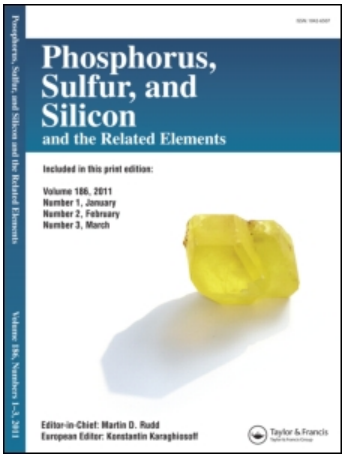


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

REVIEW. CHLOROSULFONATION OF AROMATIC AND HETERO-AROMATIC SYSTEMS

J. P. Bassin[a]; R. J. Cremlyn[a]; F. J. Swinbourne[a]
[a] School of Natural Science, Hatfield Polytechnic, Herts, England

To cite this Article Bassin, J. P. , Cremlyn, R. J. and Swinbourne, F. J.(1991) 'REVIEW. CHLOROSULFONATION OF AROMATIC AND HETERO-AROMATIC SYSTEMS', Phosphorus, Sulfur, and Silicon and the Related Elements, 56: 1, 245 — 275
To link to this Article: DOI: 10.1080/10426509108038091
URL: http://dx.doi.org/10.1080/10426509108038091

Phosphorus, Sulfur, and Silicon, 1991, Vol. 56, pp. 245–275
Reprints available directly from the publisher
Photocopying permitted by license only

Review

CHLOROSULFONATION OF AROMATIC AND HETERO-AROMATIC SYSTEMS

J. P. BASSIN, R. J. CREMLYN and F. J. SWINBOURNE
School of Natural Science,
Hatfield Polytechnic,
College Lane,
Hatfield, Herts AL10 9AB, England

(Received March 9, 1990; in final form June 18, 1990)

Key words: Chlorosulfonation; chlorosulfonic acid; sulphonyl chloride; aromatic compounds; heteroaromatic compounds.

1. INTRODUCTION

The early work on sulfonation, chlorosulfonation and the formation of sulfonyl derivatives was reviewed by Suter[1] and by Suter and Weston for aromatic hydrocarbons.[2] More recent reviews of sulfonation were carried out by Gilbert,[3,4] Hogg,[5] Cerfontain,[6] Anderson[7] and Barrett.[8] In this review of the literature since 1950, we will concentrate upon the use of chlorosulfonic acid, (chlorosulfuric acid, $ClSO_3H$), to achieve the chlorosulfonation of aromatic compounds, i.e., the replacement of one or more hydrogen atoms by the chlorosulfonyl (SO_2Cl) group. General properties of chlorosulfonic acid and specific synthesis of a variety of sulfonic acids employing this reagent have been described.[9,10]

1.1 Mechanistic Studies

In the sulfonation of aromatic compounds by sulfuric acid, although much mechanistic work has been carried out, the precise nature of the electrophile remains in doubt.[11] Sulfur trioxide is definitely involved, either free or in a combined form, however, the electrophile appears to vary according to the concentration of the sulfuric acid used. In aqueous acid (<80–85% H_2SO_4), the electrophile is probably $H_3SO_4^+$, while at higher concentrations (>85% H_2SO_4) pyrosulfuric acid ($H_2S_2O_7$) is favoured.[11]

With chlorosulfonic acid less mechanistic work has been carried out and the precise nature of the electrophilic species involved is even more uncertain. Studies of thermodynamic and experimental data indicated that when an aromatic compound reacts with an equimolar quantity of chlorosulfonic acid, the first step yields

the corresponding sulfonic acid. In the presence of an excess of the reagent, the sulfonic acid is converted more slowly into the sulfonyl chloride with liberation of sulfuric acid[11a]:

$$ArH + ClSO_3H \rightarrow ArSO_3H + HCl\uparrow \quad (1)$$

$$ArSO_3H + ClSO_3H \rightleftharpoons ArSO_2Cl + H_2SO_4 \quad (2)$$

The first step is driven to completion by removal of the hydrogen chloride liberated and the progress of the reaction can be monitored by measurement of the amount of gas evolved.[4] Early studies of the mechanism of the reaction of benzene with an equimolar amount of chlorosulfonic acid showed[12] that the major product was benzenesulfonic acid in equation (1) (Ar=Ph), together with a little diphenyl sulfone. With an excess of the reagent, benzenesulfonyl chloride was obtained in Equation (2) (Ar=Ph). Spryskov[12a] demonstrated that the second reaction was reversible and measured the equilibrium constants for several different substrates. In the benzene-chlorosulfonic acid reaction, the quantity of diphenyl sulfone was increased by addition of benzenesulfonic acid, but not by benzenesulfonyl chloride.[13] The sulfone therefore appeared to result from the reaction of benzene-sulfonic acid and benzene, under the influence of chlorosulfonic acid. Sulfone formation was relatively favoured at low temperatures; this may be due to the formation of an intermediate pyrosulfonic acid[14]:

$$ArSO_3H + ClSO_3H \rightarrow ArSO_2{\cdot}O{\cdot}SO_2OH + HCl \quad (3)$$

$$ArS_2O_6H + ArH \rightarrow ArSO_2Ar + H_2SO_4 \quad (4)$$

As the chlorosulfonation step in Equation (2) is reversible, the experimental conditions must be adjusted in order to achieve optimum yields of the desired products. An excess of chlorosulfonic acid can be used to drive this step to completion and it has been shown[15] that where reaction costs were important that a ratio of 5:1 for the ratio of reagent to substrate was desirable. However, greater efficiency has been claimed by stepwise reaction of the substrate with the reagent at moderate temperatures.[16] The yield can also be improved by removal of the sulfuric acid which is formed. This can sometimes be achieved by the addition of sodium chloride,[4] but it has been reported[17,18] that this could lead to reduced yields of the sulfonyl chloride due to the conversion of chlorosulfonic acid into the unreactive chlorosulfonate anion:

$$Cl^- + ClSO_3H \rightleftharpoons HCl + SO_3Cl^- \quad (5)$$

Sulfuric acid ideally can be removed by conversion into chlorosulfonic acid. This can be achieved by carbon tetrachloride,[4] sulfur and chlorine,[4] and also sulfur trioxide in the presence of hydrogen chloride.[16] In the latter case therefore both by-products are removed. A combination of sodium chloride and carbon tetrachloride has enabled a reduction in the amount of chlorosulfonic acid required.[4] In addition the use of the thionyl chloride, a chlorinating solvent, has also proved helpful and permitted less acid to be used.[4]

The sulfonating power of chlorosulfonic anhydride ($Cl_2S_2O_5$) is less than that of chlorosulfonic acid. However, addition of the anhydride to the reagent increases the yield of arylsulfonyl chloride.[19] The anhydride probably converts the sulfonic

acid and sulphuric acid into the sulfonyl chloride and chlorosulfonic acid respectively, Equations (6, 7):

$$ArSO_3H + ClSO_2{\cdot}O{\cdot}SO_2Cl \rightarrow ArSO_2Cl + ClS_2O_6H \quad (6)$$

$$H_2SO_4 + ClSO_2{\cdot}O{\cdot}SO_2Cl \rightarrow ClSO_3H + ClS_2O_6H \quad (7)$$

The relative rates of sulfonation of sulfonyl chlorides, sulfonic acids and sulfonate anions with chlorosulfonic acid follow the order:

$$ArSO_2Cl > ArSO_3H > ArSO_3^-$$

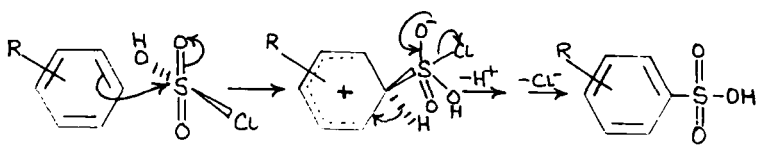
This order is in keeping with the conversion of the sulfonic acid into the sulfonyl chloride and can be explained in terms of the latter two substrates destroying part of the reagent, Equations (8, 9)[20]:

$$ArSO_3^- + ClSO_3H \rightleftharpoons ArSO_3H + SO_3Cl^- \quad (8)$$

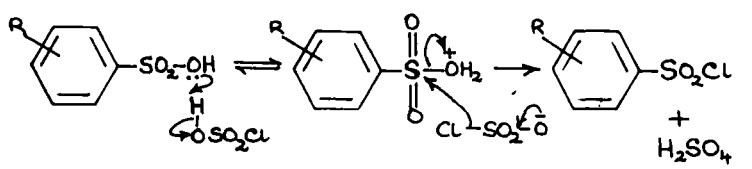
$$ArSO_3H + ClSO_3H \rightleftharpoons ArSO_3H_2^+ + SO_3Cl^- \quad (9)$$

The kinetics of the conversion of benzenesulfonic acid into the sulfonyl chloride were studied in chlorosulfonic acid.[21] The reactions between benzenesulfonyl chloride, sulfuric acid and chlorosulfonic acid at 20–50° were acid-catalysed and the equilibrium constants were practically independent of the temperature.[22]

In the reaction of the majority of aromatic compounds with an excess of chlorosulfonic acid, the mechanism of formation of the intermediate sulfonic acid and the final product may be depicted as follows, Equations (10, 11):



[10]



[11]

There is little precise information regarding the mechanistic details for these two reactions. It would appear reasonable to assume that the initial electrophilic species is chlorosulfonic acid. At higher temperatures however, reaction (12) is more pronounced:

$$ClSO_3H \rightarrow HCl + SO_3 \quad (12)$$

Hence, under these conditions, sulfur trioxide may play a significant role in the sulfonation process (10).

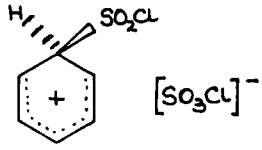
Kinetic data for the conversion of *p*-dichlorobenzene into the corresponding 2-sulfonyl chloride by chlorosulfonic acid were in agreement with the two-step reaction mechanism *via* the intermediate sulfonic acid.[23]

The sulfonation of the secondary aromatic amines, PhNHMe and PhNHEt, by chlorosulfonic acid in *o*-dichlorobenzene was a second-order reaction and involved direct reaction of the amine with HSO_3^+.[24] On the other hand, the analogous reaction with the tertiary amines, $PhNMe_2$ and $PhNEt_2$, was first order involving initial protonation of amine-sulfur trioxide complexes which rearranged to the aminobenzenesulfonic acids.[24] The kinetics of chlorination by chlorosulfonic acid of *p*-carbomethoxyaminophenylsulfonic acid have been studied photometrically at 295 nm.[25] The results indicated that the first step was addition of $2H^+$ to RSO_3H, followed by equilibration with chlorosulfonic acid. The equilibrium constant was 3.65 at 20–70°C.

Phenols with chlorosulfonic acid gave aryl sulfates which reacted with excess of the reagent to form the corresponding sulfonic acids. The kinetics of the complex reactions of 2-*t*-butylphenols have been elucidated.[26]

Sulfonation of naphthalene at 0° and 170°C gave 1,1′- and 2,2′-dinaphthyl sulfones respectively as major by-products. The isomerisation of naphthalene-1-sulfonic acid into the 2-sulfonic acid was concluded to be relatively fast in comparison with the conversion of the sulfonic acid into the sulfone.[18]

Investigations have been carried out on chlorosulfonation reactions in dichloromethane as solvent. The extent of the reaction with benzene at 0–20°C was found to be dependent upon the reaction time, increasing from 60% after a few minutes to 70% after 1 hour.[27] At low temperatures (−30° to −7°C) there was an induction period. Conflicting results were obtained from kinetic studies of chlorosulfonation reactions in dichloromethane. The reaction with benzene has been reported to be both first order and third order. It was concluded that the hydrocarbon reacted with an ion pair, $[SO_2Cl]^+$ $[SO_3Cl]^-$ to give a complex (**1**) which subsequently decomposed



(**1**)

to the sulfonyl chloride.[27] In the case of toluene and *m*-xylene, sulfonation was essentially first order with respect to chlorosulfonic acid.[27a]

The optimum conditions for the chlorosulfonation of aromatic compounds vary widely and depend upon the nature of the substrate.[4,10] In the case of electron-donating substituents in the aromatic ring (e.g., alkyl, alkoxyl, acetamido, hydroxyl), the reactions occur easily and can usually be carried out under mild conditions, the orientation being *ortho-para*-substitution. Thus, a relatively small excess of chlorosulfonic acid (a minimum of 2 equivalents) is required at comparatively low temperatures (−5° to 30°C), either in the presence or absence of a solvent, e.g., chloroform or dichloromethane. However, when electron-withdrawing substituents (e.g., nitro, carboxyl, carbonyl, sulfonyl) are present, the reactions occurred with difficulty. They required prolonged treatment with an excess of the reagent at higher temperatures, (100–150°C), and led to *m*-sulfonation.[28]

Amino and halogen substituents behave anomalously. Amino groups are usually

substantially protonated under the strongly acidic reaction conditions and hence can lead to deactivation and *m*-substitution. Although halogen groups are *ortho-/para*-directing, they are electron withdrawing and consequently cause deactivation of the substrate.

1.2 Characterization of Sulfonyl Chlorides

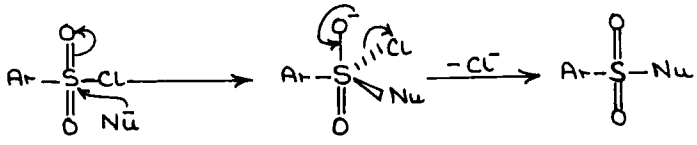
1.2.1 Derivative Formation

Sulfonyl chlorides can be readily isolated on completion of chlorosulfonation reactions, either by addition to ice-water followed by filtration, or by extraction with organic solvents. In contrast, sulfonic acids are water soluble and their isolation is tedious. As the sulfonyl chlorides are often difficult to purify and are fairly sensitive to traces of moisture which lead to decomposition, they are usually characterized chemically by treatment with nucleophilic reagents, e.g., amines, alcohols, phenols, hydrazines and azide anion.[7,8,20]

The sulfonamides in particular, after recrystallization, are generally well-defined crystalline solids.[1,7] However, in those cases where the sulfonyl chlorides are stable and amenable to purification, various chemical methods are available for their analysis.[29]

Kinetic studies of the reaction of benzenesulfonyl chloride with amines indicated an acceleration by added salts.[30] Thiophene-2-sulfonyl chloride reacted with substituted anilines slower than benzenesulfonyl chloride, indicative of a decrease in the electrophilicity of the sulfur atom. The solvolysis of arylsulfonyl chlorides in aqueous media has received considerable attention.[31,31a,31b]

The nucleophilic substitution reactions of arylsulfonyl chlorides are generally considered to follow an addition-elimination mechanism:[18,32]



It is supported by experiments involving the relative hydrolysis rates of $ArSO_2Cl$ and $ArCH_2SO_2Cl$.[33] The sulfonyl chlorides of the former series are less sensitive to substituent effects. In addition, the hydrolysis of arylsulfonyl fluorides[34] are catalysed by triethylamine and acetate anion and the alkaline hydrolysis of substituted benzenesulfonyl fluorides are particularly sensitive to substituent effects as demonstrated by the large value of the reaction constant.

The kinetics of chlorine-isotopic exchange between lithium chloride and substituted benzenesulfonyl chlorides in sulfolane solution indicated that the reaction involved a synchronous displacement mechanism of the S_N2 type, *via* a trigonal bipyramidal transition state.[35] In contrast, arylsulfonyl chlorides of the type $ArCH_2SO_2Cl$ undergo substitution *via* the sulfene mechanism and not by direct displacement at the sulfur atom:

$$ArSO_2Cl \xrightarrow{-HCL} ArCH{=}SO_2 \xrightarrow{RNH_2} ArCH_2SO_2NHR$$

1.2.2 Spectroscopic Methods

Spectroscopic methods provide important means of product characterization. Thus, infra-red spectroscopy is primarily of value for the confirmation of the presence of the sulfonyl group. Two characteristic absorption bands are usually observed at $\sim 1350\ cm^{-1}$ and $\sim 1150\ cm^{-1}$, which correspond to the asymmetric and symmetric S—O stretching frequencies respectively.[36-39]

Mass spectrometry of sulfonyl derivatives may also provide information concerning the presence of this group, with loss of SO_2 in the fragmentation pattern.[40] It is often possible to investigate the aromatic substitution pattern by proton magnetic resonance spectroscopy using approximate first-order analysis. Second-order analysis with spectral fitting by means of an iterative program such as PANIC can provide accurate values of the chemical shifts and coupling constants.

2. SUBSTRATE SYSTEMS

2.1 Hydrocarbons

2.1.1 Monocyclic Systems

Aromatic hydrocarbons are readily protonated in protic solvents, e.g., sulfuric and chlorosulfonic acid:

$$ArH + H^+ \rightleftharpoons ArH_2^+$$

The protonated form of the hydrocarbon is far less reactive to electrophilic substitution than the unprotonated form.

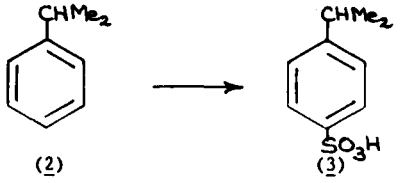
The reaction of benzene with chlorosulfonic acid gave high yields of benzenesulfonyl chloride (90–97%).[41-43] The reaction products in 1,2-dichloroethane were sensitive to the reaction conditions.[44] Addition of sodium sulphate to the reaction mixture lowered the yield of the sulfonyl chloride.[45] The product mixture usually contained the sulfonic acid, sulfonyl chloride and sulfone.[44] Benzenesulfonyl chloride was prepared in a variety of reaction conditions[14,46-49] and in a continuous process in high yield (87.6%).[50] Treatment of hexaphenylbenzene with excess chlorosulfonic acid gave hexa(chlorosulfonylphenyl)benzene,[51] where steric considerations suggested *p*-substitution.

2.1.2 Monoalkylbenzenes

The action of chlorosulfonic acid on toluene at $-80°$ to $10°$ gave the *p*-sulfonic acid,[52] whose yield decreased on lowering the temperature.[53] The reaction also gave a mixture of isomers,[54] where the yield of the *p*-isomer was increased considerably by adding ammonium chloride,[55] and by addition of catalysts.[56] In certain cases the *p*-isomer could be isolated as the sole product.[57]

The ratio of *p*- to *o*-isomers was dependent upon the molar ratios of toluene and chlorosulfonic acid.[54] The isomers of toluenesulfonyl chloride can be prepared in a continuous process.[58]

Ethyl benzene,[59,60] 1-phenyloctane,[52] phenylcyclohexane[52] and isopropylbenzene (cumene)[52,61] were chlorosulfonated in the *p*-position. The regioselectivity of chlorosulfonation of a series of alkylbenzenes (PhR; R=Me, Et, $CHMe_2$) indicated that steric effects were important.[61] Cumene (**2**) at 75°C afforded the *p*-sulfonic acid (90–95%) (**3**); the amount of the *o*-isomer was increased by conducting the reaction at lower temperatures (0–25°C) and by adding cumene to the sulfonating agent.



(2) (3)

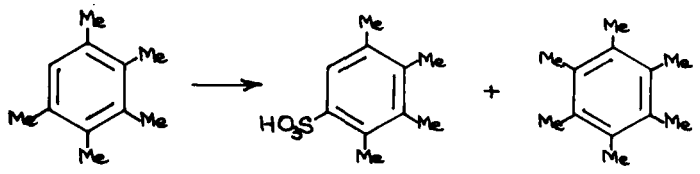
Higher molecular weight alkylbenzenes,[62] e.g., decylbenzene[63] and dodecylbenzene were converted to the corresponding benzenesulfonyl chlorides.[64,65]

In *p*-nitrotoluene, substitution by the sulfonyl chloride group occurred *ortho* to the methyl group.[66]

2.1.3 *Polyalkylbenzenes*

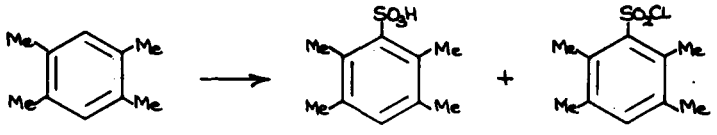
o-Xylene reacted with chlorosulfonic acid to give a low yield (26%) of 2,3-dimethylbenzenesulfonyl chloride.[67]

The sulfonation and chlorosulfonation of tetra- and penta-alkylbenzenes is often complicated by competing alkyl group rearrangements (the Jacobsen reaction).[68] Thus, pentamethylbenzene (**4**) by prolonged reaction with sulfuric acid afforded a mixture of the sulfonic acid (**5**) and hexamethylbenzene (**6**):



(4) (5) (6)

The latter resulted from rearrangement of pentamethylbenzenesulfonic acid. However, polyalkylbenzenesulfonic acids can be readily prepared because the rearrangement is slow relative to sulfonation. Thus rapid treatment of durene (**7**) with chlorosulphonic acid gave a mixture of the sulfonic acid (**8**) and the chloride (**9**):



(7) (8) (9)

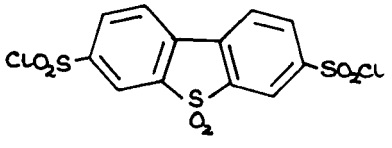
2.1.4 *Polycyclic Systems*

Chlorosulfonation of naphthalene gave a mixture of sulfonic acids and the sulfone[18,69]; the reaction has been extensively studied at low temperatures (−35° to 0°C).[70] 1,5-Naphthalenedisulfonyl chloride reacted with a very large excess (50 equivalents) of chlorosulfonic acid to give the 1,3,5-trisulfonyl chloride; these harsh conditions reflect the influence of the two deactivating sulfonyl groups on the reactivity of the substrate.[71] When the reaction was performed using an equimolar ratio of substrate and chlorosulfonic acid, the isomeric dinaphthyl sulfones were formed at both low and high temperatures.[72] The yield of mixed sulfones was highest at 160–170°C (10–11 hours).[71]

The reaction of anthracene with chlorosulfonic acid produced anthracene-1-, 2-, and 9-sulfonic acids, a mixture of anthracene-disulfonic acids, 9-chloroanthracene, 9,9′-bianathryl, and anthracene polymers. The yield and formation of each depended upon the experimental conditions and whether chloroform, dioxan, or a mixture of pyridine and isoparaffin was used as solvent.[73,74]

2.1.5 *Miscellaneous Hydrocarbons*

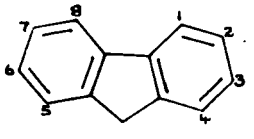
Reaction of chlorosulfonic acid with biphenyl at room temperature gave both the 4-sulfonyl chloride and 4,4′-disulfonyl chloride.[75,76] Pollak *et al.*[75] claimed the formation of dibenzothiophene-1,1-dioxide-3,6-disulfonyl chloride (**10**) in the reaction of biphenyl with chlorosulfonic acid (6 equivalents) under mild conditions.



(10)

Attempts to obtain (**10**) using the same conditions were unsuccessful, only biphenyl-4,4′-disulfonyl chloride was isolated.[76] Under forcing conditions, however, (**10**) formed in good yield from biphenyl using a large excess of chlorosulfonic acid.[76]

Diphenylmethane and bibenzyl[77]with chlorosulfonic acid each gave the corresponding 4,4′-disulfonyl chloride, but fluorene (**11**) gave a mixture of the 2- and 2,7-disulfonyl chloride even with a large excess (12 equivalents) of the reagent.[77a,77b]



(11)

2.2 *Halogeno Compounds*

The kinetics of sulfonation of chlorobenzene with chlorosulfonic acid have been studied.[78] Sulfonation of chlorobenzene,[79–81] and fluorobenzene[82,83] gave predom-

inately *p*-substitution, together with the sulfone as a by-product.[84] The yield of the sulfone can be increased under a variety of conditions.[13,85–88]

The reactions of *o*-, *m*- and *p*-dichlorobenzenes with chlorosulfonic acid have been investigated.[89] 1,2-Dichlorobenzene,[90,91] gave a good yield of 3,4,3′,4′-tetrachlorodiphenyl sulfone, although the 1,3- and 1,4-isomers[92] yielded only the expected sulfonyl chlorides. The difference arises from the lack of steric hindrance in the 4-position of 1,2-dichlorobenzene facilitating sulfone formation.

1,2,4-Trichlorobenzene and the 1,3,5-isomer[93,94] were readily converted into the trichlorobenzenesulfonyl chlorides. 1,2,3,4-Tetrachlorobenzene[95] gave the 2,3,4,5-tetrachlorobenzenesulfonyl chloride; but under drastic conditions 1,2,4,5-tetrachlorobenzene only afforded hexachlorobenzene. A possible mechanism was proposed in which the pre-formed sulfonyl chloride underwent loss of sulfur dioxide to give the pentachlorobenzene and ultimately hexachlorobenzene.[95a]

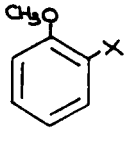
In 1-chloro-2-nitrobenzene sulfonation took place *para* to the chlorine atom as would be anticipated.[96–98] With 1-chloro-4-nitrobenzene, 2-chloro-5-nitrobenzenesulfonyl chloride[98] was obtained, while with 1-chloro-3-nitrobenzene, substitution took place *para* to the chlorine atom.[98] All these isomeric chloronitrobenzenes contained chloranil as a by-product.[98]

3-Trifluoromethylbenzenesulfonyl chlorides were prepared as intermediates in the synthesis of drugs, agrochemicals and dyes.[99] Thus, 2-chlorotrifluoromethylbenzene was reacted with a mixture of fuming sulfuric acid and chlorosulfonic acid to give 4-chloro-3-trifluoromethylbenzenesulfonyl chloride in very low yield. Chlorosulfonation of β-chloroethylbenzene gave the *p*-sulfonyl chloride.[100]

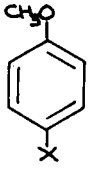
Treatment of aryl iodides with chlorosulfonic acid gave either chlorinated products or sulfones rather than the corresponding sulfonyl chlorides (see section 2.10.2).

2.3 *Ethers*

The chlorosulfonation of anisole is reported to take place *para* to the methoxyl group.[101] With *o*-(**12**) and *p*-(**13**) substituted anisoles the reactions went in high yields:



(12)



(13)

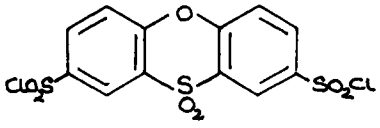
(X = Br, Cl, NO_2, OMe, NHAc)

the former reaction generally required only mild conditions.[102,103] The ease of reaction is probably due to the lack of steric hindrance in the position *para* to the methoxyl group.

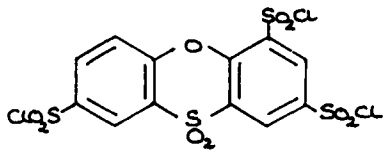
2,3,5-Trimethylanisole with chlorosulfonic acid gave 4-methoxy-2,3,6-trimethylbenzenesulfonyl chloride.[104,105]

Diphenyl ether with chlorosulfonic acid afforded the corresponding 4,4′-sulfonyl chloride[106,107]; this product was also obtained in the presence of N-containing compounds or their salts,[108] fatty acids[109] (or their derivatives) and alkali metal salts.[110]

The reaction of diphenyl ether with chlorosulfonic acid under forcing conditions afforded a mixture of the cyclic sulfones (**14**) and (**15**).[76]



(14)



(15)

The chlorosulfonation of 2′-chloro-4-nitro-diphenyl ether and 2′,6′-dichloro-4-nitrodiphenyl ether afforded very poor yields of the sulfonyl chlorides, which were very susceptible to hydrolysis due to the electron-withdrawing groups.[111,112]

2.4 *Phenols*

In the reaction of phenol with chlorosulphonic acid at temperatures of −40° to 0°C, equal amounts of 2- and 4-hydroxybenzenesulfonic acids were formed together with traces of the disulfonic acids.[113,114] The relative rate of formation of the 2-hydroxybenzenesulfonic acid compared with that of the 4-hydroxy isomer was found to increase with decreasing temperature.[113]

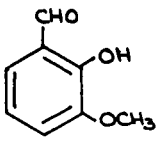
Treatment of 2,3-, 2,4-, 2,5-, 2,6-, 3,4- and 3,5-dichlorophenols with chlorosulfonic acid afforded the following substituted benzenesulfonyl chlorides: 2,3-dichloro-4-hydroxy, 3,5-dichloro-2-hydroxy, 2,5-dichloro-4-hydroxy, 3,5-dichloro-4-hydroxy, 4,5-dichloro-2-hydroxy and 2,6-dichloro-4-hydroxy respectively.[115] The orientation of chlorosulfonation is controlled by the electron-releasing hydroxyl group, so that where possible sulfonation occurred *para* to this group, however when this position is blocked by a substitutent sulfonation occurred *ortho* to the hydroxyl group.[115–118] Experiments showed that the maximum yields of sulfonyl chlorides from the appropriate dichlorophenols required the use of a large excess (approximately 5 equivalents) of chlorosulfonic acid in each case (conditions similar to those encountered with chlorosulfonation of aromatic carboxylic acids), made necessary by the condensation of chlorosulfonic acid with the phenolic hydroxyl group.[115]

The chlorosulfonation of hydroquinone,[119] higher alkyl phenols,[120] *p*-methoxyphenol,[121] and 1,2-naphthoquinone[122] have also been reported.

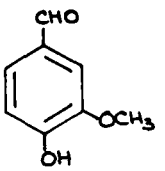
Sulfation is usually more easily effected than sulfonation.[123–126]

2.5 *Aldehydes and Ketones*

Comparatively little work has been carried out on aldehydes[127] and there were no reports of the use of chlorosulfonic acid. *o*-Vanillin (**16**) is claimed to react with oleum to give the 5-sulfonic acid.[128]



(16)



(16a)

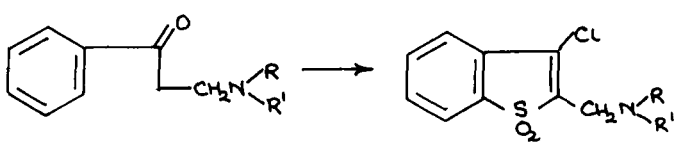
However, later work[129] failed to reproduce this result. Attempts to chlorosulfonate *o*-vanillin, vanillin (**16a**) and 2,5-dimethoxybenzaldehyde with chlorosulfonic acid under various conditions were unsuccessful and only afforded charred products.[129]

Only a small proportion of the recently published work has been concerned with the reactions of ketones with chlorosulfonic acid. The majority of these papers are due to the investigations of Cremlyn *et al.*[77,111,130–139] Some reactions have resulted in predictable products, while several novel reactions have been reported.

p-Methoxybenzophenone was chlorosulfonated much more readily (50°) than benzophenone (140°). The product from the latter reaction was the expected 3,3′-disulfonyl chloride[111] which was obtained in poor yield (15%). However, the use of more reagent at a slightly higher temperature afforded an improved yield (40–50%).[111,140] The directing influence of the substitutent is further illustrated in the case of α-naphthylchalcone[135] and of chalcone,[136] which, under less forcing conditions, gave the corresponding 4-sulfonyl chlorides. 4-Methoxychalcone was converted easily into the 3-sulfonyl chloride in good yield.[136] The methoxyl group thus provides ring activation despite the presence of steric factors.

In addition to electrophilic attack at the ring atoms, side-chain reaction may also occur. This is illustrated by the reaction of acetophenone.[132] The product was claimed to be the corresponding 2,ω-disulfonyl chloride, obtained in low yield.[140a] However, in the case of 4-substituted acetophenones, both reactions do not necessarily occur. Thus, 4-methoxyacetophenone gave the 3-sulfonyl chloride,[141] as did 4-hydroxyacetophenone.[142] The latter result is perhaps surprising in view of the 3,ω-disulfonyl chloride which was obtained from 4-methoxyacetophenone.[102]

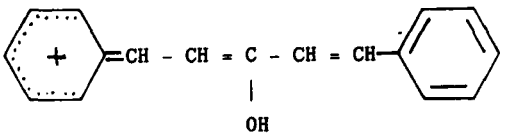
A novel cyclisation reaction occurred with propiophenone,[143] with the formation of 3-chloro-2-methylbenzothiophene-1,1-dioxide. The cyclisation of Mannich bases also proceeded smoothly:[143]



R,R′ = CH_3

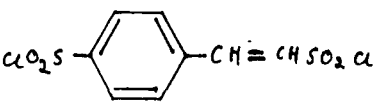
R=R′ = 

Dibenzylideneacetone was converted into the 4-sulfonyl chloride and under more forcing conditions, into the 4,4′-disulfonyl chloride.[138] The selectivity was attributed to the formation of an intermediate cation (**17**):



(17)

However, treatment of benzylideneacetone resulted in a novel reaction with the formation of styrene-4,β-disulfonyl chloride (**17a**). ω-Chlorosulfonation was proposed, as observed with acetophenone,[132] followed by elimination of mesityl oxide.



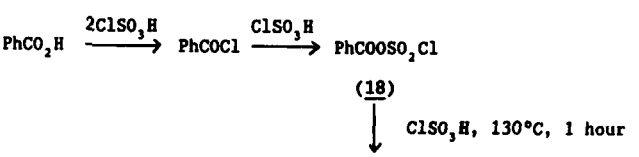
(17a)

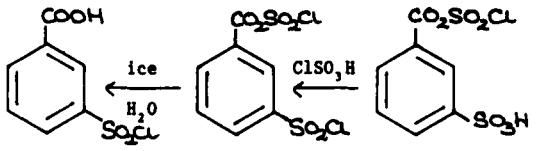
Several other benzylidene derivatives have been successfully converted into the corresponding *p*-sulfonyl chlorides by reaction with chlorosulfonic acid. Examples include 5-benzylidene and 5-cinnamylidene hydantoins,[144] 3-benzylidenecamphor[145,146] and 1,5-dibenzylidenecyclopentanone.[146a]

Benzil[133] and substituted benzils[137] undergo a novel cyclisation reaction with the formation of substituted 3-chloro-2-phenylbenzofurans. The reaction is considered to proceed *via* initial α-chlorohydrin formation, which provides the appropriate orientation and reactivity for chlorosulfonation, followed by ring closure. 1,4-Diamino-anthraquinone behaved as expected giving the 2-sulfonic acid.[147] In the case of 1,5-di(*o*-anisidino)anthraquinone, the product was 1,5-di(2-methoxy-5-chlorosulfonylanilino)anthraquinone.[130]

2.6 *Carboxylic Acids*

The reactions of chlorosulfonic acid with benzoic, cinnamic and phenylacetic acids were reported by Suter.[148] The carboxylic acid group is an electron-withdrawing substituent and consequently the chlorosulfonation of aromatic carboxylic acids generally required temperatures of more than 120°C and excess quantities of reagent. The reaction probably proceeds *via* a mixed anhydride intermediate e.g., (**18**) which would account for the comparatively large quantities of reagent required. In the case of benzoic acid[149] at least 5 equivalents of chlorosulfonic acid were needed to achieve the optimum yield of the *m*-sulfonyl chloride (**19**). The postulated mechanism is shown (Scheme 1):

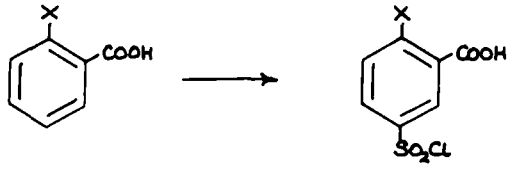




(19)

Scheme 1

Several *o*-substituted benzoic acids (**20**) (X=CH_3, OCH_3,[150] OH,[151-513] Cl, Br) have been reacted with chlorosulfonic acid (4–6 equivalents).[149] When X was an electron-donor group, chlorosulfonation occurred at 40–90°C (1–2 hours) to give the corresponding 5-sulfonyl chloride in good to excellent yields (**21**, 60–90%).



(20) (21)

The presence of X as an electron-withdrawing substituent required rather more forcing conditions, (e.g., 120–130°C, 2–3 hours). For *p*-substituted acids, the yields of the 3-sulfonyl chlorides (**22**) were lower (50%) and when electron-withdrawing groups (e.g., chloro)[154] were present the chlorosulfonation required prolonged reaction (e.g., 150°C, 2 days).

(22) (23)

Salicyclic acid has been converted into the 3,5-disulfonyl chloride and the 5-bromo and 5-chloro derivatives into the corresponding 3-sulfonyl chlorides and a range of derivatives has been reported.[151,155-157]

m-Toluic acid (**23**, X=CH_3) reacted with the chlorosulfonic acid (4 equivalents, 150°C, 2½ hours) to give a mixture of the 4- and 6-sulfonyl chlorides. The latter was claimed[149] to be the major product, possibly involving intramolecular rearrangement of the mixed anhydride intermediate. Cinnamic acid, due to the activating influence of the αβ-alkenic double bond, reacted readily with chlorosulfonic acid at 50–60°C to give the *p*-sulfonyl chloride (60%).[149]

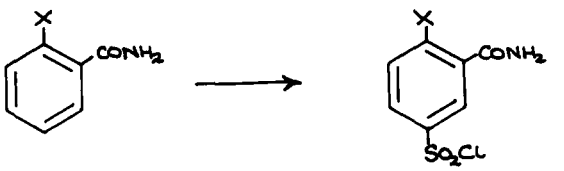
Phenoxyacetic acid was even more reactive and chlorosulfonation occurred at 0°C, but with the *o*-chloro derivative the yield of sulfonyl chloride was very low.[149] The chlorosulfonation of 2,4- and 2,5-dichlorophenoxyacetic acids has also been reported.[158]

The attempted chlorosulfonation of phenylacetic acid, *m*-nitroboenzoic acid and phthalic acid was unsuccessful.[149]

2.7 *Amides and Related Compounds*

2.7.1 *Amides*

Aromatic carboxamides react with excess chlorosulfonic acid without effect on the amide ($CONH_2$) group, cf. carboxylic acids.[149] The chlorosulfonation occurs rather more easily than with the corresponding carboxylic acid, because the amido group is a less strongly electron-withdrawing substituent probably due to the slightly greater +M effect of the amino constituent of the group compared with that of OH. Amides substituted in the 2-position by electron-donor groups (e.g., (**24**), X=CH_3, OCH_3, OH) undergo facile reaction with chlorosulfonic acid under comparatively mild conditions, (e.g., 50–70°C, ½–2 hours), to give excellent yields of the 5-sulfonyl chlorides (**25**)[159]:

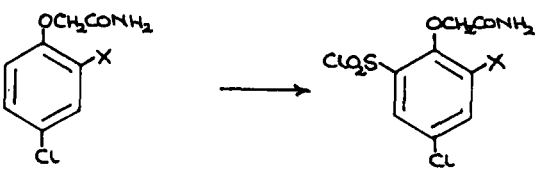


(24) (25)

With **24** (X=$OCOCH_3$), the reaction afforded a mixture of **25** (X=$OCOCH_3$) and the corresponding hydroxy compound.[159] The analogous *p*-substituted amides require rather longer reaction times due to the steric effect of the substituent; thus *p*-methoxybenzamide reacted with the reagent over 4 hours to give 5-amido-2-methoxybenzenesulfonyl chloride.

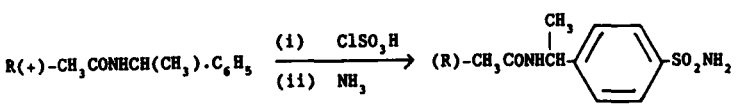
Cinnamide reacted easily with chlorosulfonic acid at 30–50°C to give the *p*-sulfonyl chloride due to the electron-donating effect of the π-electrons of the αβ-alkenic double bond.[156] Substituted cinnamides, e.g., the dimethylamide and morpholidate were similarly chlorosulfonated.[160]

Phenoxyacetamide reacted readily with chlorosulfonic acid at room temperature or at 70°C and gave an excellent yield of the *p*-sulfonyl chloride.[161] 2,4-Dichloro- and 4-chloro-2-methylphenoxyacetamide (**26**) reacted with the reagent at 80°C to give moderate yields of the corresponding 6-sulfonyl chlorides (**27**)[161]:



(26; X=Cl or CH_3) (27; X=Cl or CH_3)

1-Phenylethylacetamide (**28**) has been treated with chlorosulfonic acid followed by ammonia to give a low yield of the sulfonamide (**29**):



(28) (29)

These sulfonamides are reported to possess anti-diabetic activity.[162]

Chlorosulfonic acid is particularly useful for the conversion of acetanilide (**30**) and substituted anilides into the monosulfonyl chlorides.[163]

4-(Acetamido)benzenesulfonyl chloride (**31**), prepared by the chlorosulfonation of acetanilide (**30**), is an important intermediate in the synthesis of sulfonamide anti-bacterial drugs. A great deal of work has therefore been devoted to optimising the yield of the following reaction:

(30) (31)

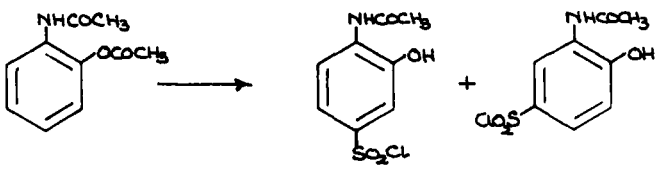
Smiles and Stewart[164] reported that chlorosulfonic acid (5 equivalents) reacted with (**30**) to give (**31**) in good yield. Studies of the reaction of (**30**) with the reagent (5 equivalents) in the temperature range of 0° to 100°C indicated that the most satisfactory temperature for formation of the monosulfonyl chloride (**31**) was 55–60°C; some disulfonation occurred above 40°C, polysulfonatin was observed above 70°C and at 100°C (2 hours) the reaction gave no sulphone.[165] Improvements in the manufacture of (**31**) involved recovery of sulfuric acid[166]; the use of more reagent (6 equivalents) at 40°C (3 hours) and subsequent treatment with dilute H_2SO_4 gave an excellent yield.[167] The reaction of (**30**) with chlorosulfonic acid in the presence of benzene (<95°C) gave a mixture of (**31**) and benzenesulfonic acid.[168] The reaction of chlorosulfonic acid with dichlorobenzenesulfonanilides gave good yields of the dichlorobenzenesulfonylsulfanilyl chlorides at low temperatures (− 10° to 10°C),[168a] although similar chlorosulfonation of carboxylic anilides occurred at 50° to 60°C. The difference in behaviour is presumably largely a reflection of the greater strength of the C—N bond (184 kcal/mol) as compared with that of the N—S bond (111 kcal/mol).[168b]

Side-chain substituted α-mono, α,α-di- and α,α,α-trichloroacetanilides reacted smoothly with chlorosulfonic acid (5 equivalents) at 60°C to give excellent yields of the corresponding *p*-sulfonyl chlorides.[169] α-Bromoacetanilide-*p*-sulfonyl chloride is used as an amide-linking agent.[170] *p*-Methyl-α,α,α-trichloroacetanilide[169] reacted with the reagent at room temperature to give the 5-sulfonyl chloride (50%), but the *p*-chloro analogue did not react. The α,α-di-and α,α,α-trichlorosulfonyl chlorides reacted with dimethylamine to give the corresponding dimethylsulfonamides without displacement of the alkyl chlorine atoms. In contrast, with the α-chloro derivative both chlorine atoms were substituted.[169]

2-, 3-Chloro, 2,5- and 2,6-dichloroacetanilides reacted with chlorosulfonic acid to give the corresponding 4-sulfonyl chlorides.[171] The reaction became increasingly difficult due to the steric and electronic effects of the chlorine atoms. 2-Chloroacetanilide afforded a 30% yield of the sulfonyl chloride after 4 hours, but the 2,6-dichloro analogue required prolonged reaction. All attempts to chlorosulfonate 2,3-dichloroacetanilide failed, possibly due to a "buttressing effect" of the acetamido group on the 2-chlorine atom.[171]

The introduction of the electron-donating methoxyl group into acetanilide greatly facilitates chlorosulfonation. Thus 2- and 4-methoxyacetanilide reacted with chlo-

rosulfonic acid at room temperature to give excellent yields of the 5- and 3-sulfonyl chlorides[102] respectively. However, 3-methoxyacetanilide gave a moderate yield of the 4-sulfonyl chloride.[102] 2-Methyl, 2-methoxy and 4-methylacetanilides with chlorosulfonic acid in boiling chloroform gave good yields of the corresponding sulfonyl chlorides. Several of the derived hydrazides/hydrazones showed anti-bacterial activity.[172] 2,5-Dimethoxyacetanilide reacted at 60°C to give the 4-sulfonyl chloride (53%)[171]; while prolonged reaction with a mixture of chlorosulfonic acid and thionyl chloride gave an increased yield (93%)[173]; the product is used in the dye industry. 2-Acetoxyacetanilide (**32**) reacted with chlorosulfonic acid in chloroform at 50–60°C with *o*-deacetylation to give a good yield of the sulfonyl chlorides (**33**, **34**); p.m.r. spectroscopy indicated that (**33**) was the major component.



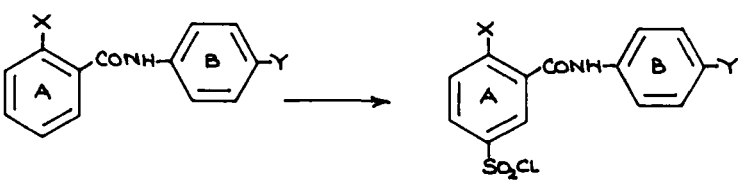
(32) (33) (34)

The 3-acetoxy analogue gave black tars but 4-acetoxyacetanilide afforded 5-acetoxy-2-hydroxybenzenesulfonyl chloride.[174]

2,4-Dimethylacetanilide reacted with chlorosulfonic acid to give 5-acetamido-2,4-dimethylbenzenesulfonyl chloride[175] and 1-acetamidonaphthalene was converted to the 4-sulfonyl chloride (45%).[176,177]

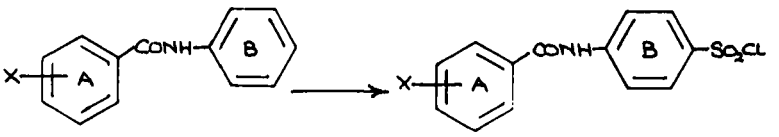
2.7.2 *Anilides*

Several *o*-substituted carboxylic acid anilides (**35**; X=OH, OCH_3, Y=H or X=OH, Y=Cl) reacted with chlorosulfonic acid (4–10 equivalents) at room temperature to give high yields of the corresponding 4-sulfonyl chlorides (**36**)[152]:



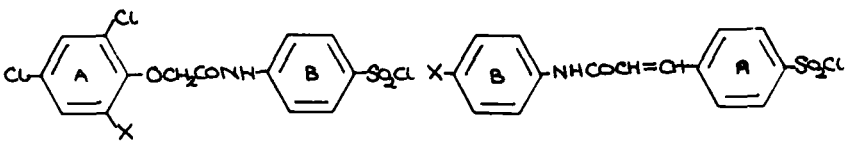
(35) (36)

Under these mild conditions, chlorosulfonation occurred selectively in ring A because this is more reactive than ring B. On the other hand, benzoic acid anilide and the 4-chloro, 3-nitro and 2,4-, 2,5- and 3,4-dichloro derivatives (**37**) reacted with warm excess chlorosulfonic acid (4 equivalents) with exclusive chlorosulfonation in ring B, which is now relatively more reactive than ring A due to the adjacent amino group, to give the *p*-sulfonyl chlorides (**38**).[178]



(37) (38)

Nicotinic acid anilide reacted similarly except that more reagent was required, possibly salt formation occurred due to the presence of the basic centre.[178] 2,4-Dichlorophenoxyacetamide reacted with warm chlorosulfonic acid to give the *p*-sulfonyl chloride (**39**; X=H) but with more reagent (7 equivalents), the disulfonyl chloride (**39**; X=SO_2Cl) was isolated.[178]

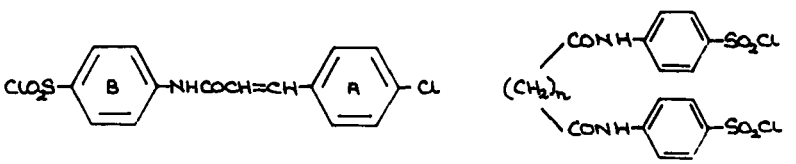


(39) (40)

The lower susceptibility of ring A relative to ring B is probably the result of some steric hindrance imposed by *o*-substitution which is absent in ring B.

Cinnamic acid anilide reacted with a large excess of chlorosulfonic acid at room temperature to give a very high yield of the disulfonyl chloride (**40**; X=SO_2Cl).[179] The corresponding *p*-chloroanilide with a large excess of the reagent at 50°C only gave the monosulfonyl chloride (**40**; X=Cl) due to steric factors and deactivation of ring B.

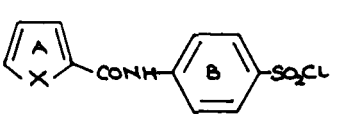
However, *p*-chlorocinnamic acid anilide reacted rapidly (5 minutes) with chlorosulfonic acid at 50°C to give a very high yield of the monosulfonyl chloride (**41**),[179] since it is now ring A that can be more easily attacked.



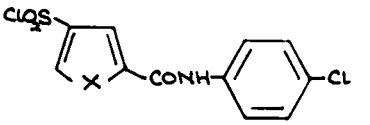
(41) (42)

Several dicarboxylic acid dianilides have been treated with large excesses of chlorosulfonic acid to give excellent yields of the 4,4′-disulfonyl chlorides (**42**). The chlorosulfonation was more difficult with oxalic acid dianilide and required treatment at 80–85°C (4 hours), the yield (60%) was also appreciably lower than that of the higher homologues: malonic (n = 1), succinic (n = 2) and glutaric (n = 3) acid dianilides. The latter generally required reaction at 50°C (10 minutes) followed by a period at room temperature (3 hours).[179,180] Oxalic acid dianilide disulfonyl chloride (**42**, n = 0) was difficult to characterize as its derivatives had very high melting points and low solubilities in organic solvents.

Furan and thiophene-2-carboxanilides reacted with warm chlorosulfonic acid and gave excellent yields of the corresponding *p*-sulfonyl chlorides (**43**; X=O,S).



(43)

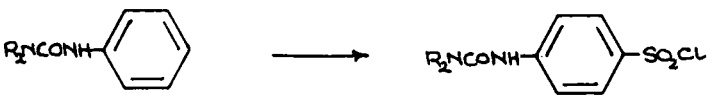


(44)

In both cases there was selective chlorosulfonation in the anilide ring B presumably due to the deactivating effect of the amide moiety on the heterocyclic ring, A.[181] However, with the *p*-chloro derivatives treatment with chlorosulfonic acid under similar conditions afforded the 4-sulfonyl chlorides (**44**) involving selective substitution in the heterocyclic ring.[181]

2.7.3 Ureas

Phenylurea[182] and N,N-dimethylphenylurea[183] (**45**), R=H, or CH_3) reacted easily with chlorosulfonic acid to give the *p*-sulfonyl chlorides (**46**).

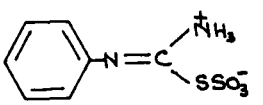


(45) (46)

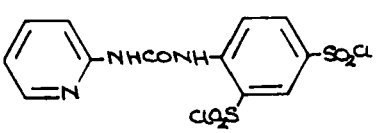
2-Substituted phenylureas reacted with chlorosulfonic acid, under similar conditions, to give the sulfonyl chlorides. 2-Chloro and 2-methylphenylurea afforded the corresponding 4-sulfonyl chlorides,[184] whereas the 2-methoxy derivative gave a better yield of the 5-sulfonyl chloride in which the orientation of sulfonation occurred with respect to the more strongly electron-donating methoxyl group.[185]

When the substituents were in the *m*- or *p*-positions, chlorosulfonation was more difficult and much lower yields were obtained. For instance, 3-methylphenylurea with chlorosulfonic acid afforded the corresponding 4-sulfonyl chloride (15%); while the 4-methyl derivative gave an even lower yield of the 2- and 3-sulfonyl chlorides.[184] The 3- and 4-chlorophenylureas failed to give sulfonyl chlorides under comparable conditions.[183]

Phenylthiourea by warming with chlorosulfonic acid behaved abnormally and gave a product considered to be the iminosulfonic acid (**47**) which did not react with phosphorus pentachloride.[185] The product could



(47)



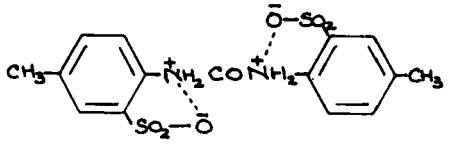
(48)

arise from sulfonation of the thiol tautomer and the proposed zwitterionic structure accounts for its inertness towards phosphorus pentachloride.

N,N'-Diphenylurea reacted normally with chlorosulfonic acid to give the 4,4'-disulfonyl chloride.[182] 4-Methyldiphenylurea reacted similarly to give the 4'-sulfonyl chloride.[185]

N-Phenyl-N'-(4-pyridyl)urea reacted normally with chlorosulfonic acid gave the 4-sulfonyl chloride[185]; however, the 2-pyridyl analogue, afforded a low yield (20%) of the 2,4-disulfonyl chloride (**48**).[185]

2,2'-Dimethyl and 3,3'-dimethyldiphenylurea were both reacted with hot chlorosulfonic acid to give moderate yields of the corresponding 4,4'-disulfonic acids, both of which were converted into the corresponding disulfonyl chlorides by heating with phosphorus pentachloride.[182] The 4,4'-dimethyl analogue afforded the 2,2'-disulfonic acid (**49**) under similar conditions, but it did not react with phosphorus pentachloride due to zwitterion formation.



(49)

The disodium salt, which cannot exist as the zwitterion, was however converted into the 2,2'-disulfonyl chloride on heating with phosphorus pentachloride.[182]

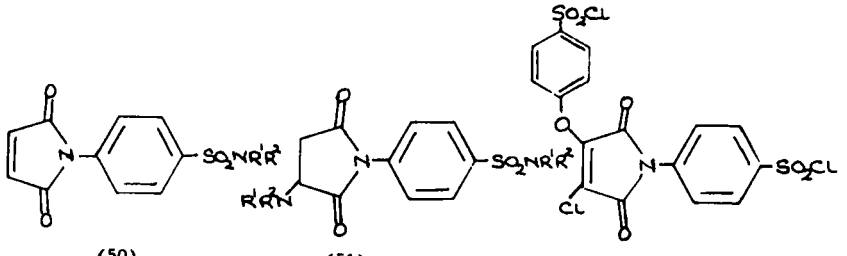
Some diarylthioureas have been treated with chlorosulfonic acid; thus N-phenyl-N'-(2-pyridyl)-N'-(2-thiazolyl)thiourea[185] reacted with chlorosulfonic acid to give the corresponding *p*-sulfonyl chlorides.[185,186]

2.7.4 *Imides*

Several N-arylmaleimides have been converted into sulfonyl chlorides by treatment with chlorosulfonic acid.

N-Phenylmaleimide reacted under mild conditions to give an excellent yield of N-(*p*-chlorosulfonylphenyl) maleimide.[187] Various N-arylmaleimides have been similarly chlorosulphonated[188] and α,α'-dichloro-N-phenylmaleimide reacted rapidly to give the corresponding *p*-sulfonyl chloride (80%).[189]

N-(*p*-Chlorosulfonylphenyl)maleimide can be used as a dienophile in Diels-Alder reactions without effect on the chlorosulfonyl moiety.[190] Treatment of N-(*p*-chlorosulfonylphenyl)maleimide with amines in acetonitrile generally gave a mixture of the sulfonamides (**50**) and (**51**).

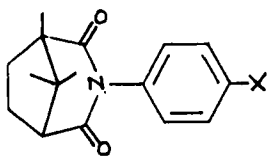


(50) (51) (52)

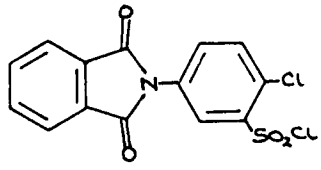
The succinimide (**51**) resulted from simultaneous Michael addition to the activated alkenic double bond, the pure imido sulfonamide (**50**) was obtained by column chromatography.[187] Other workers[191] reported that reaction of the sulfonyl chloride with aqueous ammonia gave the sulfonamide (**51**, $R^1{=}R^2{=}H$), while reaction with various substituted anilines afforded the succinimides (**51**, $R^1{=}H$, $R^2{=}NC_6H_4Y$). Reaction of α-chloro-α′-phenoxy-N-phenylmaleimide with a large excess of warm reagent gave the disulfonyl chloride (**52**).[187]

N-Phenylsuccinimide reacted similarly to give the *p*-sulfonyl chloride (87%).[156]

N-Phenylsuccinimide, -glutarimide and -comphorimide (**53**, X=H) were all converted into the corresponding *p*-sulfonyl chlorides (e.g., **53**, $X{=}SO_2Cl$) by chlorosulfonic acid—in yields of 85, 10 and 55% respectively.[192]



(53)

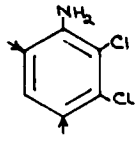


(54)

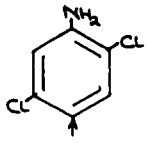
N-Phenylphthalmide and the 2-chloro derivative reacted similarly with chlorosulfonic acid to give the corresponding *p*-sulfonyl chlorides in excellent yields. 4-Chlorophenylphthalimide was similarly converted into the 3-sulfonyl chloride[193] (**54**).

2.8 *Amines*

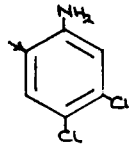
Normally aromatic amines are protected before treatment with chlorosulfonic acid, e.g., by acetylation, to avoid extensive decomposition. However, in several cases unprotected amines have given sulfonyl chlorides by direct reaction with the reagent. Sulfonation of primary amines with chlorosulfonic acid gave products which were substituted in the *o*- and/or *p*- positions with respect to the amino group.[194–198]



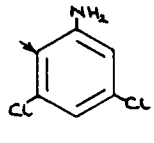
2,3-



2,5-



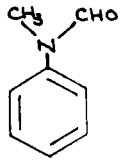
3,4-



3,5-

These dichloroanilines each reacted with a large excess of chlorosulfonic acid to give the sulfonyl chlorides as indicated by the arrows.[195] 2,5-Dichloroaniline in contrast, did not give chlorosulfonation *ortho* to the amino group,[195,199] presumably due to steric inhibition.

Sulfonation of diphenylamine with chlorosulfonic acid in nitrobenzene at 90°C gave the 4-sulfonic acid and/or the 4,4′-disulfonic acid depending upon the reagent to substrate ratio.[200] However, attempts to reproduce the reported preparation of



(55)

the 4,4′-disulfonyl chloride[201] were unsuccessful. Reaction of diphenylalmine with a large excess of chlorosulfonic acid at 80°C gave the 2,2′,4,4′-tetrasulfonyl chloride.[77] The reaction mechanism involved initial N-sulfonation.[77]

The reaction of chlorosulfonic acid with N-methylformanilide (**55**) gave the *p*-N-methylformylaminobenzenesulfonyl chloride.[202] The preparation and attempted chlorosulfonation of N,N-dimethylbenzylamine-sulfur trioxide complex were reported.[203]

Synthesis of 3-amino-6-methylbenzenesulfonic acid from *p*-toluidine,[204] 2-aminobenzene-1,3,5-trisulfonic acid[205] and 6-amino-4-methoxybenzene-1,3-disulfonyl chloride[198] from *m*-methoxyaniline were also reported.

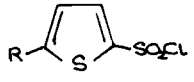
2.9 *Heterocyclic compounds*

Only a limited range of heterocyclic compounds has been studied. Interest has been shown in some monocyclic systems, notably with more than one hetero atom, and in several polycyclic systems.

2.9.1 *Monocyclic Systems*

Thiophene was converted into the 2-sulfonyl chloride in fair yield.[206] For the few derivatives which were studied only 2-substitution was reported.[207–209] It is interesting to note that this was the case with the 3—$CH_2OCH_2CF_3$ derivative,[208] where presumably initial attack at the ether oxygen directs the course of the reaction.

The kinetics of the reaction of 5-substituted-2-thiophenesulfonyl chlorides (**56**) with aniline in methanol were studied[210]:



(R = Me, Cl, Br, I, NO_2)

(56)

Imidazole-4-sulfonyl chloride was obtained from imidazole in good yield.[211] The 4-sulfonyl chloride was also obtained from 2-(*p*-chlorophenyl)imidazole—ring substitution presumably being favoured by steric and electronic factors.[212] The latter conclusion is supported by the formation of the 4′-sulfonyl chloride from 1-(β-phenoxyethyl)imidazole.[213] In this instance a mixture of chlorosulfonic acid and phosphorus pentachloride was used as the reagent.

2-Methyl-4,5-diphenyloxazole and 3,4-diphenyl-1,2,5-furazan each gave the corresponding 4′,4″-disulfonyl chloride.[214] These reactions illustrate the dominance of the +M effect of the ring oxygen atom.

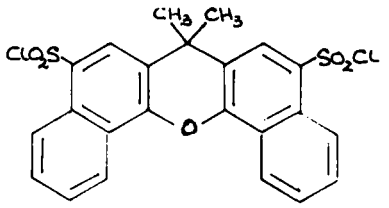
2-Amino-5-methylpyridine was converted into the 3-sulfonyl chloride under forcing conditions,[215] whereas 2,3-diphenylpyrazine gave the corresponding 3′,3″-disulfonyl chloride more easily and in excellent yield.[214] These reactions demonstrate the significant deactivation caused by the ring nitrogen atoms, particularly under acidic conditions and the product from the latter reaction, the transmission of the −M effect of the ring atoms. The deactivation of the pyridine ring can be further illustrated by the conversion of an alkyl 2-aminopyridine-3-ester into the sulfamic acid salt.[216] 2-Picoline was used as an exchange reagent in the conversion of methyl anthranilate into $2\text{-}MeO_2CC_6H_4NHSO_2NHCHMe_2$, *via* the intermediate sulfamic acid salt.[217]

2.9.2 *Polycyclic Systems*

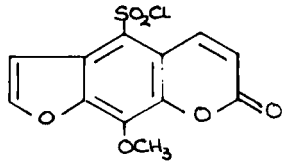
The corresponding 5-sulfonyl chloride was obtained from 2-carbomethoxy-6,7-dichloro-2,3-dihydrobenzofuran in good yield,[218] and the 5-derivative from 1-acetyl-6-chloroindoline.[219] The chlorosulfonation of carbazole[220–222] and 3,6-dinitrocarbazole[223] have been successful.

Side-chain substitution was reported in the synthesis of 3-(chlorosulfonylmethyl)-1,2-dihydrobenzisoxazole.[224] Benzimidazole was converted into the 5-sulfonic acid, but 2-(*p*-nitrophenyl)imidazole gave the 5-sulfonyl chloride.[221]

Coumarin gave the 6-sulfonyl chloride,[225,226] dimethyldinaphthopyran the bis-product, (**57**),[227] and xanthotoxin the mono-product, (**58**)[228]:



(57)

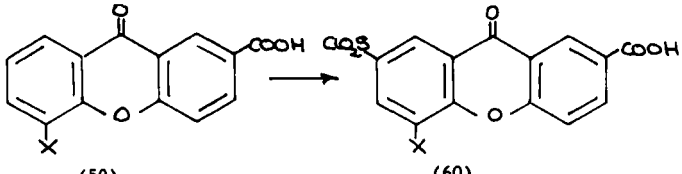


(58)

Treatment of 2-(cyanoacetyl)coumarone resulted in rearrangement and substitution, with the formation of 2-(cyanoacetyl)-3-benzofuransulfonyl chloride.[229] 8-Methoxyquinoline[230] and 2,4-dimethylquinoline[231] gave respectively the 5- and 8-sulfonyl chlorides.

6-Chloro-1,2,4-benzothiadiazine-1,1-dioxide gave the corresponding 7-sulfonyl chloride, and on reduction with stannous chloride the 7-mercapto derivative, which has application in the treatment of gout and arthritis.

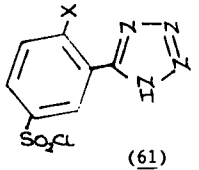
Xanthone-2-carboxylic acid (**59**) substituted in position 5 (X = methyl, ethyl, isopropoxyl, isopropyl, *n*-octyl, methoxyl, ethoxyl, *n*-propoxyl), with chlorosulfonic acid under forcing conditions gave the



(59) (60)

7-sulfonyl chloride (**60**).[232,233]

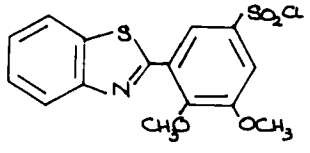
A variety of 5-aryltetrazoles (**61**) reacted with chlorosulfonic acid, with sulfonation *para* to the X group[234]:



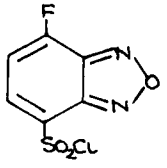
(X = Me, Cl, Br)

(61)

Treatment with chlorosulfonic acid of the following: 2-(2′,3′-dimethoxyphenyl)benzothioazole, 4-fluoro-1,2,3-benzoxadiazole, 1,2-benzisoxazole-3-acetic acid gave 3-(2′-benzothiazolyl)-4,5-dimethoxybenzenesulfonyl chloride (**62**)[235] and 4-chlorosulfonyl-7-fluoro-2-benzoxadiazole (**63**).[236]



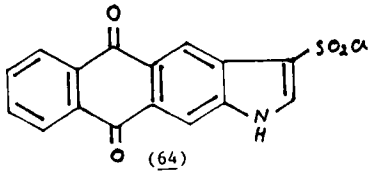
(62)



(63)

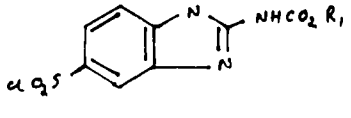
Preparation of the N-chlorosulfonamide derivative of cross-linked polystyrene made by amidation of chlorosulfonated polystryene,[236a] is useful in decreasing the COD of water. The preparation of polymerizable acrylamides containing sulphate groups have also been reported.[236b]

Treatment of naptho[2,3-*f*]indole-5,10-dione with chlorosulfonic acid in dioxane containing sodium sulphate gave the sulfonyl chloride[237] (**64**) (63%).



(64)

Treatment of a range of benzimidazol-2-ylcarbamates (R_1 = C_{1-4} alkyl) with chlorosulfonic acid at 40°C gave the 5-sulfonyl chloride[237a] (**65**).



(65)

2.10 *Miscellaneous*

2.10.1 *Further Observations*

2-(Perhaloalkyl)anilines, (up to C_6 and 13 halo substituents) were converted into the 3,5-disulfonyl chlorides,[238] whereas (2-halo-1-methyl)ethylbenzenes (Cl, Br, I) underwent 4-substitution.[238a]

The influence of the position of substitution on the reaction rate is illustrated by substituted ethyl 2-phenoxyacetates.[239] For the series studied, it was observed that the rates of substitution decreased in the order 2—Cl > 3—Cl > 4—Cl > 2,4—$(Cl)_2$ > 2,5—$(Cl)_2$.

Ferrocene has been successfully converted into the monosulfonyl chloride using a mixture of chlorosulfonic acid and phosphorus trichloride.[240].

Tetraphenoxysilane gave $(ClSO_2C_6H_4O)_{4-n}SiCl_n$ (n = 0, 1, 2, 3) which on reduction with zinc yielded 4-hydroxythiophenol.[241]

Treatment of aryl isocyanates gave sulfanilic acids.[242,243]

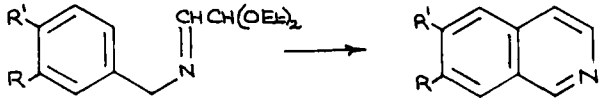
Chlorosulfonic acid was used in the formation of isoquinoline derivatives by the cyclisation of 3,4-dimethoxybenzylideneaminoacetal.[244] Cyclic phenylsulfonium salts, useful for improving the water resistance of carboxylated polymers, were prepared by cyclisation of hydroxyalkylaryl sulfides using chlorosulfonic acid.[245]

Azobenzene by prolonged heating with a large excess of chlorosulfonic acid afforded the 4,4′-disulfonyl chloride in excellent yield.[246] The comparatively drastic conditions required are probably due to initial protonation of the azido group in the strongly acid medium.

Diphenyl sulphone with chlorosulfonic acid (8 equivalents, 140°C, 4 hours) gave the 3,3′-disulfonyl chloride (77%).[111]

2.10.2 *Other Applications of Chlorosulfonic Acid*

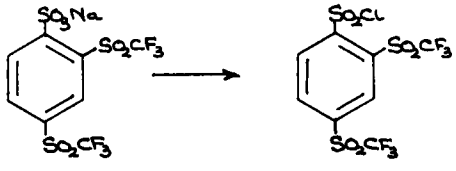
Chlorosulfonic acid was used as a cyclising agent in the conversion of benzylimino acetals (**66**) into isoquinolines:[247]



(66; R,R^1=H; MeO; MeO,H; H,Me)

In the alkylation of benzene,[248] toluene,[249] ethylbenzene[248] and halobenzenes[249] (X = F, Cl, Br, I); ethylbenzene with ethylene, propylene and but-2-ene, it proved to be a suitable catalyst. Polyalkylation was reduced and *p*-substitution increased.

Chlorosulfonic acid acts as a chlorinating agent under homolytic conditions in the conversion of nitrobenzene into pentachloronitrobenzene,[250,251] in the presence of iodine. Chlorination under heterocyclic conditions is illustrated by the following reaction:[252]



In the homolytic bromination of disubstituted benzenes[253] and the conversion of biphenyl into octabromobiphenyl,[254] chlorosulfonic acid was used as solvent.

It has been used both as an oxygenating and deoxygenating reagent; thus, 1,4-bis(trichloromethyl)benzene was converted into benzene-1,4-dicarboxylic acid[255]—the formation of the 2,5-dichloro derivative has also been reported.[256] Iodoazoxybenzene was transformed into iodoazobenzene.[257]

Examples are reported[256,258,259] of its use as a sulfating reagent.

The α-chlorination of aromatic acids of the type $Ar(CH_2)_nCO_2H$ ($n > 1$) can be mediated by chlorosulfonic acid in the presence of chlorine and oxygen.[260]

Chlorosulfonic acid functions as a chlorinating agent at elevated temperatures,[261] e.g., 1,2,4,5-tetrachlorobenzene by prolonged boiling with the reagent (165°C) yielded hexachlorobenzene.[262]

In the presence of iodine, chlorosulfonic acid has been used to chlorinate a number of aryl halides under mild conditions; thus under the optimum conditions (5 equivalents $ClSO_3H$, 2.5 equivalents of iodine), *p*-dichlorobenzene afforded hexachlorobenzene (82% yield). A mechanism for the chlorination reaction has been proposed involving both homolytic and heterolytic stages.[89] Aromatic iodo compounds behave abnormally with chlorosulfonic acid and generally yield chlorinated products, but not sulfonyl chlorides. Iodobenzene with the reagent (3 equivalents) at 60–80°C (3 hours) gave 4,4′-diododiphenylsulfone (53%).

3. CONCLUSIONS

In the period covered by this review, although the types of substrates studied are limited, a considerable number of investigations have been carried out. Chlorosulfonic acid is a versatile reagent and the experimental conditions can be modified appropriately depending upon the substrate. The sulfonyl chlorides which have been prepared are good synthetic intermediates which provide a wide range of useful derivatives by treatment with nucleophilic reagents.

There is no doubt that considerable scope exists for further work. Many other substrates remain to be studied and in several instances previous investigations could be extended, particularly where the optimum experimental conditions for the reactions have not been precisely determined. In addition, further work to define the mechanistic features of chlorosulfonation reactions would be most welcome.

ACKNOWLEDGEMENTS

Thanks are due to Roger Hancock of ICI Chemical Products for suggesting this review and providing the computer search. Thanks also to Lesley Crawshaw of the Polytechnic library and Jane Fordham for her expert typing of the review.

REFERENCES

1. C. M. Suter, *The Organic Chemistry of Sulfur*, Wiley, New York and London, 1944.
2. C. M. Suter and A. W. Weston, *Organic Reactions*, III, p. 141 (1946).
3. E. E. Gilbert, *Chem. Reviews*, **62**, p. 549 (1962).

4. E. E. Gilbert, *Sulfonation and Related Reactions*, Wiley, New York, 1965.
5. D. R. Hogg, Arenesulphonic Acids in Rodd's *Chemistry of Carbon Compounds*, Vol. III, pt A, p. 441, Elsevier, Amsterdam, 1971.
6. H. Cerfontain, *Mechanistic Aspects in Aromatic Sulfonation and Desulfonation*, Interscience Publishers, 1968.
7. K. K. Anderson, *Sulphonic Acids and their Derivatives*, in *Comprehensive Organic Chemistry*, (Eds. D. H. R. Barton and W. Ollis), Vol. 3, p. 331, Elsevier, Amsterdam 1982.
8. G. C. Barrett, in *Organic Compounds of Sulphur, Selenium and Tellurium*, (Ed. D. H. Reid), 1970, Vol. 1, Chapt. 2; 1973, Vol. 2, Chapt. 1; 1975, Vol. 3, Chapt. 1, The Chemical Society, London.
9. Ullmann's Encyclopedia of Industrial Chemistry, Vol. A7, p. 17, VCH (1986).
10. Houben-Weyl, 4th ed., Vol. 9, p. 510, 572, Georg Thieme, Stuttgart, 1955.
11. J. March, *Advanced Organic Chemistry*, 3rd ed., Wiley, New York, 1985, p. 473.
11a. B. Yu. Yasnitskii, *Zhur. Obshch. Khim.*, **23**, 107 (1953); C.A., **48**, 12689b.
12. S. M. Chizhik and B. V. Passet, *Zhur. Org. Khim.*, **11**(8), 1649 (1975); C.A., **83**, 177739n.
12a. A. A. Spryskov and Y. L. Kuz'mina, *J. Gen. Chem.*, USSR, **28**, 184 (1958).
13. A. Rieche and W. Fisher, *Angew. Chem.*, **69**, 482 (1957); C.A., **53**, 18898f.
14. V. O. Lukashevich, *Doklady Akad. Nauk. USSR*, **112**, 872 (1957); C.A., **51**, 14591g.
15. F. Cavagna, T. Grewer, O. Jaenicke and H. Zeininger, *Chem. Ing. Tech.*, **50**(1), 51 (1978); C.A., **88**, 111158u.
16. A. Swinarski, A. Grodzicki and J. Glowinska, *Przem. Chem.*, **52**(8), 553 (1973) (Pol); C.A., **80**, 59618n.
17. L. I. Levina, S. N. Patrakova and D. A. Patruskev, *J. Gen. Chem.*, USSR, **28**, 2464 (1958); C.A., **53**, 3120c.
18. V. V. Kozlov, T. I. Vol'fson, N. A. Kozlova and G. S. Tubyarskaya, *J. Gen. Chem.*, USSR, **32**, 3373 (1962); C.A., **58**, 11289d.
19. A. Spryskov and B. I. Karavaev, *Zhur. Obshch. Khim.*, **22**, 661 (1952); C.A., **47**, 8709c.
20. A. A. Spryskov and B. G. Gnedin, *Izv. Vysshikh Uehebn. Zavedenii. Khim. i. Khim. Tekhnol.*, **7**(6), 935 (1964); C.A., **62**, 14440f.
21. N. I. Rudakova and B. G. Gnedin, *Tr. Ivanov. Khim-Tekhnol. In-ta.*, **19**, 77 (1976); C.A., **86**, 139017e.
22. B. G. Gnedin, S. N. Ivanov, N. I. Rudakova and A. A. Spryskov, *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.*, **18**(7), 1039 (1975); C.A., **83**, 177735h.
23. V. I. Koshelev and S. V. Borodaev., *Zhur. Prikl. Khim.*, **53**(10), 2298 (1980); C.A., **94**, 64784g.
24. R. N. Khelevin, *Zhur. Org. Khim.*, **23**(9), 1925 (1987); C.A., **108**, 166776f.
25. V. A. Pal'm, *Doklady Akad. Nauk SSSR*, **108**, 487 (1956); C.A., **51**, 1066a.
26. A. Braendstroem, G. Strandlund and P. O. Langerstroem, *Acta Chem. Scand.*, Ser B, **B34**(7) 467 (1980); C.A., **94**, 120495c.
27. B. G. Gnedin and N. I. Rudakova, *Izv. Vyssh. Ucheb. Zaved., Khim. Khim. Tekhnol.*, **15**(5), 716 (1972); C.A.,**77**, 87401t.
27a. B. G. Gnedin and N. I. Rudakova, *Izv. Vyssh. Zaved., Khim. Khim. Tekhnol.*, **17**(12), 1820 (1974); C.A., **82**, 97324n.
28. R. B. Wagner and H. D. Zook, *Synthetic Organic Chemistry*, Wiley, New York, 1965, p. 822.
29. M. R. F. Ashwith, *The Determination of Sulphur Containing Groups*, Academic Press, London and New York, 1972, p. 51.
30. S. D. Ross, M. Finkelstein and F. S. Dunkl, *J. Org. Chem.*, **39**, 134 (1974).
31. M. E. Aberlin and C. A. Burton, *J. Org. Chem.*, **35**, 1825 (1970).
31a. M. L. Tarpet and A. N. Hambly, *Aust. J. Chem.*, **24**, 703 (1971).
31b. S. E. Creasey and R. D. Guthrie, *Chem. Comn.*, 801 (1971).
32. E. Ciuffarin and L. Senatore, *Tetrahedron Letters*, 1635 (1974).
33. R. V. Vizgent, I. M. Tuchapskii and Y. G. Skrypnik, *Reakts. sposobn. org. Soedin*, **11**, 21 (1974); C.A., **82**, 42576r.
34. J. L. Kice and E. A. Lunney, *J. Org. Chem.*, **40**, 2125 (1975).
35. R. J. Cremlyn, P. H. Gore, A. O. O. Ikejiani and D. F. C. Morris, *J. Chem. Research*, 194 (1982).
36. L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, Methuen, London, 1958.
37. L. J. Bellamy, *Advances in Infrared Group Frequencies*, Methuen, London, 1968.
38. L. J. Bellamy, *The Infrared Spectra of Organic Sulfur Compounds*, in *Organic Sulfur Compounds*, (Ed. N. Karasch) Vol. 1, p. 47, Pergamon Press, New York and Oxford, 1961.
39. R. J. Cremlyn and D. N. Waters, *J. Chem. Soc.*, 6243 (1964).
40. Private communication from P. B. Sattur, Regional Research Laboratory, Hyderabad, 500 007, India.
41. H. U. Blank, *Ger. Offen.*, 2,721,429 (1978); C.A., **90**, 87032s.

42. W. Schenk, H. U. Blank, F. Hugeduzn and W. Evertz, *Ger. Offen.*, 2,743,540 (1979); C.A., **91**, 391286.
43. T. Pfister, W. Schenk and H. U. Blank, *Ger. Offen.*, 2,743,541 (1979); C.A., **91**, 39129c.
44. B. G. Gnedin, N. I. Rudakova and A. A. Sprykov, *Izv. Vyssh. Ucheb. Zaved., Khim. Khim. Tekhnol.*, **14**(10), 1530 (1971); C.A., **76**, 24842w.
45. L. I. Levina, S. N. Patrakova and D. A. Patrushev, *Zhur. Obshch. Khim.*, **28**, 2427 (1958); C.A., **53**, 3120c.
46. M. Badzysnki, R. Bardyga, M. Domoradzki, E. Sobczak and W. Korpal, *Pol.*, **95**, 319 (1978); C.A., **90**, 103635y.
47. Henkel and Cie. G. m.b.H., *Ger. Offen.*, 840,238 (1952); C.A., **47**, 3876f.
48. H. U. Blank, *Ger. Offen.*, 2,635,281 (1978); C.A., **88**, 152242k.
49. H. U. Blank, *Ger. Offen.*, 2,635,279 (1978); C.A., **88**, 152243m.
50. R. Aurnhammer and W. Ludwig, *Ger. Offen.*, 2,135,087 (1973); C.A., **78**, 97324e.
51. P. Bergmann, *Z. Chem.*, **11**(11), 423 (1971); C.A., **77**, 101021c.
52. G. H. Birum and R. F. Jansen, *US*, 4,713,489 (19897); C.A., **109**, 6216v.
53. A. A. Spryskov and B. G. Gnedin, *Zhur. Obshch. Khim.*, **33**(4), 1082 (1963); C.A., **59**, 9748b.
54. A. B. Kulkarri and R. C. Shah, *J. Indian Chem. Soc., Ind. and News Ed.*, **18**, 22 (1955); C.A., **50**, 7735h.
55. J. Ofem and G. Schaffen, *US*, 3,686,300 (1972); C.A., **77**, 1396121m.
56. I. Ognyanov and A. Zayorora, *Zhur. Priklad. Khim.*, **29**, 1299 (1956); C.A., **51**, 1879e.
57. Korea Institute of Science and Technology, *Japan Kokai*, JP 58,162,570 [83, 162, 570] (1983); C.A., **100**, 51268j.
58. R. Aurnhammer and R. Koening, *Ger. Offen.*, 1,172,258 (1964); C.A., **61**, 6961d.
59. J. F. Batchelor and J. H. Gorvin, *Ger. Offen.*, 2,344,799 (1974); C.A., **80**, 133258p.
60. H. F. Hodson and J. F. Batchelor, *US*, 4,103,015 (1978); C.A., **90**, 22816f.
61. E. N. Krylor and E. N. Odintsova, *Zhur. Org. Khim.*, **18**(9), 1936 (1982); C.A., **97**, 215203g.
62. R. J. Lee, *US*, 3,772,373 (1973); C.A., **80**, 26946q.
63. Purdue Research Foundation, *Neth. Appl.*, 7,413,366 (1976); C.A., **85**, 186819g.
64. M. J. Virnig, *US*, 4,100,163 (1978); C.A., **89**, 215238g.
65. Societe anon. des produits Purs, de Courcelles, *Belg.*, 495,433 (1950); C.A., **49**, 4018g.
66. J. Saito, T. Tamura, Y. Kurahashi, S. Uzawa, N. Matsumoto and N. Yumagrchi, *Eur. Pat. Appl. EP*, 173918 (1986); C.A., **105**, 56341r.
67. G. P. Chudinova, B. G. Gnedin, A. A. Vinogradov, M. I. Zaitseva and T. V. Nikolaeva, *Izv. Vyssh. Ucheb. Zaved., Khim. Khim. Tekhnol.*, **20**(1), 54 (1977); C.A., **86**, 189389y.
68. C. M. Suter, *The Organic Chemistry of Sulfur*, Wiley, New York and London, 1944, p. 212.
69. J. Zaloudek, J. Valik and J. Matoulek, *Czech.*, 143,091 (1971); C.A., **77**, 75071x.
70. B. G. Gnedin, A. A. Spryskov and E. G. Lokshina, *Izv. Vyssh. Ucheb., Khim. Khim. Tekhnol.*, **10**(7), 774 (1967); C.A., **67**, 116736g.
71. A. A. Spryskov, *Zhur. Obshch. Khim. (J. Gen. Chem.)*, **21**, 2022 (1951); C. A., **46**, 6608d.
72. V. V. Kozlov, T. I. Vol'fson, N. A. Kozlova and G. S. Tubyanskaya, *Zhur. Obshch. Khim.*, **32**, 3440 (1962); C.A., **58**, 11289d.
73. J. O. Morley, *J. Chem. Soc., Perkin Trans. 2*, **13**, 1560 (1976).
74. J. O. Morley, *J. Chem. Soc., Perkin Trans. 2*, **13**, 1554 (1976).
75. J. Pollak, M. Heinsberg-Krass, E. Katschen and O. Lustig, *Mh. Chem.*, **55**, 358 (1930); C.A., **24**, 4005.
76. J. P. Bassin, Hatfield Polytechnic, Private communication (1989).
77. J. M. Lynch, PhD thesis, CNAA, Hatfield Polytechnic, 1989.
77a. A. Chrzaszcaewska and T. Machlanski, *Lodz Tow. Nauk, Wydz. III, Acta Chem.*, **11**, 143 (1966); C.A., **66**, 37689.
77b. P. C. Dutta and D. Mandal, *J. Indian Chem. Soc.*, **33**, 410 (1956); C. A., **51**, 724.
78. G. L. Afraimovich, S. M. Danov, V. A. Dozorov, B. V. Danova, S. V. Makarov and G. A. Malova, *Osnovn. Organ. Sintez i Neftekhimiya*, **9**, 122 (1978). From *Zh. Khim.* 1979. Abstr. No. IN203; C.A., **90**, 151255w.
79. Mitsui Toatsu Chemicals, Inc., *Japan Kodai*, JP 58,49,360 [83,49,360] (1983); C.A., **99**, 22122n.
80. Mitsui Toatsu Chemicals, Inc., Jpn., *Japan Kokai*, JP 58,38,253 [83,382,53] (1983); C.A., **99**, 38224h.
81. M. Kato and S. Watanuki, *Japan Kokai*, 75,100,035 (1975); C.A., **84**, 16958p.
82. D. Taylor and G. C. Vincent, *J. Chem. Soc.*, 3218 (1952).
83. R. Nodzu, T. Osaka, H. Kitano and K. Fukui, *Nippon, Kagaku Zasshi*, **76**, 775 (1951); C.A., **51**, 17793.
84. T. Papenfuhs, *Ger. Offen.*, DE 3302647 (1984); C.A., **102**, 24, 282m.
85. G. Schaefer and P. Neumann, *Ger. Offen.*, DE 3704932 (1987); C.A., **109**, 210705d.
86. A. E. Erickson, *US*, 2,860,168 (1958); C.A., **53**, 9152f.

87. Konishi Kagaku Kogyo Co., Ltd., *Japan Kokai Koho*, JP 58,206,553 [83,206,553] (1983); C.A., **100**, 156364r.
88. Konishi Kagaku Kogyo Co., Ltd., *Japan Kokai*, JP 58,206,551 [83,206,551] (1983); C.A., **100**, 156363q.
89. R. J. Cremlyn and T. Cronje, *Phosphorus and Sulfur*, **6**, 495 (1979).
90. V. J. Leslie and J. B. Rose, *US*, 3,830,781 (1974); C.A., **82**, 171675w.
91. V. J. Leslie and J. B. Rose, *US*, 3,917,715 (1975); C.A., **84**, 31898n.
92. A. A. Spryskov and Yu. L. Kuzmina, *Zhur. Obshch. Khim.*, **21**, 1887 (1951); C.A., **46**, 6608d.
93. S. Hussain, P. A., Swaroop, M. Kifayahulla, R. Narsimha and R. Vaidyeswaran, *Indian IN* 150,341 (1982); C.A., **99**, 139483x.
94. W. V. Farrar, *J. Chem. Soc.*, 3063 (1960).
95. I. R. A. Bernard, G. E. Chivers, R. J. Cremlyn and R. G. Mootoosamy, *Aust. J. Chem.*, **27**, 171 (1974).
95a. G. E. Chivers, R. J. Cremlyn and R. A. Martin, *Chemistry and Industry*, 130 (1975).
96. G. W. Seymoor, V. S. Salvin and W. D. Jones, *US*, 2,511,547 (1950); C.A., **45**, 653a.
97. W. Brodt and T. Papenfuhs, *Ger. Offen.*, DE, 3,618,219 (1987); C.A., **108**, 133408j.
98. E. V. Zakharov, V. I. Zetkin, M. Ya. Fishkis and V. S. Nakhshynov, *Zhur. Organ. Khim.*, **1**(10), 1866 (1965); C.A., **65**, 3394h.
99. Y. Fukuraya, T. Asano and M. Una, *Japan Kokai*, JP 63,104,952 [88,104,952] (1988); C.A., **110**, 7850a.
100. K. M. Roizen and I. M. Bilik, *Metody Poluch. Khim. Reaktiv. Prep.*, **20**, 118 (1969); Zhur. Khim., 1971, Abstr. No. 2Zh 248; C.A., **76**, 59123q.
101. L. A. Carpino and B. Cohen, *US*, 4575541 (1986); C.A., **105**, 7069q.
102. R. J. Cremlyn and R. Hornby, *J. Chem. Soc. (C)*, 1341 (1969).
103. P. Jacob III, G. Anderson III, C. K. Meshul, A. T. Shulgin and N. Jr. Castagnoli, *J. Med. Chem.*, **20**(10), 1235 (1977).
104. M. Fujine, M. Wakimasu and C. Kihada, *J. Chem. Soc. Chem. Commun.*, **8**, 445 (1982).
105. M. Fujino, M. Wakimasu and C. Kihada, *Chem. Pharm. Bull.*, **29**, 2825 (1981); C.A., **96**, 85948v.
106. R. J. Thomas, *US*, 3,845,015 (1974); C.A., **82**, 112647r.
107. H. Motokawa, K. Okusa, K. Tsuji and E. Mitsui, *Japan. Kokai*, 7,691,230 (1976); C.A., **85**, 159675a.
108. E. Ehama, Y. Hirose, T. Tsukuru, T. Tomimoto and M. Taniguchi, *Japan Kokai*, JP 7,445,034 (1974); C.A., **81**, 105009k.
109. T. Ehama, Y. Hirose, T. Tsukuru, T. Tomimoto and M. Taniguchi, *Japan Kokai*, JP 7,445,035 (1974); C.A., **81**, 105010d.
110. T. Ehama, Y. Hirose, T. Tsukuru, T. Tomimoto and M. Taniguchi, *Japan Kokai*, JP 7,436,652 (1974); C. A., **81**, 105012f.
111. R. J. Cremlyn, S. Montgomery, Y. Ng and D. Simpson, *Phosphorus and Sulfur*, **12**(3), 341 (1982).
112. R. J. Cremlyn, T. Cronje and K. Goulding, *Aust. J. Chem.*, **32**, 445 (1979).
113. A. A. Spryskov and B. G. Gnedin, *Zhur. Organ. Khim.*, **1**(11), 1946 (1965); C.A., **64**, 9534d.
114. A. A. Spryskov and B. G. Gnedin, *Izv. Vysshikh Uchebn. Zaved. Khim. i. Khim. Tekhnol.*, **7**(6), 935 (1964); C.A., **62**, 14440.
115. R. J. Cremlyn and T. Cronje, *Phosphorus and Sulfur*, **6**, 413 (1979).
116. American Cyanamid Co., *Belg.*, **845**, 158 (1977); C.A., **88**, 46391y.
117. T. A. Sullivan and V. G. Witterhalt, *US*, 4,556,733 (1985); C.A., **104**, 148503c.
118. H. J. Millen and J. L. Sandeno, *US*, 3,658,965 (1972); C.A., **77**, 48059t.
119. S. J. Esteve, *Span. ES*, 512,680 (1983); C.A., **99**, 104969h.
120. I. G. Turynachik, E. K. Blinova, E. V. Lebeder and B. S. Shaporal, *Sb. Tu. Vses. Ob'edin Neftekhim.*, **11**, 88 (1976); *Zh., Kihm.*, Abstr. No. 9P161 (1977); C.A., **87**, 134268y.
121. T. Higuchi, and T. Nishihata, **US**, 4,470,980 (1981); C.A., **101**, 216440v.
122. U. Lohmann and K. Hartke, *Arch. Pharm.* (Weinheim. Ger), **317**(4), 313 (1984); C.A., **101**, 54671s.
123. G. Doucet-Bundry, *C. R. Acad. Sci. Paris Serc. C.*, **267**(17), 1057, (1968); C.A., **70**, 37346p.
124. E. J. Chogoe Jr., R. L. Smith and G. E. Stokker, *Ger. Offen.*, 2723 635 (1977); C.A., **88**, 89358k.
125. R. Iden, *Ger. Offen.*, DE 3628090 (1988); C.A., **109**, 8023g.
126. A. M. Leone, P. L. Francis and B. McKenzie-Gray, *J. Pineal Res.*, **5**(4), 367 (1988); C.A., **109**, 231493y.
127. C. M. Suter, *The Organic Chemistry of Sulfur*, Wiley, New York and London, 1944, p 224.
128. Von E. Profft and E. Geilser, *J. Prakt. Chem.*, **9**, 136 (1959).
129. C. Mizon, GRSC Project Thesis, Hatfield Polytechnic (1983).
130. T. Davies, M. A. Weaver and R. R. Giles, *US*, 4,403,092 (1983), C.A., **99**, 195567q.

131. Yamanouchi Pharmaceutical Co., Ltd., *Japan Kokai*, JP 57,136,561 [82,136,561] (1982); C.A., **98**, 16433c.
132. R. J. Cremlyn and L. Wu, *Phosphorus and Sulfur*, **39**, 165 (1988).
133. R. J. Cremlyn, O. O. Shode and F. J. Swinbourne, *J. Chem. Soc., Perkin Trans. I*, 2181 (1983).
134. D. M. Duckworth, *Eur. Pat. Appl.*, EP 91, 749 (1983); C.A., **100**, 138735h.
135. R. J. Cremlyn, F. J. Swinbourne and E. Mookerjee, *Indian J. Chem.*, **25B**, 562 (1986).
136. R. J. Cremlyn, F. J. Swinbourne and O. O. Shode, *J. Chinese Chem. Soc.*, **31**, 383 (1984).
137. R. J. Cremlyn, F. J. Swinbourne, O. O. Shode and J. Lynch, *J. Heterocyclic Chem.*, **24**, 117 (1987).
138. R. J. Cremlyn, F. J. Swinbourne, P. Fitzgerald, N. Godfrey, P. Hedges, J. Lapthorne and C. Mizon, *Indian J. Chem.*, **23B**, 962 (1984).
139. R. J. Cremlyn, F. J. Swinbourne and L. Goodman, *Phosphorus and Sulfur*, **28**, 395 (1986).
140. J. L. Work and J. E. Herweh, *J. Poly. Sci.*, pt. A-1, **6**, 2028 (1968).
140a. A. W. Weston and C. M. Suter, *J. Am. Chem. Soc.*, **61**, 389 (1939).
141. G. Nakai, M. Abe and H. Takagaki, *Japan. Kokai*, JP 63234059 [87234059] (1987); C.A., **109**, 54493a.
142. R. E. Philion, *Ger. Offen.*, 2728641 (1978); C.A., **90**, 137468m.
143. R. F. Meyer, *J. Heterocyclic Chem.*, **3**(2), 174 (1966).
144. R. J. Cremlyn, S. Jethwa, G. Joiner and D. White, *Phosphorus and Sulfur*, **36**, 99 (1988).
145. R. J. Cremlyn, M. Bartlett and L. Wu, *Phosphorus and Sulfur*, **39**, 173 (1988).
146. R. J. Cremlyn, M. Bartlett and J. Lloyd, *Phosphorus and Sulfur*, **40**, 91 (1988).
146a. R. J. Cremlyn and S. Graham, Hatfield Polytechnic, unpublished observations (1988).
147. Sumitomo Chemical Co., Ltd., *Japan Kokai*, JP 8254162(1982); C.A., **47**, 127301g.
148. C. M. Suter, *The Organic Chemistry of Sulfur*, Wiley, New York and London, 1944, p. 225.
149. R. J. Cremlyn, *J. Chem. Soc. (C)*, 11(1968).
150. M. S. Hadley and E. A. Watts, *Eur. Pat. App.* EP 4270S (1981); C. A., **96**, 163011a.
151. A. M. Islam, I. B. Hannout and M. M. Atwa, *Egypt. J. Chem.*, **17**(5), 689 (1974); C.A., **86**, 171047a.
152. R. J. Cremlyn, F. J. Swinbourne, J. Atherall, L. Courtney, T. Cronje, P. Davis, S. Langston and M. Rogers, *Phosphorus and Sulfur*, **9**, 155 (1980).
153. R. J. Cremlyn, F. J. Swinbourne, S. Plant, D. Saunders and C. Sinderson, *Phosphorus and Sulfur*, **10**(3), 323 (1981).
154. G. B. Jackman, V. Petrow, O. Stephenson and A. Wild, *J. Pharm. Pharmacol.*, **14**, 679 (1962).
155. A. M. El-Naggar, I. M. Ismail, M. R. Zahen and M. H. El-Hakin, *Glas. Hem. Dras. Beograd*, **49**(9), 527 (1984); C.A., **103**, 716737a.
156. R. J. Cremlyn, K. Thandi and R. Wilson, *Indian J. Chem.*, **23B**, 94 (1984).
157. G. R. Brown, J. K. Landquist and D. R. Summers, *J. Chem. Soc., Perkin I*, 633 (1978).
158. Gh. Bohez and C. Onisciu, *Bull. Inst. Politech. Iasi.*, **10**(3–4), 139; C.A., **64**, 635a.
159. R. J. Cremlyn, F. J. Swinbourne and R. Mguni, *Phosphorus and Sulfur*, **8**, 321 (1980).
160. R. J. Cremlyn, O. Obiorah and G. Singh, *Indian J. Chem.*, **25B**, 599 (1986).
161. R. J. Cremlyn and R. W. Pannell, *Aust. J. Chem.*, **31**, 2669 (1978).
162. H. Ahrens and C. Rufer, *Ger. Offen.*, 2153 528 (1973); C.A., **79**, 18755r.
163. C. M. Suter, *The Organic Chemistry of Sulfur*, Wiley, New York and London, 1944, p. 459.
164. S. Smiles and J. Stewart, *Org. Synth. Coll.*, Vol. I, p. 8, Wiley, New York, 1941.
165. B. G. Yasnitskii, *Zhur. Obshch. Khim.*, **26**, 2346 (1956); C.A., **51**, 4985.
166. K. Matsuura, *Japan Kokai*, 7,712,697 (1977); C.A., **86**, 157722k.
167. K. Matsuura, H. Ikeda, *Japan Kakai*, 7,712,146 (1977); C.A., **87**, 39114m.
168. M. Badzynski, R. Bardyga, M. Domoradzk, W. Korapl, and E. Sobczak, *Pol.*, 98,199 (1978); C.A., **91**, 140557r.
168a. R. J. Cremlyn, F. J. Swinbourne, P. Devlukia and O. O. Shode, *Indian J. Chem.*, **23B**, 249 (1984).
168b. Handbook of Chemistry and Physics, CRC Press Inc. Boca Raton, Florida, F186 (1986).
169. R. J. Cremlyn and O. O. Shode, *J. Chem. Soc. Pakistan*, **8**, 409 (1986).
170. Wakunaga Pharmaceutical Co., Ltd., *Japan Kokai*, JP 58,162,847 [83,152,847] (1983); C.A., **100**, 85428b.
171. R. J. Cremlyn, *J. Chem. Soc. (C)*, 77 (1967).
172. A. Badawi, El-Bayoaki and V. R. Zakuria, *Orient J. Chem.*, **1**(2), 78 (1985); C.A., **104**, 3315.
173. W. Raunder, R. Fischer, H. P. Korthals, H. Laqua, E. Schlenz, D. Merkel and L. Zoelch, *Gen*(Egypt) DD, 222304 (1985); C.A., **104**, 109213p.
174. R. J. Cremlyn, K. Burrell, K. Fish, I. Hough and D. Mason, *Phosphorus and Sulfur*, **12**(2), 197 (1982).
175. W. L. F. Armarego, *Aust. J. Chem.*, **25**(1), 221 (1972).
176. R. J. Cremlyn, *J. Chem. Soc.*, 1329 (1963).

177. L. N. Goldyrev and I. Ya. Postovskii, *J. Appl. Chem.* (USSR), **11**, 316 (1938) (see ref. 172 p. 1331).
178. R. J. Cremlyn, F. J. Swinbourne, R. Honeyman, D. Nash, O. O. Shode and A. Patel, *Indian J. Chem.*, **22B**, 1029 (1983).
179. R. J. Cremlyn, F. J. Swinbourne, J. G. Bloy, K. Pathak and O. O. Shode, *J. Chem. Soc. Pakistan*, **7**, 111 (1985).
180. R. J. Cremlyn, S. D. Lewis and R. J. Nunes, *J. Chem. Soc. Pakistan*, **8**(4), 491 (1986).
181. R. J. Cremlyn, F. J. Swinbourne and O. O. Shode, *Pakistan J. Chem.*, **8**(3), 323 (1986).
182. R. J. Cremlyn, D. Leonard and R. Motwani, *J. Chem. Soc., Perkin I*, 500 (1973).
183. G. E. Chivers, R. J. Cremlyn, R. Guy, R. Honeyman and P. Reynolds, *Aust. J. Chem.*, **28**, 413 (1975).
184. R. J. Cremlyn and R. A. Martin, *Aust. J. Chem.*, **27**, 435 (1974).
185. N. Akhtar, N. V. Badami, R. J. Cremlyn and K. J. Goulding, *Phosphorus and Sulfur*, **3**, 293 (1977).
186. N. V. Badami, R. J. Cremlyn and F. J. Swinbourne, *Aust. J. Chem.*, **30**, 1793 (1977).
187. R. J. Cremlyn and R. Nunes, *Phosphorus and Sulfur*, **31**, 245 (1987).
188. A. D. Biba, A. A. Rositskii and A. S. Bespalyi, *USSR* 418472 (1974); C.A., **80**, 133070w.
189. R. J. Cremlyn, F. J. Swinbourne and R. J. Nunes, *Quimica Nova*, **7**(2), 118 (1984).
190. R. J. Cremlyn, F. J. Swinbourne and R. Nunes, *Phosphorus and Sulfur*, 65 (1987).
191. M. M. Kremler, N. E. Kullchitskaya, A. D. Biba and V. D. Romanenko, *Ikr. Khim. Zh.*, **37**(9), 924(1971); C.A., **77**, 19296n.
192. R. J. Cremlyn and R. Nunes, *Gazz. Chim. Ital.*, **117**, 183 (1987).
193. R. J. Cremlyn, F. J. Swinbourne and R. J. Nunes, *Quimica Nova*, 61(1985).
194. W. Logemann, P. Giraldi and S. Galimbenhi, *Ann. Chem.*, **623**, 157 (1959).
195. J. H. Short and U. Biermacher, *J. Am. Chem. Soc.*, **82**, 1135 (1960).
196. H. L. Yale, K. Losee and J. Bernstein, *J. Am. Chem. Soc.*, **82**, 2042 (1960).
197. K. Inukai and K. Hosokawa, *J. Chem. Soc. Japan*, **66**, 1402 (1963) (Ref. 6, p. 108).
198. S. R. Tamat and D. E. Moore, *J. Pharm. Sci.*, **72**(2), 180 (1983).
199. B. I. Kissin, G. A. Timokhin and N. N. Faeshkina, *USSR*, 633,858, (1978); C.A., **90**, 87035v.
200. K. Dziewonski and M. Russocki, *Bull. Intern. Acad. Polanaisc A*, 1929 (1931); C.A., **25**, 1503.
201. R. T. Thampi, B. H. Iyer and P. C. Guhi, *Science and Culture*, **11**, 285 (1946).
202. K. Carpenter, B. J. Heywood, E. W. Parnell, J. Metivier and R. Boesch, *US*, 3,823,008 (1974); C.A., **83**, 92404z.
203. G. F. Grillot and R. N. Ciccardi, *J. Org. Chem.*, **26**, 1665 (1961).
204. Y. Chen, *Huaxue Shijie*, **29**(10), 444 (1988); C.A., **110**, 136957q.
205. G. Booth, *Synth. Commun.*, **13**(8), 659 (1983); C.A., **99**, 194541q.
206. T. E. Willian, V. Van Germent and B. W. William, *J. Org. Chem.*, **43**(1), 101 (1978).
207. L. H. Edwards, **US**, 3996243 (1976); C.A., **86**, 106359q.
208. F. Kimura, T. Hoga, K. Maeda, K. Hayashi, M. Ikeguchi and T. Yoshida, *Braz. Pedido*, PI BR 8602, 648 (1987); C.A., **108**, 37636m.
209. L. H. Edwards, *US*, 3991081 (1976); C.A., **86**, 72424q.
210. E. Maccarone, G. Musumarra and G. A. Tomaselli, *Annali di*, **63**, 861 (1973); C.A., **83**, 8686n.
211. R. L. Ellis, *US*, 3932444 (1976); C.A., **84**, 136515p.
212. J. J. Baldwin and F. C. Novello, *US*, 4110456 (1978); C.A., **90**, 87462g.
213. P. E. Cross, R. P. Dickinson, M. J. Parry and M. J. Randall, *J. Med. Chem.*, **28**, 1427 (1985).
214. R. J. Cremlyn, F. J. Swinbourne and O. O. Shode, *J. Heterocyclic Chem.*, **22**, 1211 (1985).
215. Y. Morisawa, M. Katoaka, K. Kihano and K. Kusano, *Japan Kokai*, 78,21,171 (1978); C.A., **89**, 6238t.
216. H. Menkle, A. Mueller, G. Hamprecht and G. Reissenweber, *Ger. Offen.*, DE 3428837 (1986); C.A., **105**, 78675e.
217. N. Stabile, R. Motta and G. Gasso, *Eur. Pat. App.*, EP 70,467 (1983); C.A., **99**, 5362y.
218. H. Harada, Y. Mahsushta, M. Nakamura and Y. Yonehani, *Eur. Pat. App.* EP. 173899 (1986); C.A., **105**, 114890g.
219. E. J. Glamkowski and P. A. Reitano, *J. Med. Chem.*, **22**(1), 106 (1979).
220. T. I. Prosheahkina, V. I. Shishkina and G. M. Norikova, *USSR*, 270, 729 (1970): C.A., **73**, 98795t.
221. V. G. Sayapin, A. M. Simonov and V. V. Kuzmenko, *Khim. Geterotsikl. Soedin*, **5**, 681 (1970); C.A., **73**, 45409p.
222. N. E. Makismova and V. I. Shishkina, *Khimiya i Tekhanl. Krasheniya Sinteza Krasitelei i Polimer Materialov Iranovo.*, 26, (1981), (Russ.); C.A., **97**, 40299p.
223. G. M. Novikova, V. I. Shishkina and N. T. Igonina, *Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.*, **17**(a), 1360 (1974); C.A., **82**, 72722c.

224. K. Matsumoto, H. Miyazaki, T. Fujii, A. Kagemoto, T. Maeda and M. Nashimoto, *Arzneim. Forsch*, **33**(7), 961(1983); C.A., **99**, 98746q.
225. M. V. Rubtzov and V. M. Fedossova, *J. Gen. Chem.*, (USSR), **14**, 857 (1944).
226. R. J. Cremlyn and S. M. Clowes, *J. Chem. Soc. Pakistan*, **10**(1), 97(1988).
227. F. D. Hamb and J. C. Wilson, *US*, 3902904 (1975); C.A., **84**, 45190n.
228. M. A. Louffy, Abu-Shady, A. Hamed, *Pharmazie*, **32**(4), 240 (1977); C.A., **87**, 68200s.
229. A. Solovena and G. I. Arbuzov, *Zhur. Obshch. Khim.*, **21**, 765 (1951); C.A., **45**, 9524i.
230. A. L. Tachilkin, G. A. Darydova, I. N. Gracheva, I. R. Kovelman and S. I. Kirillova, *USSR, SU* 1074869 (1984); C.A., **100**, 220924c.
231. A. Sturis, V. Purmole, T. I. Dichko, J. Asoks, P. I. Brusilovskii and Yu. A. Bankorskii, *Latr. PSR Zinat. Akad. Vestis, Khim. Ser.*, **2**, 181 (1979); C.A., **91**, 39289e.
232. J. R. Pfisher, I. T. Harrison and J. H. Fried, *US*, 3,989,720 (1976); C.A., **86**, 72443w.
233. J. R. Pfisher, I. T. Harrison and J. H. Fried, *US*, 3,989,721 (1976); C.A., **86**, 7244w.
234. G. F. Holland, *US*, 3894003 (1975); C.A., **83**, 206282r.
235. T. Tanaka, H. Umekawa, M. Saitoh, T. Ishikawa, T. Shin, M. Ito, H. Itoh, Y. Kauamatsu, H. Sugihara and H. Niroysohip, *Mal. Pharmacal.*, **29**(3), 264 (1986); C.A., **104**, 184072v.
236. T. Toshimasa and I. Kazuhino, *Anal. Chem.*, **56**(13), 2461 (1984); C.A., **101**, 160558s.
236a. S. C. Gupta, S. K. Jain, Archna Mehna, N. K. Mathur and C. K. Narang, *J. Polym. Mater.*, **6**(1), 57 (1989); C.A., **111**, 40393x.
236b. H. Nagorski and K. Dahmer, *Ger. Offen.*, DE 3,717,439; C.A., **111**, 58489t.
237. S. L. Vorobera, V. N. Buyanov, I. I. Levina and N. N. Suvorov, *Zh. Vses. Khim. O-va. im. D.I. Mendeleeva*, **34**(1), 129 (1989); C.A., **111**, 173943y.
237a. F. Sperber, C. Huszar, A. Nemeth, E. Somfai and I. Pali, *Ger. Offen.*, DE 3,826,036 (1989); C.A., **111**, 57733f.
238. H. H. Mrozik, *US*, 4001406 (1977); C.A., **86**, 9616j.
238a. R. D. Rossi and D. K. Ray-Chandhuri, *US*, 4510324 (1985); C.A., **103**, 37200m.
239. C. Oniscu and G. Botez, *Bul. Inst. Politech. Iasi, Sect. 2*, **22**(1–2), 73 (1976); C.A., **86**, 71291g.
240. D. W. Slocum and W. Achermann, *Synth. Reac. Inorg. Met-Org. Chem.*, **12**(4), 397 (1982); C.A., **97**, 72525a.
241. S. Higeta and K. Marayama, *Japan Kokai*, JP. 60 17H 762 [85,174,762] (1985); C.A., **104**, 33856c.
242. I. B. Theodore, *J. Am. Chem. Soc.*, **75**, 1405 (1953).
243. B. Gerhard and K. Frich, *Ger. Offen.*, 2238340 (1974); C.A., **80**, 120541a.
244. K. Kido and Y. Watanobe, *Yakugaku Zasshi*, **95**(a), 1038 (1975); C.A., **84**, 43790j.
245. D. L. Schmidt, H. B. Smith, M. J. Hatch and W. E. Broxterman, *Ger. Offen.*, 2,434,594 (1975); C.A., **84**, 5824r.
246. R. J. Cremlyn, *J. Chem. Soc.*, 6235 (1964).
247. K. Kido and Y. Watanobe, *Daiichi Yakka Daigaku Kenkyn Nenpo*, **14**, 1 (1983); C.A., **101**, 38326c.
248. T. Kiersznicki, *Zesz. Nank. Politech. Slask. Chem.*, **76**, 57 (1976); C.A., **86**, 170969v.
249. T. Kiersznicki, *Zesz. Nank. Politech. Slask. Chem.*, **76**, 93, (1976); C.A., **86**, 170974p.
250. M. Umemoto, M. Ura, S. Kosho and H. Hashimoto, *Japan Kokai*, JP62,252,745 (87,252,745)(1987); C.A., **109**, 10991d.
251. V. I. Zetkin, E. V. Zakharov, V. Sh. Gurevich, R. V. Dzhagatspanyan, I. M. Kolesnikov and I. I. Kupriyanov, *Khim. Prom.*, **44**(5), 334 (1968); C.A., **69**, 67023c.
252. S. G. Sheiko, R. V. Vizgent, V. N. Boiko, L. Z. Gandelsman and L. M. Yaqupolskii, *Zhur. Org. Khim.*, **14**(11), 237 (1987); C.A., **90**, 137404n.
253. A. L. Hashem, *J. Appl. Chem. Biotechnol.*, **23**(8), 621 (1973); C.A., **80**, 26872n.
254. H. Fujii and I. Ohro, *Japan Kokai*, 174 11689 (1974); C.A., **82**, 3939s.
255. S. Jiang, Z. Xiang, L. Wang and T. Yao, *Huaxue Shijie*, **24**(1), 8 (1983); C.A., **99**, 104891b.
256. A. Tzikas, *Eur. Pat. Appl.*, EP 36,840 (1981); C.A., **96**, 36888s.
257. J. Yamamoto, H. Kunikaha and M. Omezu, *Nippon Kugaku Kaishi*, **1**, 78(1983); C.A., **98**, 178840k.
258. F. C. Novello, *Ger. Offen.*, 2,313,573 (1972); C.A., **80**, 3559b.
259. F. Garrido, J. Ibanez, E. Gonalons and A. Giraldez, *Eur. J. Med. Chem. Chim. Ther.*, **10**(2), 143 (1975); C.A., **83**, 131401t.
260. Y. Ogata, T. Sugimoto and M. Inuishi, *Org. Synthesis*, Coll. Vol. VI, p. 90, Wiley, New York (1988).
261. M. Ballesher and S. Olivella, *Aromatic and Alkaromatic Chlorocarbons* in *Polychloroaromatic Compounds*, (Ed. H. Suschitzky), Plenum Press, London, 1976.
262. R. J. Cremlyn, G. E. Chivers, T. N. Cronje and R. A. Martin, *Aust. J. Chem.*, **29**, 1573 (1976).