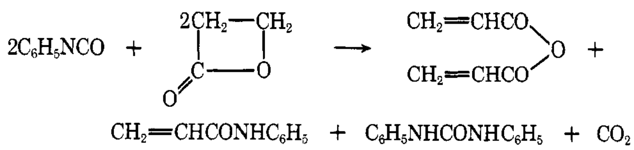
Phenyl isocyanate and ethylene carbonate in the presence of a tertiary amine give a 1:1 addition product at 70°, and at 130° 3-phenyloxazolidone-2 (**138**) is obtained in good yield.



138

2. *Reaction with β-Propiolactone*[369]

Phenyl isocyanate and β-propiolactone in the presence of a tertiary amine give acrylic anhydride, acrylanilide, *N,N'*-diphenylurea, and carbon dioxide in an exothermic reaction.



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(360) T. W. Campbell and J. J. Monagle, *J. Amer. Chem. Soc.*, **84**, 1495 (1962).

(361) T. W. Campbell, J. J. Monagle, and V. S. Foldi, *ibid.*, **84**, 3673 (1962).

(362) J. J. Monagle, T. W. Campbell, and H. F. McShane, *ibid.*, **84**, 4288 (1962).

(363) H. Ulrich, B. Tucker, and A. A. R. Sayigh, *Tetrahedron Lett.*, 1731 (1968).

(364) H. Ulrich and A. A. R. Sayigh, *J. Chem. Soc.* (*London*), 5558 (1963).

(365) H. Ulrich, *J. Org. Chem.*, **32**, 1360 (1967).

(366) T. W. Campbell and K. C. Smeltz, *ibid.*, **28**, 2069 (1963).

(367) D. J. Lyman and N. Sadri, *Makromol. Chem.*, **67**, 1 (1963).

(368) R. Tsuzuki, K. Ichikawa, and M. Kase, *J. Org. Chem.*, **25**, 1009 (1960).

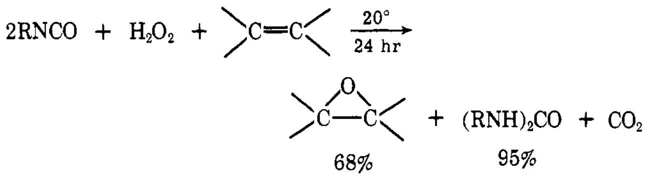
(369) R. Tsuzuki, K. Ichikawa, and M. Kase, *ibid.*, **26**, 1808 (1961).

(370) R. F. Layton and Q. Quick, *Anal. Chem.*, **40**, 1158 (1968).

(371) N. Matsumura, N. Sonoda, and S. Tsutsumi, *Tetrahedron Lett.*, 2029 (1970).

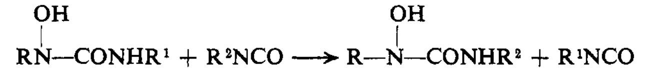
I. REACTIONS WITH HYDROGEN PEROXIDE AND OLEFINS

An isocyanate and hydrogen peroxide form a complex.[370] Epoxidation of olefins with hydrogen peroxide using an isocyanate as coreactant has been reported.[371]



J. REACTION WITH *N*-HYDROXY UREAS[372]

When an isocyanate reacts with an *N*-hydroxy urea, the corresponding product of transisocyanation can be isolated in a yield of 40–98% at 20–25°.



$$\mathrm{R\overset{OH}{\underset{|}{N}}{-}CONHR^1 + R^2NCO \longrightarrow R{-}\overset{OH}{\underset{|}{N}}{-}CONHR^2 + R^1NCO}$$

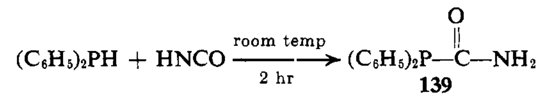
For convenience, the reactions of isocyanates are summarized in Table V.

IV. Reactions of Certain Isocyanates

A. REACTIONS OF ISOCYANIC ACID

1. Reaction with Phosphine

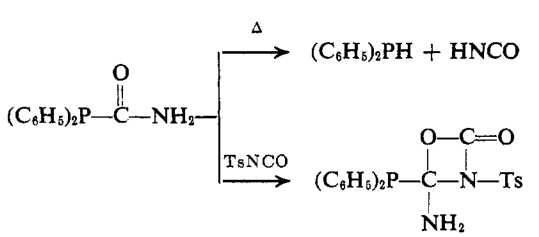
Diphenylphosphine and isocyanic acid add at room temperature to give carbamoyldiphenylphosphine (**139**).[373]



$$(C_6H_5)_2PH + HNCO \xrightarrow[2\ hr]{room\ temp} (C_6H_5)_2P{-}\overset{O}{\overset{\|}{C}}{-}NH_2$$

139

When heated, **139** dissociates into starting materials. The addition of **139** to *p*-toluenesulfonyl isocyanate gives 4-amino-4-diphenylphosphinyl-3-*p*-toluenesulfonyl-1,3-oxazetidinone (**140**).[374]

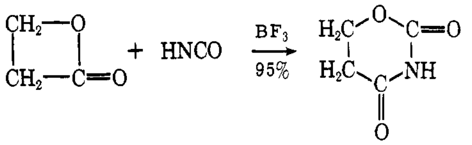


140

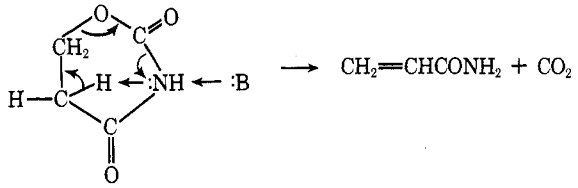
2. Reaction with *β*-Propiolactone[306]

β-Propiolactone and isocyanic acid in ether at −20° for 12 hr and then at 0° for 10 days in the presence of boron trifluoride etherate produces 2,4-dioxo-3,4,5,6-tetrahydro-2*H*-1,3-dioxazine (**141**) as a colorless crystalline solid.

Heated at 180°, **141** gives a polyacrylamide and carbon dioxide, but at 85° in the presence of triethylamine, monomeric acrylamide and carbon dioxide are obtained.

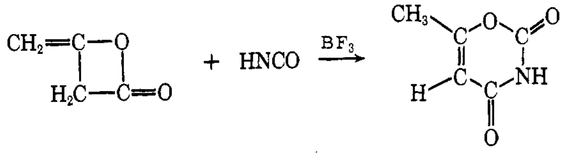


141



3. Reaction with Diketene[375]

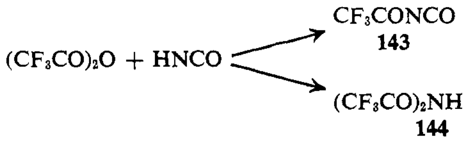
The addition of isocyanic acid to *β*-propiolactone is similar to its addition to diketene which gives 6-methyl-3,4-dihydro-2,4-dioxo-2*H*-1,3-oxazine (**142**).



142

4. Reaction with Trifluoroacetic Acid Anhydride[376]

Trifluoroacetic acid and isocyanic acid mixed at −196° and heated to room temperature gradually, afford trifluoroacetyl isocyanate (**143**) when isocyanic acid is in excess. On the other hand, hexafluorodiacetimide (**144**) is produced when trifluoroacetic acid anhydride is in excess.

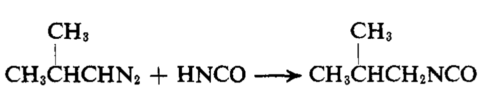


$(CF_3CO)_2O + HNCO \rightarrow CF_3CONCO$ **143**

$(CF_3CO)_2O + HNCO \rightarrow (CF_3CO)_2NH + CO_2$ **144**

5. Reaction with Diazoalkane[377]

Isobutyl isocyanate (**145**) is produced when isocyanic acid as



$$\mathrm{CH_3\overset{CH_3}{\overset{|}{C}}HCHN_2 + HNCO \longrightarrow CH_3\overset{CH_3}{\overset{|}{C}}HCH_2NCO}$$

145

a gas is introduced into the methylene dichloride solution of 2-methyldiazopropane.

6. Reaction with Polyvinyl Alcohols[378,379]

The reactions of polyvinyl alcohol and isocyanic acid were carried out in solid–liquid or solid–vapor phases. The products have the following structures.

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(372) N. V. Hostantinova, G. S. Shvindlerman, and Yu. A. Baskakov, *Zh. Org. Khim.*, **5**, 384 (1964).

(373) G. P. Papp and S. A. Buckler, *J. Org. Chem.*, **31**, 588 (1966).

(374) L. G. Vaughan and R. V. Lindsey, Jr., *ibid.*, **33**, 3088 (1968).

(375) Mitsui Toatsu Chemicals Co., Japanese Patent 44-12735 (1969).

(376) W. C. Firth, *J. Org. Chem.*, **33**, 441 (1968).

(377) N. Groving and A. Holm, *Acta Chem. Scand.*, **19**, 1768 (1965).

(378) M. Amagasa, Y. Kasuga, Y. Saito, T. Yamaichi, and H. Takagawa, *Kobunshi Kagaku*, **28**, 42 (1971).

(379) Mitsui Toatsu Chemicals Co., Japanese Patent 608901 (1971).

Table V

Reactions of Isocyanates

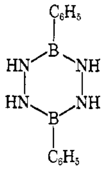
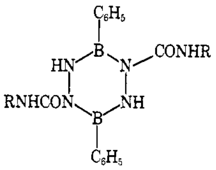
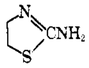
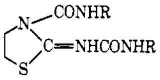
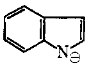
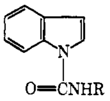
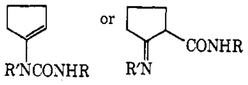
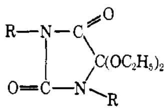
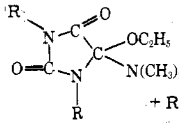
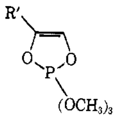
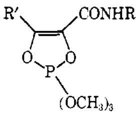
RNCO+	*Product*	*Subsection*	*RNCO+*	*Product*	*Subsection*
		A. Addition Reactions			
NH_3	$RNHCONH_2$		R_2NOH	$RNHCOONR_2'$	
$R'NH_2$	$RNHCONHR'$		$R_3'SiOH$	$RNHCOOSiR_3'$ or	
H_2NOH	$RNHCONHOH$			$RNHCONHR + R_3'SiOSiR_3'$	
H_2NNH_2	$RNHCONHNHCONHR$				A. 1
H_2O	$(RNHCOOH) \longrightarrow$ $RNHCONHR + CO_2$				A. 1
H_2S	$(RNHCOSH) \longrightarrow$ $RNHCONHR + COS$				
H_2O_2	$(RNHCOO)_2 \longrightarrow$ $RN{=}NR + 2CO_2$				A. 1
$R'NHCONH_2$	$RNHCONHCONHR'$				
$R'NHCOOR^2$	$RNHCONR'COOR^2$		$R'NHC({=}NH)NH_2$	$RNHCONHC({=}NH)NHR'$	
$R'—C({=}NH)NH_2$	$RNHCON{=}CR'NHCONHR$				A. 1
H_2NCN	$RNHCONHCN$				A. 1
$R'OH$	$RNHCOOR'$				
$R'SH$	$RNHCOSR'$		$(CH_3)_2\overset{O}{\overset{\uparrow}{S}}{=}NH$	$(CH_3)_2\overset{O}{\overset{\uparrow}{S}}{=}NCONHR$	A. 1
PH_3	$(RNHCO)_3P$		$R'SO_3H$	$RNHCOOSO_2R'$	A. 4
HCl	$RNHCOCl$		C_6H_6	C_6H_5CONHR	A. 5
HCN	$RNHCOCN$		$RC(OC_2H_5)_3$ (no catalyst)	$RNHCOC(OC_2H_5)_3 \longrightarrow$	A. 6
$R'COOH$	$RNH\overset{O}{\overset{\Vert}{C}}O\overset{O}{\overset{\Vert}{C}}R' \longrightarrow$ $RNHCOR' + CO_2$ or $RNHCONHR + (R'CO)_2O + CO_2$			$R\underset{O{=}CNHR}{\underset{\vert}{N}}COC(OC_2H_5)_3 \longrightarrow$ 	
$CH_2(COOR)_2$	$RNHCOCH(COOR)_2$				
$NaHSO_3$	$RNHCOSO_3Na$		$HC(OC_2H_5)_3$ (BF_3)	$R\underset{HC(OC_2H_5)_2}{\underset{\vert}{N}}COOC_2H_5$	
$CH_2(OC_2H_5)_2$	$R\underset{CH_2OC_2H_5}{\underset{\vert}{N}}COC_2H_5$	A. 7	$CH_3SO_2CH_3$	$(RNHCO)_2CHSO_2CH_3$	A. 10
$(C_2H_5)_2\overset{H}{\overset{\vert}{C}}N(CH_3)_2$	 $+ RNHCOOC_2H_5$	A. 8	$R'_2N\overset{O}{\overset{\uparrow}{S}}NR'_2$	$RN{=}C—O^-$ $R'_2—\overset{\vert}{N}—\underset{O}{\underset{\downarrow}{S}}—NR'_2$	A. 11
$(CH_3)_2\overset{+}{S}—\overset{-}{C}COOC_2H_5$	$(CH_3)_2S{=}\underset{CONHR}{\underset{\vert}{C}}COOC_2H_5$	A. 9			A. 12
$R'CH{=}P(C_6H_5)_3$	$R'\underset{\underset{(C_6H_5)_3}{P^-}}{\underset{\vert}{C}}H—\underset{O^-}{\underset{\vert}{C}}{=}NR$	A. 9			

Table V (Continued)

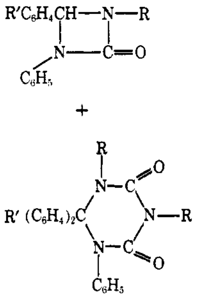
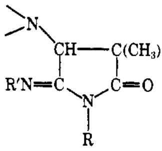
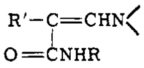
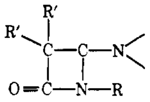
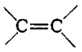
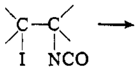
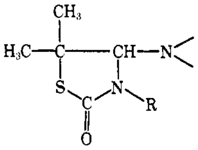
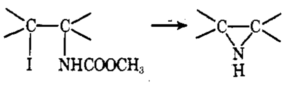
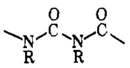
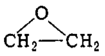
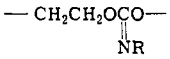
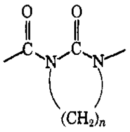
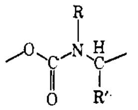
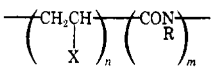
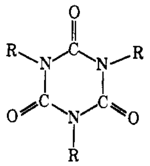
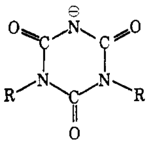
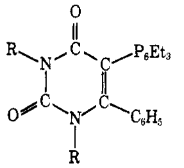
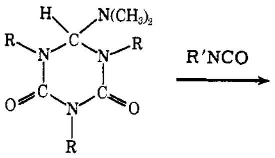
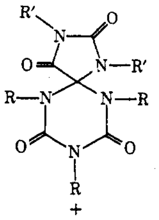
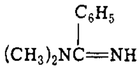
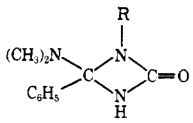
RNCO +	*Product*	*Subsection*	*RNCO +*	*Product*	*Subsection*
		B. Addition Reactions to Double Bonds			
$R'C_6H_4CH{=}NC_6H_5$		B. 1	$(CH_3)_2C{=}CHN\!<$ + R'NC		B. 2
			$R'HC{=}CHN\!<$	 $R'{-}\underset{O=CNHR}{C}{=}CHN\!<$	B. 2
$R'_2C{=}CHN\!<$		B. 2	 INCO		B. 3
$(CH_3)_2C{=}CHN\!<$ + S		B. 2			
		C. Polymerizations and Copolymerizations			
A^-		C	 (A⁻)	 $—CH_2CH_2O\underset{NR}{\overset{\|}{C}}O—$	C. 5
$OCN(CH_2)_nNCO$		C. 2	R'CHO		C. 6
$CH_2{=}CHX$		C. 4	catalyst		C. 8
		D. Ring Formation Reactions			
MOCN		D. 1	$Et_3PbC{\equiv}CC_6H_5$		D. 2
DMF	$RN{=}CHN(CH_3)_2 \xrightarrow{RNCO}$   + $R'NHCON(CH_3)_2$	D. 3	 $(CH_3)_2N\overset{C_6H_5}{C}{=}NH$		D. 3

Table V (*Continued*)

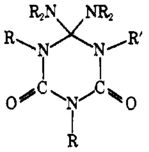
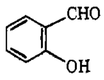
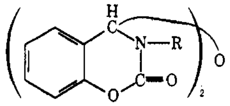
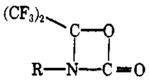
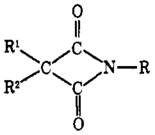
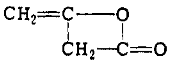
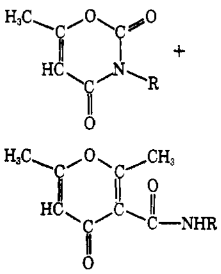
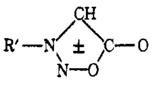
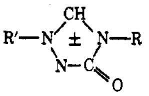
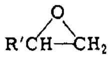
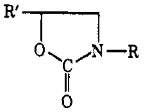
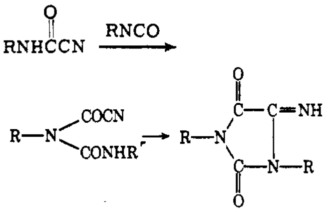
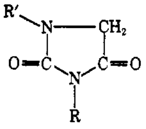
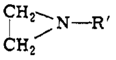
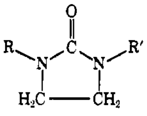
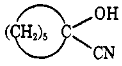
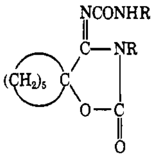
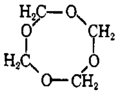
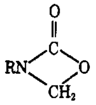
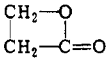
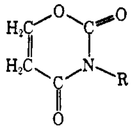
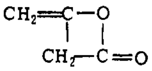
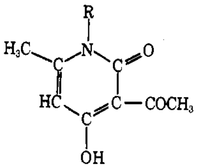
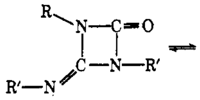
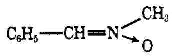
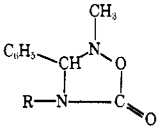
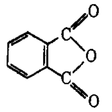
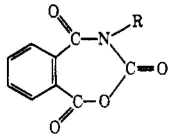
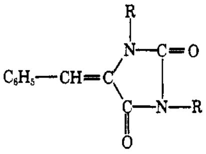
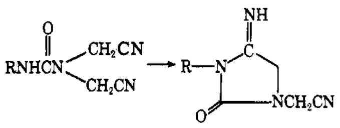
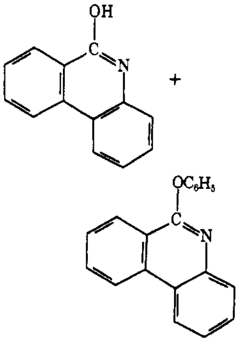
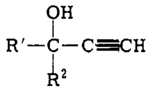
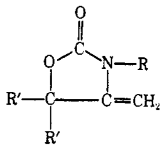
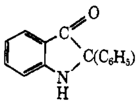
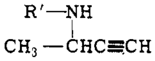
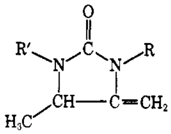
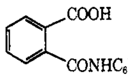
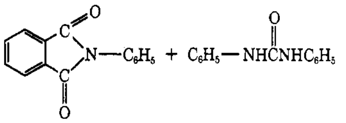
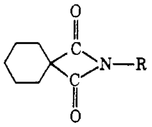
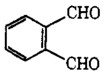
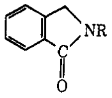
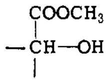
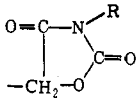
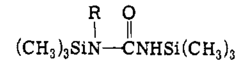
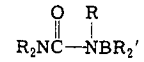
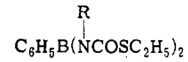
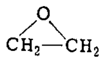
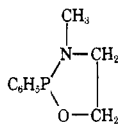
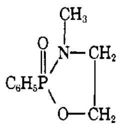
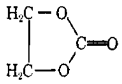
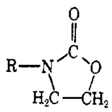
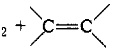
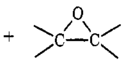
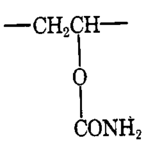
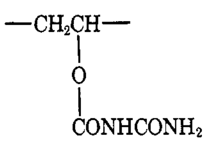
RNCO +	*Product*	*Subsection*
 $R_2N\overset{\overset{NR'}{\Vert}}{C}NR_2$		D. 4
		D. 6
CF_3COCF_3		D. 8
$R'R^2C{=}C{=}O$		D. 10
 (acidic)		D. 11
		D. 14
		D. 16
HCN		D. 18
$R'NHCH_2COOH$		D. 20
		D. 22
		D. 5
		D. 7
		D. 9
 (basic)		D. 11
$R'N{=}C{=}NR'$	 $RN{=}C{=}NR' + R'NCO$	D. 12
		D. 13
		D. 15
$C_6H_5{-}C{\equiv}CH$		D. 17
$HN(CH_2CN)_2$		D. 19
 (C_6H_5NCO)		D. 21

Table V (Continued)

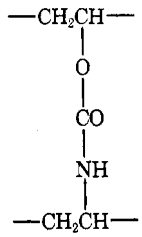
RNCO +	*Product*	*Subsection*	*RNCO +*	*Product*	*Subsection*
 $R'-\overset{OH}{\underset{R^2}{C}}-C\equiv CH$		D. 23			
			$(C_6H_5)_2CN_2$, $h\nu$ (C_6H_5NCO)		D. 25
 $CH_3-\overset{R'-NH}{CH}C\equiv CH$					D. 27
C_6H_5COCl		D. 24			D. 28
			 $-\overset{COOCH_3}{CH}-OH$		D. 29
		E.	Insertion Reactions		
$(CH_3)_3SiNHSi(CH_2)_3$	 $(CH_3)_3Si\overset{R}{N}-\overset{O}{C}NHSi(CH_3)_3$	E. 1	$CH_3OCON(CH_3)CH_2OCH_3$	$CH_3O-CO-N(CH_3)CH_2-NRCOOCH_3$	E. 5
R_2NBR_2'	 $R_2N\overset{O}{C}-\overset{R}{N}BR_2'$	E. 2	$Ti(OR')_4$	$(R'O)_{4-n}Ti(-NRCOOR')_n$	E. 6
$C_6H_5B(SC_2H_5)_2$	 $C_6H_5B(\overset{R}{N}COSC_2H_5)_2$	E. 3	$(Bu_3Sn)_2O$	$Bu_3SnNRCOOSnBu_3 \rightarrow$ $Bu_3SnNRCONRSnBu_3 + CO_2$	E. 7
 $(P(NCO)_3)$	$OCNP(OCH_2CH_2NCO)_2$	E. 4			
			$In(C_2H_5)_3$	$(C_2H_5)_2In\ NRCOC_2H_5$	E. 8
	F. Deoxy Reaction		G. Carbodiimide Formation Reactions		
			Catalysts	$RN{=}C{=}NR$	G
	RNC + 	F	 adducts		H
			H_2O_2 + 	$(RNHCO)_2$ +  + CO_2	I
			$R^1NHCON(OH)R^2$	$R^1NCO + RNHCON(OH)R^2$	J



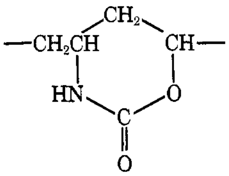
$-CH_2\underset{\underset{CONH_2}{O}}{CH}-$



$-CH_2\underset{\underset{CONHCONH_2}{O}}{CH}-$



$\begin{array}{c} -CH_2CH- \\ O \\ CO \\ NH \\ -CH_2CH- \end{array}$



7. *Preparation of Melamines*[380]

Isocyanic acid heated with ammonia in the presence of catalyst produces melamine (see eq 8).

8. *Miscellaneous Reactions*

Reactions with olefins, vinyl ethers, aldehydes, acid chlorides, silyl chlorides, and phosphorus chlorides have been discussed.

B. REACTIONS OF ACYL ISOCYANATES

The present discussion complements Tsuge's review[10] on acyl isocyanates. Enhanced reactivity of the isocyanate group by

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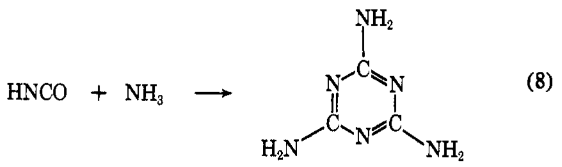
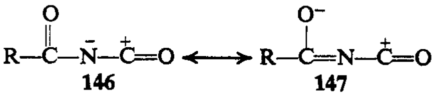
(380) Oesterreichische Stickstoffwerke A.-G., Japanese Patent 46-4744 (1971).

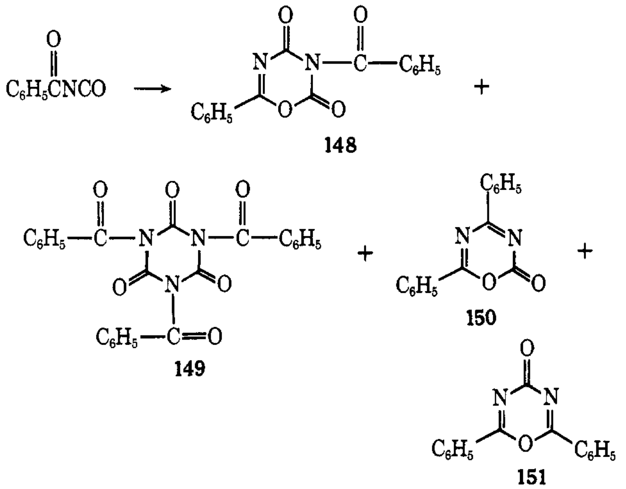

(8)

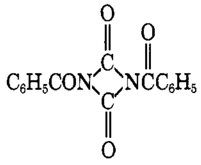
the electron-attracting acyl group and a considerable contribution from both a 1,4-dipolar structure (**147**) and a 1,2-dipolar structure (**146**) are to be expected.


146 **147**

1. Dimerizations and Trimerizations

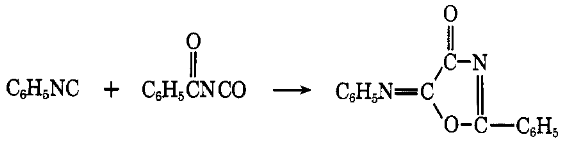
Para-substituted benzoyl isocyanates kept between room temperature and 80° in the presence of catalysts such as triethylamine or stannic chloride give four compounds, **148**–**151**.[381, 382] The isocyanate dimer **152** with a uretidinone structure was not obtained. The product **148** is generated from a 1,4-dipolar structure, and **149** from a 1,2-dipolar structure.


148 **149** **150** **151**


152

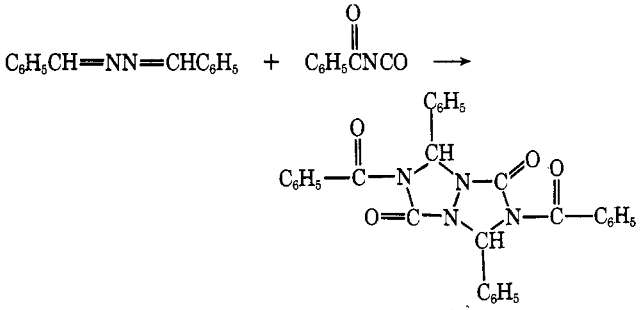
2. Reaction with Isonitriles[383–385]

The reaction of an acyl isocyanate with phenyl isocyanide gives an iminooxazolone (**153**).


153

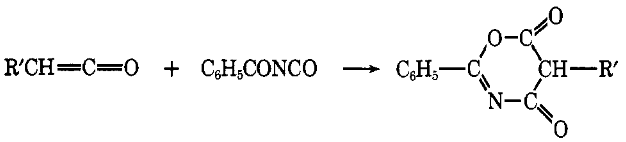
3. Reaction with Azines[386]

When an aldazine and benzoyl isocyanate are heated under reflux in xylene, a criss-cross bicyclic adduct (**154**) is obtained.


154

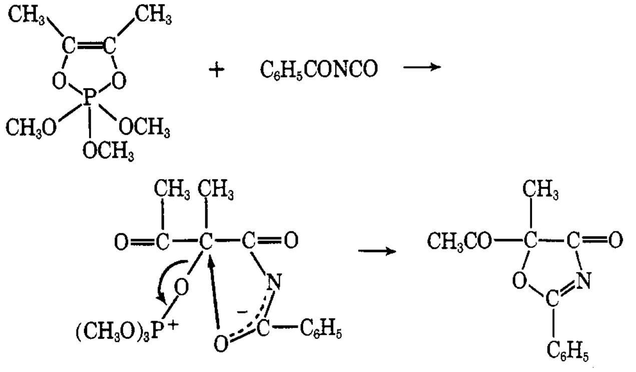
4. Reaction with Ketenes[387, 388]

An exothermal reaction between a substituted ketene and benzoyl isocyanates gives a 4*H*-1,3-oxazine-4,6(5*H*)-dione (**155**).


155

5. Reaction with Dioxaphospholenes[389]

2,2,2-Trialkoxy-2,2-dihydro-1,3,2-dioxaphospholene and benzoyl isocyanate give an oxazolone (**156**).


156

6. Reaction with Epoxides[390]

Para-substituted benzoyl isocyanate and styrene oxide give 5- and 4-substituted oxazolidin-2-ones.

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(381) O. Tsuge and R. Mizuguchi, *Nippon Kagaku Zasshi*, **86**, 325 (1965); *Chem. Abstr.*, **63**, 4299e (1965).

(382) O. Tsuge and R. Mizuguchi, *Kogyo Kagaku Zasshi*, **69**, 939 (1966).

(383) R. Neidlein, *Chem. Ber.*, **97**, 3476 (1964).

(384) R. Neidlein, *Angew. Chem.*, **76**, 440 (1964).

(385) R. Neidlein, *ibid.*, **76**, 500 (1964).

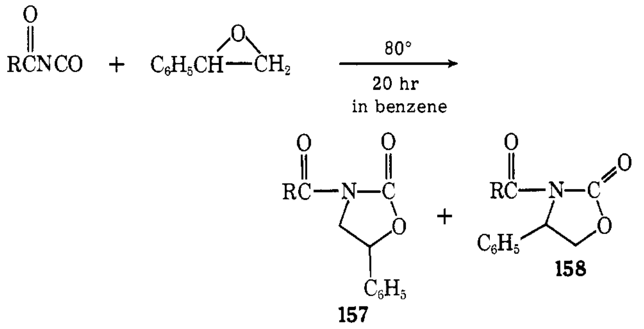
(386) O. Tsuge and S. Kanamasa, 22nd Meeting of the Chemical Society of Japan, No. 20502, Tokyo, 1969.

(387) Eastman Kodak Co., U. S. Patent 3394132 (1968).

(388) J. C. Martin, R. B. Burpitt, P. G. Gott, M. Harris, and R. H. Meen, *J. Org. Chem.*, **36**, 2205 (1971).

(389) F. Ramirez and C. D. Telefus, *ibid.*, **34**, 376 (1969).

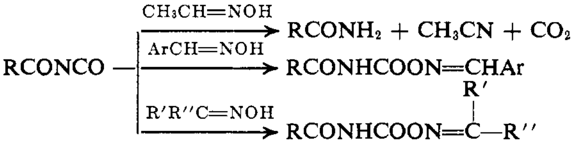
(390) O. Tsuge, T. Itoh, and K. Sakai, *Nippin Kagaku Zasshi*, **90**, 1031 (1969).



157 **158**

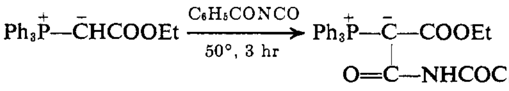
7. *Reactions of Aldoximes*[391] *and Ketoximes*[392]

Ketoximes and benzaldoxime give similar reactions with an acyl isocyanate, but aliphatic aldoximes react differently.



8. *Reaction with Phosphonium Ylides*[393]

The reaction between carbethoxymethylenetriphenylphosphorane (**159**) and benzoyl isocyanate gives the stable ylide **160** in good yield.



$$\overset{+}{\mathrm{Ph_3P}}-\overset{-}{\mathrm{C}}\mathrm{HCOOEt} \xrightarrow[50°,\ 3\ \mathrm{hr}]{\mathrm{C_6H_5CONCO}} \overset{+}{\mathrm{Ph_3P}}-\underset{\mathrm{O=C-NHCOC_6H_5}}{\overset{-}{\mathrm{C}}}-\mathrm{COOEt}$$

159 **160**

C. SULFONYL ISOCYANATES

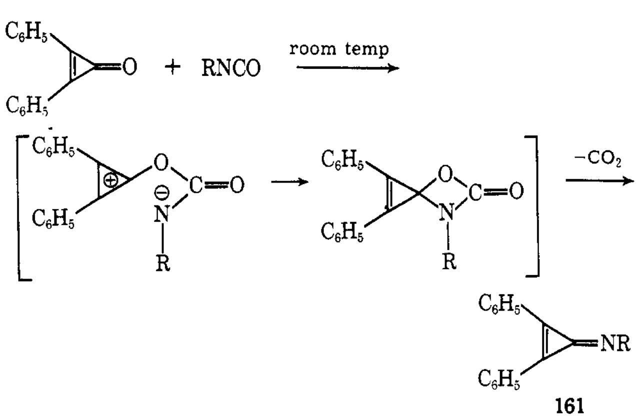
Alkyl and aryl sulfonyl isocyanates have been studied extensively and have been reviewed by Ulrich[6] in 1965. Chlorosulfonyl isocyanates have received similar attention and have been reviewed by Graf[8] in 1968. Only new and selected reports will be mentioned here.

With the strong electron-attracting power of the sulfonyl group, sulfonyl isocyanates are more reactive than other isocyanates. Chlorosulfonyl isocyanate is more reactive than either an alkyl- or an arylsulfonyl isocyanate.

1. *Alkyl- or Arylsulfonyl Isocyanates*

a. Reaction with Diphenylcyclopropenone[394]

Diphenylcyclopropenone and a sulfonyl isocyanate react at room temperature to give an iminocyclopropene (**161**) and carbon dioxide.

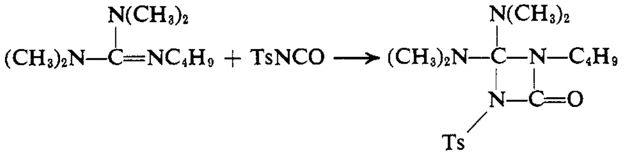


161

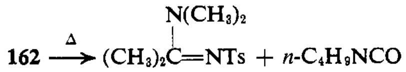
R = p-Ts, COCl, SO_2Cl, $COCCl_3$

b. Reaction with Amidine and Guanidine[395]

When N,N,N',N'-tetramethyl-N''-n-butylguanidine and p-toluenesulfonyl isocyanate are mixed in benzene, an exothermic reaction produces a 1:1 crystalline adduct (**162**), mp 158–160°. Heated in o-dichlorobenzene **162** releases n-butyl isocyanate, and N,N,N',N'-tetramethyl-N''-p-toluenesulfonylguanidine remains as a residue. In this way an n-butyl group and the p-toluenesulfonyl group are exchanged.



162



$$\mathbf{162} \xrightarrow{\Delta} \mathrm{(CH_3)_2}\overset{\mathrm{N(CH_3)_2}}{\mathrm{C}}\mathrm{=NTs} + n\text{-}\mathrm{C_4H_9NCO}$$

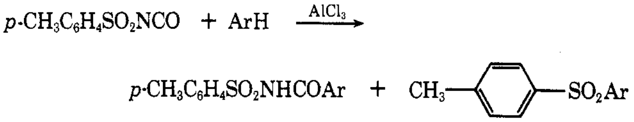
Other reactions between a normal isocyanate and a guanidine have been discussed (section III.D.4).

c. Reaction with Carbodiimides[396]

The reaction is substantially the same as that mentioned in section III.D.12.

d. Reaction with Aromatic Compounds[397]

The reaction of p-toluenesulfonyl isocyanate with benzene in the presence of aluminum chloride gives a mixed amide at room temperature and a sulfone at higher temperature.



e. Reaction of Diazomethane

A sulfonyl isocyanate and diazomethane may react to give a 1,2,3-oxathiazol-4-one 2-oxide (**163**).[398] A different reaction

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[391] K. A. Nuridzhanyan, L. M. Nesterova, A. F. Vasilev, and N. L. Aryutkina, *Zh. Org. Khim.*, **5**, 874 (1969).

[392] K. A. Nuridzhanyan, L. M. Nesterova, A. F. Vasilev, and V. V. Negrebetsskii, *ibid.*, **5**, 874 (1969).

[393] Y. Ohshiro, Y. Mori, M. Komatsu, and T. Agawa, *J. Org. Chem.*, **36**, 2029 (1971).

[394] L. A. Paquette, T. J. Barton, and N. Horton, *Tetrahedron Lett.*, 5039 (1967).

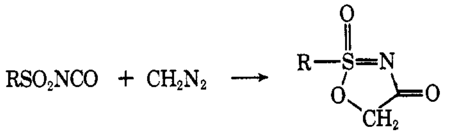
[395] H. Ulrich, B. Tucker, and A. A. R. Sayigh, *Angew. Chem., Int. Ed. Engl.*, **7**, 291 (1968).

[396] H. Ulrich, B. Tucker, and A. A. R. Sayigh, *J. Amer. Chem. Soc.*, **90**, 528 (1968).

[397] J. W. McFarland and L. C. Yao, *J. Org. Chem.*, **35**, 123 (1970).

[398] G. Lohaus, *Tetrahedron Lett.*, 127 (1970).

between phenyl isocyanate and diazomethane has been described.[399]



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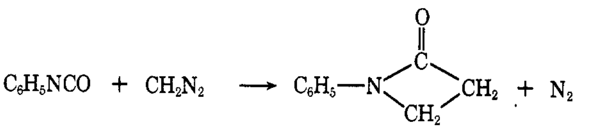
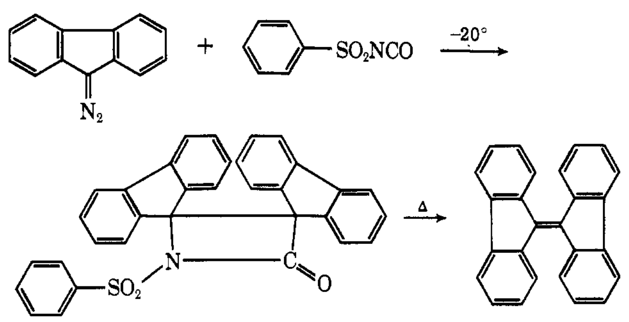


Diazofluorene and an arylsulfonyl isocyanate give a lactam (**164**).[398]



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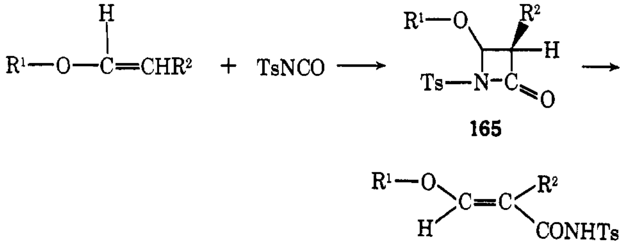
f. Reaction with Enol Ethers[400–402]

N-Tosylazetidin-2-ones (**165**) are formed *via* a stereospecific cis addition of an enol ether and *p*-toluenesulfonyl isocyanate. Configuration, isomerization, and rearrangement of the azetidin-2-ones have been studied.

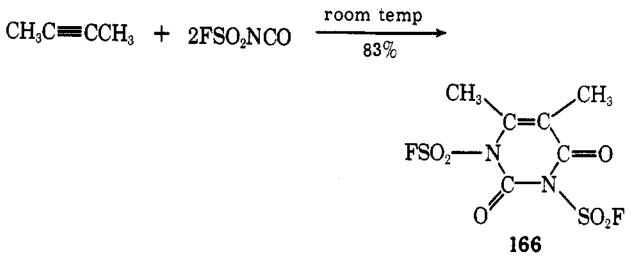


2. *Halosulfonyl Isocyanates*

a. Reactions with Acetylenic Compounds

Butyne-2 and 2 mol of fluorosulfonyl isocyanate give a difluorosulfonyluracil (**166**).[403]

Chlorosulfonyl isocyanate and 3-hexyne give a 1:1 adduct (**167**).[404]



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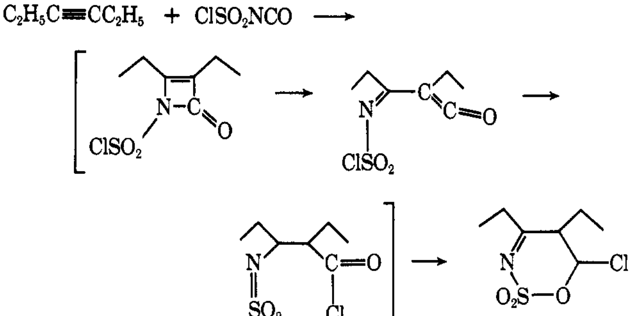

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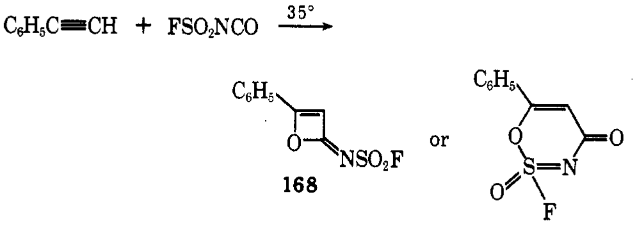
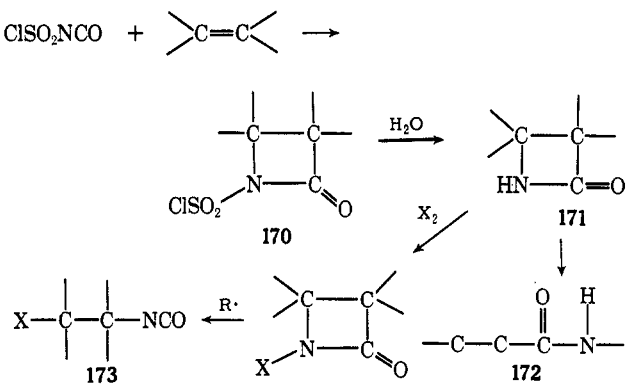
The reaction between phenylacetylene and fluorosulfonyl isocyanate gives 2-fluorosulfonylimido-4-phenyloxetene (**168**) or a 1,2,3-oxathiazinone-4 derivative (**169**).[405]



b. Reactions with Olefinic Compounds

Chlorosulfonyl isocyanate[8] adds to a double bond. The adduct (**170**) may be hydrolyzed into a β-lactam (**171**). The latter polymerizes into 3-nylon (**172**). When halogenated the β-lactam gives a β-haloalkyl isocyanate (**173**).



When cyclooctatetraene is treated with chlorosulfonyl isocyanate, a 1,4 cycloaddition occurs (see below).[406]

Hexamethyl(Dewar benzene) and chlorosulfonyl isocyanate add to give an azasemibullvalene derivative (**174**), perhaps by the mechanism proposed.[407]

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(400) F. Effenberger and G. Kiefer, *Angew. Chem., Int. Ed. Engl.*, **6**, 951 (1967).

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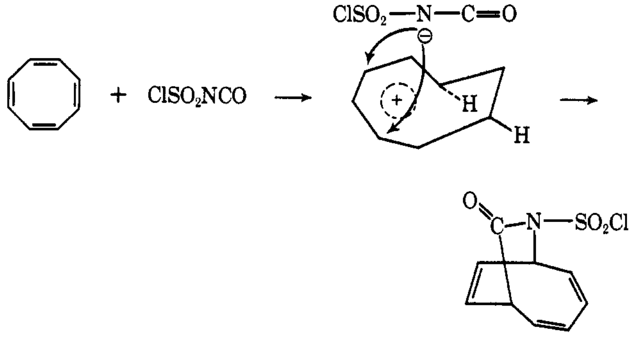
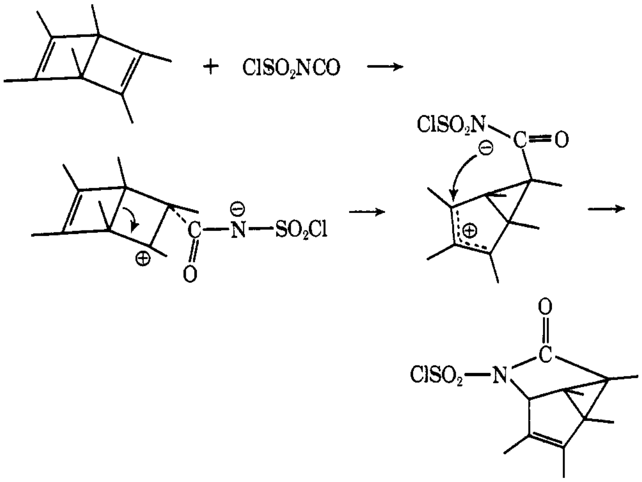
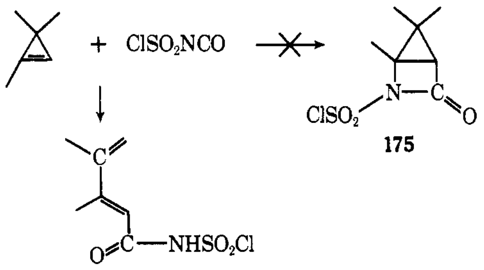




174

Addition of chlorosulfonyl isocyanate to a cyclopropene[408] does not give a β-lactam (**175**), in contrast with the reaction between β-chlorsulfonyl isocyanate and olefins; instead **176** and **177** were obtained.



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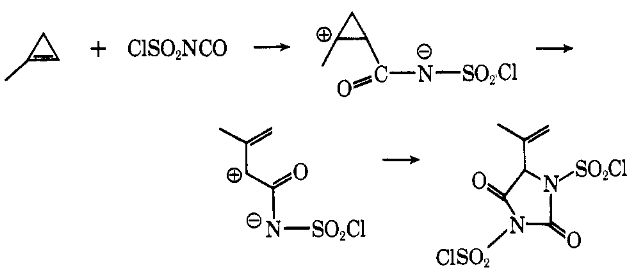
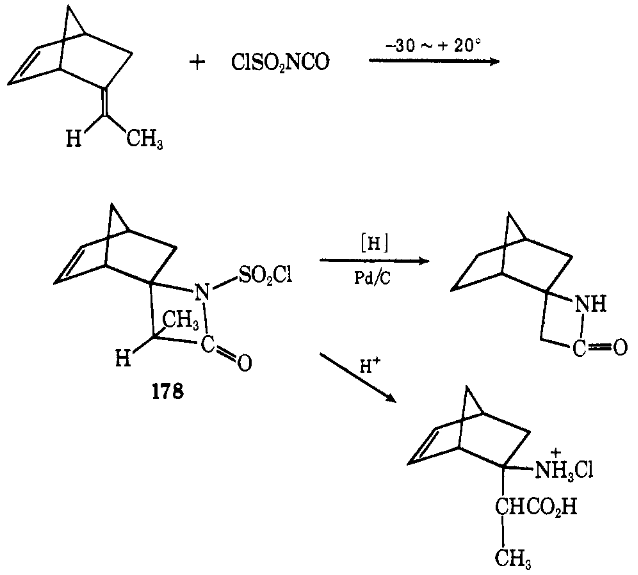


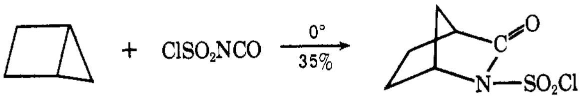
177

The treatment of 5-ethylidenebicyclo[2.2.1]hept-2-ene with chlorosulfonyl isocyanate led to the formation of 1-chlorosulfonyl-3-methyl-2-azetidinone-4-spiro-5′-bicyclo[2.2.1]hept-2′-ene (**178**) by an exclusive attack at the exocyclic double bond.[409]



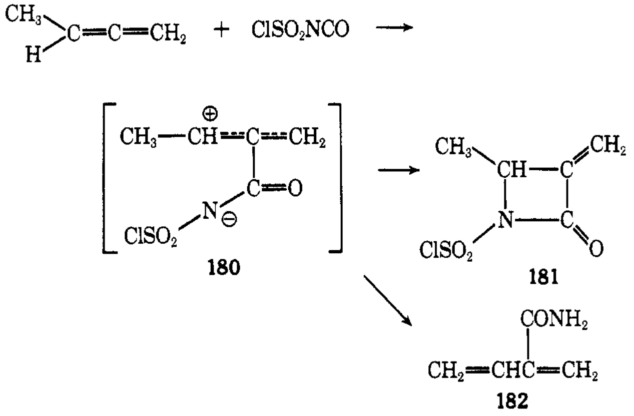
178

The treatment of bicyclo[2.1.0]pentane with chlorosulfonyl isocyanate for 12 hr at 0° afforded 2-chlorosulfonyl-2-aza-3-ketobicyclo[2.2.1]heptane (**179**).[410]



179

From the addition of chlorosulfonyl isocyanate to an allene initial electrophilic attack at the central carbon atom of the allenic system produced a zwitterion (**180**). Isolated products were β-lactam derivatives (**181**) and/or 2-carboxamido-1,3-butadiene (**182**).[411]



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V. Conclusion

The chemistry of the isocyanate group is old and has been studied extensively; nevertheless, new discoveries are constantly appearing. In *Chemical Abstracts* five pages are needed to list isocyanates semiannually, and in *Chemical Titles* there

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(408) J. J. Barton, R. Rogido, and J. C. Clardy, *Tetrahedron Lett.*, 2081 (1970).

(409) E. J. Moriconi and C. C. Jalandoni, *J. Org. Chem.*, **35**, 2073 (1970).

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are about ten reports semimonthly. Newer synthetic methods for isocyanates and especially a new industrial preparation for tolylene diisocyanate appear promising.

Industrial demand for isocyanates is increasing. Aliphatic diisocyanates are used for nonyellowing purposes. Examples include hexamethylene diisocyanate, dimeryl diisocyanate, methylenebis(cyclohexyl diisocyanate), isopropyridenebis(cyclohexyl diisocyanate), lysine diisocyanate, and 3-isocyanatomethyl-3,5,5-trimethylcyclohexyl isocyanate.

Many new reactions have not yet received industrial applications. In the future they will be valuable in preparing polyurethanes, pharmaceutical and agricultural chemicals, and other useful products.

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