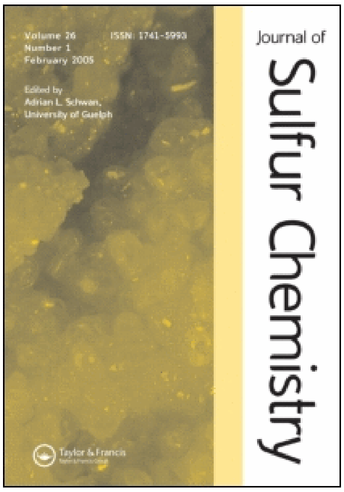

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Sulfonyl Isocyanates and Sulfonyl Isothiocyanates

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SULFONYL ISOCYANATES AND SULFONYL ISOTHIOCYANATES

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The literature dealing with sulfonyl isocyanates since 1972 is reviewed. Along with the sulfonyl isocyanates, the preparations and reactions of sulfonyl isothiocyanates are also reviewed. The paper is divided into three sections—Introduction, Preparations and Reactions.

The chief sources of sulfonyl isocyanates are reactions of sulfonamides with phosgene, of sulfonyl ureas with phosgene, and of sulfonyl halides with metal cyanates. The principal sources of sulfonyl isothiocyanates are iminothiocarbamate salts when treated with thionyl chloride, phosphorus halides, or methyl chlorocarbonate. The iminothiocarbamate salts are prepared from sulfonamides, carbon disulfide, and metal hydroxides.

The reactions of the isocyanates and isothiocyanates are categorized under reactions with azides, carbon-carbon unsaturated bonds, carbon-nitrogen double bonds, hydroxyl groups, amines, amino acids, amino alcohols, amides, aldehydes and ketones, C-H acidic compounds, phosphorus compounds, silicon compounds, tin compounds, other organometallics, and miscellaneous reactions.

I. INTRODUCTION

The chemistry of sulfonyl isocyanates was reviewed by Ulrich in 1965[1] and by McFarland in 1972.[2] This report will cover only the literature dealing with sulfonyl isocyanates which has appeared since the last review and previous work necessary for clarity of discussion.

Sulfonyl isothiocyanates will be reviewed along with sulfonyl isocyanates inasmuch as the chemistry of the two classes of compounds is often very similar. The NCO group and the NCS group are highly activated by an adjacent sulfonyl group. As would be expected from what is known of ordinary isocyanates and isothiocyanates, the sulfonyl isocyanates are considerably more reactive in most reactions than are the sulfonyl isothiocyanates. The strongly electron-withdrawing sulfonyl group causes the carbon atom of the NCO or NCS group to be a strong electrophile. In reactions with nucleophiles the transient negative charge on nitrogen is stabilized by the adjacent SO_2 group.

This review is divided into two major sections—methods of preparation and reactions. Both aliphatic and aromatic sulfonyl isocyanates and sulfonyl isothiocyanates are covered. The halosulfonyl isocyanates and isothiocyanates are only discussed when they appear with the above types.

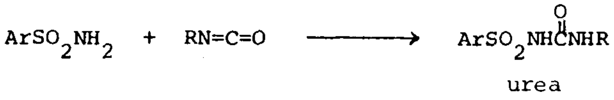
II. PREPARATIONS

The preferred method for preparing sulfonyl isocyanates is the treatment of sulfonamides with phosgene.[2–7] Improvements in yield and purity of sulfonyl isocyanate have been realized by allowing the sulfonamide to react with phosgene in the presence of primary amines such as propylamine, butylamine, or 1,6-diaminohexane.[8]

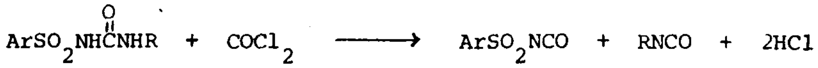
$$R\text{-}C_6H_4SO_2NH_2 + COCl_2 \xrightarrow[125\text{-}130^\circ C]{RNH_2} R\text{-}C_6H_4SO_2NCO \quad (1)$$

$$(R = \underline{p}\text{-Me}, \underline{p}\text{-Cl}, \underline{o}\text{-Me}) \qquad < 95\%$$

Further study of the effect of the presence of alkyl isocyanates on the reaction of sulfonamides with phosgene has been carried out.[9] As pointed out earlier,[2] ureas are probably intermediates in the isocyanate-catalyzed phosgenation of sulfonamides. These ureas are known to react

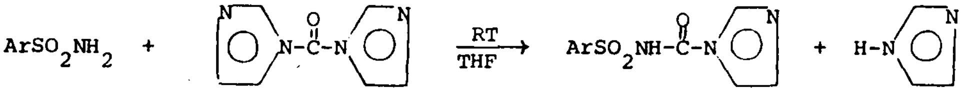

(2)

$$ArSO_2NH_2 + RN{=}C{=}O \longrightarrow \underset{\text{urea}}{ArSO_2NH\overset{O}{\overset{\|}{C}}NHR}$$


(3)

$$ArSO_2NH\overset{O}{\overset{\|}{C}}NHR + COCl_2 \longrightarrow ArSO_2NCO + RNCO + 2HCl$$

with phosgene to give aliphatic isocyanate, sulfonyl isocyanate, and hydrogen chloride.[10,11] Sulfonamides react with N,N′-carbonyldiimidazole to give intermediates which upon heating with P_2O_5 afford the sulfonyl isocyanates.[12]



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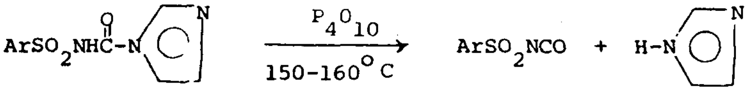


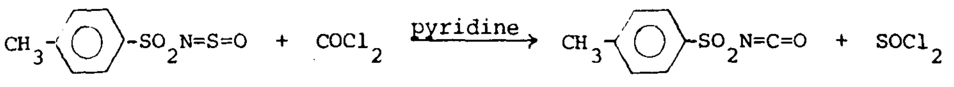
(5)

Sulfonyl urethanes have been reported to give sulfonyl isocyanates when heated in xylene or treated with chlorine.[13]

$$R\text{-}C_6H_4SO_2NHCOSCH_3 \xrightarrow[\text{or } Cl_2]{\text{xylene, heat}} R\text{-}C_6H_4SO_2NCO + CH_3SH \quad (6)$$

$$(R = \underline{p}\text{-Br}, H, \underline{m}\text{-}NO_2, \underline{p}\text{-Me}, \underline{o}\text{-Me})$$

N-Sulfinylamines and N-sulfinylsulfonamides react with phosgene in the presence of pyridine or N,N-dimethylformamide to afford isocyanates and thionyl chloride.[14] The reaction is reversible, resulting in N-sulfinyl compounds when isocyanates react with thionyl chloride under certain conditions.



(7)

The earliest method for sulfonyl isocyanate preparation was the treatment of sulfonyl halides with metal cyanates, especially silver cyanate.[15] Japanese workers claim an improved method using metal cyanates such as KOCN, organic sulfonyl halides in organic solvents containing nitrile groups, metal salts, and phosphorus pentoxide.[16]

$$R\text{-}SO_2Cl \quad + \quad KOCN \quad \xrightarrow[\substack{CH_3CN,\ reflux \\ 5\ hours}]{LiI,\ P_4O_{10}} \quad RSO_2NCO \quad + \quad KCl \tag{8}$$

$$(R = CH_3,\ \underline{p}\text{-}CH_3C_6H_4,\ \underline{p}\text{-}ClC_6H_4,\ \underline{o}\text{-}CH_3C_6H_4)$$

Trifluoromethanesulfonyl isocyanate and trifluoromethanesulfonyl isothiocyanate result from the reactions of the silver salts of the corresponding sulfonamides with phosgene and thiophosgene, respectively.[17]

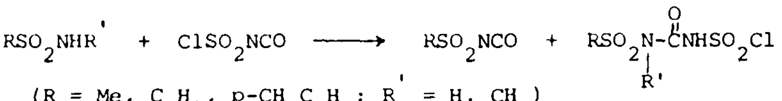
$$CF_3SO_2NAg_2 \quad + \quad COCl_2 \quad \longrightarrow \quad CF_3SO_2N{=}C{=}O \quad + 2\ AgCl \tag{9}$$

$$CF_3SO_2NAg_2 \quad + \quad CSCl_2 \quad \longrightarrow \quad CF_3SO_2N{=}C{=}S \quad + 2\ AgCl \tag{10}$$

The above trifluoromethanesulfonyl isothiocyanate may also be prepared from the sulfonyl isocyanate and phosphorus pentasulfide at elevated temperatures.[18]

$$CF_3SO_2N{=}C{=}O \quad + \quad P_2S_5 \quad \xrightarrow[pressure]{160^\circ\ C} \quad CF_3SO_2N{=}C{=}S \tag{11}$$

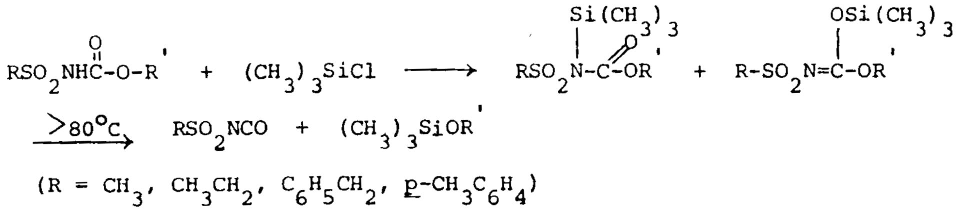
Alkane and aromatic sulfonyl isocyanates result from the reaction of primary and secondary sulfonamides with chlorosulfonyl isocyanate.[19] Other products are also obtained.



$$RSO_2NHR' \quad + \quad ClSO_2NCO \quad \longrightarrow \quad RSO_2NCO \quad + \quad RSO_2\underset{R'}{\underset{|}{N}}\text{-}\overset{O}{\overset{\|}{C}}NHSO_2Cl \tag{12}$$

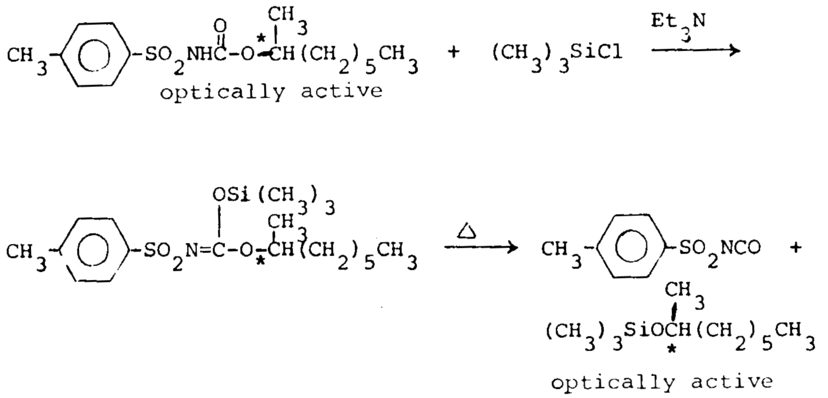
$$(R = Me,\ C_6H_5,\ \underline{p}\text{-}CH_3C_6H_4;\ R' = H,\ CH_3)$$

Sulfonyl carbamates are silylated at low temperatures in the presence of tertiary amines by trialkylsilyl halides. The silylated carbamates decompose above 80°C to sulfonyl isocyanates and trialkylalkoxysilanes.[20] Thermolysis of trimethylsilylated O-neopentyl-N-*p*-toluenesulfonylcarbamate exhibits first-order kinetics and optically active O-2-octyl-N-*p*-toluenesulfonylcarbamate yields trimethyl-2-octyloxysilane with retention of configuration.



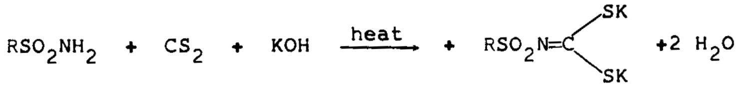
$$RSO_2NHC({=}O)\text{-}O\text{-}R' + (CH_3)_3SiCl \longrightarrow RSO_2N(Si(CH_3)_3)\text{-}C({=}O)\text{-}OR' + R\text{-}SO_2N{=}C(OSi(CH_3)_3)\text{-}OR' \xrightarrow{>80^\circ C} RSO_2NCO + (CH_3)_3SiOR' \qquad (13)$$

$(R = CH_3,\ CH_3CH_2,\ C_6H_5CH_2,\ p\text{-}CH_3C_6H_4)$



(14)

Sulfonyl isothiocyanates are generally prepared by the reaction of sulfonyl iminothiocarbamate salts with phosgene, thionyl chloride, a phosphorus halide, or methyl chlorocarbonate.[21,22] The iminothiocarbamate salts are, in turn, available from sulfonamides, carbon disulfide, and base.



$$RSO_2NH_2 + CS_2 + KOH \xrightarrow{heat} + RSO_2N{=}C(SK)_2 + 2\ H_2O \qquad (15)$$

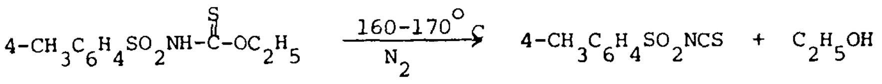
$$RSO_2N{=}C(SK)_2 + SOCl_2 \xrightarrow[reflux]{C_6H_6} RSO_2N{=}C{=}S + 2\ KCl + S_2O \qquad (16)$$

The direct formation of sulfonyl isothiocyanates from sulfonamides and thiophosgene has also been reported.[23] The reaction is carried out in the presence of a hydrophobic inert solvent and aqueous alkali.

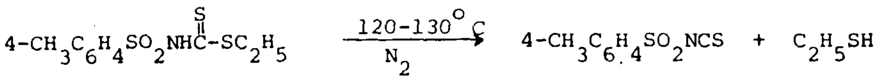
$$p\text{-}R\text{-}C_6H_4SO_2NH_2 + CSCl_2 \xrightarrow[aq.\ NaOH]{CHCl_3,} p\text{-}R\text{-}C_6H_4SO_2NCS \qquad (17)$$

$(R = CH_3,\ Cl)$

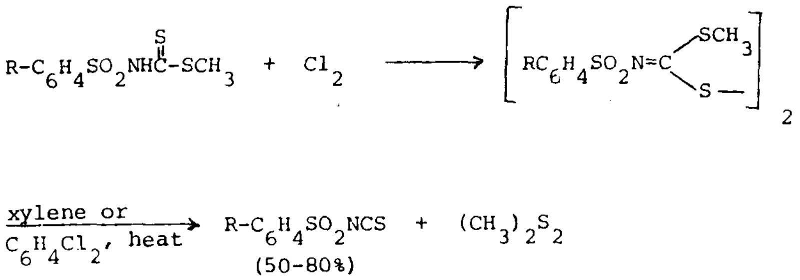
N-Sulfonylthiocarbamates[24] and N-sulfonyldithiocarbamates[25] may be pyrolyzed to sulfonyl isothiocyanates. Alternatively, the dithiocarbamates are converted by chlorine into dimers which are pyrolyzed to the corresponding isothiocyanates.[26]



$$4\text{-}CH_3C_6H_4SO_2NH\text{-}\overset{S}{\overset{\|}{C}}\text{-}OC_2H_5 \xrightarrow[N_2]{160\text{-}170^\circ C} 4\text{-}CH_3C_6H_4SO_2NCS + C_2H_5OH \tag{18}$$

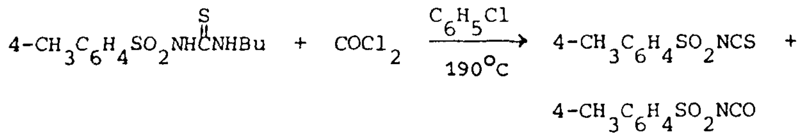


$$4\text{-}CH_3C_6H_4SO_2NH\overset{S}{\overset{\|}{C}}\text{-}SC_2H_5 \xrightarrow[N_2]{120\text{-}130^\circ C} 4\text{-}CH_3C_6H_4SO_2NCS + C_2H_5SH \tag{19}$$



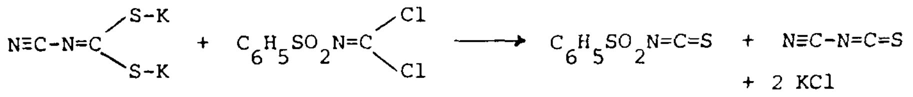
(20)

Phosgenation of sulfonyl thioureas has been reported to give sulfonyl isothiocyanates, along with sulfonyl isocyanates, at high temperatures.[27]



$$4\text{-}CH_3C_6H_4SO_2NH\overset{S}{\overset{\|}{C}}NHBu + COCl_2 \xrightarrow[190^\circ C]{C_6H_5Cl} 4\text{-}CH_3C_6H_4SO_2NCS + 4\text{-}CH_3C_6H_4SO_2NCO \tag{21}$$

Sulfonyl iminodichlorides react with cyanoiminothiocarbamate salts to give sulfonyl isothiocyanates.[28]

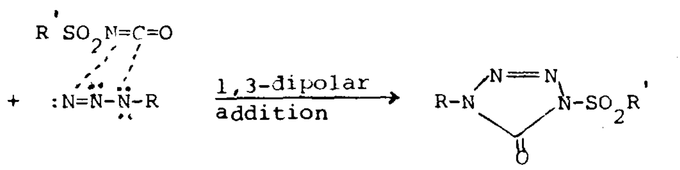


(22)

III. REACTIONS

A. *With Azides*

The reactions of azides with sulfonyl isocyanates and sulfonyl isothiocyanates are similar to many of the reactions with unsaturated molecules and generally lead to cycloadditions. Although there are exceptions, sulfonyl isocyanates usually add across their C=N bond while the sulfonyl isothiocyanates tend to add across their C=S bond.[29] Vandensavel, Smets, Denecker, and L'Abbé have shown that the reactions of alkyl azides with sulfonyl isocyanates lead to alkyl-4-arylsulfonyl-2-tetrazolin-5-ones.[30-32] Some of the products ("masked isocyanates") were used as crosslinking agents for polymers such as epichlorohydrin 2,2-*bis*-(4-hydroxyphenyl)-propane copolymer.



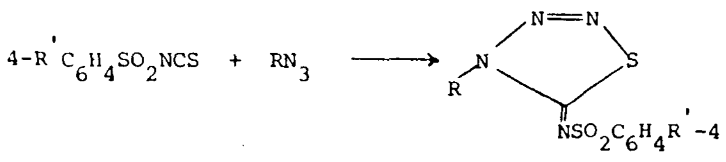
(23)

1-alkyl-4-arylsulfonyl-Δ^2-tetrazolin-5-one

(R = Bu, C_6H_5, p-$CH_3C_6H_4$, p-anisyl; R' = p-$CH_3C_6H_4$, C_6H_5, p-ClC_6H_4, Cl, p -and m-$O_2NC_6H_4$)

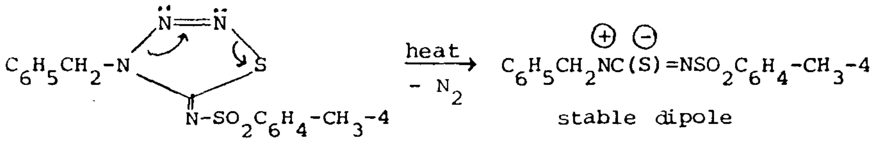
The 1 : 1 cycloaddition products undergo cycloreversion upon heating. Both cycloaddition and cycloreversion reactions are accelerated by the presence of electron-withdrawing groups on the isocyanate moiety. The energies of activation and heats of reaction have been determined for cycloreversions.[31]

In contrast to the isocyanates, sulfonyl isothiocyanates react with alkyl azides across their C=S bond to afford 4-alkyl-5-sulfonylimino-Δ^2-1,2,3,4-thiatriazolines.[33] The thiatriazolines thermolyze to stable dipoles which undergo cycloaddition with enamines and ynamines.



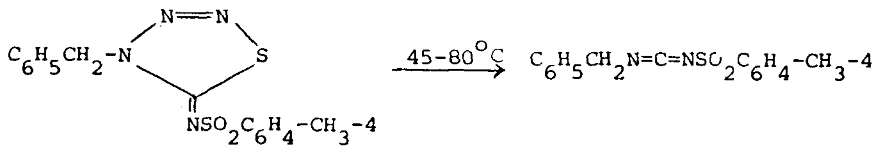
(24)

(R = Bu, $PhCH_2$; R' = H,Me, Cl) thiatriazoline derivative



(25)

Thiatriazolines from sulfonyl isothiocyanates and azides are also reported to thermolyze to carbodiimides.[34] When heated in the presence of enamines or ynamines, they give rise to substituted thiazolidines and thiazolines, respectively.



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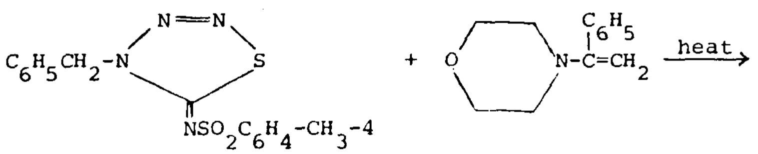

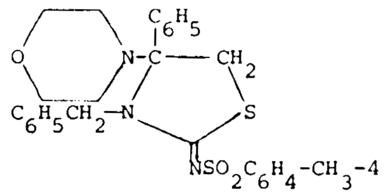

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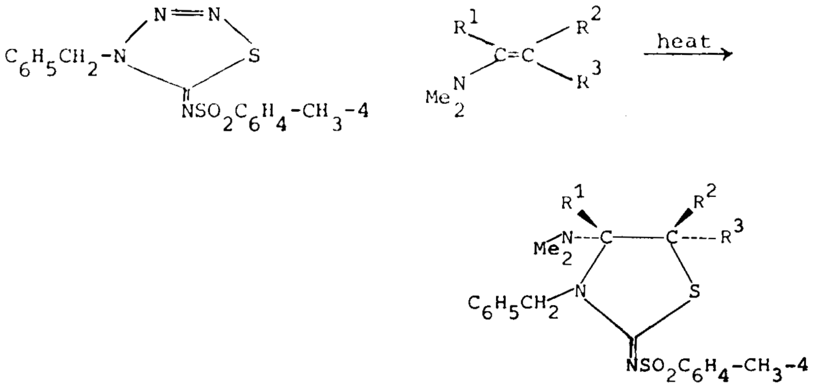

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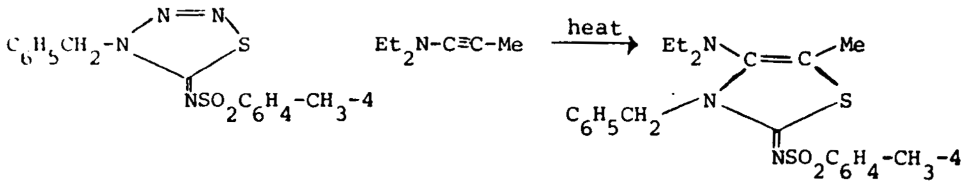
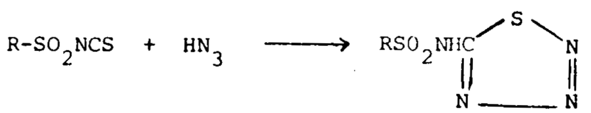


(29)

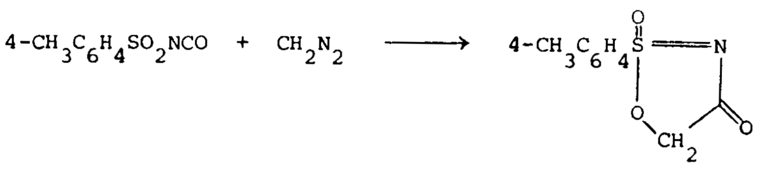
Reactions similar to those above occur between hydrazoic acid and sulfonyl isothiocyanates.[35,36]



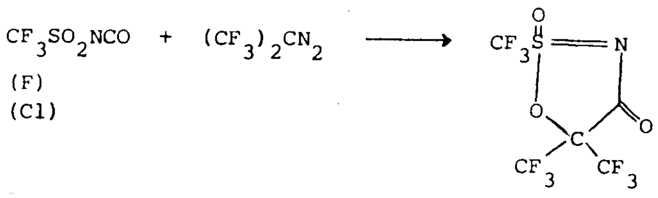
(30)

(R = Me, Et, C_6H_5, o-and p-$CH_3C_6H_4$, 4-ClC_6H_4, 3-$O_2NC_6H_4$, NMe_2)

On the basis of limited reports it appears that sulfonyl isocyanates and sulfonyl isothiocyanates react differently toward diazomethane and some of its derivatives. Lohans found that *p*-toluenesulfonyl isocyanate reacts with diazomethane to give a cyclic product involving oxygen of the original sulfonyl group.[2,37] A similar reaction has been reported for *bis*-(trifluoromethyl)-diazomethane.[38]

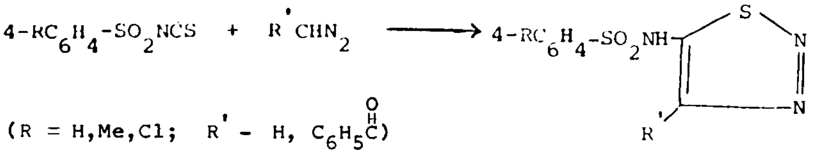


(31)



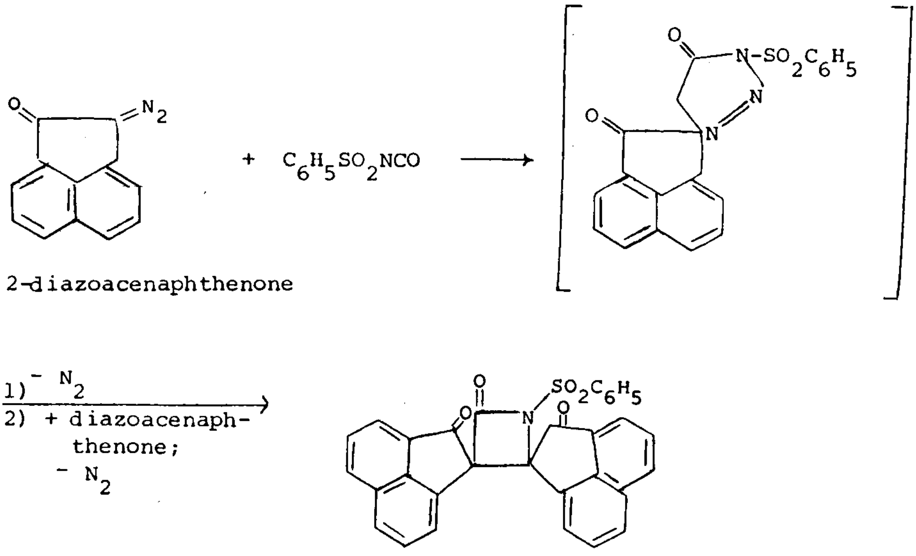
(32)

On the other hand, diazomethane and benzoyldiazomethane react as typical 1,3-dipoles in reactions with sulfonyl isothiocyanates.[36]



(33)

The reaction of 2-diazoacenaphthenone with phenylsulfonyl isocyanate is apparently initially a 1,3-dipolar cycloaddition. The final product results from one mole of isocyanate and two moles of diazo ketone.[39] The diazo ketone does not react with phenyl isocyanate or phenyl isothiocyanate.

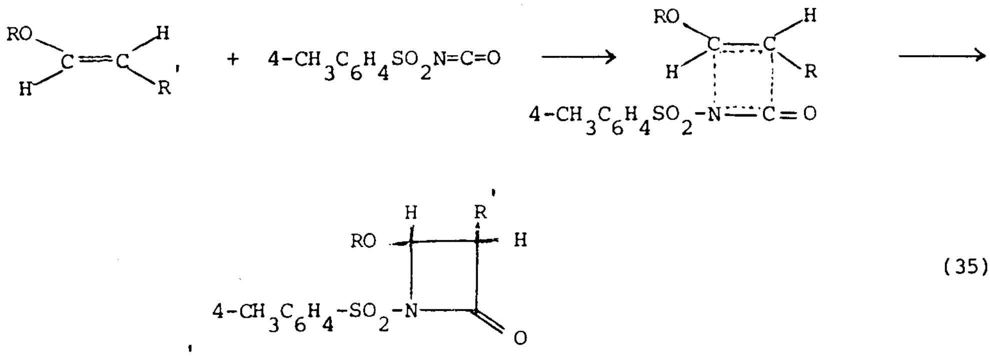


(34)

(mixture of two stereoisomers)

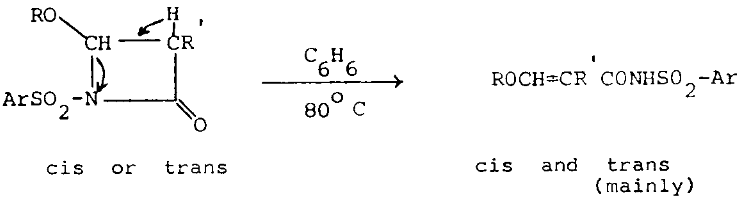
B. Additions to Carbon—Carbon Double Bonds

Sulfonyl isocyanates undergo stereospecific *cis*-addition to enol ethers.[40,41] The 2-azetidinones initially formed isomerize to a mixture of mainly *trans* compounds. Stereochemical results, activation parameters, and influence of substituents and solvent polarity on rates of cycloaddition and isomerization, indicate that cycloaddition proceeds in a concerted manner via a transition state with partial charges.



(35)

(R = Me,Et; R' = Me,Et)

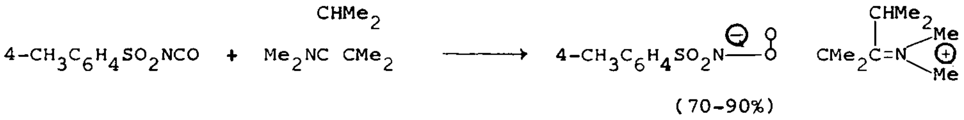


(36)

Sulfonyl isocyanates[42,43] and sulfonyl isothiocyanates[44] react with enamines to give 1,4-dipoles. In non-polar solvents the dipoles are often in equilibrium with cyclic structures.

(37)

(R = Me,MeO,Ph;R^1R^2 = Me,Et,etc.)



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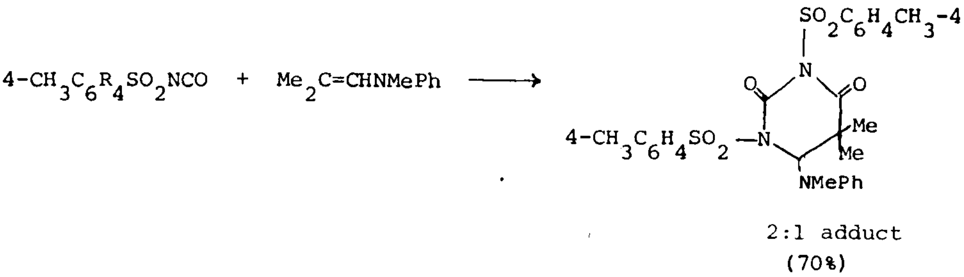

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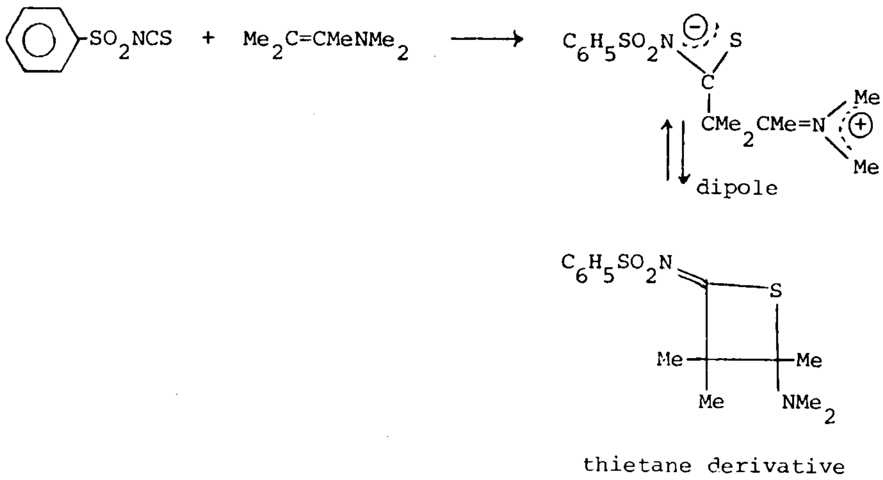

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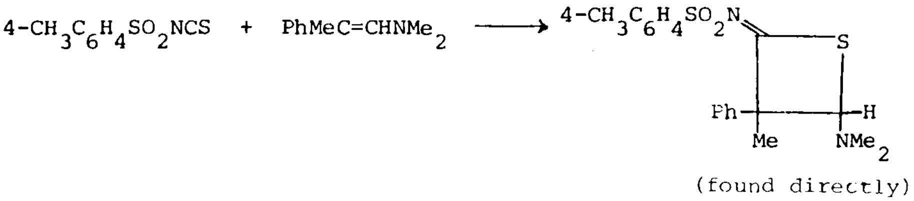
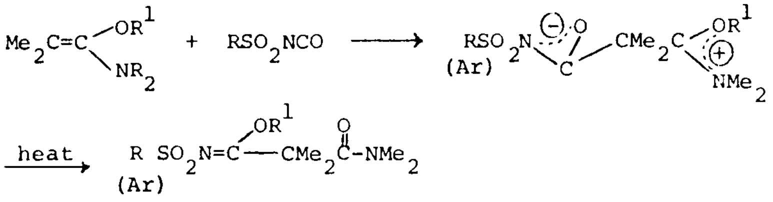


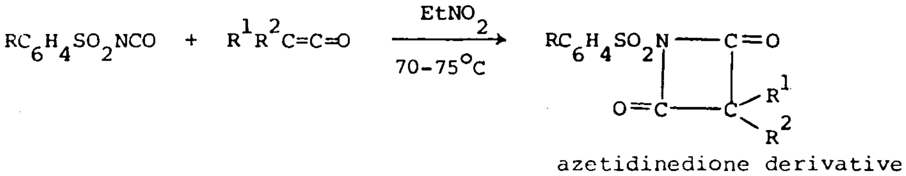
(41)

Ketene O,N-acetals react with sulfonyl isocyanates and isothiocyanates to afford dipoles which may be rearranged thermally.[45]

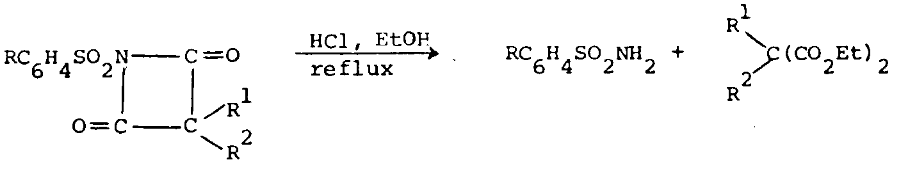


(42)

Further studies of the reactions of ketenes,[46] acylketenes,[47] and ketenimines[48] have been carried out since the last review. The products from ketene reactions have been hydrolyzed to malonic esters.

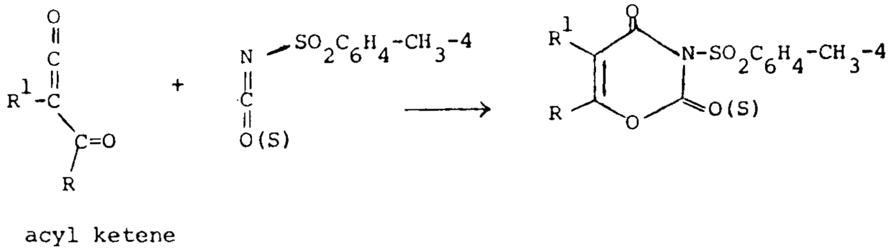


(43)



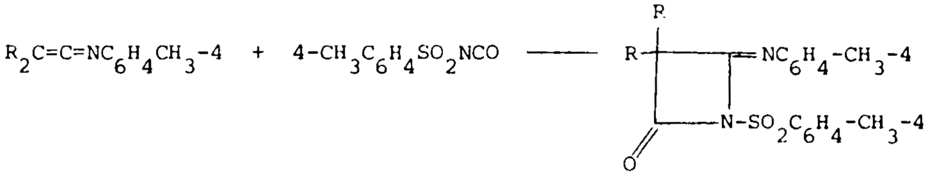
(44)

The acylketenes act as 1,4-dipoles in their reactions with isocyanates and isothiocyanates. The reaction is not specific for the sulfonyl compounds.



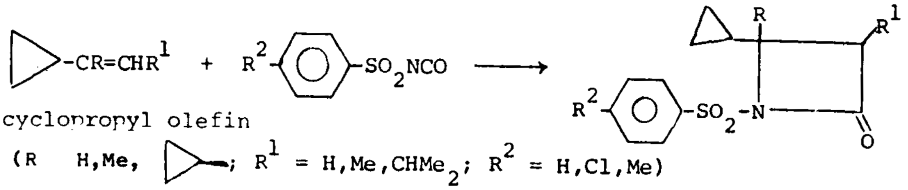
(45)

Ketenimines normally add across their carbon-carbon double bond, resulting in 4-iminoazetidin-2-ones.



(46)

Other reactions of sulfonyl isocyanates with carbon-carbon double bonds include those with cyclopropyl olefins,[49] alkenylidenecyclopropanes,[50] and methylenenorbornadiene.[51]



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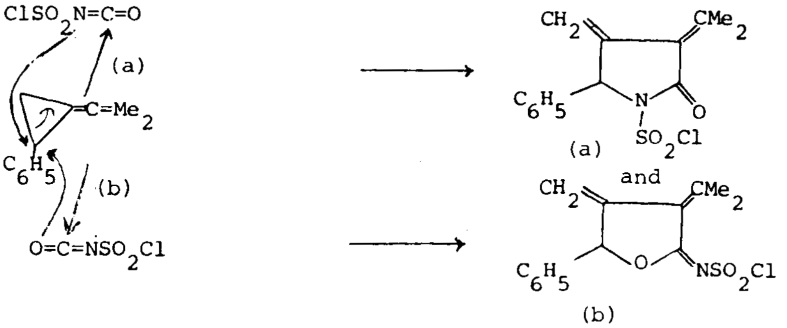
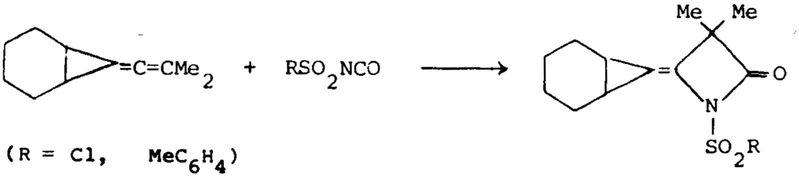
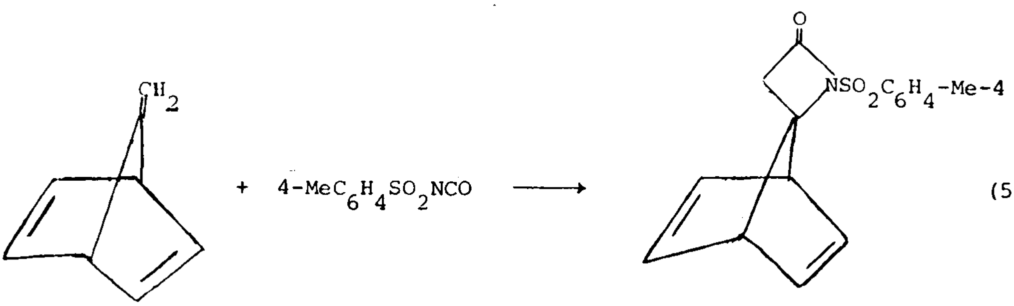


(48)



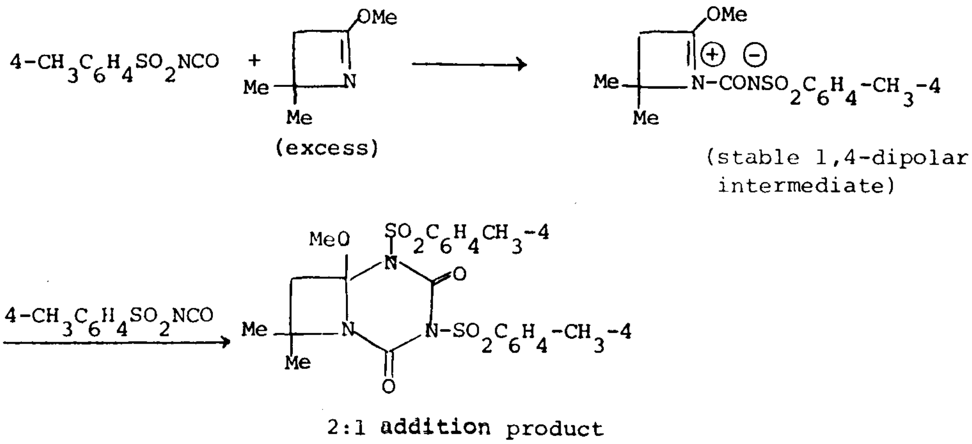
(49



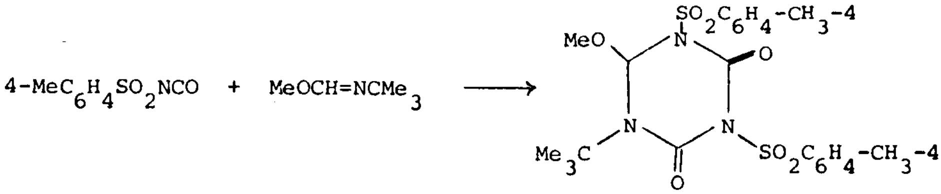
(50)

C. *Addition to Carbon-Nitrogen Double Bonds*

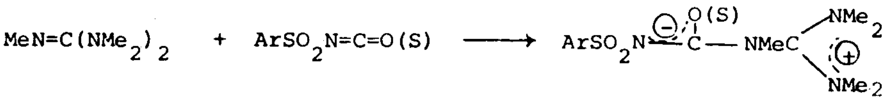
Imines react with sulfonyl isocyanates[52,53] to afford various cyclic and dipolar products, depending upon the conditions, the structure of the imine, and the structure of the isocyanate or isothiocyanate.



(51)

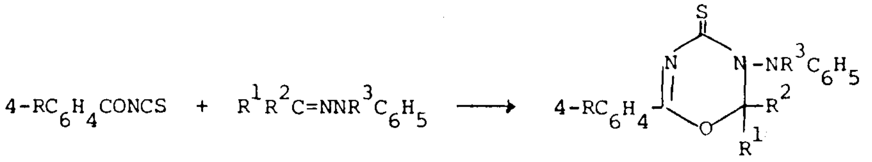


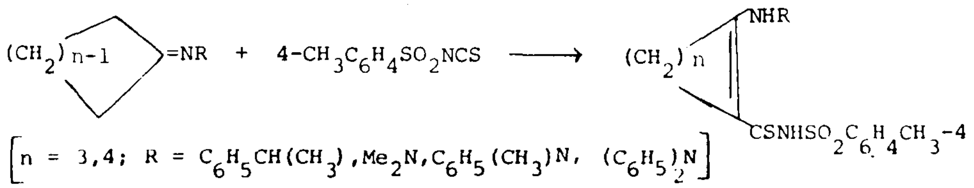
(52)



(53)

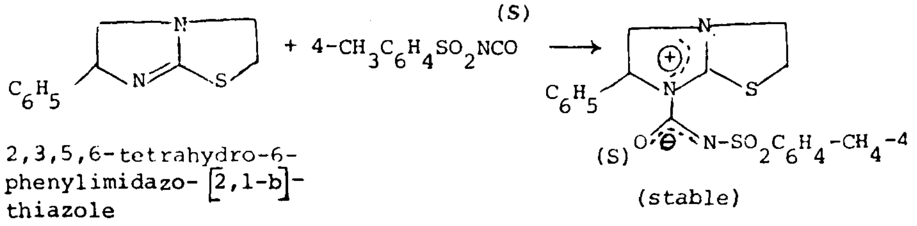
The sometimes contrasting reactions of the very reactive acyl and sulfonyl isothiocyanates are illustrated below.[54]


(54)


(55)

$[n = 3,4;\ R = C_6H_5CH(CH_3), Me_2N, C_6H_5(CH_3)N, (C_6H_5)_2N]$

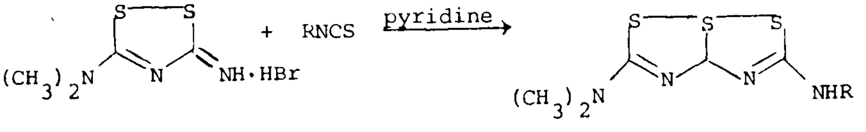
While 2,3,5,6-tetrahydro-6-phenylimidazo-[2,1-b]-thiazole reacts with aryl isothiocyanates to give unstable dipolar 1:1 adducts and aryl and alkyl isocyanates afford cyclic 2:1 adducts, sulfonyl and acyl isocyanates and isothiocyanates produce stable dipolar 1:1 adducts.[55]


(56)

2,3,5,6-tetrahydro-6-phenylimidazo-[2,1-b]-thiazole

(stable)

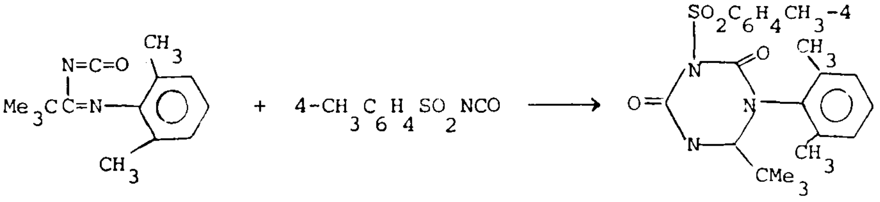
Imino-1,2,4-dithiazoles undergo 1,3-dipolar additions with isothiocyanates and other unsaturated species.[56] This behavior is ascribed to donation of electrons into the system by ring sulfur, causing sulfur to be electrophilic and imino nitrogen nucleophilic.

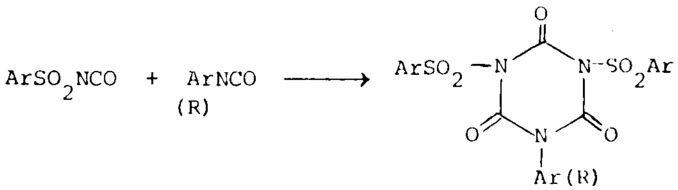

(57)

imino-1,2,4-dithiazole derivative (1,3-dipolar addition product)

(R = alkyl, aryl, $C_6H_5SO_2$)

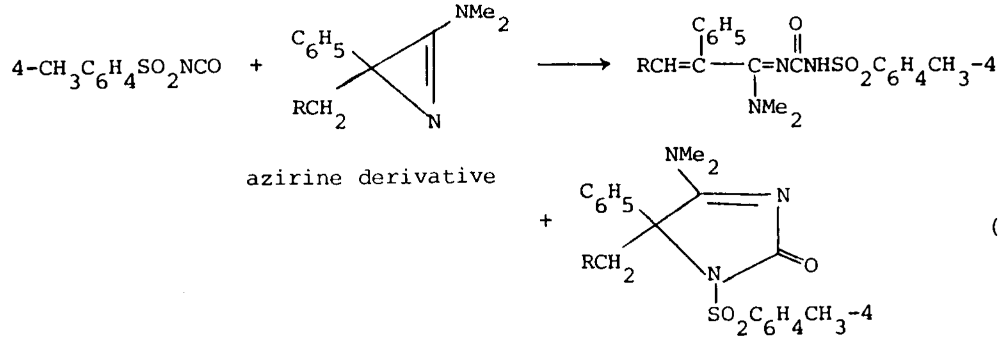
Sulfonyl isocyanates add 1,4 to conjugated imino isocyanates[57] and give 2:1 adducts with alkyl and aryl isocyanates.[58]


(58)

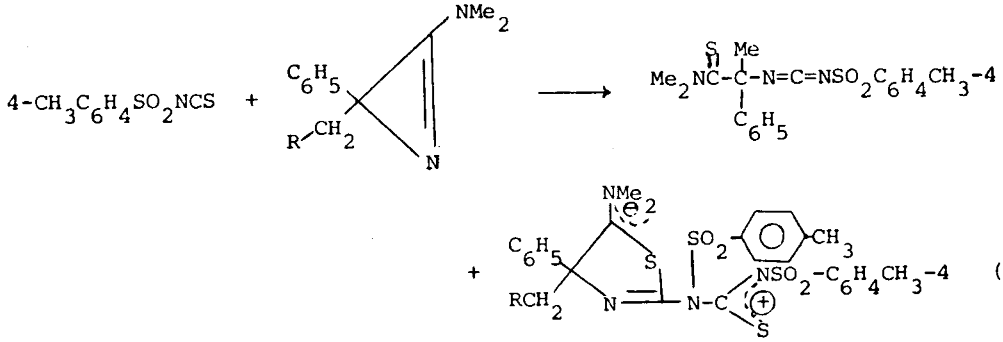


(59)

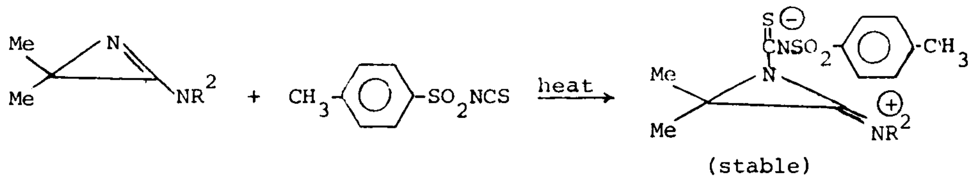
Other interesting reactions involving carbon-nitrogen bonds include azirines,[59] diazacyclopropanones[60] and isothioureas.[61]



(60)



(61)



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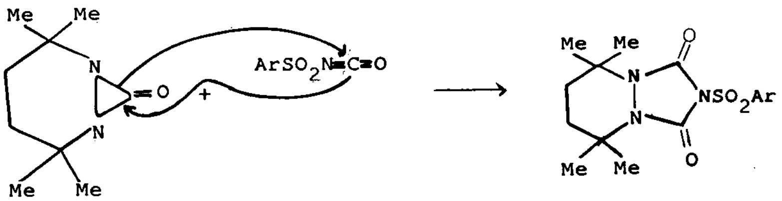
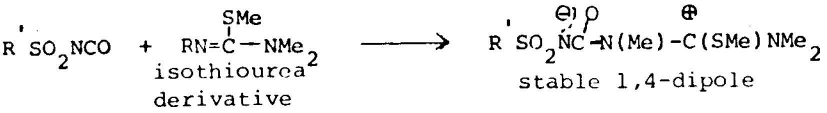


(63)

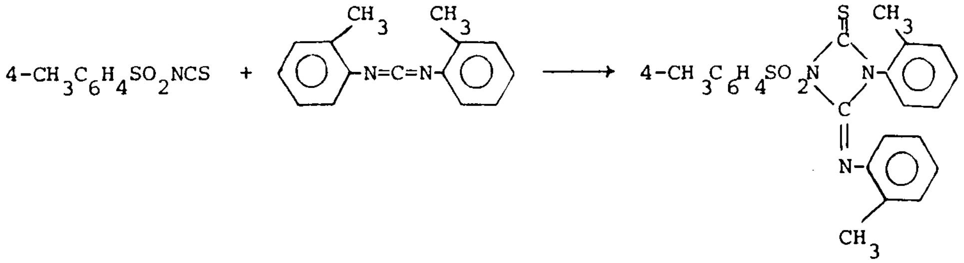
2,2,5,5-tetramethyl-
1,6-diazabicyclo[4:1:0]-
heptan-7-one



$$R'SO_2NCO + RN{=}\overset{SMe}{C}{-}NMe_2 \longrightarrow R'SO_2\overset{\ominus}{N}\overset{O}{C}{-}\overset{\oplus}{N}(Me){-}C(SMe)NMe_2 \qquad (64)$$

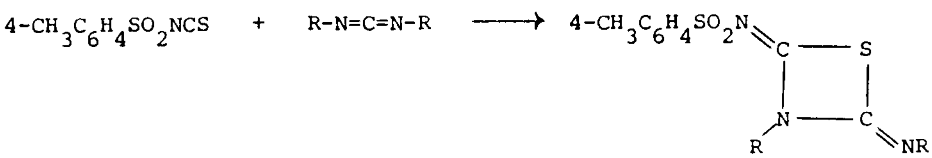
$(R = Me;\ R' = 4\text{-}MeC_6H_4,\ 2,6\text{-}Me_2C_6H_3,\ C_6H_5, Cl)$

Sulfonyl isothiocyanates and carbodiimides undergo (2+2) cycloadditions to give 1,3-diazetidine-2-thiones[62] and 1,3-thiazetidine derivatives.[63] Although



(65)

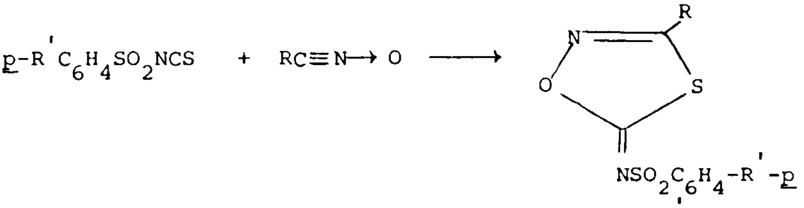
1,3-diazetidine-2-thione derivative



(66)

the usual addition is across the C=S bond of the isothiocyanate, some reactions involve addition across the N=C bond.

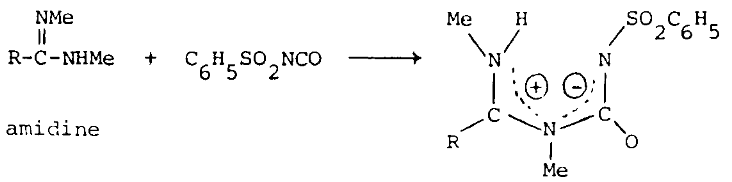
Sulfonyl isothiocyanates undergo 1,3-dipolar cycloadditions with nitrile oxides to afford 3-substituted 5-(arylsulfonyl)-imine-1,4,2-oxathiazoles.[64]



(67)

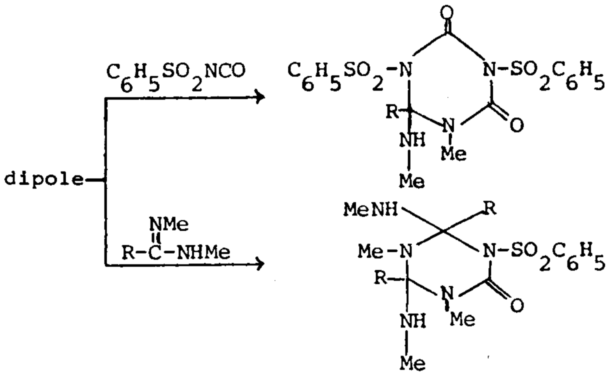
$(R = C_6H_5,\ p\text{-}CH_3C_6H_4,\ \text{mesityl},\ CO_2Et,\ Me,\ Me_3C;\ R' = H, Me)$

Amidines react with sulfonyl and other strongly electrophilic isocyanates to give dipoles which react with dipolarophiles to afford cyclic compounds.[65]



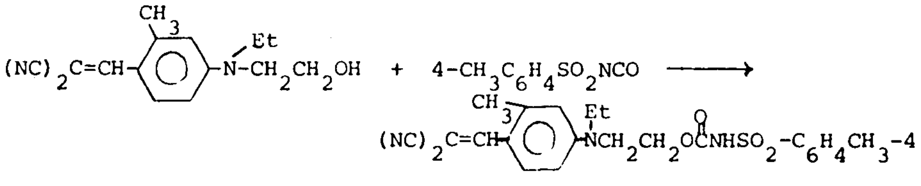
(68)

unstable dipole

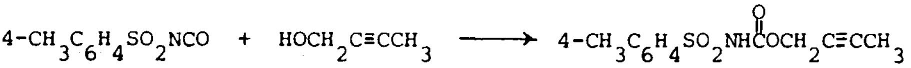

(69)

D. *Reactions of the O—H Group (Alcohols, Peroxides, Acids and Oximes)*

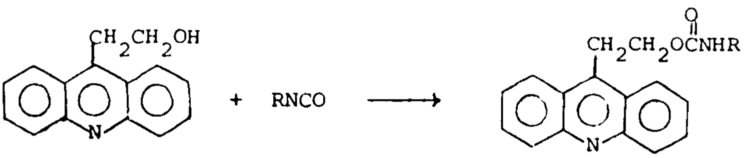
The reactions of alcohols and phenols with sulfonyl isocyanates have been thoroughly studied.[2] Most alcohols lead to sulfonyl carbamates, while those alcohols which tend to form carbonium ions give N-substituted sulfonamides. Most of the recent work with alcohols has been directed toward the synthesis of useful chemicals such as styryl, azo, anthraquinone, and nitro dyes for acetate, polyamide, acrylic, and polyester fibers,[66] antidotes for herbicides,[67] and biologically interesting acridyl compounds.[68]


(70)

styryl dye


$$4\text{-}CH_3C_6H_4SO_2NCO + HOCH_2C\equiv CCH_3 \longrightarrow 4\text{-}CH_3C_6H_4SO_2NH\overset{O}{\overset{\|}{C}}OCH_2C\equiv CCH_3 \quad (71)$$

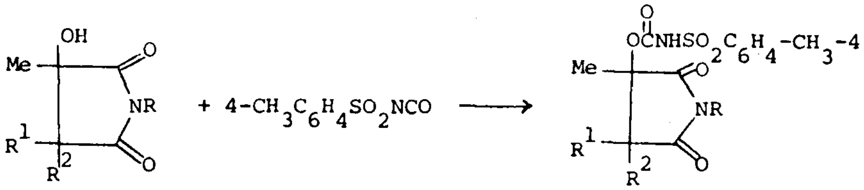
(antidotes for herbicides)


(72)

2-(9-acridyl)-ethanol

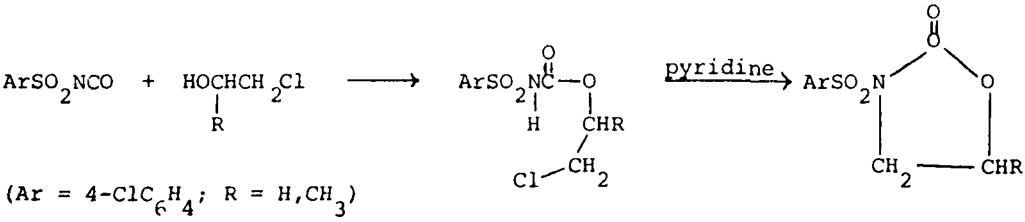
(R = alkyl, aryl, tosyl)

p-Toluenesulfonyl isocyanate, as well as other isocyanates, is reported to react with the hydroxyl group of pyrrolidinedione derivatives to give useful chemical intermediates.[69] McFarland and coworkers report that chloro alcohols react with sulfonyl isocyanates[70] and sulfonyl isothiocyanates[22,70] to produce 1:1 adducts which may be cyclized to oxazolidin-2-ones and oxazolidine-2-thiones.



(73)

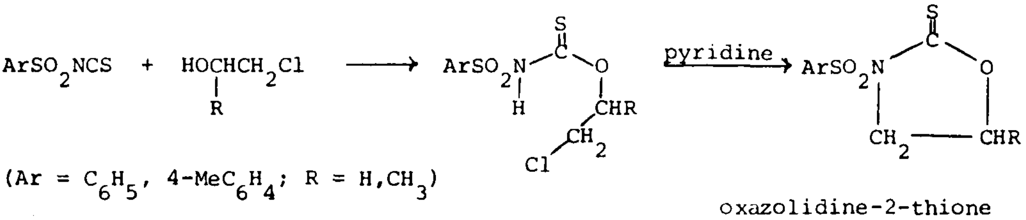
pyrrolidinedione derivative



$(Ar = 4\text{-}ClC_6H_4;\ R = H,CH_3)$

(74)

4-substituted 5-aryl-sulfonyl-oxazolidin-2-one

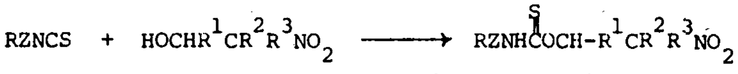


$(Ar = C_6H_5,\ 4\text{-}MeC_6H_4;\ R = H,CH_3)$

(75)

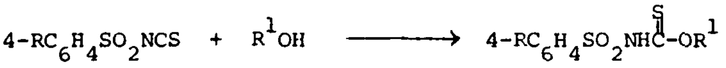
oxazolidine-2-thione derivative

Reaction products from sulfonyl isothiocyanates and nitro alcohols are claimed to have bactericidal and fungicidal activity and are, therefore, used in deodorants, creams, and cleaning compounds.[71] Other sulfonyl thiocarbamates have been found to be useful intermediates in the preparation of remedies for diabetes mellitus.[72]



$$RZNCS + HOCHR^1CR^2R^3NO_2 \longrightarrow RZNH\overset{S}{\overset{\|}{C}}OCH\text{-}R^1CR^2R^3NO_2 \qquad (76)$$

$(R = C_6H_5,\ 4\text{-}ClC_6H_4,\ 2\text{-furyl};\ R^1 = H,Me;\ R^2 = H,Br;\ R^3 = H,Me,Et;$
$Z = SO_2,CO)$



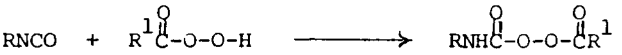
$$4\text{-}RC_6H_4SO_2NCS + R^1OH \longrightarrow 4\text{-}RC_6H_4SO_2NH\overset{S}{\overset{\|}{C}}\text{-}OR^1 \qquad (77)$$

$(R = Me,Cl;\ R^1 = Me,Et,Pr)$ antidiabetic

Alkyl peroxides,[73] peracids,[74] and oximes[75] also react with sulfonyl isocyanates in a similar manner as do the alcohols. The products are alkyl arylsulfonylcarbamoyl peresters, acyl arylsulfonylcarbamoyl acyl peroxides, and O-aryl-sulfonylcarbamoyl oximes, respectively.

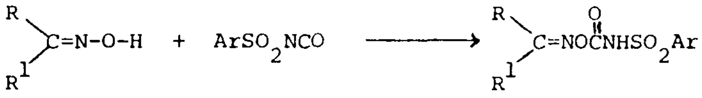
$$RZNCO + Me_3C\text{-}O\text{-}O\text{-}H \longrightarrow RZNH\overset{O}{\overset{\|}{C}}\text{-}O\text{-}O\text{-}CMe_3 \qquad (78)$$

($R = C_6H_5$, 4-$CH_3C_6H_4$, etc.; Z = SO_2,CO) alkyl perester



$$RNCO + R^1\overset{O}{\overset{\|}{C}}\text{-}O\text{-}O\text{-}H \longrightarrow RNH\overset{O}{\overset{\|}{C}}\text{-}O\text{-}O\text{-}\overset{O}{\overset{\|}{C}}R^1 \qquad (79)$$

(R = aryl, ArCo, $ArSO_2$; R^1 = C_6H_5,aryl,Me$(CH_2)_{10}$) carbamoyl acyl peroxide

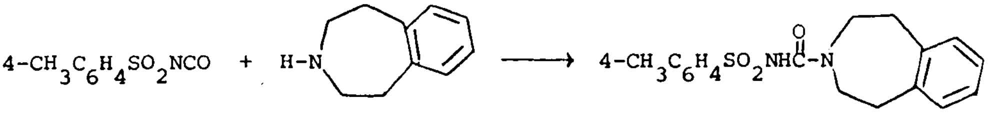


(80)

carbamoyl oxime

E. Reactions with Amines

Considerable research has been carried out toward the synthesis of biologically active ureas and thioureas starting with sulfonyl isocyanates or sulfonyl isothiocyanates and primary or secondary amines. Hypoglycemic activity has been found to exist in sulfonyl ureas prepared from sulfonyl isocyanate and benzazepines,[76] 4,5-dihydropyrazole,[77] aminodicyclopentadienes,[78] as well as azabicyclo compounds.[79]

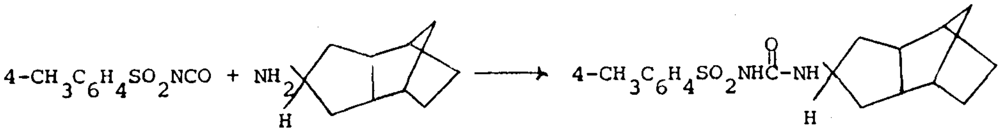


(81)

1,2,4,5-tetrahydro-3H-3-benzazepine

(82)

4,5-dihydro-pyrazole



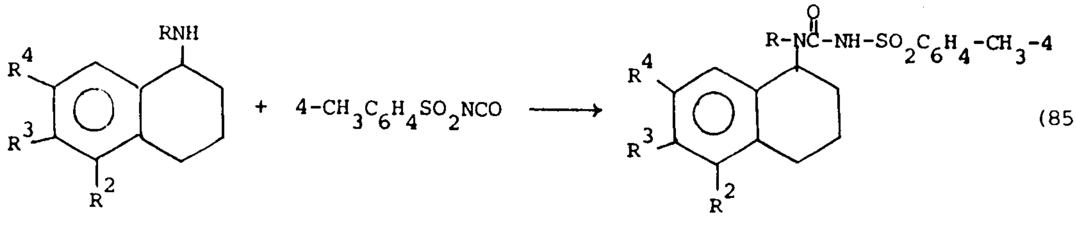
(83)

2-endo-aminotetra-hydro-endo-dicyclo-pentadiene

Sulfonyl isothiocyanates likewise react with alkyl amines to give hypoglycemic agents.[80,81]

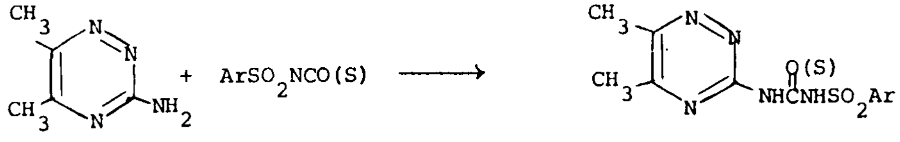
$$\underline{p}\text{-}R'\text{-}C_6H_4SO_2NCS + RNH_2 \longrightarrow \underline{p}\text{-}R'\text{-}C_6H_4SO_2NH\overset{S}{\overset{\|}{C}}\text{-}NHR \quad (84)$$

Herbicidal activity is found in sulfonyl ureas from sulfonyl isocyanates with amino tetralines,[82] aminotriazines,[83] and substituted pyridazinones.[84]



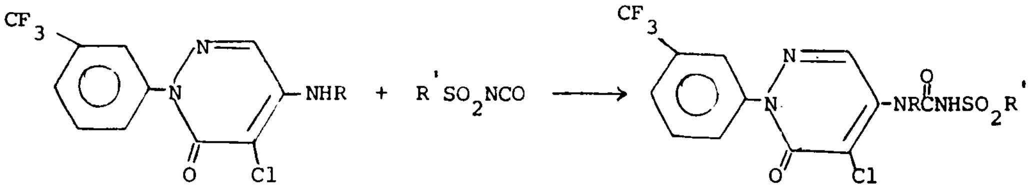
(85)

aminotetraline derivative



(86)

1,2,4-triazine derivative
(also 1,3,5-triazine)

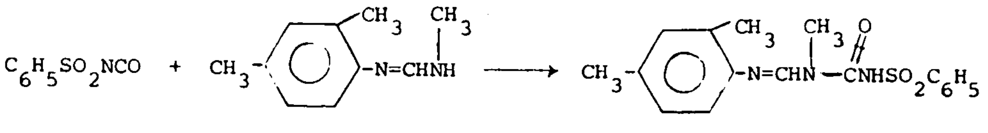


(87)

pyridazinone derivative

$(R = Me,Et;\ R' = C_6H_5,\ 4\text{-}CH_3C_6H_4)$

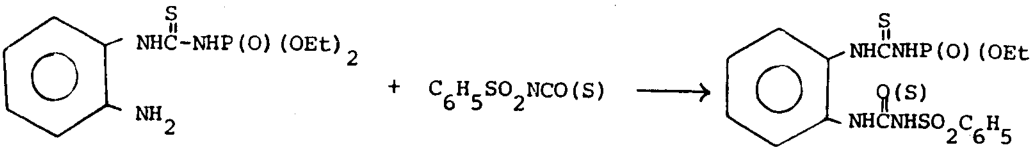
Arylformamidines combine with sulfonyl isocyanates to give (sulfonyl-carbamoyl) phenylformamidines, some of which exhibit activity as acaricides, nemotocides, agricultural fungicides, and insecticides.[85]



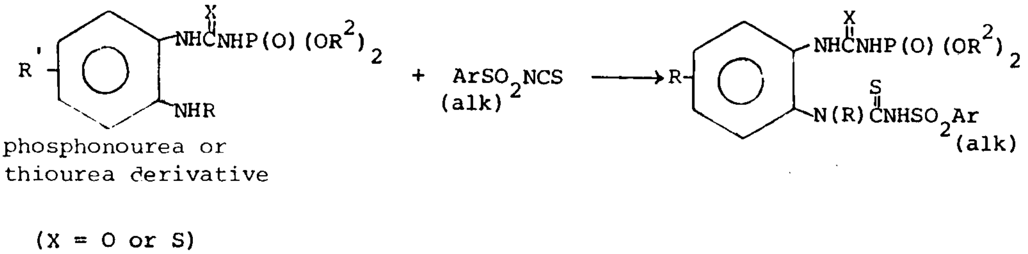
(88)

aryl formamidine derivative

Anthelmintics and nematocides have been prepared from amino substituted phosphonothioureas and sulfonyl isocyanates[86,87] as well as sulfonyl isothiocyanates.[86,88-91]

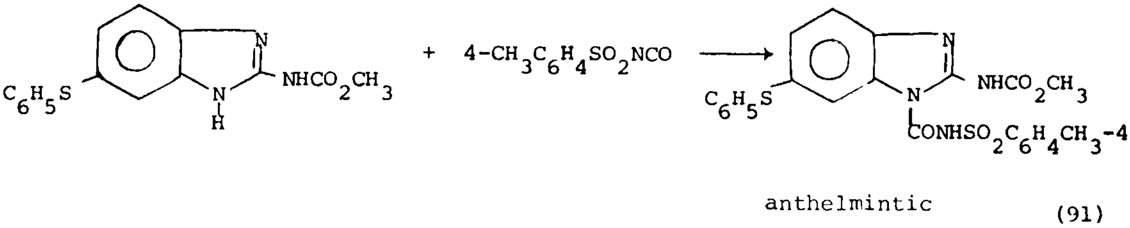


(89)



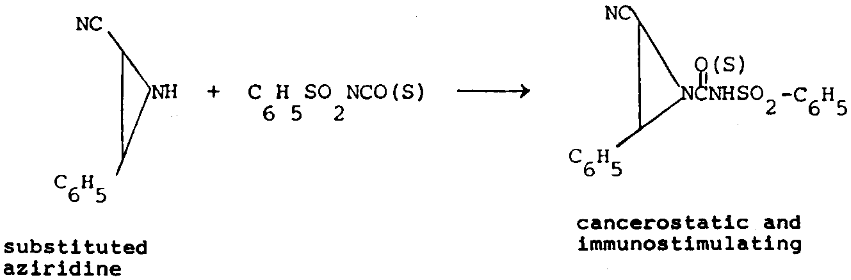
(90)

Sulfonylcarbamidobenzimidazoles, prepared as below, control hookworms in dogs and sheep.[92]

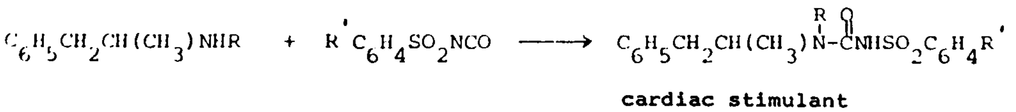


(91)

Certain aziridines along with sulfonyl isocyanates or isothiocyanates give ureas which are cancerostatic and immunostimulating,[93] while certain other amines and sulfonyl isocyanates are reported to lead to products which are cardiac stimulants.[94]

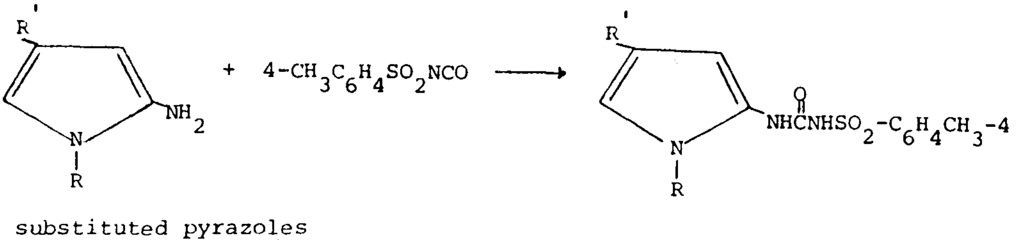


(92)



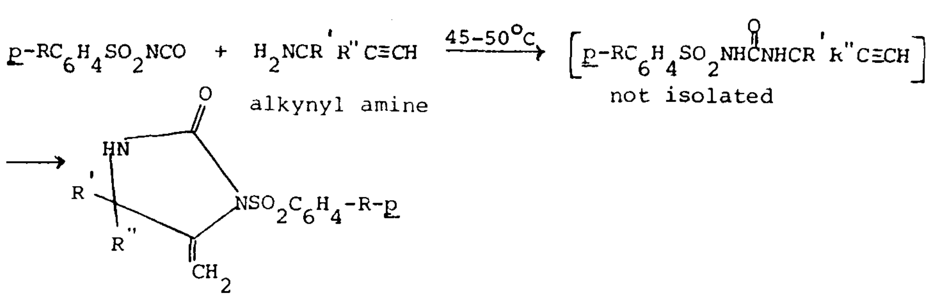
$$C_6H_5CH_2CH(CH_3)NHR + R'C_6H_4SO_2NCO \longrightarrow C_6H_5CH_2CH(CH_3)\overset{R}{N}\text{-}\overset{O}{\overset{\|}{C}}NHSO_2C_6H_4R' \quad (93)$$

Other reported reactions of sulfonyl isocyanates with amines include the reactions with 5-aminopyrazoles,[95] alkynyl amines,[96] aminothiazole oxides,[97] alkyl amines,[98] and substituted thiazines.[99]

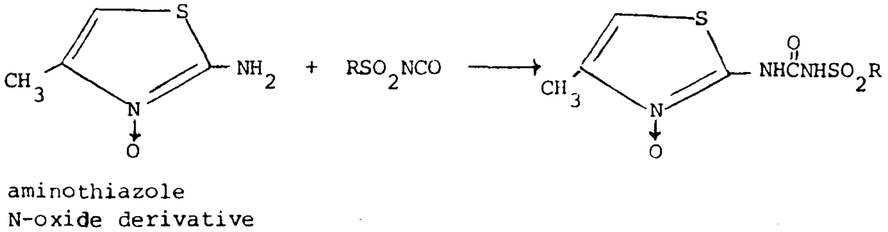


(94)

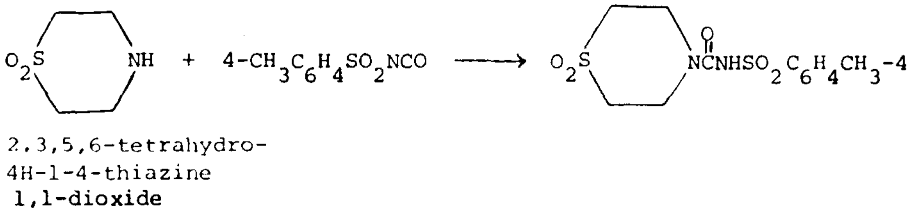
(R = CH_3, C_6H_5, 4-$O_2NC_6H_4$, 4-ClC_6H_4; R' = H, CH_3, C_6H_5, 4-$O_2NC_6H_4$, 4-ClC_6H_4)



(95)

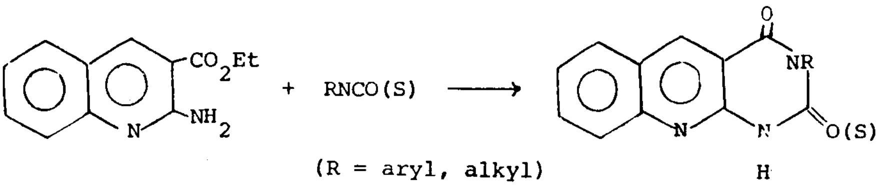


(96)

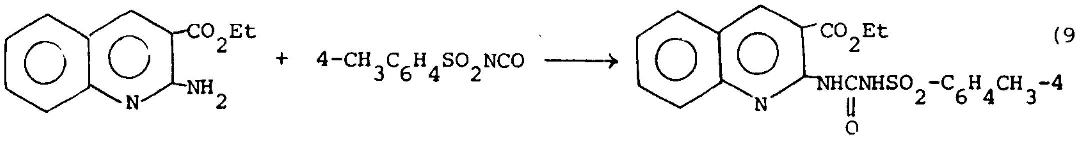


(97)

Aminoquinolinecarboxylates react with aromatic and alkyl isocyanates to give tricyclic compounds, whereas *p*-toluenesulfonyl isocyanate affords only open-chain products.[100]

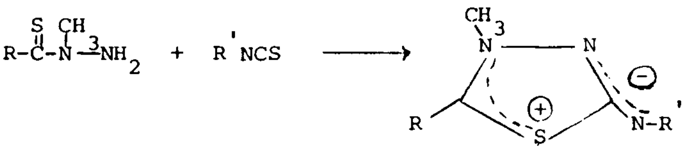


(98)



(99)

Mesoionic 2-acylimino-1,3,4-thia- and oxadiazoles are reported from the reactions of thioaroylhydrazines and isothiocyanates.[101]

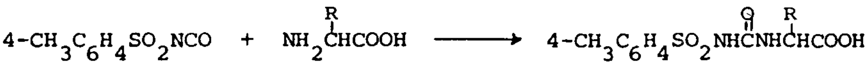


(100)

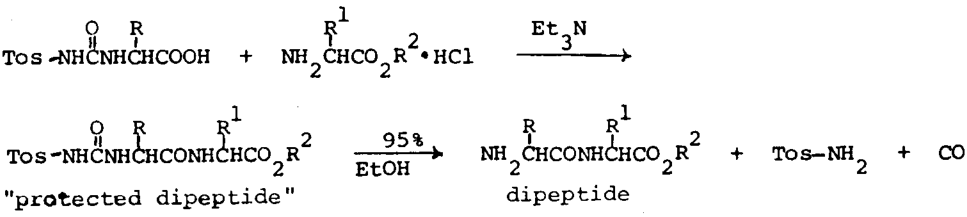
$(R = C_6H_5,\ 4\text{-}CH_3C_6H_4,\ 4\text{-}CH_3OC_6H_4;\ R' = C_6H_5CO,\ C_6H_5SO_2,\ CH_3CO)$

F. Reactions with Amino Acids

The tosylaminocarbonyl* group has been used as an amino protecting group in the synthesis of peptides.[102] Deblocking may be accomplished by heating "protected" peptides in 95% aqueous ethanol, propanol, or butanol. No racemization occurs.



$$4\text{-}CH_3C_6H_4SO_2NCO + NH_2\overset{R}{C}HCOOH \longrightarrow 4\text{-}CH_3C_6H_4SO_2NH\overset{O}{\overset{\|}{C}}NH\overset{R}{C}HCOOH \qquad (101)$$

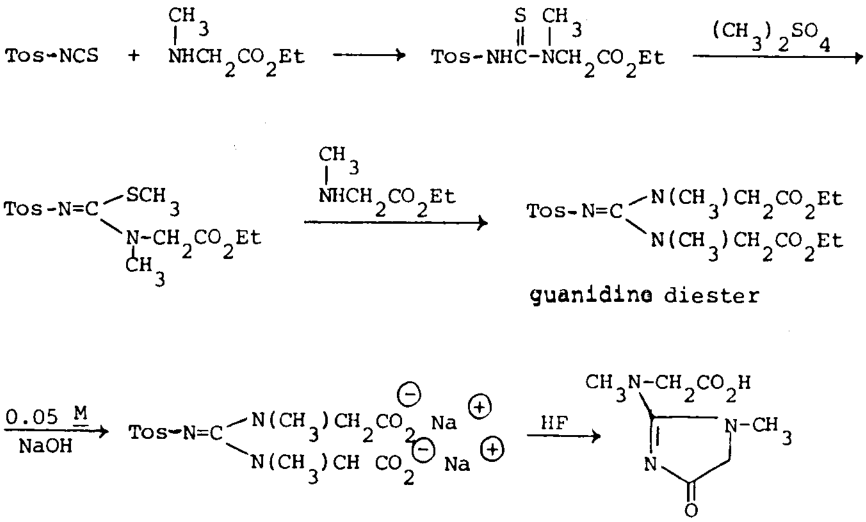


$$\text{Tos-NH}\overset{O}{\overset{\|}{C}}NH\overset{R}{C}HCOOH + NH_2\overset{R^1}{C}HCO_2R^2\cdot HCl \xrightarrow{Et_3N}$$

$$\underset{\text{"protected dipeptide"}}{\text{Tos-NH}\overset{O}{\overset{\|}{C}}NH\overset{R}{C}HCONH\overset{R^1}{C}HCO_2R^2} \xrightarrow[EtOH]{95\%} \underset{\text{dipeptide}}{NH_2\overset{R}{C}HCONH\overset{R^1}{C}HCO_2R^2} + \text{Tos-NH}_2 + CO_2 \qquad (102)$$

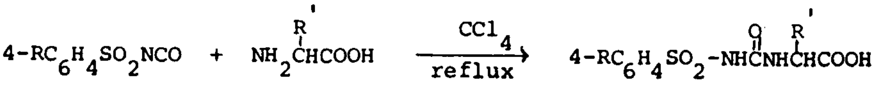
*Tosyl or Tos = $4\text{-}CH_3C_6H_4SO_2$.

Esters of amino acids, when treated with sulfonyl isothiocyanates, lead to intermediates for the synthesis of guanidine diesters.[103] The latter are detosylated and cyclized by hydrogen fluoride.



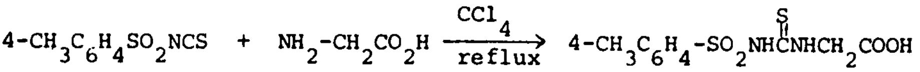
(103)

Russian workers found a similar reaction between 6-aminohexanoic acid and aromatic sulfonyl isothiocyanates,[104] while McFarland and coworkers studied the reactions of various amino acids with both sulfonyl isocyanates and isothiocyanates.[105] The reaction products from the sulfonyl isothiocyanates are especially useful for the synthesis of substituted imidazolidinonethiones.



$$4\text{-}RC_6H_4SO_2NCO + NH_2\overset{R'}{C}HCOOH \xrightarrow[\text{reflux}]{CCl_4} 4\text{-}RC_6H_4SO_2\text{-}NH\overset{O}{C}NH\overset{R'}{C}HCOOH \qquad (104)$$

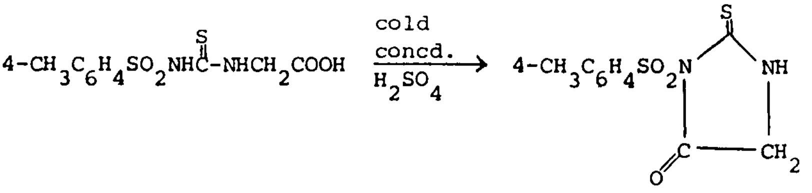
$(R = CH_3,Cl;\ R' = H,CH_3,\ C_6H_5CH_2)$



$$4\text{-}CH_3C_6H_4SO_2NCS + NH_2\text{-}CH_2CO_2H \xrightarrow[\text{reflux}]{CCl_4} 4\text{-}CH_3C_6H_4\text{-}SO_2NH\overset{S}{C}NHCH_2COOH$$

N-(4-toluenesulfonyl)-N'-(carboxymethyl)-thiourea

(105)

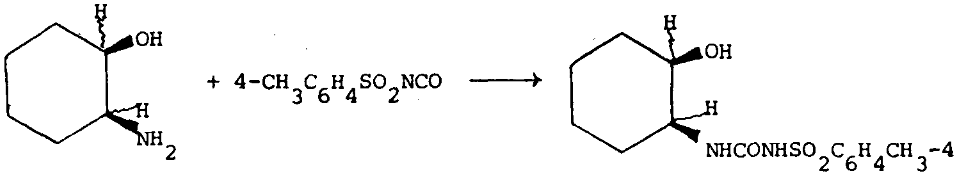


(106)

1-(4-toluenesulfonyl)-imidazolidin-5-one-2-thione

G. *Reactions with Amino Alcohols*

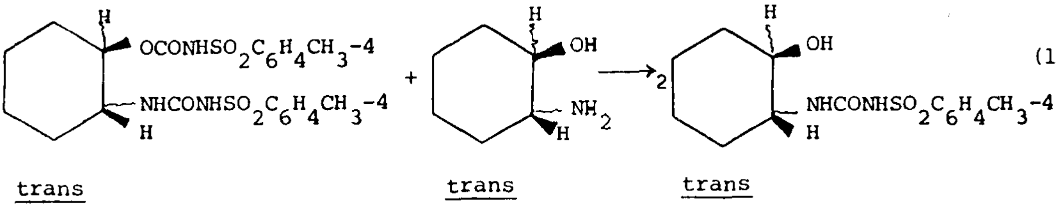
In Sections D and E it was shown that both alcohols and amines react readily with sulfonyl isocyanates and sulfonyl isothiocyanates. Several workers have found that under controlled conditions the amino group in amino alcohols will selectively react with sulfonyl isocyanates. For example, *cis*-2-aminocyclohexanol and tosyl isocyanate give *cis*-2-(tosylureido)-cyclohexanol.[106] (See also references 108 and 109.)



(107)

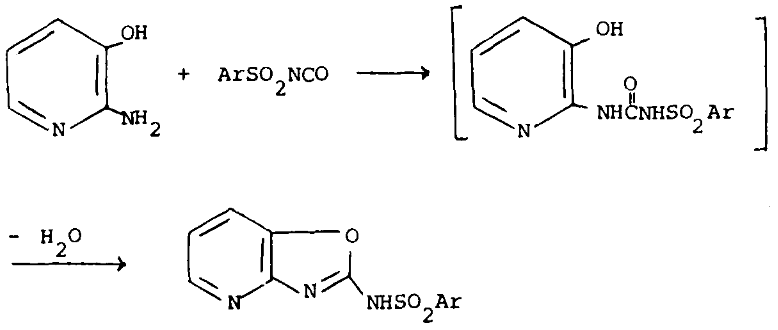
cis-2-(tosylureido) cyclohexanol

The use of two moles of sulfonyl isocyanate causes both hydroxyl and amino groups to react. It is possible, however, to displace the tosylaminocarbonyl group from oxygen by amino alcohol.[107]



(108)

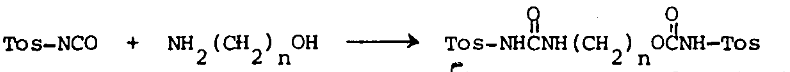
2-Amino-3-hydroxypyridine and arylsulfonyl isocyanates lead to 2-aminoxazolo [4,5-b]-pyridines which are anti-inflammatory, anticonvulsive, and diuretic compounds.[110] Presumably the first reaction is with the amino group, followed by cyclization.



(109)

oxazolopyridine derivative

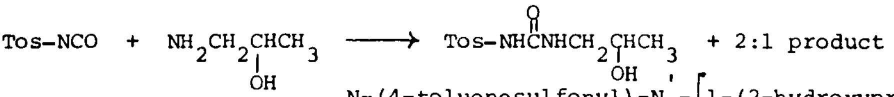
The results of an extensive study of various amino alcohols with sulfonyl isocyanates and isothiocyanates illustrate the difficulties involved in obtaining 1:1 adducts from the extremely reactive isocyanates.[105] 4-Toluenesulfonyl isocyanate reacts with 2-aminoethanol and 3-amino-1-propanol to give only 2:1 isocyanate/amino alcohol products. 1-Amino-2-propanol gives both 1:1 and 2:1 adducts, while 2-amino-2-methyl-1-propanol affords only a 1:1 adduct. The less reactive sulfonyl isothiocyanate gives only 1:1 adducts with the first three amino alcohols.



$$\text{Tos-NCO} + NH_2(CH_2)_nOH \longrightarrow \text{Tos-NH}\overset{O}{\overset{\|}{C}}NH(CH_2)_nO\overset{O}{\overset{\|}{C}}NH\text{-Tos} \quad (110)$$

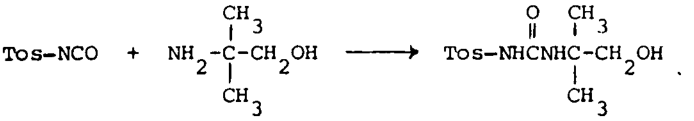
(n = 2 or 3)

2-[(N-4-toluenesulfonyl)-N'-ureido]-alkyl 4-toluenesulfonyl carbamate

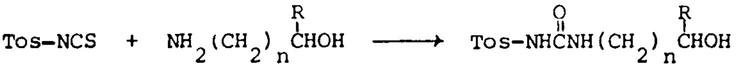


$$\text{Tos-NCO} + NH_2CH_2\underset{OH}{CH}CH_3 \longrightarrow \text{Tos-NH}\overset{O}{\overset{\|}{C}}NHCH_2\underset{OH}{CH}CH_3 + 2{:}1\ \text{product} \quad (111)$$

N-(4-toluenesulfonyl)-N'-[1-(2-hydroxypropyl)]-urea



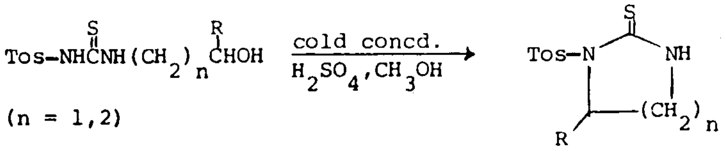
$$\text{Tos-NCO} + NH_2\text{-}\overset{CH_3}{\underset{CH_3}{C}}\text{-}CH_2OH \longrightarrow \text{Tos-NH}\overset{O}{\overset{\|}{C}}NH\overset{CH_3}{\underset{CH_3}{C}}\text{-}CH_2OH \quad (112)$$



$$\text{Tos-NCS} + NH_2(CH_2)_n\overset{R}{C}HOH \longrightarrow \text{Tos-NH}\overset{O}{\overset{\|}{C}}NH(CH_2)_n\overset{R}{C}HOH \quad (113)$$

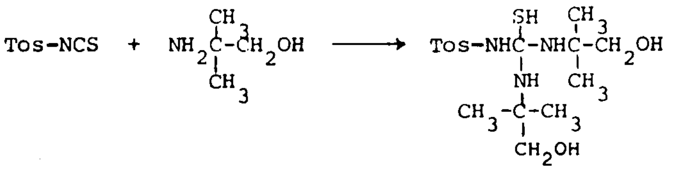
A: R = H, n = 1
B: R = CH_3, n = 1
C: R = H, n = 2

The 1:1 adducts from the isothiocyanates are cyclized by concentrated sulfuric acid to imidazolidine-2-thiones and hexahydropyrimidine-2-thiones.



(114)

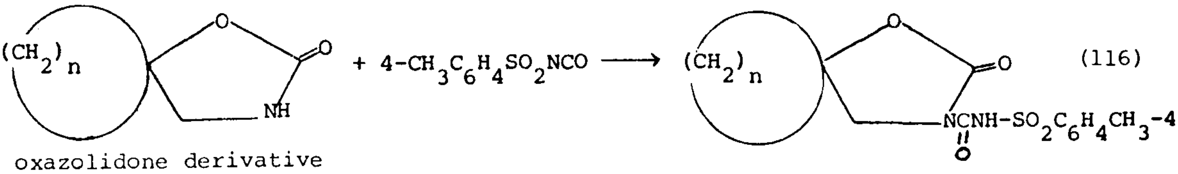
2-Amino-2-methyl-1-propanol leads to a 1:2 isocyanate/amino alcohol product.



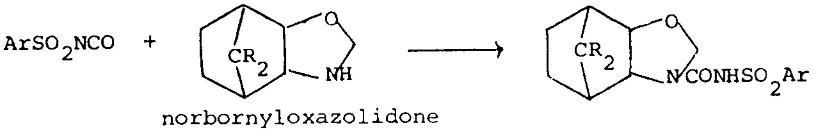
(115)

H. Reactions with Amides and Thioamides

The nitrogen atoms of amides and thioamides are not as nucleophilic as are the nitrogens of amines. Consequently, reactions are usually slower. Sulfonyl isocyanates are, however, strong electrophiles and readily undergo reactions with amides and thioamides to afford N-sulfonyl-N'-acylureas or N-sulfonyl-N'-thioacylureas. 2-Oxazolidones and sulfonyl isocyanates give arylsulfonylcarbamoyl derivatives of the oxazolidones.[111,112] Other similar reactions



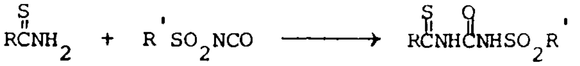
(116)



(117)

have also been reported.[113,114]

Thioamides also react with sulfonyl isocyanates in organic solvents such as benzene and methyl ethyl ketone.[115]



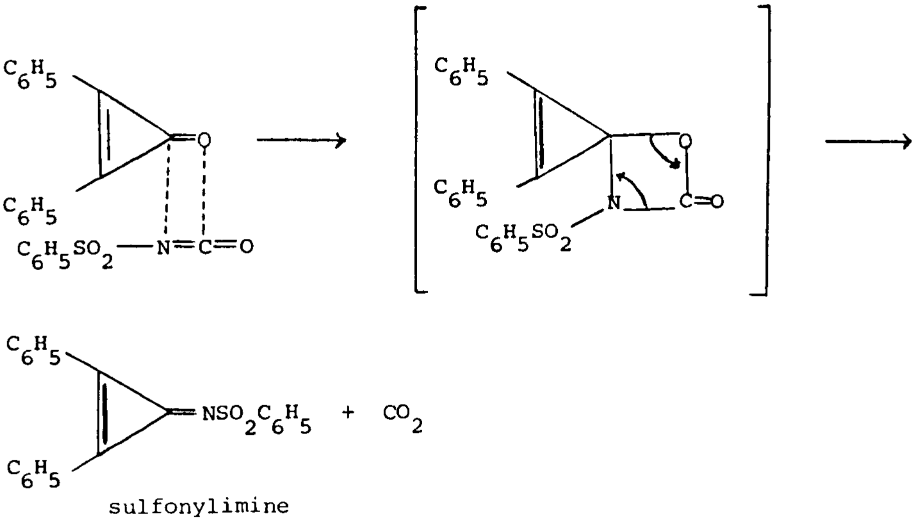
$$R\overset{S}{\overset{\|}{C}}NH_2 + R'SO_2NCO \longrightarrow R\overset{S}{\overset{\|}{C}}NH\overset{O}{\overset{\|}{C}}NHSO_2R'$$

(118)

(R = C_6H_5, subst'd C_6H_5, 1-naphthyl, 2-furyl, 2-thienyl; R' = CH_3, C_6H_5, 4-$CH_3C_6H_4$, 4-ClC_6H_4)

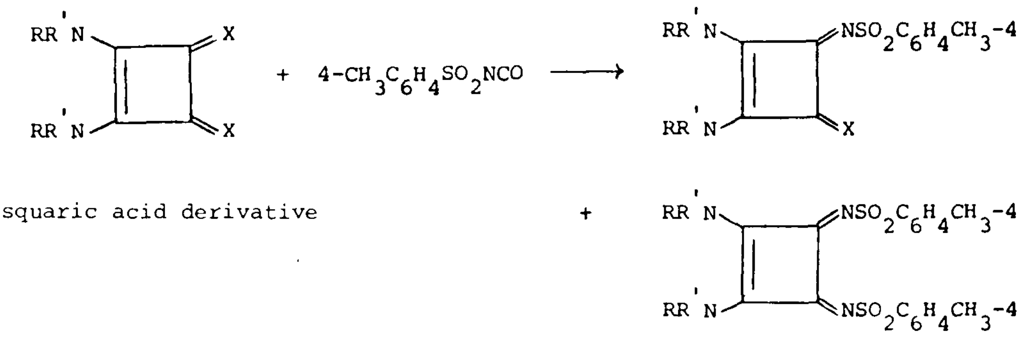
I. Reactions with Aldehydes and Ketones

It was reported in the earlier review[2] that aldehydes and some ketones react with sulfonyl isocyanates to give sulfonylimines and CO_2. Furthermore, it was indicated that the reactions are 1,2-dipolar additions and a mechanism for the reaction of benzenesulfonyl isocyanate and diphenylcyclopropenone was proposed.[116]



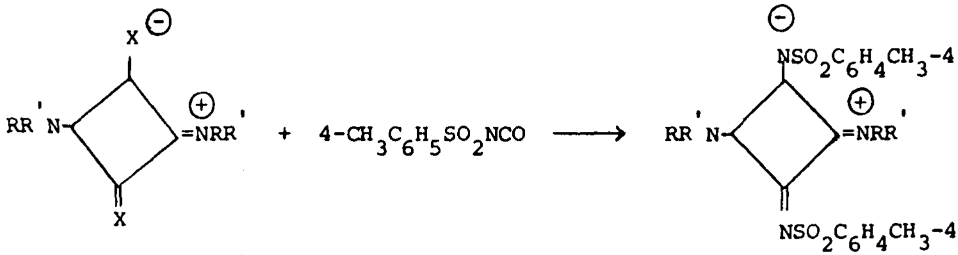
(119)

Treatment of squaric acid derivatives or their thio analogs with sulfonyl isocyanates replaces either one or both of the carbonyl oxygen atoms by sulfonylimino groups.[117,118]



squaric acid derivative

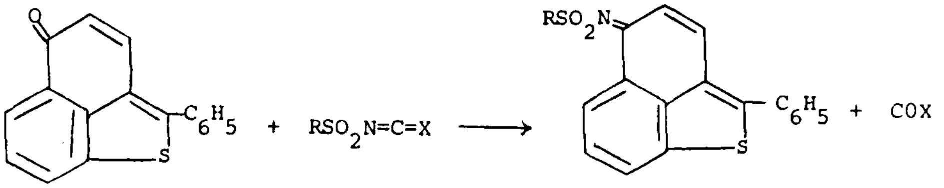
(120)



(121)

(R = R' = CH_3; RR'N = piperidino; X = O or S)

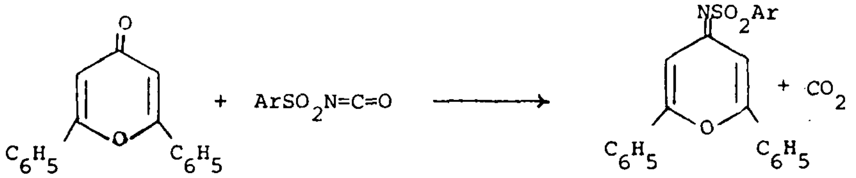
Recent studies have also shown that both sulfonyl isocyanates and isothiocyanates react similarly with substituted naphthothiophenes[119-121] and 4-pyrones[122] to give sulfonylimines and CO_2 or COS.



(122)

2-phenyl-5-oxonaphtho
[1,8-be]thiophene

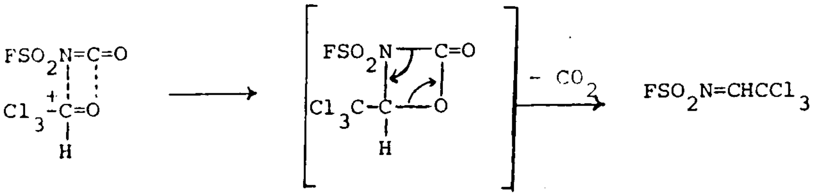
(R = aryl, Cl; X = O,S)



(123)

2,6-diphenyl-4H-
4-pyrone

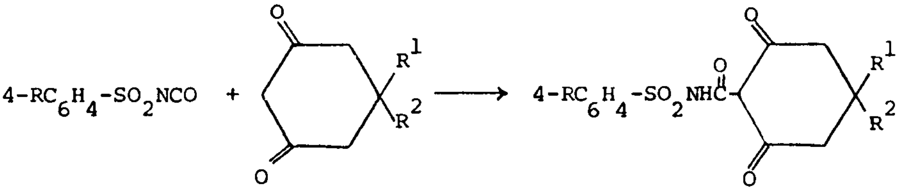
Halosulfonyl isocyanates also enter into such reactions as illustrated by the reaction of fluorosulfonyl isocyanate with chloral.[123]



(124)

J. Reactions with C-H Acidic Compounds

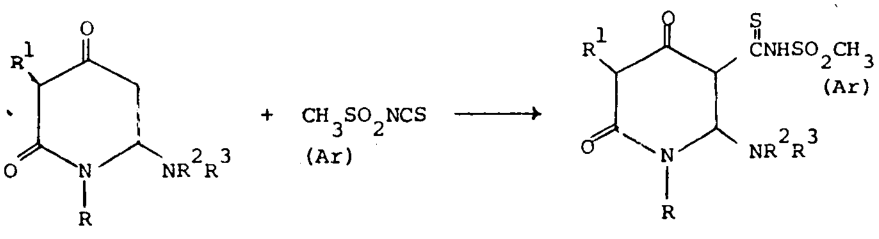
Hydrogens on carbon adjacent to carbonyl are known to be activated. Substances containing such hydrogens may react in the enol form to give C-substituted or O-substituted products. Many of these reactions involve highly reactive isocyanates and isothiocyanates. 1,3-Cyclohexanediones react with sulfonyl isocyanates to give substances which exhibit antidiabetic activity.[124]



(125)

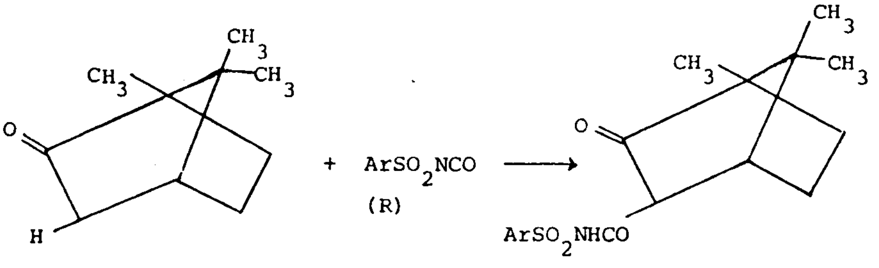
$(R = CH_3Cl,H;\ R^1 = H,CH_3;\ R^2 = C_{1-5}\text{alkyl},C_6H_5;\ R^1R^2 = (CH_2)_5)$

Other examples include the reactions of sulfonyl isothiocyanates with uracils[125] and camphor derivatives with sulfonyl isocyanates.[126]



uracil derivative

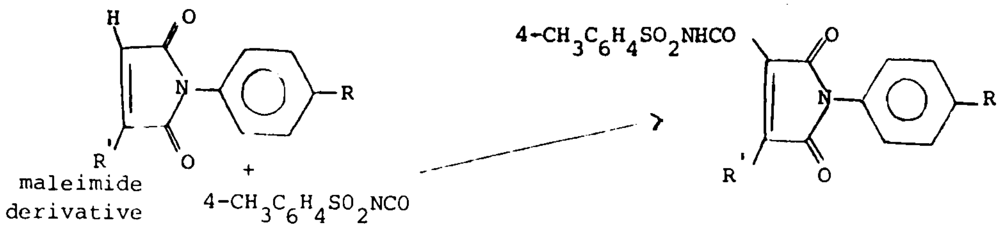
(126)



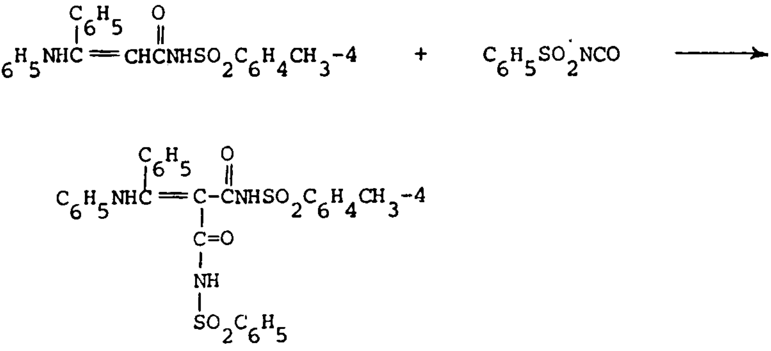
camphor derivative

(127)

α, β-Unsaturated carbonyl compounds also react to place the sulfonylaminocarbonyl group on unsaturated carbon of maleimides[127] and other α, β-unsaturated amides.[128]



(128)

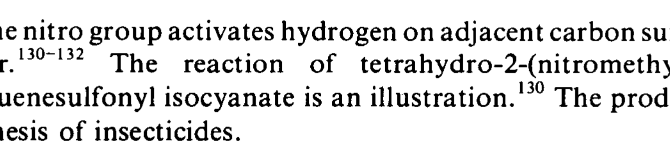


$$C_6H_5NH\overset{C_6H_5}{C}{=}CH\overset{O}{\overset{\|}{C}}NHSO_2C_6H_4CH_3\text{-}4 + C_6H_5SO_2NCO \longrightarrow$$

$$C_6H_5NH\overset{C_6H_5}{C}{=}\underset{\underset{\underset{SO_2C_6H_5}{|}}{\underset{NH}{|}}}{\underset{C=O}{|}}{C}\text{-}\overset{O}{\overset{\|}{C}}NHSO_2C_6H_4CH_3\text{-}4$$

(129)

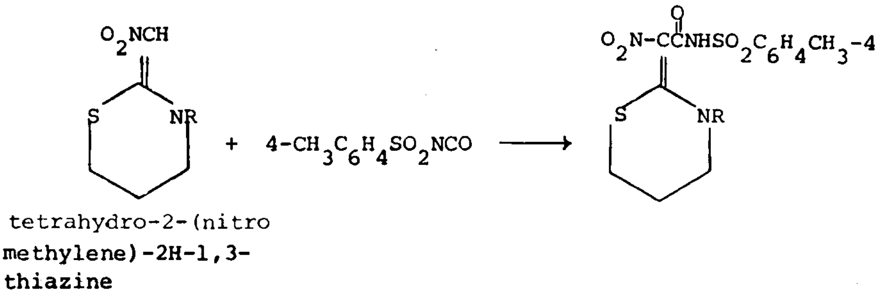
1,2-Cyclohexanedione reacts and gives O-acylation, indicating reaction via the enol form.[129]



(130)

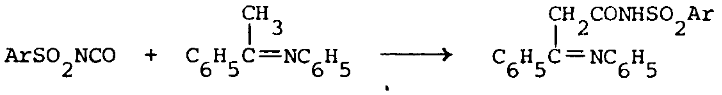
(R = 4-$CH_3C_6H_4SO_2$, 4-ClC_6H_4, 4-BrC_6H_4, $C_6H_5CH_2$, C_6H_5CO, 4-$CH_3C_6H_4CO$)

The nitro group activates hydrogen on adjacent carbon sufficiently to cause addition to occur.[130–132] The reaction of tetrahydro-2-(nitromethylene)-2H-1,3-thiazine with p-toluenesulfonyl isocyanate is an illustration.[130] The product is an intermediate in the synthesis of insecticides.



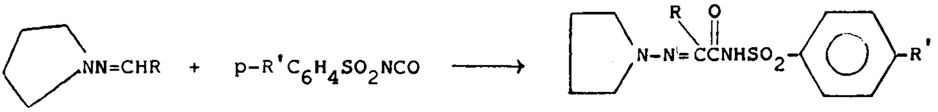
(131)

Reactions of hydrogen on carbon include those on carbon adjacent to a carbon-nitrogen double bond,[133] hydrogen which is on the carbon of a carbon-nitrogen double bond,[134] and ethylenic hydrogen adjacent to a sulfur atom.[135]



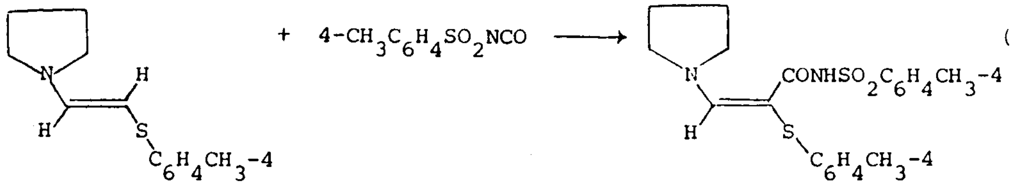
$$ArSO_2NCO + C_6H_5\overset{\overset{\displaystyle CH_3}{|}}{C}{=}NC_6H_5 \longrightarrow C_6H_5\overset{\overset{\displaystyle CH_2CONHSO_2Ar}{|}}{C}{=}NC_6H_5 \quad (132)$$

(Ar = C_6H_5, 4-$CH_3C_6H_4$)



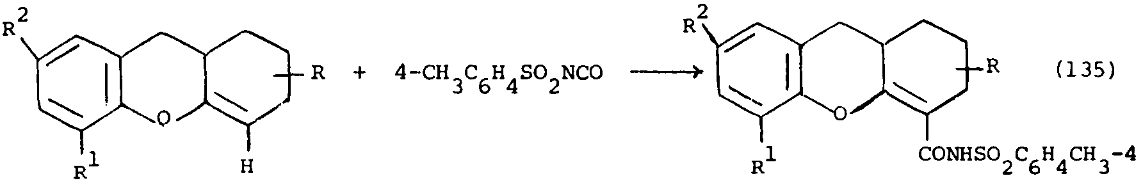
(133)

(R = H, CH_3, CH_3CH_2, $CH(CH_3)_2$; R' = H, CH_3)



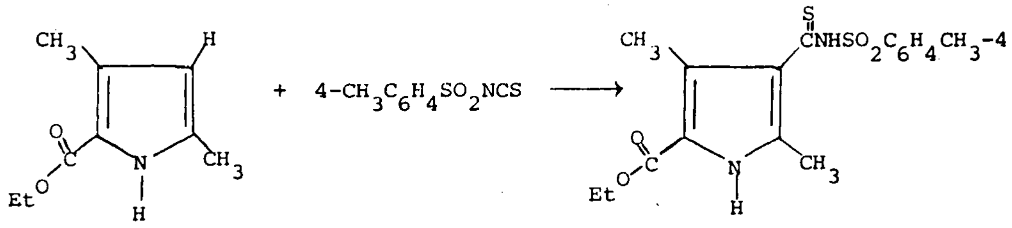
(134)

Finally, xanthenes[136] and pyrroles[137] react with sulfonyl isocyanates and isothiocyanates to replace hydrogen by a sulfonylaminocarbonyl or thiocarbonyl group. The reaction with pyrrole may very well be considered to be an electrophilic aromatic substitution.



(135)

substituted xanthene

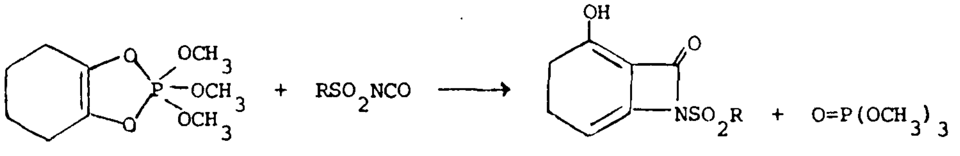


(136)

substituted pyrrole

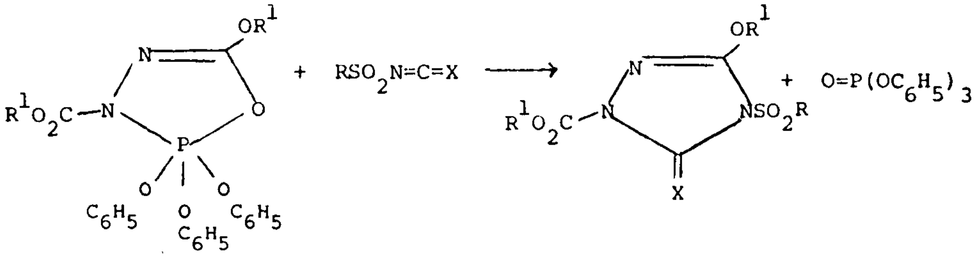
K. Reactions with Phosphorus Compounds

In Section E, phosphonoureides and phosphonothioureides, prepared from sulfonyl isocyanates and sulfonyl isothiocyanates, were discussed as anthelmintic agents.[90] The reactions involving isocyanates and isothiocyanates were, however, with amino groups in compounds containing phosphorus. Several papers have appeared in which sulfonyl isocyanates and sulfonyl isothiocyanates reacted with phospholenes to displace trialkyl or triaryl phosphate. The research has been done by Neidlein and Mosebach.[138-140]



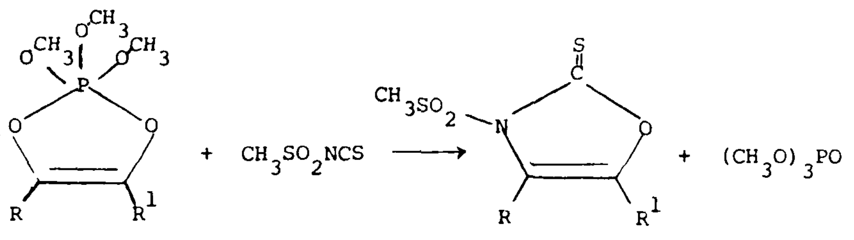
(137)

(R = 4-$CH_3C_6H_4$, 4-ClC_6H_4)



(138)

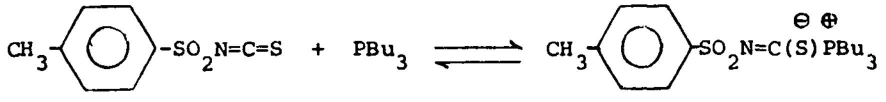
(R = C_6H_5, substd C_6H_5, CH_3, CH_3CH_2; R^1 = CH_3, CH_3CH_2; X = O,S)



(139)

(R = CH_3CH_2,C_6H_5; R^1 = H,CH_3)

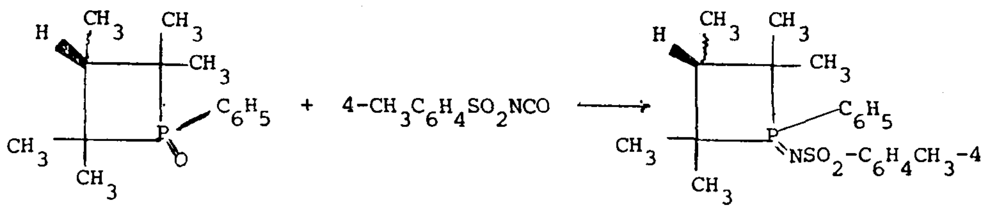
p-Toluenesulfonyl isothiocyanate, as well as other isothiocyanates, and tributyl phosphine give a dipolar adduct which is in equilibrium with starting materials.[141] The equilibrium



(140)

constants have been determined by ^{31}P NMR.

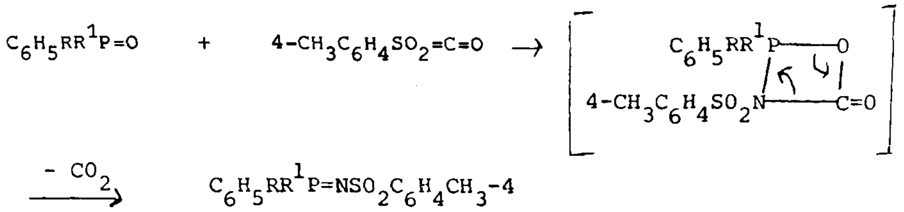
Cyclic and acyclic phosphine oxides behave toward sulfonyl isocyanates and sulfonyl isothiocyanates as do aldehydes and ketones. The products are phosphinimines and CO_2 or COS, respectively.[142-144] Whereas in the cyclic compounds



(141)

cis-2,2,3,4,4-pentamethyl-1-phenylphosphetane 1-oxide

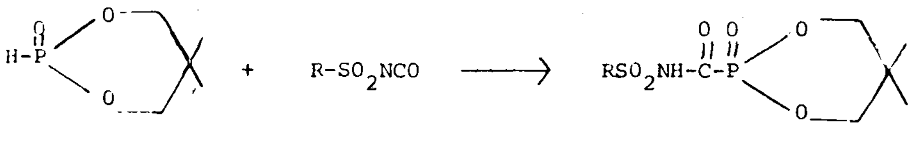
cis- phosphinimine (retention of configuration)



(142)

phosphinimine formation occurs with retention of configuration, in the acyclic compounds racemization occurs faster than does phosphinimine formation.

Hydrogen phosphonates react with sulfonyl isocyanates to give products which are useful as flame retardants for polymers.[145]

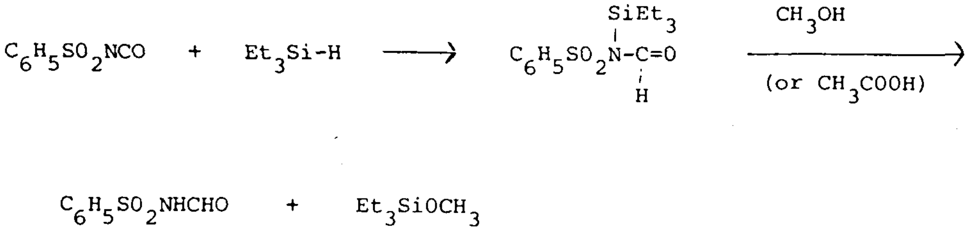


(143)

flame retardants

L. Reactions with Silicon Compounds

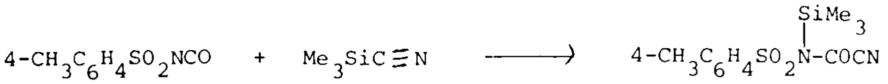
Paralleling the increased activity in organosilicon chemistry has been the interest in the reactions of these compounds with sulfonyl isocyanates. Some reactions involve breaking an Si-X bond, but most are reactions at other functional groups in the molecule. Trialkylsilanes add to sulfonyl isocyanates, silicon (the more positive element) adding to nitrogen and hydrogen to carbon.[146] The result is a silicon-substituted formamide which can be solvolyzed to a sulfonyl formamide by methanol or acetic acid.



$$C_6H_5SO_2NCO + Et_3Si\text{-}H \longrightarrow C_6H_5SO_2\overset{SiEt_3}{N}\text{-}\underset{H}{C}{=}O \xrightarrow[\text{(or } CH_3COOH)]{CH_3OH} C_6H_5SO_2NHCHO + Et_3SiOCH_3$$

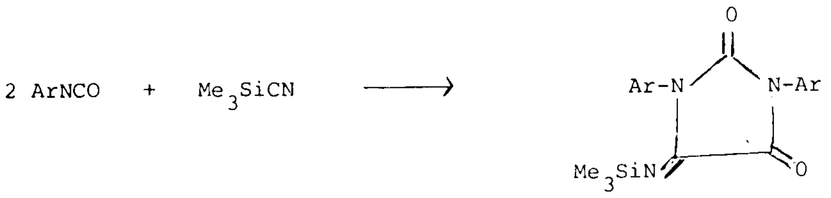
(144)

Reactions with trialkylsilyl cyanides involve breaking the carbon-silicon bond.[147]



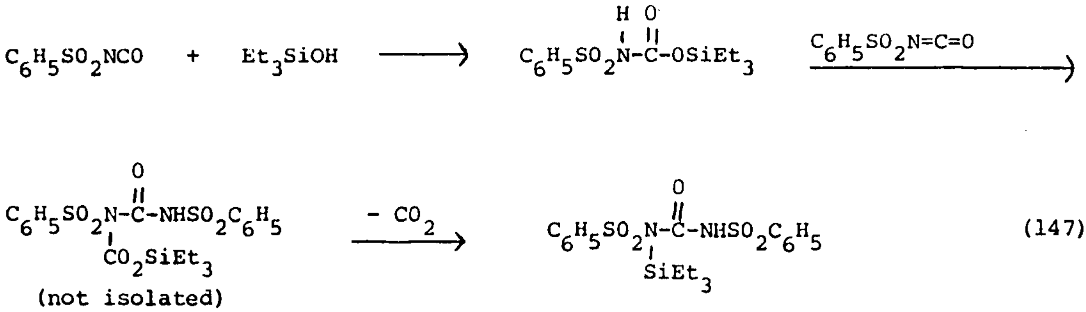
$$4\text{-}CH_3C_6H_4SO_2NCO + Me_3SiC{\equiv}N \longrightarrow 4\text{-}CH_3C_6H_4SO_2N(SiMe_3)\text{-}COCN \quad (145)$$

It is interesting that two moles of aromatic (non-sulfonyl) isocyanates react with silyl cyanides to give cyclic products.



(146)

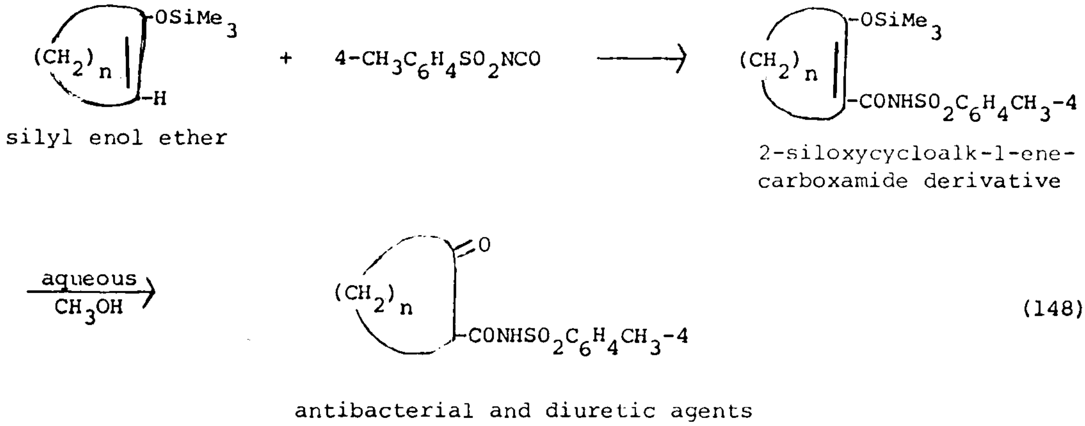
Triethylsilanol behaves like an alcohol in its reactions with sulfonyl isocyanates.[148] A second mole of isocyanate will, however, react with the 1:1 adduct.



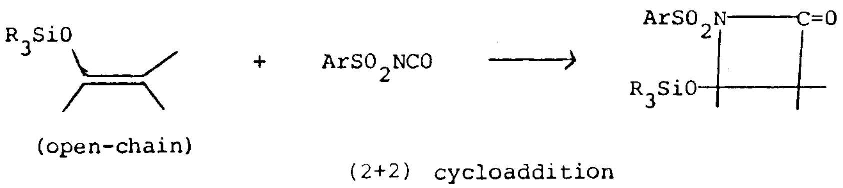
$$C_6H_5SO_2NCO + Et_3SiOH \longrightarrow C_6H_5SO_2NH\text{-}\overset{O}{\overset{\|}{C}}\text{-}OSiEt_3 \xrightarrow{C_6H_5SO_2N=C=O}$$

$$\underset{\text{(not isolated)}}{C_6H_5SO_2N(CO_2SiEt_3)\text{-}\overset{O}{\overset{\|}{C}}\text{-}NHSO_2C_6H_5} \xrightarrow{-\,CO_2} C_6H_5SO_2N(SiEt_3)\text{-}\overset{O}{\overset{\|}{C}}\text{-}NHSO_2C_6H_5 \quad (147)$$

Silyl enol ethers react with isocyanates giving 2-siloxycycloalk-1-enecarboxamides or 4-siloxyazetidin-2-ones depending upon the structure of the silyl enol ether.[149,150] The first type of products may be hydrolyzed to substances having antibacterial and diuretic activity.

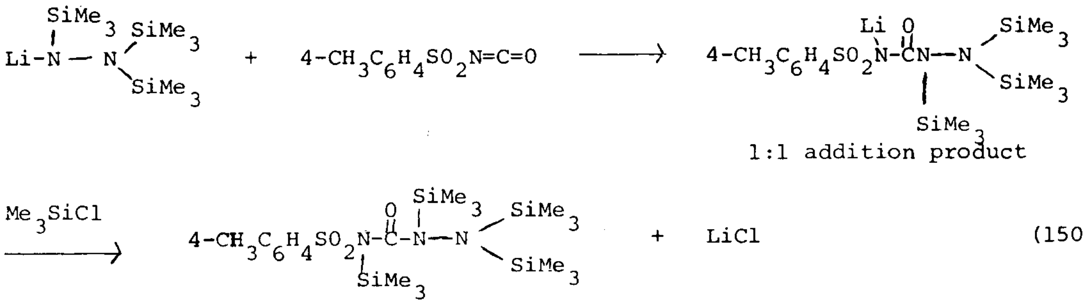


(148)



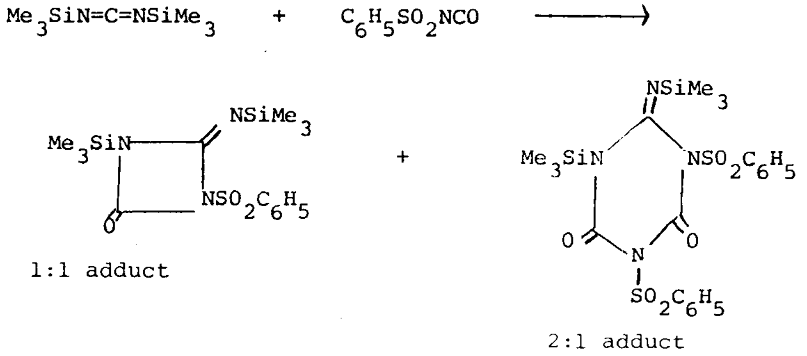
(149)

Lithium silyl hydrazides react with isocyanates to afford 1:1 adducts which further react with trimethylsilyl chloride to give silylated isocyanates.[151]



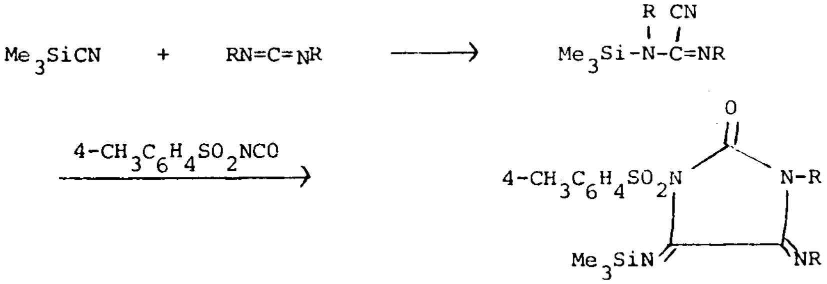
(150)

Organosilyl, as well as organogermyl and organostannyl, carbodiimides react with sulfonyl isocyanates to afford 1:1 and 2:1 isocyanate/carbodiimide adducts[152] in the case of organosilicon compounds. (See also Section N.)



(151)

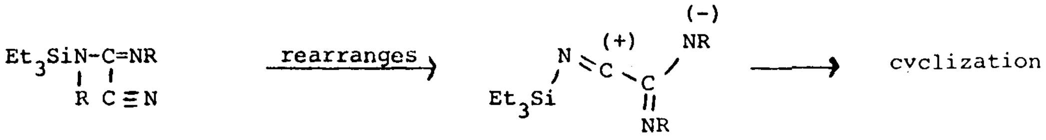
Trimethylsilyl cyanide reacts with carbodiimides to afford silylated amidines. The latter enter into cycloadditions with sulfonyl isocyanates.[153]



(152)

$(R = (CH_3)_2CH$, cyclohexyl, $4\text{-}CH_3C_6H_4)$

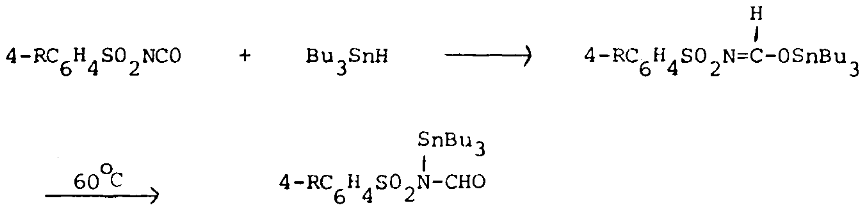
A possible mechanism for the above reaction involves the rearrangement of the silylated amidine to a 1,3-dipole which cyclizes with isocyanate.



$$Et_3Si\underset{R}{N}\text{-}\underset{C\equiv N}{C}{=}NR \xrightarrow{\text{rearranges}} \underset{Et_3Si}{N}{\overset{(+)}{=}}C\text{-}\underset{NR}{\overset{}{C}}\text{-}\overset{(-)}{NR} \longrightarrow \text{cyclization}$$

M. Reactions with Tin Compounds

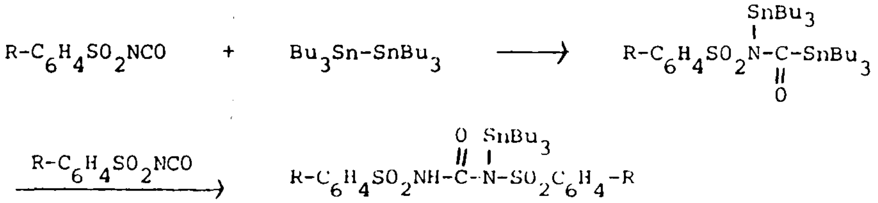
Organotin compounds have been found to react with sulfonyl isocyanates by breaking either the tin-hydrogen bond, the tin-tin bond, the tin-oxygen bond, or the oxygen-hydrogen bond in hydroxides. Illustrative of the first type of reaction is the addition of trialkyltin hydrides to sulfonyl isocyanates.[154] The initial addition is across the C=O bond of the isocyanate. Heating the first product at about 60°C causes isomerization to stannyl formamides.



$$4\text{-}RC_6H_4SO_2NCO + Bu_3SnH \longrightarrow 4\text{-}RC_6H_4SO_2N{=}\overset{H}{C}\text{-}OSnBu_3 \xrightarrow{60^\circ C} 4\text{-}RC_6H_4SO_2\overset{SnBu_3}{N}\text{-}CHO \qquad (153)$$

$(R = H, CH_3O, CH_3)$

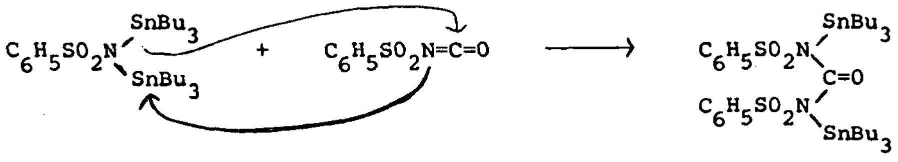
Hexabutyltin is reported to give 1:1 adducts with sulfonyl isocyanates, but further reaction may occur with another molecule of isocyanate.[155]



$$R\text{-}C_6H_4SO_2NCO + Bu_3Sn\text{-}SnBu_3 \longrightarrow R\text{-}C_6H_4SO_2\overset{SnBu_3}{N}\text{-}\underset{O}{C}\text{-}SnBu_3 \xrightarrow{R\text{-}C_6H_4SO_2NCO} R\text{-}C_6H_4SO_2NH\text{-}\overset{O}{C}\text{-}\overset{SnBu_3}{N}\text{-}SO_2C_6H_4\text{-}R \qquad (154)$$

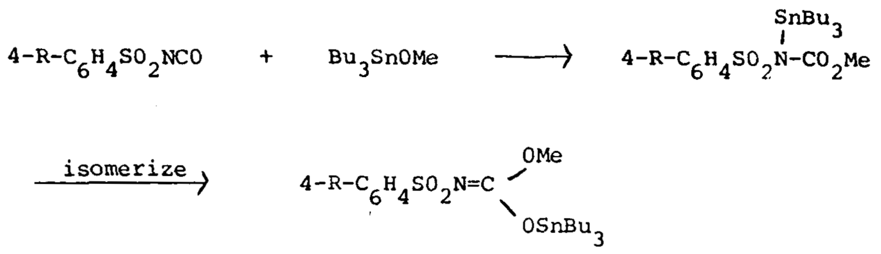
$(R = 4\text{-}CH_3, 4\text{-}CH_3O, 3\text{-}Cl)$

Distannylated sulfonamides also react with sulfonyl isocyanates.



(155)

The reaction of alkoxytrialkyltins with sulfonyl isocyanates causes cleavage of the tin-oxygen bond and formation of N-stannyl-N-sulfonylcarbamic acid esters.[156] The latter are reported to isomerize to the corresponding O-stannyl derivatives.

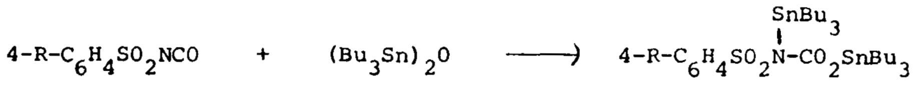


$$4\text{-R-}C_6H_4SO_2NCO + Bu_3SnOMe \longrightarrow 4\text{-R-}C_6H_4SO_2\overset{SnBu_3}{\overset{|}{N}}\text{-}CO_2Me \xrightarrow{\text{isomerize}} 4\text{-R-}C_6H_4SO_2N{=}C\begin{matrix}\diagup OMe\\ \diagdown OSnBu_3\end{matrix} \qquad (156)$$

(156)

$(R = H, CH_3, CH_3O, Cl)$

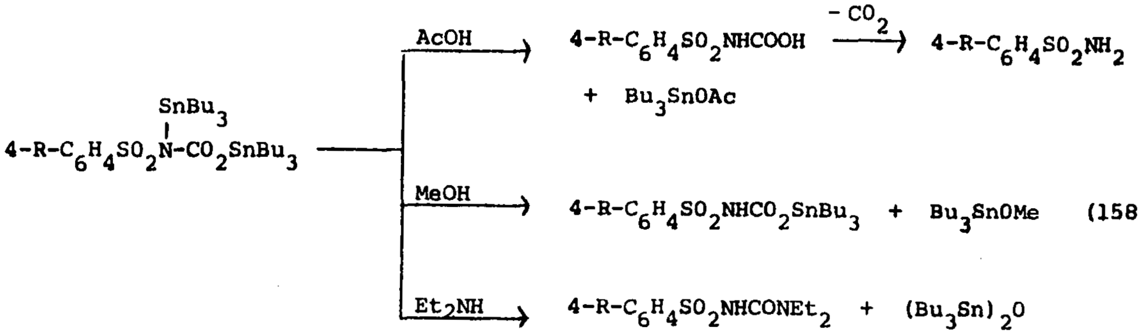
Trialkyltin oxides also add to isocyanates accompanied by breakage of the tin-oxygen bond.[157] The 1:1 adducts may be converted to carbamic acids, carbamic acid tin salts, and ureas by acetic acid, methanol, and amines, respectively.



$$4\text{-R-}C_6H_4SO_2NCO + (Bu_3Sn)_2O \longrightarrow 4\text{-R-}C_6H_4SO_2\overset{SnBu_3}{\overset{|}{N}}\text{-}CO_2SnBu_3 \qquad (157)$$

(157)

$(R = H, CH_3, CH_3O, Cl)$

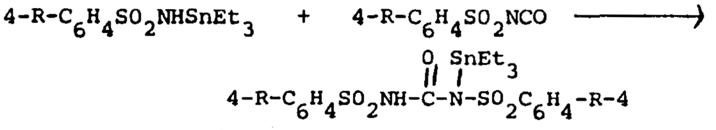


$$4\text{-R-}C_6H_4SO_2\overset{SnBu_3}{\overset{|}{N}}\text{-}CO_2SnBu_3 \longrightarrow \begin{cases} \xrightarrow{AcOH} 4\text{-R-}C_6H_4SO_2NHCOOH \xrightarrow{-CO_2} 4\text{-R-}C_6H_4SO_2NH_2 \\ \quad + Bu_3SnOAc \\ \xrightarrow{MeOH} 4\text{-R-}C_6H_4SO_2NHCO_2SnBu_3 + Bu_3SnOMe \\ \xrightarrow{Et_2NH} 4\text{-R-}C_6H_4SO_2NHCONEt_2 + (Bu_3Sn)_2O \end{cases} \qquad (158)$$

(158)

Organotin hydroxides give 1:1 adducts or decarboxylated 1:1 adducts with sulfonyl isocyanates depending upon the nature of the organic groups.[158] For example, the principal product from triethyltin hydroxide and arylsulfonyl isocyanates is an N-stannylated sulfonamide. The latter reacts with more sulfonyl isocyanate if present.

$$4\text{-R-}C_6H_4SO_2NCO + Et_3SnOH \longrightarrow 4\text{-R-}C_6H_4SO_2NHSnEt_3 + CO_2 \qquad (159)$$

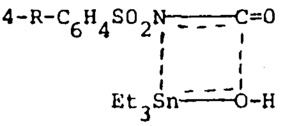


$$4\text{-R-}C_6H_4SO_2NHSnEt_3 + 4\text{-R-}C_6H_4SO_2NCO \longrightarrow 4\text{-R-}C_6H_4SO_2NH\text{-}\overset{O}{\overset{\|}{C}}\text{-}\overset{SnEt_3}{\overset{|}{N}}\text{-}SO_2C_6H_4\text{-R-4} \qquad (160)$$

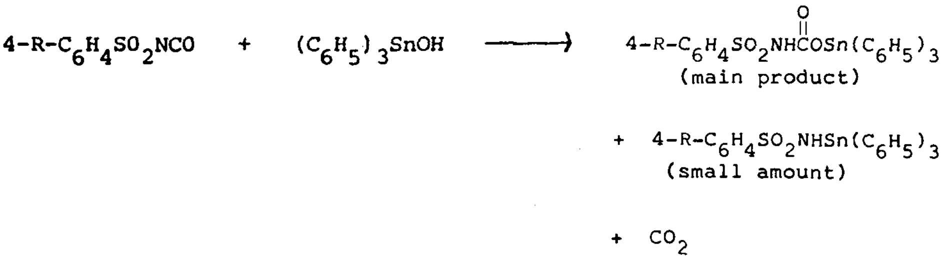
(160)

$(R = H, CH_3, CH_3O, Cl)$

It has been proposed that the reaction[159] proceeds through a cyclic intermediate which loses CO_2.



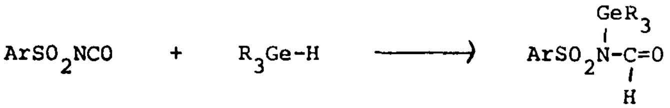
When the organic groups on tin are aromatic the main products are 1:1 adducts, indicating addition of oxygen and hydrogen (from the OH group of the tin compound) across the nitrogen-carbon double bond of the isocyanate.



$$4\text{-R-}C_6H_4SO_2NCO + (C_6H_5)_3SnOH \longrightarrow 4\text{-R-}C_6H_4SO_2NH\overset{O}{\overset{\|}{C}}OSn(C_6H_5)_3 \text{ (main product)} + 4\text{-R-}C_6H_4SO_2NHSn(C_6H_5)_3 \text{ (small amount)} + CO_2 \qquad (161)$$

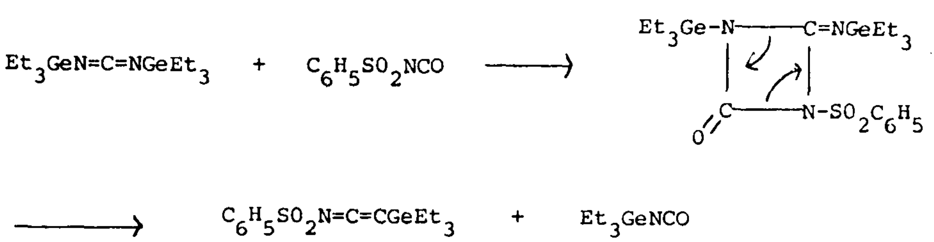
N. Reactions with Other Organometallic Compounds

Like trialkylsilanes, trialkylgermanes add to sulfonyl isocyanates to give N-substituted formamides.[146]



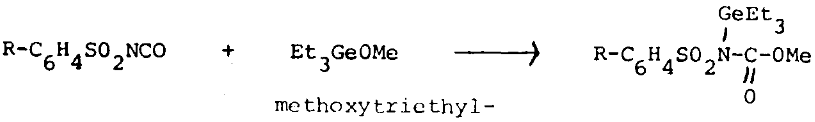
$$ArSO_2NCO + R_3Ge\text{-}H \longrightarrow ArSO_2\overset{GeR_3}{\overset{|}{N}}\text{-}\underset{H}{\underset{|}{C}}{=}O \qquad (162)$$

Organogermyl carbodiimides react with benzenesulfonyl isocyanates to produce sulfonyl carbodiimide and trialkylgermanium isocyanate.[152] (See also Section L.)



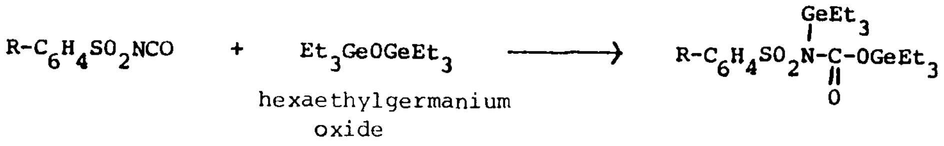
(163)

Alkoxytrialkylgermaniums and trialkylgermanium oxides[159] behave as do the corresponding tin compounds[156,157] in their reactions with sulfonyl isocyanates. In each case the metal-oxygen bond is broken and addition is across the nitrogen-carbon double bond of the isocyanate.



$$R\text{-}C_6H_4SO_2NCO + Et_3GeOMe \longrightarrow R\text{-}C_6H_4SO_2\overset{GeEt_3}{\overset{|}{N}}\text{-}\underset{O}{\underset{\|}{C}}\text{-}OMe \qquad (164)$$

methoxytriethyl-
germanium

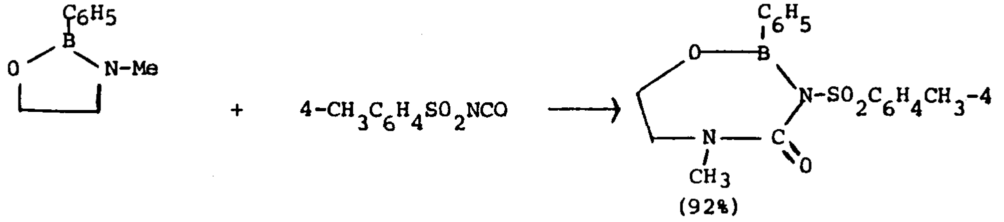


$$R\text{-}C_6H_4SO_2NCO + Et_3GeOGeEt_3 \longrightarrow R\text{-}C_6H_4SO_2\overset{GeEt_3}{N}\text{-}\underset{O}{\overset{\|}{C}}\text{-}OGeEt_3$$

(165)

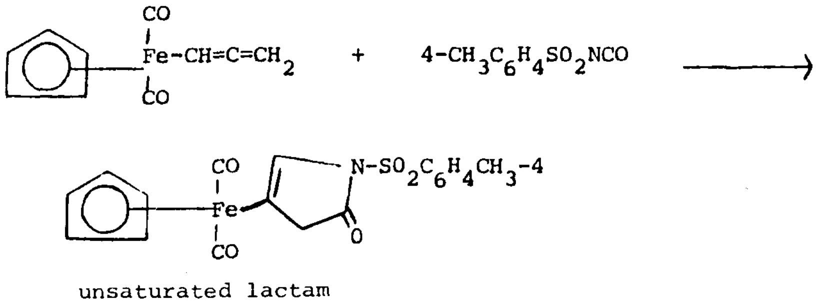
(R = H, m-Cl)

Five-membered ring compounds containing boron, oxygen, and nitrogen react with sulfonyl isocyanates to expand the ring to seven members.[160] The boron-nitrogen bond is broken in the process.



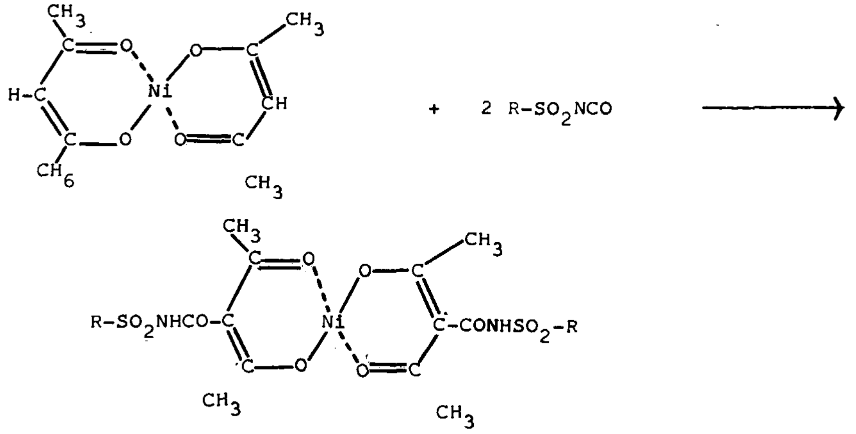
(166)

Allenylironcarbonyl compounds are reported to enter into cycloaddition reactions with sulfonyl isocyanates.[161,162] The metal is believed to assist the cycloaddition to unsaturated lactams.

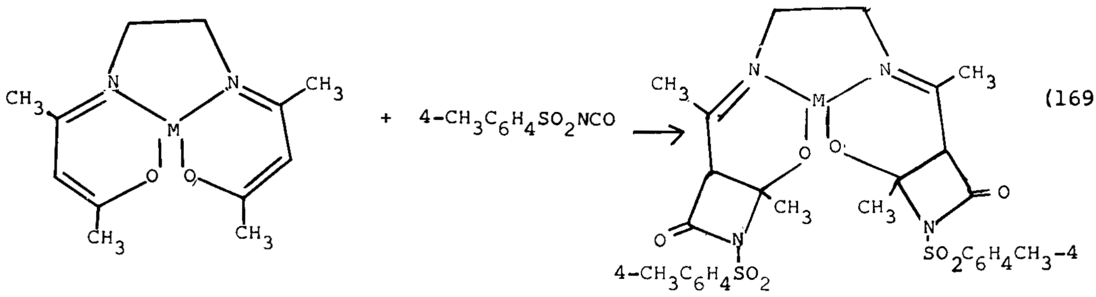


(167)

Organonickel and organocopper compounds have been shown to react with isocyanates as illustrated below.[163,164]



(168)



(169)

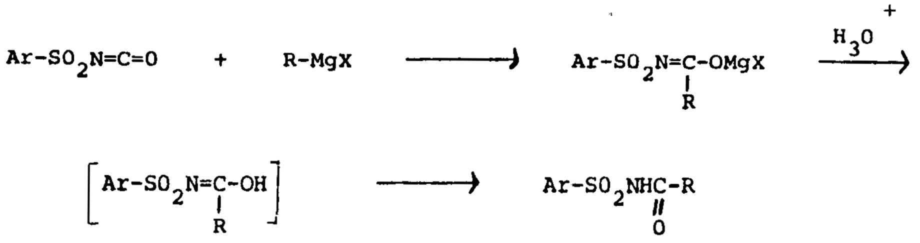
(M = Ni, Cu)

Low oxidation state complexes of transition metals such as rhodium, ruthenium, platinum, and palladium give complexes with isocyanates, including sulfonyl isocyanates.[165,166]

$$\left[\overset{+}{Rh}\left[P(C_6H_5)_3\right]_3\right]\overset{-}{Cl} + 2\ RSO_2NCO \longrightarrow \left[\overset{3+}{Rh}\left[P(C_6H_5)_3\right]_2\left[RSO_2\overset{-}{N}-CO-\overset{-}{N}SO_2R\right]\right]^{+}\overset{-}{Cl} + P(C_6H_5)_3 + CO \qquad (170)$$

$$\left[\overset{0}{Ru}(CO)_3\left[P(C_6H_5)_3\right]_2\right] + 2\ 4\text{-}CH_3C_6H_4SO_2NCO \longrightarrow \left[\overset{2+}{Ru}(CO)_2\left[P(C_6H_5)_3\right]_2\left[4\text{-}CH_3C_6H_4SO_2\overset{-}{N}\text{-}CO\text{-}\overset{-}{N}SO_2C_6H_4\text{-}CH_3\text{-}4\right]\right] + 2\ CO \qquad (171)$$

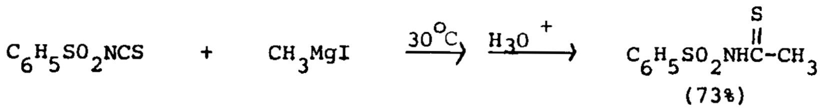
The reactions of Grignard reagents with sulfonyl isocyanates have been thoroughly studied and were reported in a previous review.[2,167]



$$Ar\text{-}SO_2N{=}C{=}O + R\text{-}MgX \longrightarrow Ar\text{-}SO_2N{=}\underset{R}{\underset{|}{C}}\text{-}OMgX \xrightarrow{H_3O^+} \left[Ar\text{-}SO_2N{=}\underset{R}{\underset{|}{C}}\text{-}OH\right] \longrightarrow Ar\text{-}SO_2NH\underset{O}{\underset{\|}{C}}\text{-}R$$

(172)

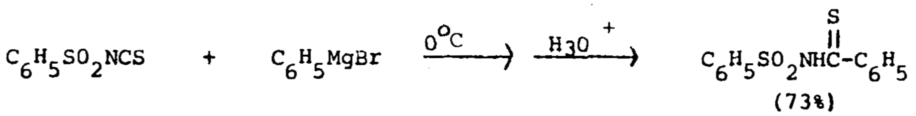
McFarland and Houser found that methylmagnesium iodide and phenylsulfonyl isothiocyanate behave as expected at ambient temperature to give the thioamide.[22]



$$C_6H_5SO_2NCS + CH_3MgI \xrightarrow{30^{\circ}C} \xrightarrow{H_3O^+} C_6H_5SO_2NH\overset{S}{\overset{\|}{C}}\text{-}CH_3\ (73\%)$$

(173)

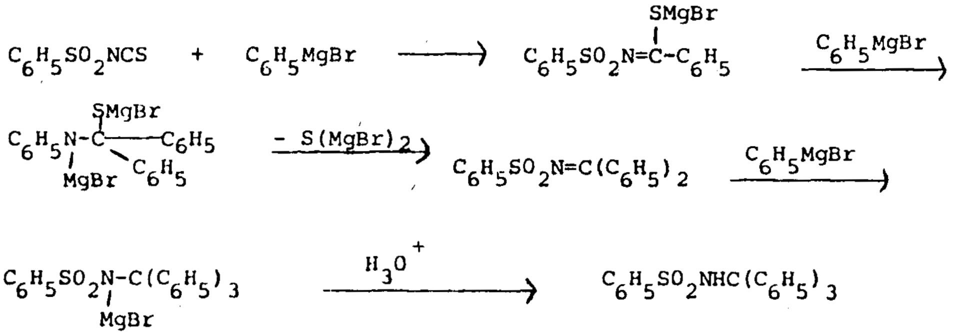
At 0°C phenyl magnesium bromide also gives thioamide, but at room temperature the isolated product is N-(triphenylmethyl)-benzenesulfonamide (27% and 50% yields at 1:1 and 1:3 isothiocyanate/Grignard reagent ratios, respectively).



$$C_6H_5SO_2NCS + C_6H_5MgBr \xrightarrow{0^{\circ}C} \xrightarrow{H_3O^+} C_6H_5SO_2NH\overset{\overset{S}{\|}}{C}-C_6H_5 \quad (73\%) \qquad (174)$$

$$C_6H_5SO_2NCS + C_6H_5MgBr \xrightarrow{25-30^{\circ}C} \xrightarrow{H_3O^+} C_6H_5SO_2NHC(C_6H_5)_3 \qquad (175)$$

The following mechanism was proposed for the latter reaction.



$$C_6H_5SO_2NCS + C_6H_5MgBr \longrightarrow C_6H_5SO_2N{=}\overset{\overset{SMgBr}{|}}{C}-C_6H_5 \xrightarrow{C_6H_5MgBr}$$

$$C_6H_5\underset{\underset{MgBr}{|}}{N}-\overset{\overset{SMgBr}{|}}{C}(C_6H_5)-C_6H_5 \xrightarrow{-S(MgBr)_2} C_6H_5SO_2N{=}C(C_6H_5)_2 \xrightarrow{C_6H_5MgBr} \qquad (176)$$

$$C_6H_5SO_2\underset{\underset{MgBr}{|}}{N}-C(C_6H_5)_3 \xrightarrow{H_3O^+} C_6H_5SO_2NHC(C_6H_5)_3$$

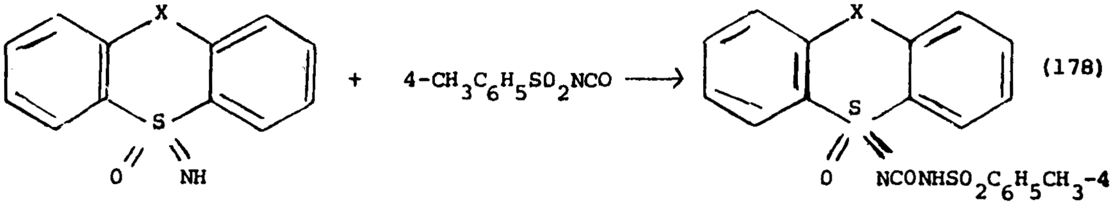
More recently Walter and Roehr have extensively studied the reactions of sulfonyl isothiocyanates with Grignard reagents and found that under controlled conditions the thioamides may be obtained in good yields in all cases studied.[168] The thioamides were found to be relatively acidic and to exist partially in the thioenol form. The stereochemistry of the products was determined.

$$R-SO_2NCS + R^1MgX \longrightarrow R-SO_2NHCSR^1 \qquad (177)$$

$$(R = CH_3,\ C_6H_5;\ R^1 = CH_3,\ CH_3CH_2,\ (CH_3)_2CH,\ C_6H_5CH_2,\ C_6H_5)$$

O. Miscellaneous Reactions

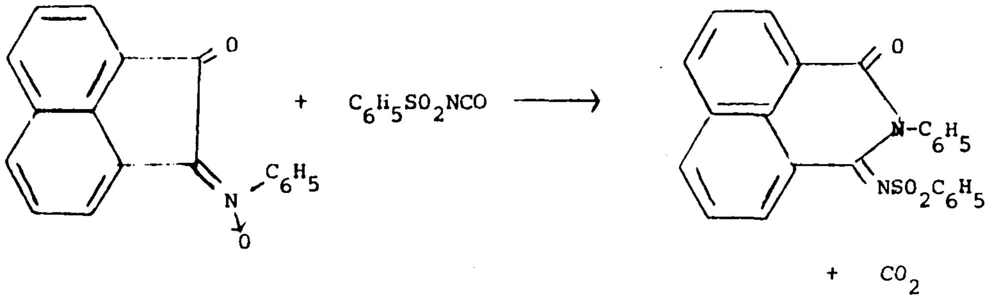
Sulfoximides with substituents on nitrogen are reported to be useful as antihistamines, antitussives, inflammation inhibitors, sedatives, and diuretics. The sulfonyl carbamoyl derivatives are prepared from simple sulfoximides and sulfonyl isocyanates.[169]



(178)

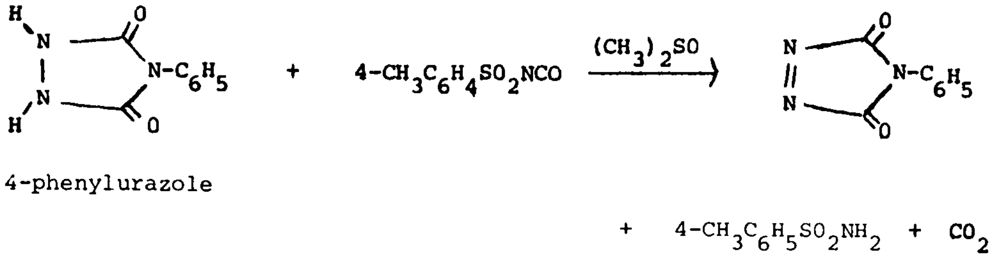
$(X = O,\ S,\ CH_2,\ CO,\ NR)$

Ketonitrones enter into an extremely interesting reaction with sulfonyl isocyanates.[170] Ring expansion occurs along with loss of CO_2.



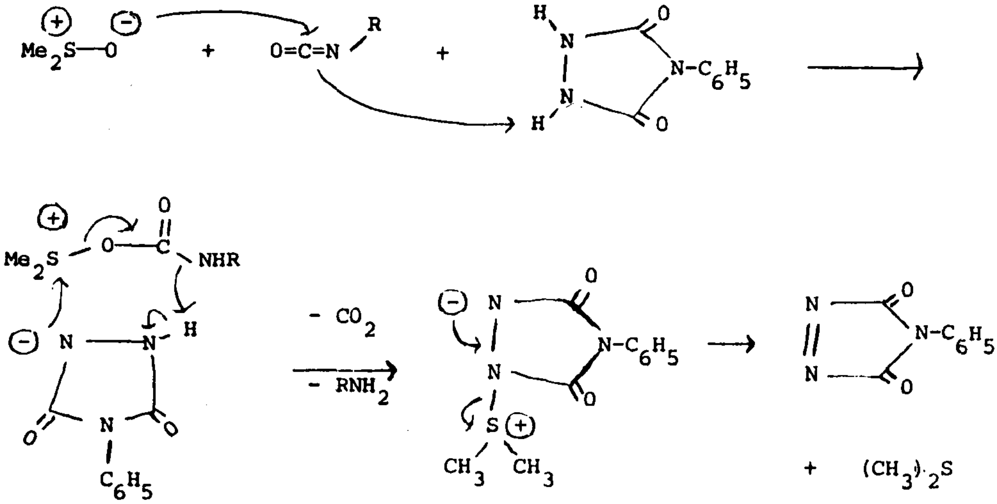
(179)

4-Phenylurazole is oxidized in the presence of dimethyl sulfoxide and activated isocyanates.[171]



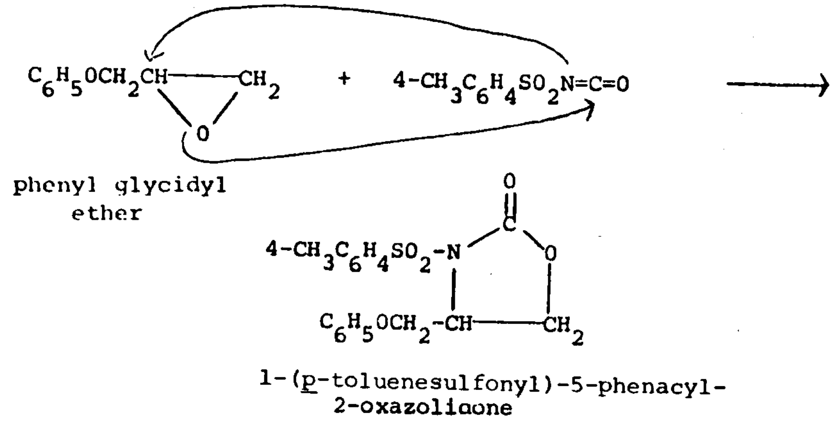
(180)

A mechanism has been proposed for the reaction.

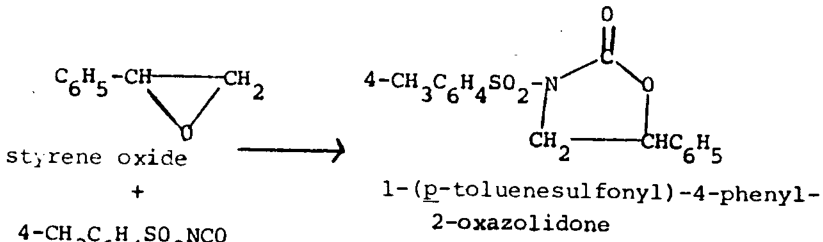


(181)

Phenylglycidyl ether reacts with *p*-toluenesulfonyl isocyanate to produce 1-(*p*-toluenesulfonyl)-5-phenacyl-2-oxazolidone as the principal product with a hydrocarbon-soluble adduct of Bu_3PO and LiBr as catalyst.[172] In contrast to conventional isocyanates, however, the sulfonyl isocyanate gives principally the 4-isomer with styrene oxide.

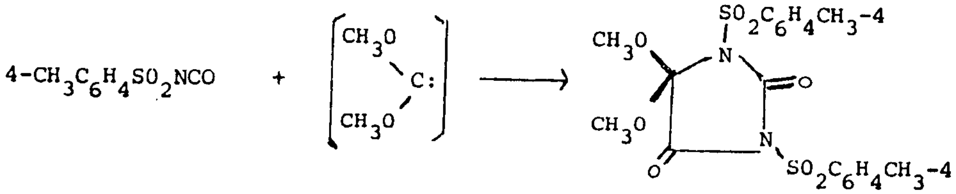


(182)



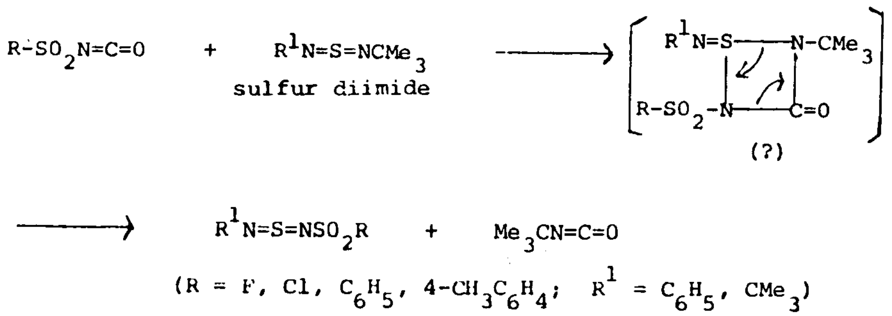
(183)

Carbenes react with isocyanates and isothiocyanates.[173] Dimethoxycarbene, generated from either 1,2,3,4-tetrachloro-6-phenyl-7,7-dimethoxynorbornadiene or trimethoxymethane, combines with two moles of *p*-toluenesulfonyl isocyanate to give hydantoin derivatives.



(184)

Sulfur diimides enter into exchange reactions with sulfonyl isocyanates to produce N-sulfonyl sulfur diimides.[174]



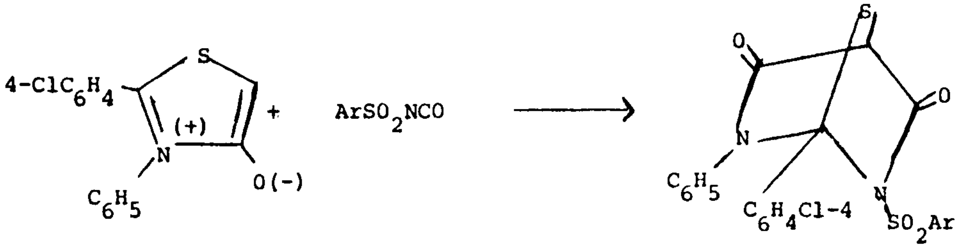
(185)

Halosulfonyl isocyanates also react with sulfinylamines to exchange CO for SO.[174]

$$\text{Hal-SO}_2\text{N=C=O} \quad + \quad \text{RN=S=O} \quad \longrightarrow \quad \text{Hal-SO}_2\text{N=S=O} \quad + \quad \text{RN=C=O} \qquad (186)$$

$$(\text{Hal} = \text{F, Cl}; \quad \text{R} = \text{CMe}_3)$$

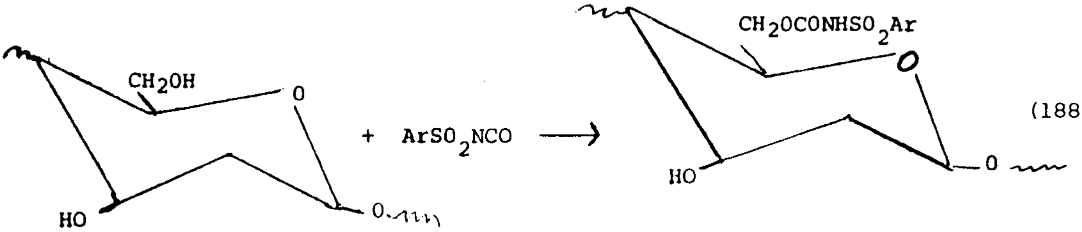
Mesoionic compounds such as anhydro-2-(4-chlorophenyl)-4-hydroxy-3-phenylthiazolium hydroxide combine with activated isocyanates at room temperature to afford 1:1 primary adducts with 2,6-diaza-7-thiacyclo [2.2.1] heptane structures.[175,176]



(187)

anhydro-2-(4-chlorophenyl)-4-hydroxy-3-phenylthiazolium hydroxide

Sulfonyl isocyanates react with cellulose substrates in pyridine solvents to give cellulose N-arylsulfonyl carbamates, useful as ion exchange resins.[177]



(188)

cellulose unit

ion exchange resin

$$(\text{ArSO}_2\text{NCO} = \text{C}_6\text{H}_5\text{SO}_2\text{NCO},\ 4\text{-CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{NCO},\ 1\text{-CH}_3\text{-2,4-(OCNSO}_2)_2\text{C}_6\text{H}_3)$$

Alkali-soluble binders for light-sensitive printing plates are obtained from mixing *p*-toluenesulfonyl isocyanate with poly-(vinylbutyral) and then with trimethylolpropane triacrylate.[178] Immobilization of enzymes such as trypsin is studied by binding the trypsin to polyether 4-aminobenzenesulfonyl carbamate support with glutaraldehyde.[179] The sulfonylated carbamate is prepared by reaction of 4-nitrobenzenesulfonyl isocyanate with a bisphenol A-epichlorohydrin copolymer, followed by reduction of the nitro groups with sodium dithionite. Immobilized enzymes have been shown to be more active in basic media than the free enzymes.

Finally, aromatic isocyanates *i.e.*, [(p-OCNC$_6$H$_4$)$_2$CH$_2$ and *p*- or *m*-(OCNCH$_2$)$_2$C$_6$H$_4$] are stabilized against discoloration and polymerization by the addition of 0.001 to 1% of acyl or sulfonyl isocyanates.[180]

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