THE CHEMISTRY OF SULFONYL ISOCYANATES

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CONTENTS

I. Introduction 369
II. Preparation of Sulfonyl Isocyanates 369
A. From Sulfonamides 369
B. From Sulfonyl Chlorides and Sulfonic Anhydrides 370
C. From Sulfonylureas 370
D. Miscellaneous Methods 370
III. Physicochemical Data 371
A. General 371
B. Spectral Data 372
IV. Chemical Behavior 372
A. Reactions with Oxygen–Hydrogen Bonds 372
B. Reactions with Sulfur–Hydrogen Bonds 372
C. Reactions with Nitrogen–Hydrogen Bonds 373
D. Reactions with Carbon–Hydrogen Bonds 374
E. 1,2-Dipolar Addition Reactions 374
V. Uses of Sulfonyl Isocyanates 375
VI. References 376

I. INTRODUCTION

This review is concerned with the chemistry of sulfonyl isocyanates, *i.e.*, compounds with an isocyanato group attached to the sulfur atom of a sulfonyl moiety. Sulfonyl isocyanates have the general formula RSO_2NCO, where R may be a halogen, an alkyl, an aryl, or an isocyanato group. Although other substituents such as cyano, isothiocyanato, etc., could be envisaged, only representatives of the aforementioned groups have been reported in the literature. Exceptions are the pyrosulfuryl compounds $ClSO_2OSO_2NCO$ and $O(SO_2NCO)_2$ which for the sake of completion are included in the review article.

While isocyanates have been extensively reviewed in the past (5, 53, 54, 62), sulfonyl isocyanates were not included in the review articles. Owing to the polar sulfonyl group attached to the cumulative double bond system, the reactivity of the isocyanato group toward nucleophilic attack on the center carbon atom is vastly enhanced in sulfonyl isocyanates. Also the polarization of the C=N double bond is sufficiently influenced by the sulfonyl group to change the regular reaction pattern observed in isocyanates.

Billeter (8) first obtained sulfonyl isocyanates in 1903 and studied some of their reactions. The classical method of synthesis involves the reaction of sulfonyl chlorides with silver cyanate. Methane as well as benzenesulfonyl isocyanate were obtained in low yield. The tedious work-up procedures as well as exaggerated statements in regard to their stability virtually prevented further work in this area.

In 1951 Krzikalla (43) reported the direct high temperature phosgenation of *p*-toluenesulfonamide to *p*-toluenesulfonyl isocyanate. Although this route is simple and attractive, subsequent work was limited to *p*-toluenesulfonyl isocyanate and *p*-chlorobenzenesulfonyl isocyanate. Considerable improvement of the direct phosgenation of arylsulfonamides discovered in our laboratory (59) allowed for the first time the synthesis of a variety of substituted arylsulfonyl isocyanates. Another useful new method is the direct phosgenation of sulfonylureas which enabled us to synthesize the novel isocyanatobenzenesulfonyl isocyanates and aryldisulfonyl diisocyanates (57).

Recent work of Graf made chlorosulfonyl isocyanate (22, 26) and sulfonyl diisocyanate (48) readily available.

The availability of a variety of mono- and difunctional sulfonyl isocyanates and their utility in organic synthesis prompted this review in order to collect the available data and stimulate further research. The bibliography covers references up to July 1964.

II. PREPARATION OF SULFONYL ISOCYANATES

A. FROM SULFONAMIDES

The direct phosgenation of sulfonamides is sluggish as evidenced by the fact that sulfanilamide can be selectively phosgenated to *p*-isocyanatobenzenesulfonamide (21).

$$p\text{-}H_2NC_6H_4SO_2NH_2 + COCl_2 \rightarrow p\text{-}OCNC_6H_4SO_2NH_2$$

However, Krzikalla (43) discovered that in trichlorobenzene, *i.e.*, at a temperature above 200°, sulfonamides

can be phosgenated to sulfonyl isocyanates in yields of >80%. More recent work could not verify the claimed high yields. King (42), repeating Krzikalla's procedure, obtained only a 54% yield of *p*-toluenesulfonyl isocyanate.

$$p\text{-}CH_3C_6H_4SO_2NH_2 + COCl_2 \rightarrow p\text{-}CH_3C_6H_4SO_2NCO$$

Effenberger and Gleiter (16) phosgenated *p*-chlorobenzenesulfonamide for 18 hr. in 1,2,4-trichlorobenzene and obtained a 65% yield of *p*-chlorobenzenesulfonyl isocyanate. The required fractionation indicated cleavage of the S–N bond with formation of the corresponding sulfonyl chloride as a by-product.

Cyclohexanesulfonyl isocyanate has also been synthesized by direct phosgenation of cyclohexanesulfonamide, but neither yield nor experimental details were reported (17).

Recently Ulrich and Sayigh (59) conducted the phosgenation of arylsulfonamides in the presence of a catalytic amount of an isocyanate allowing rapid phosgenation at temperatures ranging from 130 to 180°. Thus, a wide variety of substituted arylsulfonyl isocyanates were synthesized for the first time, generally in high yields.

B. FROM SULFONYL CHLORIDES AND SULFONIC ANHYDRIDES

The classical synthesis of sulfonyl isocyanates involves the reaction of methane- (8, 10) and benzenesulfonyl chloride (8, 9) with silver cyanate in benzene; however, the yields are low (5–38%). More recently a 65% yield of *p*-toluenesulfonyl isocyanate was reported for the reaction of *p*-toluenesulfonyl chloride and potassium cyanate (20).

$$RSO_2Cl + AgNCO \rightarrow RSO_2NCO$$

Sulfonyl diisocyanate also can be prepared from chlorosulfonyl isocyanate and silver cyanate (2).

$$OCNSO_2Cl + AgNCO \rightarrow SO_2(NCO)_2$$

The intermediacy of methanesulfonic anhydride in the reaction of methanesulfonyl chloride and silver cyanate (8, 10) was postulated by Field and Settlage (19), who obtained methanesulfonyl isocyanate from methanesulfonic anhydride and silver cyanate in a 38% yield.

$$(CH_3SO_2)_2O + AgNCO \rightarrow CH_3SO_2NCO$$

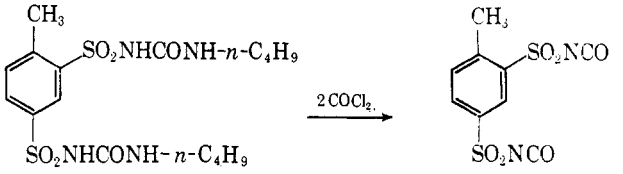
C. FROM SULFONYLUREAS

The direct phosgenation of 1-arylsulfonyl-3-alkylureas proceeds well at temperatures above 50° and both arylsulfonyl isocyanate and alkyl isocyanate are obtained in high yield (57).

$$p\text{-}CH_3C_6H_4SO_2NHCONH\text{-}n\text{-}C_4H_9 + COCl_2 \rightarrow p\text{-}CH_3C_6H_4SO_2NCO + n\text{-}C_4H_9NCO$$

Since 1-arylsulfonyl-3-alkylureas are readily available from arylsulfonamides and alkyl isocyanates (44), and the alkyl isocyanates are regenerated in the reaction, the over-all reaction amounts to the conversion of a sulfonamide to a sulfonyl isocyanate. Preferably a low boiling alkyl isocyanate should be used in order to achieve a good separation from the relatively high boiling sulfonyl isocyanate.

Arylbissulfonylureas react similarly to yield the previously unreported aryldisulfonyl diisocyanates (57).

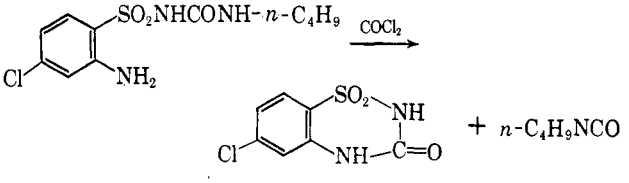


$$+ \; 2\,n\text{-}C_4H_9NCO$$

If *m*- or *p*-sulfanilylureas are reacted with phosgene, the hitherto unknown *m*- or *p*-isocyanatobenzenesulfonyl isocyanates are obtained (57).

$$p\text{-}H_2NC_6H_4SO_2NHCONH\text{-}n\text{-}C_4H_9 + COCl_2 \rightarrow p\text{-}OCNC_6H_4SO_2NCO + n\text{-}C_4H_9NCO$$

This reaction failed with *o*-sulfanilylureas because ring closure is faster than elimination. Thus from 1-(2-amino-4-chlorobenzenesulfonyl)-3-*n*-butylurea and phosgene, 6-chloro-2H-1,2,4-benzothiadiazin-3(4H)-one 1,1-dioxide and *n*-butyl isocyanate were obtained (57).



$$+ \; n\text{-}C_4H_9NCO$$

D. MISCELLANEOUS METHODS

Upon reaction of cyanogen chloride and sulfur trioxide Graf (22, 26) obtained a mixture of products from which chlorosulfonyl isocyanate and chloropyrosulfuryl isocyanate can be isolated.

$$ClCN + SO_3 \rightarrow ClSO_2NCO + ClS_2O_5NCO$$

Under certain conditions chlorosulfonyl isocyanate ($ClSO_2NCO$) can be obtained as the main reaction product.

A minute amount of chlorosulfonyl isocyanate was obtained from urea and chlorosulfonic acid (3).

$$H_2NCONH_2 + ClSO_3H \rightarrow ClSO_2NCO$$

From cyanogen bromide and sulfur trioxide, sulfonyl diisocyanate and pyrosulfuryl diisocyanate can be obtained directly (29).

$$BrCN + SO_3 \rightarrow SO_2(NCO)_2 + S_2O_5(NCO)_2$$

Sulfonyl diisocyanate can also be prepared by pyrolysis of chlorosulfonyl isocyanate (48).

$$2ClSO_2NCO \rightarrow SO_2(NCO)_2 + SO_2 + Cl_2$$

The separation of sulfonyl diisocyanate from pyrosulfuryl chloride has been accomplished by treating the

TABLE I

INORGANIC SULFONYL ISOCYANATES

Compound	M.p., °C.	B.p., °C. (mm.)	Method	Yield, %	Ref.
FSO_2NCO		62 (760)	D	85	4
			D	97	38
			D	70	61
$ClSO_2NCO$		106–107 (760)	D	81	22, 26
ClS_2O_4NCO	−32 to −31	67–68 (10)	D	53	22, 26
$SO_2(NCO)_2$		139 (760)	B	80	2
		40–41 (10)	D	40	29
			D	47.5	48
$S_2O_5(NCO)_2$	26		D		1
	26.8	46 (0.2)	D	17	29

mixture at 330–340° with cyanogen chloride which converts pyrosulfuryl chloride to chlorosulfonyl isocyanate. Chlorosulfonyl isocyanate is subsequently separated by fractional distillation (33).

Pyrosulfuryl diisocyanate was also obtained by Appel and Gerber (1) from potassium cyanate and sulfur trioxide.

$$KOCN + 2SO_3 \rightarrow KOCN \cdot 2SO_3 \rightarrow S_2O_5(NCO)_2$$

The fluorination of chlorosulfonyl isocyanate with HF (38) or NaF (61) afforded fluorosulfonyl isocyanate in excellent yield.

$$ClSO_2NCO + HF \rightarrow FSO_2NCO$$

The reaction of sulfonyl diisocyanate with fluorosulfonic acid gave fluorosulfonyl isocyanate (4).

$$SO_2(NCO)_2 + FSO_3H \rightarrow FSO_2NCO$$

The sulfonyl isocyanates synthesized according to methods A, B, C, and D are listed in Tables I and II.

III. PHYSICOCHEMICAL DATA

A. GENERAL

Sulfonyl isocyanates are colorless or light yellow (nitro derivatives) liquids or low melting solids which can be distilled *in vacuo* without decomposition. They are generally easily soluble in inert organic solvents such as chloroform, carbon tetrachloride, benzene, halogenated benzenes, dioxane, etc. However, reaction occurs upon solution in such highly polar solvents as dimethylformamide and dimethyl sulfoxide.

While isocyanates form carbodiimides and triisocyanurates upon heating with and without a catalyst (53), sulfonyl isocyanates are thermally remarkably stable (58). Also its color stability is far superior to aryl isocyanates. On exposure to light no discoloration was observed on long standing (58). The rate of reaction of sulfonyl isocyanates with active hydrogen compounds is extremely fast. Onodera (50) found that the reaction velocity constant of sulfonyl diisocyanate using 2-ethylhexyl alcohol as the substrate in benzene at 30° was $>150 \times 10^{-4}$ sec.$^{-1}$.

The vastly enhanced reactivity of sulfonyl isocyanates can be attributed to their ability to stabilize a developing negative charge on the nitrogen atom in the transition state of a nucleophilic reaction.

The electronic effects of substituents on the reactivity of substituted benzenesulfonyl isocyanates were less pronounced than in substituted phenyl isocyanates (58). This observation is not at all surprising, since the effect of substituents in benzenesulfonyl isocyanates

TABLE II

ORGANIC SULFONYL ISOCYANATES

Compound	M.p., °C.	B.p., °C. (mm.)	Method	Yield, %	Ref.
CH_3SO_2NCO	31	73.5–75 (10)	B	5	10
			B	38	19
$C_6H_{11}SO_2NCO$		88–94 (0.5)	A		17
$C_6H_5SO_2NCO$		139 (13.5)	B	29–38.5	9
		79–83 (0.7)	A	85.5	59
$4\text{-}CH_3C_6H_4SO_2NCO$			B	65	20
		90–93 (0.05)	A	54	42
		91–92 (0.5)	A	92.5	59
		119–120 (4.0)	C	85.6	57
$2,5\text{-}(CH_3)_2C_6H_3NCO$		95–97 (0.5)	A	60.5	59
$4\text{-}FC_6H_4SO_2NCO$		94–95 (0.9)	A	73	59
$4\text{-}ClC_6H_4SO_2NCO$		78–79 (0.005)	A	65	16
		92–93 (0.4)	A	89	59
		94–95 (0.8)	C	57.9	57
$2,5\text{-}(Cl)_2C_6H_3SO_2NCO$		118–120 (0.5)	A	32	59
$3,4\text{-}(Cl)_2C_6H_3SO_2NCO$		128–130 (0.6)	A	91.3	59
$4\text{-}BrC_6H_4SO_2NCO$	38–40	117–120 (1.2)	A	89.5	59
$4\text{-}CH_3OC_6H_4SO_2NCO$		130–133 (0.4)	A	87.8	59
$4\text{-}O_2NC_6H_4SO_2NCO$	70–73	137–143 (0.4)	A	81.1	59
$3\text{-}O_2NC_6H_4SO_2NCO$	84–86	152–153 (1.0)	A	78	59
$4\text{-}OCNC_6H_4SO_2NCO$	40–44	120 (0.4)	C	64.3	57
$3\text{-}OCNC_6H_4SO_2NCO$		135–136 (1.1)	C	45.7	57
$2\text{-}CH_3C_6H_3\text{-}1,4\text{-}(SO_2NCO)_2$		171–175 (1.8)	C	38.8	57

is merely reflected in slight differences in the polarization of the sulfonyl group, rather than in a direct influence on the electrophilic carbon atom of the isocyanato group. The sulfonyl group thus effectively isolates the isocyanato group from the aryl moiety.

B. SPECTRAL DATA

Both the ultraviolet and the n.m.r. spectra of benzenesulfonyl isocyanates reflect the features of the phenyl nucleus. However, the infrared spectra show characteristic absorptions attributed to ν_{as}–NCO (2240–2220 cm.$^{-1}$), $\nu_{as}SO_2$ (1390–1370 cm.$^{-1}$), and ν_sSO_2 (1190–1180 cm.$^{-1}$). Interestingly, the isocyanate absorption is slightly shifted to higher wave length owing to the influence of the neighboring polar sulfonyl group. We have observed a similar shift for sulfonyl isothiocyanates and an opposite shift in sulfonyl carbodiimides (60). A comparison of the three cumulative double bond systems is shown in Table III.

TABLE III

Class of compounds	ν_{as}N=C=X, cm.$^{-1}$	Description of absorption band
Aryl-NCO	2275–2250	Strong, medium-broad
Aryl-SO_2NCO	2240–2220	Strong, sharp
Aryl-NCS	2040	Strong, broad
Aryl-SO_2NCS	1905	Strong, sharp
Aryl-N=C=NR	2140–2130	Strong, medium-broad
Aryl-SO_2N=C=NR	2183–2174	Strong, medium-broad

IV. CHEMICAL BEHAVIOR

A. REACTION WITH OXYGEN–HYDROGEN BONDS

The reaction of sulfonyl isocyanates with water differs from alkyl and aryl isocyanates because the generated sulfonamide is not capable of reacting with unreacted sulfonyl isocyanate to afford 1,3-disubstituted ureas. The reaction is extremely rapid and quantitative, thus allowing an easy quantitative determination of sulfonyl isocyanates.

$$RSO_2NCO + H_2O \rightarrow [RSO_2NHCOOH] \rightarrow RSO_2NH_2 + CO_2$$

Similarly, sulfonyl diisocyanate reacts with water to form sulfamide (2).

$$SO_2(NCO)_2 + 2H_2O \rightarrow SO_2(NH_2)_2 + 2CO_2$$

In chlorosulfonyl (23) and fluorosulfonyl isocyanates (41) the reaction can be stopped at the sulfamoyl halide stage.

$$ClSO_2NCO + H_2O \rightarrow ClSO_2NH_2 + CO_2$$

Sulfamoyl chloride is an excellent sulfamidation agent. Thus, under Friedel–Crafts conditions sulfonamides are formed (23).

$$C_6H_6 + ClSO_2NH_2 \xrightarrow{AlCl_3} C_6H_5SO_2NH_2$$

With alcohols and phenols, sulfonyl isocyanates react similarly to isocyanates to afford urethanes (9). The reaction is instantaneous and needs no catalysis.

$$C_6H_5SO_2NCO + ROH \rightarrow C_6H_5SO_2NHCOOR$$

Sulfonyl diisocyanate reacts with a number of alcohols to afford bisurethanes (2, 50). With ethylene glycol a polysulfonylurethane was obtained (2). Also chlorosulfonyl isocyanate reacts with 1 equiv. of an alcohol or phenol to afford the corresponding urethane-N-sulfonyl chlorides (24).

$$ClSO_2NCO + ROH \rightarrow ClSO_2NHCOOR$$

The reaction of sulfonyl isocyanates with carboxylic acids is not too well investigated. Chlorosulfonyl isocyanate reacts with acetic acid to yield acetylsulfamoyl chloride (27).

$$ClSO_2NCO + CH_3COOH \rightarrow [ClSO_2NHCOOCOCH_3] \rightarrow ClSO_2NHCOCH_3 + CO_2$$

Rudinger (52) reports that *p*-toluenesulfonyl isocyanate reacts with carboxylic acids similarly to form N-substituted *p*-toluenesulfonamides. However, we observed that *p*-toluenesulfonyl isocyanate reacts with acetic acid in benzene to form 1,3-bis-*p*-toluenesulfonylurea and acetic anhydride (58). The reaction most likely proceeds *via* the following sequence of steps.

$$p\text{-}CH_3C_6H_4SO_2NCO + CH_3COOH \rightarrow [p\text{-}CH_3C_6H_4SO_2NHCOOCOCH_3] \rightarrow [(p\text{-}CH_3C_6H_4SO_2NHCO)_2O] + (CH_3CO)_2O$$
$$\downarrow$$
$$(p\text{-}CH_3C_6H_4SO_2NH)_2CO + CO_2$$

Sulfonyl diisocyanate reacts with chlorosulfonic and fluorosulfonic acid to the corresponding imidodisulfuryl halide (4).

$$SO_2(NCO)_2 + 2ClSO_3H \rightarrow HN(SO_2Cl)_2$$

Apparently, formation of chlorosulfonyl isocyanate is the first step in this reaction, because in the reaction of sulfonyl diisocyanate with fluorosulfonic acid the intermediate fluorosulfonyl isocyanate can be obtained in high yield (4).

While isocyanates react with hydrogen chloride to form carbamoyl chlorides, the basicity of the nitrogen atom in sulfonyl isocyanates is lowered to such an extent that, for instance, benzenesulfonyl isocyanate does not react with hydrogen chloride (9). With hydrogen iodide, however, a 1:1 adduct is formed (9).

$$C_6H_5SO_2NCO + HI \rightarrow C_6H_5SO_2NHCOI$$

B. REACTIONS WITH SULFUR–HYDROGEN BONDS

In a recent patent (56) the reaction of chlorosulfonyl isocyanate with dodecyl mercaptan is described. The intermediate thiourethane was subsequently reacted with aniline to form phenylsulfamoyl dodecylthiocarbamate.

$$ClSO_2NCO + C_{12}H_{25}SH \rightarrow ClSO_2NHCOSC_{12}H_{25}$$

$$ClSO_2NHCOSC_{12}H_{25} + C_6H_5NH_2 \rightarrow C_6H_5NHSO_2NHCOSC_{12}H_{25}$$

This reaction sequence is another example of the different reactivity of both functions in chlorosulfonyl

isocyanate. Graf (24) also reacted urethane-N-sulfonyl chlorides (obtained from chlorosulfonyl isocyanate and alcohols or phenols) with amines to form the corresponding sulfamoyl carbamates.

$$ClSO_2NCO + ROH \rightarrow ClSO_2NHCOOR$$

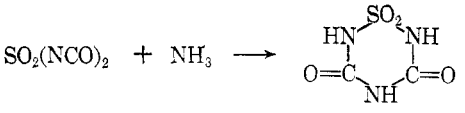
$$ClSO_2NHCOOR + R'NH_2 \rightarrow R'NHSO_2NHCOOR$$

C. REACTIONS WITH NITROGEN–HYDROGEN BONDS

With ammonia, benzenesulfonyl isocyanate gave benzenesulfonylurea (9).

$$C_6H_5SO_2NCO + NH_3 \rightarrow C_6H_5SO_2NHCONH_2$$

Sulfonyl diisocyanate reacts with ammonia to form a cyclic urea derivative which was isolated as the diammonium salt (2).

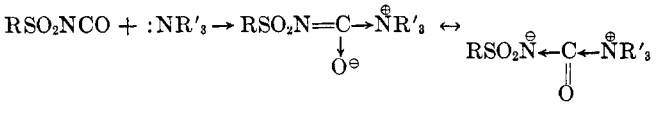


Primary and secondary amines react with sulfonyl isocyanates similarly to form the corresponding sulfonylureas (9). Recently, a host of patents claiming

$$RSO_2NCO + R'NH_2 \rightarrow RSO_2NHCONHR'$$

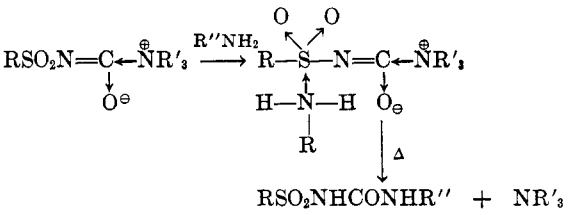
the reaction of alkyl- and arylsulfonyl isocyanates with primary amines for the synthesis of hypoglycemic-active sulfonylureas have been issued; however, only in a few instances (11, 17, 18) have experimental data been reported. With aliphatic diamines the corresponding bissulfonylureas were obtained (37).

The reaction of sulfonyl diisocyanate with mono- and diamines has been investigated, and in all instances mono- and polysulfonylureas were obtained (51). With tertiary amines, sulfonyl isocyanates form stable 1:1 adducts, thus demonstrating the strong electrophilicity of the center carbon atom in the cumulative double bond system (6, 12–14, 31, 55).



The formation of tertiary amine complexes of sulfonyl isocyanates was perhaps first discovered by Graf (31) on chlorosulfonyl isocyanate. The chlorosulfonyl isocyanate adducts react in the same manner as the free isocyanate, but ice–water can be used as solvent (31). However, some tertiary amine complexes liberate CO_2 on exposure to moisture with formation of the corresponding sulfonamide and regeneration of the tertiary amine.

Upon addition of a primary alkylamine a new set of complexes is formed (14). This complex on heating should form the corresponding sulfonylurea with regeneration of the tertiary amine.

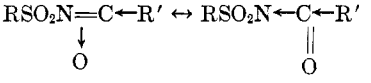


Also on reaction with primary amine hydrochlorides the tertiary amine complexes of sulfonyl isocyanates form sulfonylureas and tertiary amine hydrochlorides (6).

The physical data of tertiary amine complexes of sulfonyl isocyanates are listed in Tables IV and V.

TABLE IV

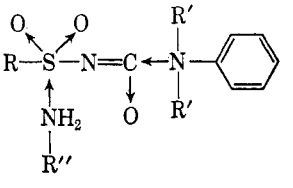
TERTIARY AMINE ADDUCTS OF SULFONYL ISOCYANATES



R	R'	M.p., °C.	Yield, %	Ref.
Cl	Pyridine	52–56		31
C_6H_5	Triethylamine	116–119		6
C_6H_5	Diethylaniline	241–243		13
C_6H_5	Pyridine	117–120		6
		91–96		13
C_6H_5	γ-Picoline	125–128		6
C_6H_5	Isoquinoline	171–174		6
p-$CH_3C_6H_4$	Trimethylamine	124–127		6
p-$CH_3C_6H_4$	Triethylamine	96–99		6
		75–83	90	55
p-$CH_3C_6H_4$	Pyridine	76–79		6
		45–51	98	55
p-$CH_3C_6H_4$	Isoquinoline	156–159		6
p-$CH_3C_6H_4$	1,2-Dimethylbenzimidazole	160–165	85	55
p-ClC_6H_4	Diethylaniline	180–181.5		13
p-ClC_6H_4	Pyridine	118–121		6
p-ClC_6H_4	α-Picoline	106–110		6
p-ClC_6H_4	γ-Picoline	96–99		6
p-ClC_6H_4	Isoquinoline	161–164		6

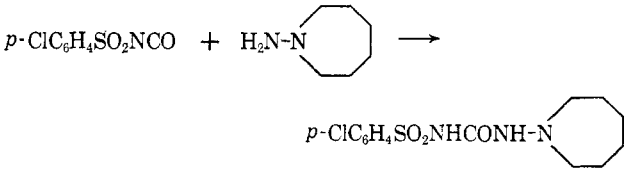
TABLE V

TERTIARY AMINE–PRIMARY AMINE ADDUCTS OF SULFONYL ISOCYANATES



R	R'	R''	M.p., °C.	Ref.
C_6H_5	Ethyl	n-Butyl	177–178.5	14
p-$CH_3C_6H_4$	Methyl	n-Butyl	221–223	14
p-$CH_3C_6H_4$	Ethyl	n-Butyl	178.5–180	14
p-$CH_3C_6H_4$	Methyl	Benzyl	211–212	14
p-ClC_6H_4	Ethyl	n-Butyl	192–193	14

Hydrazine derivatives react with sulfonyl isocyanates to form the corresponding semicarbazides (59).



O-Alkylhydroxylamines react with arylsulfonyl isocyanates to form 1-arylsulfonyl-3-alkoxyureas (7).

$$RSO_2NCO + R'ONH_2 \rightarrow RSO_2NHCONHOR'$$

With amides, such as acetamide and benzamide, benzenesulfonyl isocyanate reacted at elevated temperature as expected to produce the corresponding ureas (9); analogously, sulfonamides afforded disulfonylureas (9).

$$RSO_2NCO + R'CONH_2 \rightarrow RSO_2NHCONHCOR'$$

$$RSO_2NCO + R'SO_2NH_2 \rightarrow RSO_2NHCONHSO_2R'$$

N-Monoalkylamides react with *p*-toluenesulfonyl isocyanate by both substitution (Eq. 1) and elimination (Eq. 2) apparently depending upon the structure of the alkyl substituents (42).

$$RSO_2NCO + CH_3CONHCH_2CH(CH_3)_2 \rightarrow RSO_2NHCON(COCH_3)CH_2CH(CH_3)_2 \quad \text{(Eq. 1)}$$

$$RSO_2NCO + CH_3CONHCH(CH_3)CH_2CH_3 \rightarrow RSO_2N{=}C(CH_3){-}NHCH(CH_3)CH_2CH_3 + CO_2 \quad \text{(Eq. 2)}$$

Monosubstituted formamides react exclusively according to Eq. 2 to yield formamidines (45–47). If the alkyl substituent is *t*-butyl the formamidines are formed already at room temperature indicating a 1,2-dipolar addition mechanism (47).

Dialkylformamides react at room temperature with *p*-toluenesulfonyl isocyanate (42) according to Eq. 2. This reaction is discussed in more detail in section E.

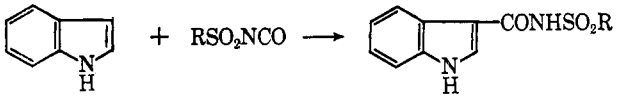
D. REACTION WITH CARBON–HYDROGEN BONDS

Since very little information in regard to the mechanism of the interaction of sulfonyl isocyanates with carbon–hydrogen bonds is available in the literature, most reactions which formally can be considered to result by displacement of an activated hydrogen on a carbon atom are reviewed in this section. However, this author feels that except for the Friedel–Crafts type reaction most proceed by a two-step or concerted 1,2-dipolar addition mechanism.

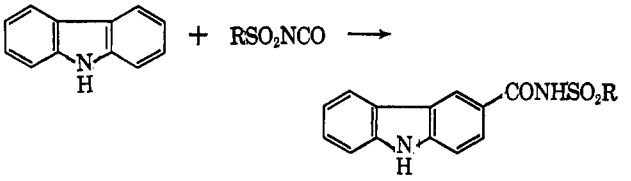
Aromatic tertiary amines with a free *para* position react with arylsulfonyl isocyanates to afford substituted sulfonamides (55).

$$RSO_2NCO + C_6H_5N(CH_3)_2 \rightarrow RSO_2NHCOC_6H_4N(CH_3)_2$$

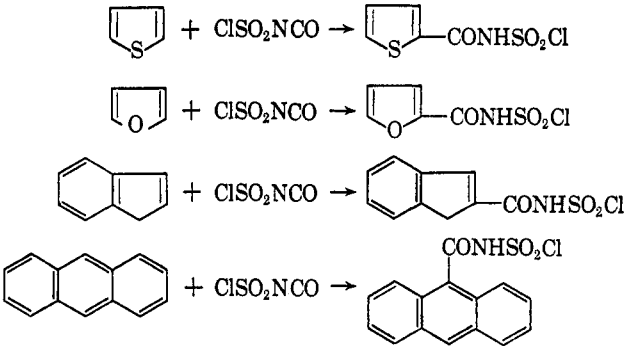
A number of heterocycles react with *p*-toluenesulfonyl isocyanate in a similar fashion. Pyrrole and indole react especially readily undergoing substitution in the activated 3-position (55).



Carbazoles react by substitution in the *para* position to the heterocyclic nitrogen atom (55).



The facile interaction of sulfonyl isocyanates with a variety of heterocycles was first observed by Graf (25, 30), who reacted chlorosulfonyl isocyanate with a number of heterocycles and reactive hydrocarbons.



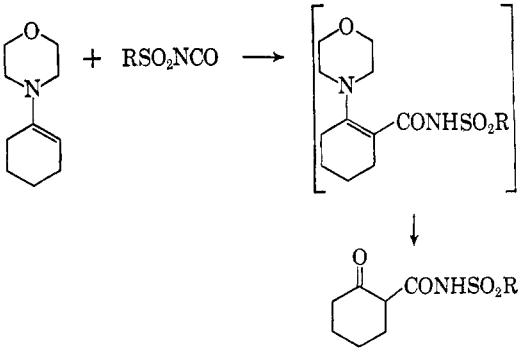
Under Friedel–Crafts conditions arylsulfonyl isocyanates react with benzene to afford N-benzoylarylsulfonamides (9, 15) and diarylsulfones, the latter being the main products (15).

$$RSO_2NCO + C_6H_6 \xrightarrow{AlCl_3} RSO_2NHCOC_6H_5 + RSO_2C_6H_5$$

Chlorosulfonyl isocyanate reacts similarly; however, the N-sulfonyl chloride is hydrolyzed to the corresponding amide (23, 32).

$$ClSO_2NCO + C_6H_6 \xrightarrow{AlCl_3} [(ClSO_2NHCOC_6H_5] \xrightarrow{H_2O} H_2NCOC_6H$$

Enamines react with *p*-toluenesulfonyl isocyanate. Thus, from 1-morpholinocyclohexene-(1), N-*p*-toluenesulfonylcyclohexanone-(2)-carboxamide was obtained (40).



E. 1,2-DIPOLAR ADDITION REACTIONS

Cumulative double bond systems are known to undergo 1,2-dipolar addition reactions quite readily. Thus, isocyanates add preferentially across the C=N double bond. In sulfonyl isocyanates this tendency is

increased owing to the polarizing effect of the neighboring sulfonyl group.

Aldehydes react with sulfonyl isocyanates with formation of sulfonylimines and elimination of CO_2 (34, 42).

$$ClSO_2NCO + C_6H_5CHO \rightarrow \left[\begin{array}{l} C_6H_5CH\!-\!O \\ \quad\vdots\quad\ \vdots \\ ClSO_2N\!-\!C\!=\!O \end{array}\right] \rightarrow C_6H_5CH{=}N{-}SO_2Cl + CO_2$$

If isobutyraldehyde is used, the intermediate imine reacts with excess aldehyde to form the final product (42).

$$RSO_2NCO + (CH_3)_2CH{-}CHO \rightarrow RSO_2N{=}CH{-}CH(CH_3)_2 \rightarrow RSO_2NH{-}\underset{\displaystyle (CH_3)_2C{-}CHO}{\underset{|}{CH}}{-}CH(CH_3)_2$$

The 1,2-dipolar addition reaction proceeds especially rapidly with N,N-disubstituted amides. Dimethylformamide and dimethylacetamide react with *p*-toluenesulfonyl isocyanate at room temperature to afford the corresponding amidines in good yields (42).

$$RSO_2NCO + (CH_3)_2N{-}CHO \rightarrow \left[\begin{array}{l} RSO_2N\!-\!C\!=\!O \\ \quad\vdots\quad\ \vdots \\ (CH_3)_2N\!-\!CH\!-\!O \end{array}\right] \rightarrow RSO_2N{=}CH{-}N(CH_3)_2 + CO_2$$

Chlorosulfonyl isocyanate reacts similarly with a wide variety of N,N-disubstituted straight-chain and cyclic amides (35).

Ketene adds very readily to sulfonyl isocyanates to form a four-membered ring adduct (25, 36). In the case of chloro- and fluorosulfonyl isocyanate the adducts are only stable at low temperatures (36).

$$RSO_2NCO + CH_2{=}C{=}O \rightarrow RSO_2N\underset{\displaystyle O{=}C{-}CH_2}{\underset{|}{-}}C{=}O$$

Chloro- and fluorosulfonyl isocyanate even react with a number of olefins to form 1,2-dipolar addition products. Generally, the reaction proceeds to form both the initial cyclic intermediate as well as the straight-chain isomer as demonstrated here on isobutylene (25).

$$CH_2{=}\underset{\displaystyle CH_3}{\underset{|}{C}}{=}CH_2 + ClSO_2NCO \rightarrow \begin{cases} ClSO_2{-}N(\overset{\displaystyle CH_3}{\overset{|}{C}}{-}CH_2){-}C{=}O \quad 70\% \\ ClSO_2HN{-}CO{-}\overset{\displaystyle CH_3}{\overset{|}{C}}{=}CH_2 \quad 30\% \end{cases}$$

While styrene forms the four-membered ring adduct, 1,1-diphenylethylene and 1,1-diphenyl-2-methylethylene form the linear isomer. No reaction was observed with tetraphenylethylene (25).

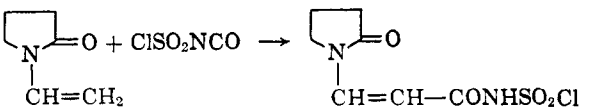
Dienes react faster than monoolefins to form 1:1 adducts (39).

$$CH_3CH{=}CH{-}CH{=}CH_2 + ClSO_2NCO \rightarrow CH_3CH{=}CH{-}CH{=}CH{-}CONHSO_2Cl$$

Vinyl ethers react with sulfonyl isocyanates to form both the cyclic and the linear adduct (16).

$$ROCH{=}CH_2 + RSO_2NCO \rightarrow \begin{cases} RO{-}CH{-}CH_2 \\ \quad\vdots\quad\ \vdots \\ RSO_2{-}N{-}C{=}O \end{cases} \quad \begin{cases} RO{-}CH{=}CH \\ RSO_2{-}NH{-}C{=}O \end{cases}$$

Upon solution of the reaction mixture in dimethyl sulfoxide, isomerization of the cyclic to the linear adduct was observed (16). Similarly, vinylamides react with chlorosulfonyl isocyanate to form acrylamide derivatives (49).



Dimethyl sulfoxide reacts with *p*-toluenesulfonyl isocyanate to form a sulfilimine derivative (42).

$$(CH_3)_2S{\rightarrow}O + RSO_2NCO \rightarrow \left[\begin{array}{l} RSO_2N\!-\!C\!=\!O \\ \quad\vdots\quad\ \vdots \\ (CH_3)_2S\!-\!O \end{array}\right] \rightarrow RSO_2N{=}S(CH_3)_2 + CO_2$$

V. USES OF SULFONYL ISOCYANATES

Sulfonyl isocyanates are highly reactive intermediates for the synthesis of a variety of sulfonylcarbamoyl derivatives. Due to their rapid and quantitative reaction with active hydrogen compounds the yields are generally high and no side reactions occur. Thus, in numerous patents dealing with the synthesis of sulfonylureas as potential useful hypoglycemic agents sulfonyl isocyanates are described as reactants.

Chlorosulfonyl isocyanate has been used to prepare phenylsulfamoyl dodecylthiocarbamate, a herbicide with good activity in concentrations of less than 0.1% (56).

Furthermore, the difunctional sulfonyl isocyanates, such as sulfonyl diisocyanate and halosulfonyl isocyanate, are intermediates in the synthesis of polymeric materials. From sulfonyl diisocyanate, polysulfonylurethanes (2, 50) and polysulfonylureas (51) have been prepared. Also isocyanatobenzenesulfonyl isocyanate and aryldisulfonyl diisocyanates are reactive monomers for the synthesis of sulfonylpolyurethanes, -polyamides, -polyureas, and -polysemicarbazides. Especially, the isocyanatobenzenesulfonyl isocyanates could be ex-

ceedingly useful in the preparation of prepolymers, since the sulfonylisocyanato group is considerably more reactive than the isocyanato group attached to the phenyl nucleus.

We also found that sulfonyl isocyanates stabilize isocyanates against deterioration and discoloration (57).

VI. REFERENCES

(1) Appel, R., and Gerber, H., *Angew. Chem.*, **70**, 271 (1958).
(2) Appel, R., and Gerber, H., *Chem. Ber.*, **91**, 1200 (1958).
(3) Appel, R., and Eisenhauer, G., *Chem. Ber.*, **95**, 1753 (1962).
(4) Appel, R., and Rittersbacher, H., *Chem. Ber.*, **97**, 849 (1964).
(5) Arnold, R. G., and Nelson, J. A., *Chem. Rev.*, **57**, 47 (1957).
(6) Aumüller, W., and Weyer, R., German Patent 1,100,618 (March 2, 1961); *Chem. Abstr.*, **55**, 24680 (1961).
(7) Aumüller, W., Weyer, R., Weber, H., Korger, G., and Bänder, A., German Patent 1,139,830 (Nov. 22, 1962); *Chem. Abstr.*, **58**, 10121 (1963).
(8) Billeter, O. C., *Ber.*, **36**, 3213 (1903).
(9) Billeter, O. C., *Ber.*, **37**, 690 (1904).
(10) Billeter, O. C., *Ber.*, **38**, 2013 (1905).
(11) Breuer, H., and Hoehn, H., U. S. Patent 3,102,115 (Aug. 27, 1963); *Chem. Abstr.*, **60**, 1707 (1964).
(12) Brzozowski, Z., and Zacharewicz, W., *Roczniki Chem.*, **34**, 1839 (1960).
(13) Brzozowski, Z., and Zacharewicz, W., *Roczniki Chem.*, **35**, 1163 (1961); *Chem. Abstr.*, **57**, 16447 (1962).
(14) Brzozowski, Z., and Zacharewicz, W., *Roczniki Chem.*, **36**, 291 (1962); *Chem. Abstr.*, **57**, 16448 (1962).
(15) Effenberger, F., and Gleiter, R., *Chem. Ber.*, **97**, 472 (1964).
(16) Effenberger, F., and Gleiter, R., *Chem. Ber.*, **97**, 1576 (1964).
(17) Farbwerke Hoechst A.-G., British Patent 808,072 (Jan. 28, 1959); *Chem. Abstr.*, **53**, 12221 (1959).
(18) Farbwerke Hoechst A.-G., British Patent 935,980 (Sept. 4, 1963); *Chem. Abstr.*, **60**, 1653 (1964).
(19) Field, L., and Settlage, P. H., *J. Am. Chem. Soc.*, **76**, 1222 (1954).
(20) Franz, J. E., U. S. Patent 2,974,164 (March 7, 1961); *Chem. Abstr.*, **55**, 16485 (1961).
(21) Geigy Co., French Patent 862,626; Houben-Weyl, "Methoden der organischen Chemie," Vol. 8, 4th Ed., Georg Thieme Verlag, Stuttgart, 1952, p. 128.
(22) Graf, R., *Chem. Ber.*, **89**, 1071 (1956).
(23) Graf, R., *Chem. Ber.*, **92**, 509 (1959).
(24) Graf, R., *Chem. Ber.*, **96**, 56 (1963).
(25) Graf, R., *Ann.*, **661**, 111 (1963).
(26) Graf, R., German Patent 928,896 (June 13, 1955); *Chem. Abstr.*, **51**, 4419 (1957).
(27) Graf, R., German Patent 931,225 (Aug. 4, 1955); *Chem. Abstr.*, **50**, 7861 (1956).
(28) Graf, R., German Patent 937,645 (Jan. 12, 1956); *Chem. Abstr.*, **51**, 4419 (1957).
(29) Graf, R., German Patent 940,351 (March 15, 1956); *Chem. Abstr.*, **52**, 12344 (1958).
(30) Graf, R., German Patent 941,847 (April 19, 1956); *Chem. Abstr.*, **51**, 14789 (1957); see also German Patent 1,119,227 (Dec. 14, 1961).
(31) Graf, R., German Patent 1,000,807 (Jan. 17, 1957); *Chem. Abstr.*, **54**, 1555 (1960).
(32) Graf, R., German Patent 1,010,958 (June 27, 1957); *Chem. Abstr.*, **54**, 2269 (1960).
(33) Graf, R., German Patent 1,084,714 (July 7, 1960); *Chem. Abstr.*, **55**, 20966 (1961).
(34) Graf, R., German Patent 1,109,667 (Jan. 22, 1960); *Chem. Abstr.*, **56**, 8632 (1962).
(35) Graf, R., Günther, D., Jensen, H., and Matterstock, K., German Patent 1,144,718 (March 7, 1963); *Chem. Abstr.*, **59**, 6368 (1963).
(36) Graf, R., and Mundlos, E., German Patent 1,098,515 (Feb. 2, 1961); *Chem. Abstr.*, **56**, 452 (1962).
(37) Habicht, E., U. S. Patent 2,962,530 (Nov. 29, 1960); *Chem. Abstr.*, **56**, 5889 (1962).
(38) Hahn, H., German Patent 1,083,791 (June 23, 1960); *Chem. Abstr.*, **55**, 17509 (1961).
(39) Hoffmann, H., and Diehr, H. J., *Tetrahedron Letters*, **27**, 1875 (1963).
(40) Hünig, S., Hübner, K., and Benzing, E., *Chem. Ber.*, **95**, 926 (1962).
(41) Jonas, H., and Voigt, D., *Angew. Chem.*, **70**, 572 (1958).
(42) King, C., *J. Org. Chem.*, **25**, 352 (1960).
(43) Krzikalla, H., German Patent 817,602 (Oct. 18, 1951); *Chem. Abstr.*, **47**, 2206 (1953); British Patent 692,360 (June 3, 1953); *Chem. Abstr.*, **47**, 8771 (1953); U. S. Patent 2,666,787 (Jan. 19, 1954); *Chem. Abstr.*, **48**, 3995 (1954).
(44) Kurzer, F., *Chem. Rev.*, **50**, 1 (1951).
(45) Logemann, W., and Artini, D., *Chem. Ber.*, **90**, 2527 (1957).
(46) Logemann, W., Artini, D., Tosolini, G., and Piccinni, F., *Chem. Ber.*, **91**, 951 (1958).
(47) Logemann, W., Artini, D., and Tosolini, G., *Chem. Ber.*, **91**, 2566 (1958).
(48) Matterstock, K., and Graf, R., German Patent 1,152,093 (Aug. 1, 1963).
(49) Matterstock, K., and Jensen, H., German Patent 1,160,432 (Jan. 2, 1964); *Chem. Abstr.*, **60**, 9247 (1964).
(50) Onodera, N., *Kogyo Kagaku Zasshi*, **65**, 790 (1962); *Chem. Abstr.*, **57**, 14933 (1962).
(51) Onodera, N., *Kogyo Kagaku Zasshi*, **66**, 481 (1963); *Chem. Abstr.*, **59**, 13820 (1963).
(52) Rudinger, J., "Congress Lectures, XIXth International Congress of Pure and Applied Chemistry," London, 1963, p. 354.
(53) Saunders, J. H., and Frisch, K. C., "Polyurethanes, Chemistry and Technology," Part I, Interscience, Publishers, Inc., New York, N. Y., 1962.
(54) Saunders, J. H., and Slocombe, R. J., *Chem. Rev.*, **43**, 203 (1948).
(55) Seefelder, M., *Chem. Ber.*, **96**, 3243 (1963).
(56) Sheers, E. H., U. S. Patent 3,113,857 (Dec. 10, 1963); *Chem. Abstr.*, **60**, 5395 (1964).
(57) Ulrich, H., U. S. patent application pending.
(58) Ulrich, H., unpublished work.
(59) Ulrich, H., and Sayigh, A. A. R., U. S. patent application pending.
(60) Ulrich, H., and Sayigh, A. A. R., *Angew. Chem.* **76**, 781 (1964).
(61) Voigt, D., German Patent 1,043,293 (Nov. 13, 1958); *Chem. Abstr.*, **55**, 7298 (1961).
(62) Wilson, C. V., *Org. Chem. Bull.* (published by the research laboratories of the Eastman Kodak Co.), **35**, No. 2 and No. 3 (1963).