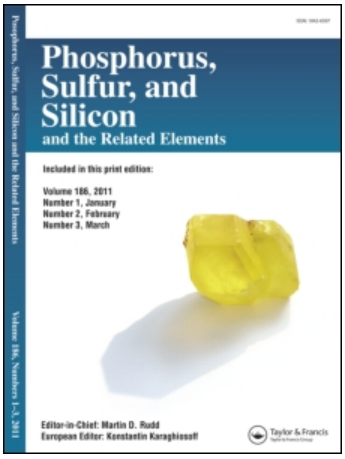

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

STUDIES IN THE HETEROCYCLIC COMPOUNDS V[1]. SOME REACTIONS OF 5-CHLORO-2-THIOPHENESULFONYL DERIVATIVES

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To cite this Article Obafemi, Craig A.(1982) 'STUDIES IN THE HETEROCYCLIC COMPOUNDS V[1]. SOME REACTIONS OF 5-CHLORO-2-THIOPHENESULFONYL DERIVATIVES', Phosphorus, Sulfur, and Silicon and the Related Elements, 13: 1, 119 — 131
To link to this Article: DOI: 10.1080/03086648208078988
URL: http://dx.doi.org/10.1080/03086648208078988

Phosphorus and Sulfur, 1982, Vol. 13, pp. 119–131
0308-664X/82/1301-0119/$06.50/0

STUDIES IN THE HETEROCYCLIC COMPOUNDS V[1]. SOME REACTIONS OF 5-CHLORO-2-THIOPHENESULFONYL DERIVATIVES

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(*Received November 10, 1981*)

The reactions of 5-chloro-2-thiophenesulfonyl chloride are described. Treatment of the sulfonyl chloride with ammonia, hydrazine hydrate, sodium azide, indole and imidazole gave the sulfonamides (**5**), sulfonohydrazide (**4**), sulfonyl azide (**3**), 1-(5-chloro-2-thiophenesulfonyl)indole (**27**) and 1-(5-chloro-2-thiophenesulfonyl)-imidazole (**26**), respectively. The sulfonyl chloride was reacted further with 20 aryl- and cycloalkyl-amines to give the corresponding sulfonamides (**6**)–(**25**). Attempted chlorination of the sulfonyl chloride (**2**) with sulfuryl chloride or bromination of the sulfonyl azide (**3**) with pyridinium bromide perbromide failed. However, nitration of the sulfonyl chloride (**2**) with fuming nitric acid gave the 4-nitro-sulfonyl chloride (**28**), which with sodium azide afforded the 5-chloro-4-nitro-sulfonyl azide (**29**). The sulfonyl azides, (**3**) and (**29**), have been reacted with triphenylphosphine, triethylphosphite, norbornene and cyclohexene. The azides reacted further with indole and 1-methylindole to give the 2-sulfonyl-iminoindolines (**34**)–(**36**). The infra-red spectra and mass spectra of some of the substituted thiophenesulfonyl derivatives are discussed.

INTRODUCTION

Organosulfonyl compounds are well known to show marked biological activities.[2,3] Of particular interest are the heteroarylsulfonyl derivatives, including thiophenesulfonyl derivatives, some of which has recently been reported to exhibit some antifungal and antibacterial activities.[4] We reported previously the synthesis, reactions and mass spectra of some unsubstituted 2-thiophenesulfonyl derivatives,[5,6] and in continuation of our studies on the reactions of heterocyclic sulfonyl compounds, this paper describes the preparation and reactions of some substituted 2-thiophenesulfonyl derivatives in order to obtain new compounds with potential biological properties.

RESULTS AND DISCUSSION

The reaction of 2-chlorothiophene (from thiophene and sulfuryl chloride)[7] with a mixture of chlorosulfonic acid and phosphorus pentachloride gave the 5-chloro-2-thiophenesulfonyl chloride (**2**)[8] which was reacted with 23 aryl- and heteroaryl-amines, indole and imidazole to give the sulfonamides (**5**)–(**27**). With hydrazine hydrate, the chloride gave the sulfonohydrazide (**4**) and with sodium azide, it gave the sulfonyl azide (**3**). 5-Chloro-2-thiophenesulfonyl chloride (**2**) was refluxed with equimolar amount of sulfuryl chloride in benzene for 12 h. to give only the unreacted sulfonyl chloride (**2**) (ir, nmr and ms evidences). Similarly, the sulfonyl azide (**3**), upon treatment with pyridinium bromide perbromide in methanol, failed to give any brominated product (ir, ms and nmr evidences). However, when the sulfonyl chloride (**2**) was reacted with fuming nitric acid, a good yield of the 4-nitro

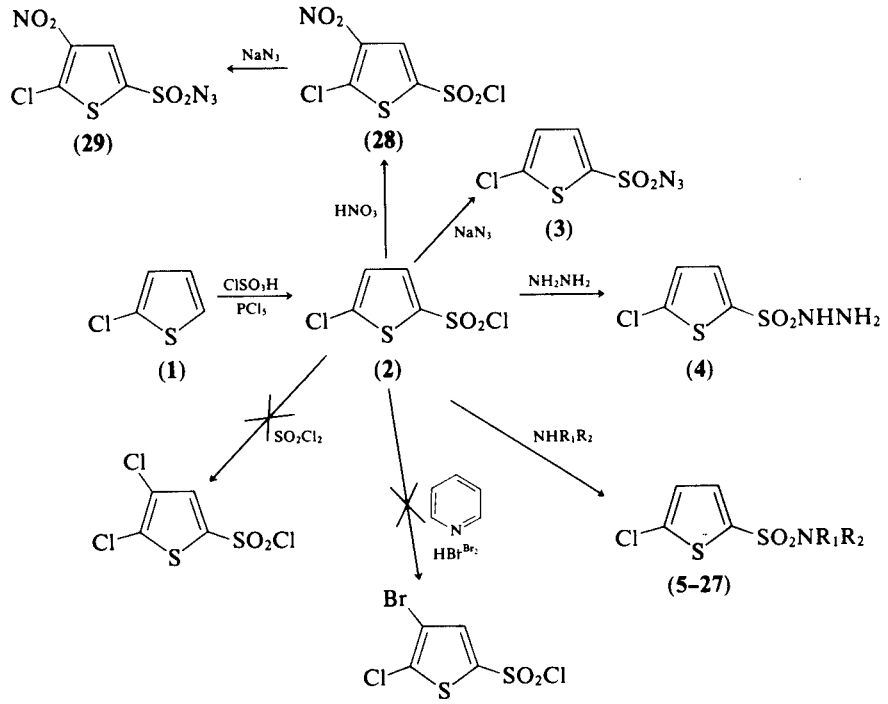
sulfonyl chloride derivative (**28**) was obtained. Reaction of the nitro-sulfonyl chloride (**28**) with sodium azide gave the sulfonyl azide (**29**). The preparation and reactions of the 5-chloro-2-thiophenesulfonyl chloride (**2**) are shown in Scheme 1 while the properties of the sulfonamides are given in Table I.

The sulfonyl azides (**3**) and (**29**) undergo the reactions shown in Scheme 2.

They reacted with triphenylphosphine and triethylphosphite to give the iminophosphoranes (**30**) and (**31**), while they undergo the 1,3-dipolar addition reactions with norbornene affording the aziridines (**32**) and (**33**), respectively. With indole and *N*-methyl-indole, the azides (**3**) and (**29**) attacked at the 2,3-double bond giving rise to the thiophenesulfonyliminoindolines (**34**)–(**36**), in a reaction similar to the reaction of sulfonyl azides with indoles.[1,9]

In contrast to the addition reaction observed with norbonene, the azides (**3**) and (**29**) reacted with cyclohexene to give mainly, after work-up, the thiophenesulfonamides (**5**) and (**37**), respectively, as was observed for the reaction of unsubstituted thiophenesulfonyl azide with cyclohexene.[5] The infra-red and nmr spectra of the crude product (brown oil), obtained when either sulfonyl azide (**3**) or (**29**), was treated with cyclohexene at 140, showed the major products to be cyclohexenylsulfonamide (**39**) (NH absorption at ν_{max} around 3285 cm^{-1}, for both crude products, and NH signals at δ 6.60 and 5.77, for crude product obtained with sulfonyl azide (**3**), and at δ 7.0, 6.60 and 6.0, for the crude product obtained from sulfonyl azide (**29**), all the signals being removed upon D_2O treatment) and the sulfonylimine (**38**) (with the characteristic C=NSO_2 absorption in the ir at around 1605 cm^{-1}).[1]

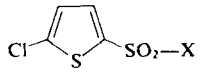
The brown oil was cooled in the fridge overnight to give a solid which was recrystallized from EtOH/H_2O to give pure crystals of the sulfonamides (**5**) and (**37**) (the band at ν_{max} 3285 cm^{-1} disappeared and replaced with characteristic SO_2NH_2 ab-



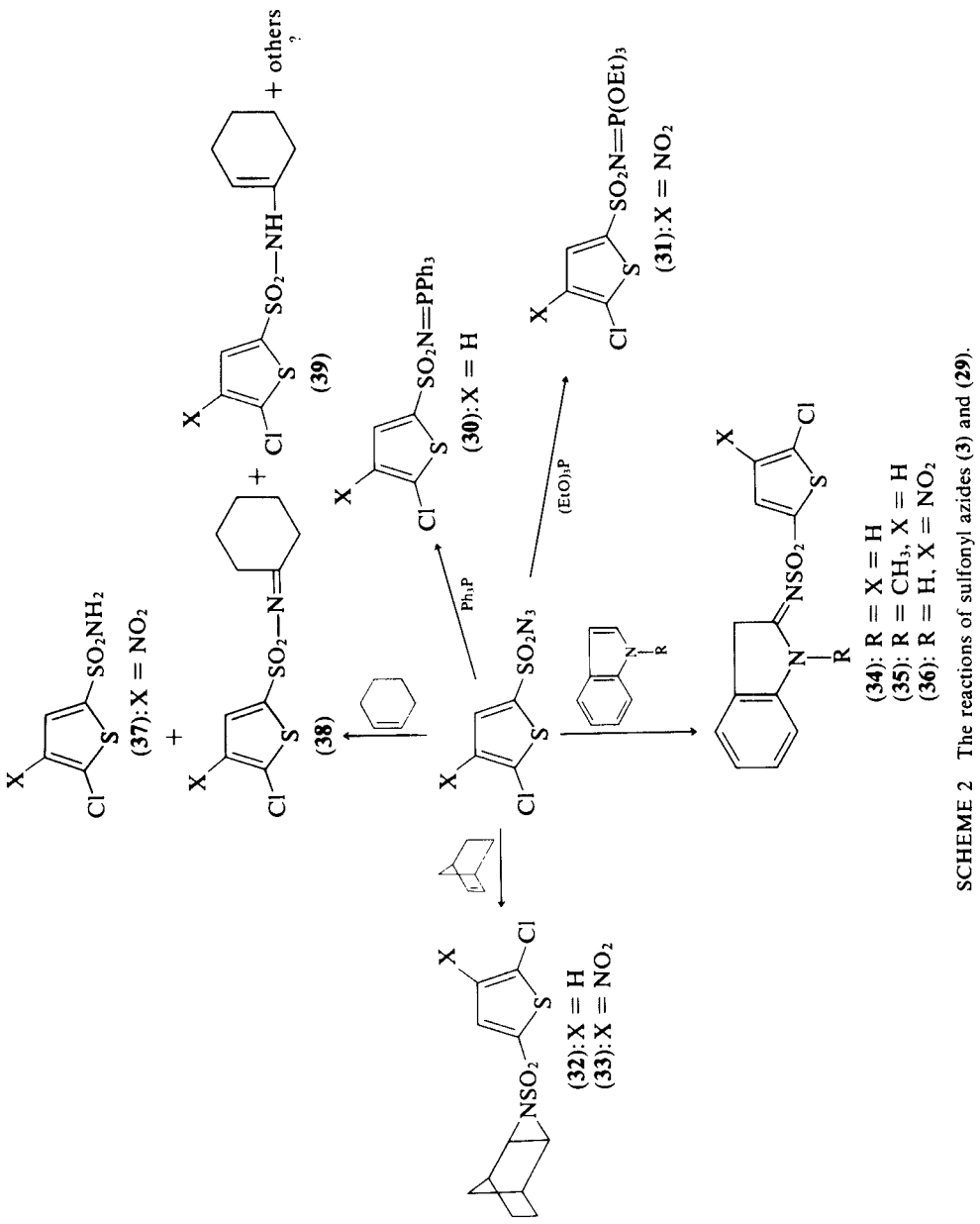
SCHEME 1 The reactions of 5-chloro-2-thiophenesulfonyl chloride.

TABLE I

Properties of the 5-chloro-2-thiophenesulfonamides



Compd. No	X	Yield (%)	Mp (°C)	Formula	Analysis C (%) Found (reqd.)	H (%) Found (reqd.)	N (%) Found (reqd.)
5	NH_2	62	114–116	lit.[19] 115–116°			
6	NHPh	39	83–84	lit.[19] 84–85°			
7	NCH_3(Ph)	69	77–79	$C_{11}H_{10}ClNO_2S_2$	45.81(45.91)	3.48(3.50)	4.85(4.86)
8	NHPh-4′-Br	75	122–124	$C_{10}H_7BrClNO_2S_2$	33.82(34.06)	2.0(2.0)	3.98(3.97)
9	NHPh-4′-Cl	71	111–113	$C_{10}H_7Cl_2NO_2S_2$	38.82(38.97)	2.30(2.29)	4.51(4.54)
10	NH—C_6H_{11}	59	74–76	$C_{10}H_{14}ClNO_2S_2$	43.0(42.93)	5.10(5.04)	5.0(5.01)
11	NHPh-2′-OH	55	130–132	$C_{10}H_8ClNO_3S_2$	41.32(41.45)	2.95(2.78)	4.86(4.83)
12	NHPh-4′-OH	68	137–138	$C_{10}H_8ClNO_3S_2$	41.30(41.45)	2.80(2.78)	4.92(4.83)
13	NHPh-2′-OCH_3	69	61–62	$C_{11}H_{10}ClNO_3S_2$	43.75(43.49)	3.51(3.32)	4.45(4.61)
14	NHPh-4′-OCH_3	58	98–99	$C_{11}H_{10}ClNO_3S_2$	43.74(43.49)	3.61(3.32)	4.50(4.61)
15	NHPh-2′-CH_3	62	80–82	$C_{11}H_{10}ClNO_2S_2$	46.13(45.91)	3.32(3.47)	4.63(4.87)
16	NHPh-3′-CH_3	65	72–73	$C_{11}H_{10}ClNO_2S_2$	46.09(45.91)	3.40(3.47)	4.77(4.87)
17	NHPh-4′-CH_3	60	102–104	$C_{11}H_{10}ClNO_2S_2$	45.71(45.91)	3.25(3.47)	4.81(4.87)
18	NHPh-3′-NO_2	52	113–114	$C_{10}H_7ClN_2O_4S_2$	37.59(37.68)	2.20(2.21)	8.86(8.79)
19	NHPh-4′-NO_2	69	124–125	$C_{10}H_7ClN_2O_4S_2$	37.60(37.68)	2.18(2.21)	8.85(8.79)
20	NH-Napthyl-β	72	106–107	$C_{14}H_{10}ClNO_2S_2$	51.88(51.93)	3.11(3.11)	4.20(4.33)
21	NHPh-2′-Ph	78	100–101	$C_{16}H_{12}ClNO_2S_2$	54.99(54.93)	3.51(3.46)	3.95(4.0)
22	NHPh-4′-$N(CH_3)_2$	63	139–140	$C_{12}H_{13}ClN_2O_2S_2$	45.39(45.49)	4.02(4.14)	8.95(8.84)
23	NH-Pyridil-α	75	214–215	$C_9H_7ClN_2O_2S_2$	39.51(39.35)	2.59(2.57)	10.11(10.20)
24	NH-Pyridil-β, α-Cl	72	175–177	$C_9H_6Cl_2N_2O_2S_2$	34.67(34.96)	1.88(1.96)	9.17(9.06)
25	NH-isoquinolyl-4′	69	180–181	$C_{13}H_9ClN_2O_2S_2$	48.29(48.07)	2.81(2.79)	8.61(8.62)
26	N-imidazolyl	32	64–66	$C_7H_5ClN_2O_2S_2$	33.78(33.81)	2.0(2.03)	11.15(11.26)
27	N-indolyl	45	58–59	$C_{12}H_8ClNO_2S_2$	48.27(48.40)	2.69(2.71)	4.79(4.70)



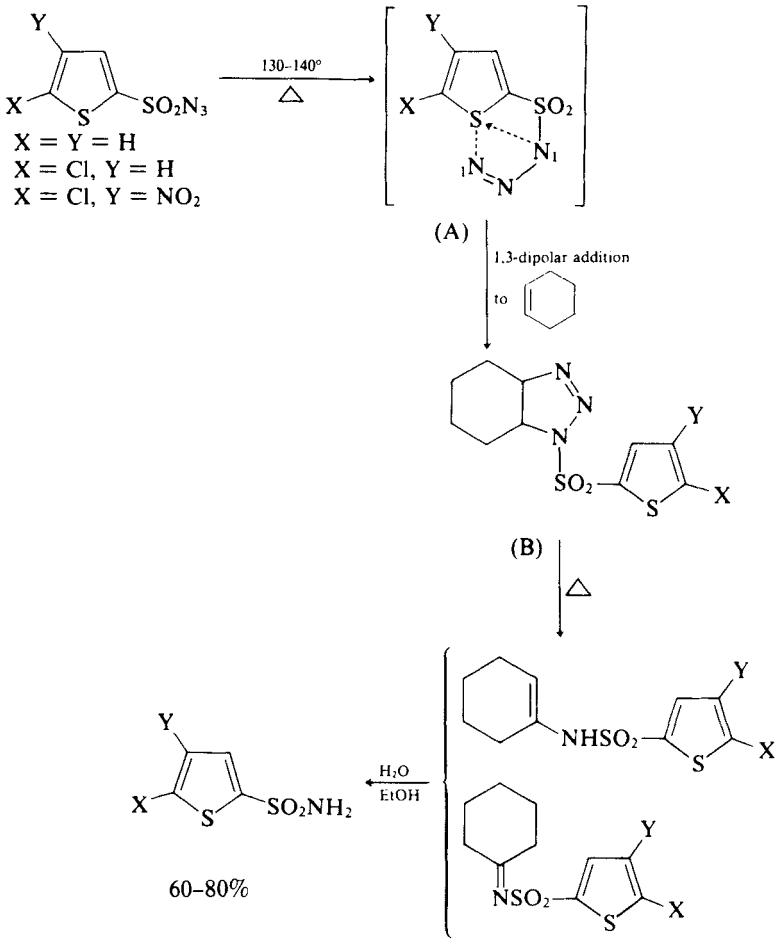
SCHEME 2 The reactions of sulfonyl azides (3) and (29).

sorptions at ν_{max} 3375–3355 and 3285–3265 in the ir, and in the nmr, a singlet, broad absorption at δ 6.60 (6.97) which disappeared upon treatment with D_2O).

Apparently, the sulfonylimine (**38**) had been hydrolyzed during recrystallization giving rise to the sulfonamides and cyclohexanone, the presence of cyclohexanone was confirmed by the presence of C=O absorption at ν_{max} 1700 cm^{-1} from the crude oil obtained from the mother liquor and the disappearance of the absorption band at around ν_{max} 1605 cm^{-1}.

In contrast to the above observations, treatment of benzene-sulfonyl azide with cyclohexene, under identical conditions used for the thiophenesulfonyl azides, did not give the corresponding sulfonyl amide in agreement with earlier observation by Franz and Osuch.[10] The sulfonamide was only obtained through a metal-catalyzed thermal decomposition in cyclohexene.[11]

A possible explanation for the formation of the thiophenesulphonamides involves an interaction between the thiophene ring sulfur atom and the azido-group forming an intermediate complex (A in Scheme 3) which then enhances the 1,3-dipolar addition to cyclohexene to give triazole B leading to the formation of sulfonylimine (**38**)



SCHEME 3 Possible reaction path of 2-thiophenesulfonyl azide derivatives with cyclohexene at 130–140 C.

and enamine (**39**), in a manner similar to copper-catalyzed decomposition of benzenesulfonyl azide in cyclohexene.[11,12] (Scheme 3)

The infra-red spectra of the various thiophenesulfonyl derivatives, in KBr discs or neat films, showed the usual thiophene C—H stretching vibration in the region 3125–3100 cm^{-1}. In the two thiophenesulfonamides (**5**) and (**37**), the NH_2 group showed two characteristic bands in the regions 3375–3355 and 3285–3265, while in all the compounds (**2**)–(**39**), the sulfonyl group showed two characteristic bands (asymmetric and symmetric) in the range 1380–1320 cm^{-1} and 1170–1130 cm^{-1} according to literature data,[13] and in the sulfonamides (**6**) and (**8**)–(**25**), the NH stretching vibrations showed in the range 3345–3240 cm^{-1} (associated form).[14] These absorptions due to the stretching vibrations of the SO_2, NH_2, NH and including the S—N vibrations are given in Table II.

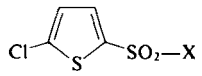
The nmr data of some of the compounds are given in the experimental section.

The mass spectra of six of the compounds were examined and compared with those of reported unsubstituted thiophenesulfonyl- and arylsulfonyl-derivatives.[6,15–17] The mass spectra of the compounds (**2**), (**3**) and (**5**) exhibit intense parent peaks, 58.6% in the azide (**3**) to 82.5% in the sulfonamide (**5**), while in the 4-nitro-derivatives (**28**) and (**29**), the intensities of the parent peaks are 19.9% and 8.1%, respectively. The most important ions (≥3%) in the mass spectra of the sulfonyl derivatives are given in Table III.

It has been reported[6,17] that the mass spectra of some aryl-sulfonyl chlorides ex-

TABLE II

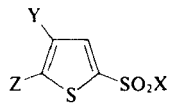
Infra-red stretching frequencies of 5-chloro-2-thiophenesulfonamides



Compound No	X	SO_2 asym.	SO_2 sym.	N—H	S—N
5	NH_2	1340	1158	3375, 3285	900m
6	NHPh	1330	1145	3240	930m
7	$N(CH_3)Ph$	1350, 1170, 1144			870s
8	NHPh-4'-Br	1330	1145	3270	902m
9	NHPh-4'-Cl	1330	1150	3268	904m
10	$NH\text{-}C_6H_{11}$	1335	1160	3245	885s
11	NHPh-2'-OH	1328	1144	3260	910m
12	NHPh-4'-OH	1332	1153	3263	905m
13	$NHPh\text{-}2'\text{-}OCH_3$	1342	1160	3265	925m
14	$NHPh\text{-}4'\text{-}OCH_3$	1332	1154	3273	908m
15	$NHPh\text{-}2'\text{-}CH_3$	1325	1146	3285	910m
16	$NHPh\text{-}3'\text{-}CH_3$	1328	1160	3263	935m
17	$NHPh\text{-}4'\text{-}CH_3$	1335	1155	3255	900m
18	$NHPh\text{-}3'\text{-}NO_2$	1338	1145	3250	885s
19	$NHPh\text{-}4'\text{-}NO_2$	1340	1150	3380	910m
20	NH-Napthyl-β	1350	1148	3265	915m
21	NHPh-2'-Ph	1338	1160	3275	910s
22	$NHPh\text{-}4'\text{-}N(CH_3)_2$	1330	1142	3258	905s
23	NH-Pyridil-α	1350	1130	3260w	958m
24	NH-Pyridil-β, α-Cl	1338	1155		920m
25	NH-isoquinolyl-4'	1340	1168	3345	890s
26	N-imidazolyl	1362	1170, 1130		935m
27	N-indolyl	1370	1165, 1120		940m

TABLE III

The mass spectra of some substituted thiophenesulfonyl derivatives at 70 ev.



m/e[a]	X = Cl[6] Y = Z = H	X = Cl Y = H Z = Cl	X = N_3 Y = H Z = Cl	X = NH_2 Y = H Z = Cl	X = NCH_3Ph Y = H Z = Cl	X = Cl Y = NO_2 Z = Cl	X = N_3 Y = NO_2 Z = Cl
30					4.6	15.8	15.3
37						9.0	13.4
38		4.3	4.5	5.9	4.8		
39	100				15.2		
45	42.6	8.1	8.8	8.2		7.1	6.2
48	17					3.0	3.5
51					18.0		
55	10						
57	37.2	8.7	9.1	7.9	3.3		
63					4.7		
64	24	7.1	5.0	8.3	3.3	3.7	4.9
65					5.3		
69						25.1	21.6
71	10						
72						14.2	18.1
73		65.2	69.5	64.7	16.2		
74						4.4	4.1
75		22.2	21.8	20.1	4.8		
77					80.8		
78					16.3		
79		7.9	6.1	6.0	26.7	10.1	10.5
81		12.1	13.5	12.9		46.6	49.8
82		17.1	17.9	18.5	5.2	3.2	3.3
83	27						
96		11.8	11.0	16.4			
99	34.4						
104					12.7		
105		23.8	20.0	21.8	9.9		
106					100		
107		8.3	7.9	8.3	7.8		
116						28.0	22.9
117		32.4	26.1	28.8			
118						10.1	8.5
119		10.8	8.7	10.1			
133		44.4	47.5	51.7			
135		15.8	18.0	19.2			
147	95.7						
150						4.7	5.2
165			5.7	6.9			
181		100	100	100	3.5		
182	28.4[M]$^+$	16.2	15.0	7.2	9.4		
183		38.5	35.4	36.4			
184	10.6		5.5		3.3		
188					12.0		
197				82.5[M]$^+$			
199				27.0			
216		62.5[M]$^+$					
218		45.3					
220		10.4					

TABLE III (*Continued*)

m/e[a]	X = Cl[6] Y = Z = H	X = Cl Y = H Z = Cl	X = N_3 Y = H Z = Cl	X = NH_2 Y = H Z = Cl	X = NCH_3Ph Y = H Z = Cl	X = Cl Y = NO_2 Z = Cl	X = N_3 Y = NO_2 Z = Cl
223			58.6[M]$^{+\cdot}$	49.5			
224			4.0	7.4			
225			22.6	17.5			
226						100	100
227						6.1	5.9
228						38.0	36.9
261						19.9[M]$^{+\cdot}$	
263						14.8	
265						3.5	
268							8.1[M]$^{+\cdot}$
270							3.1
287					2.7[M]$^{+\cdot}$		

[a] Parent peak is denoted by [M]$^{+\cdot}$. All peaks $\geq$ 3% of base peak included.

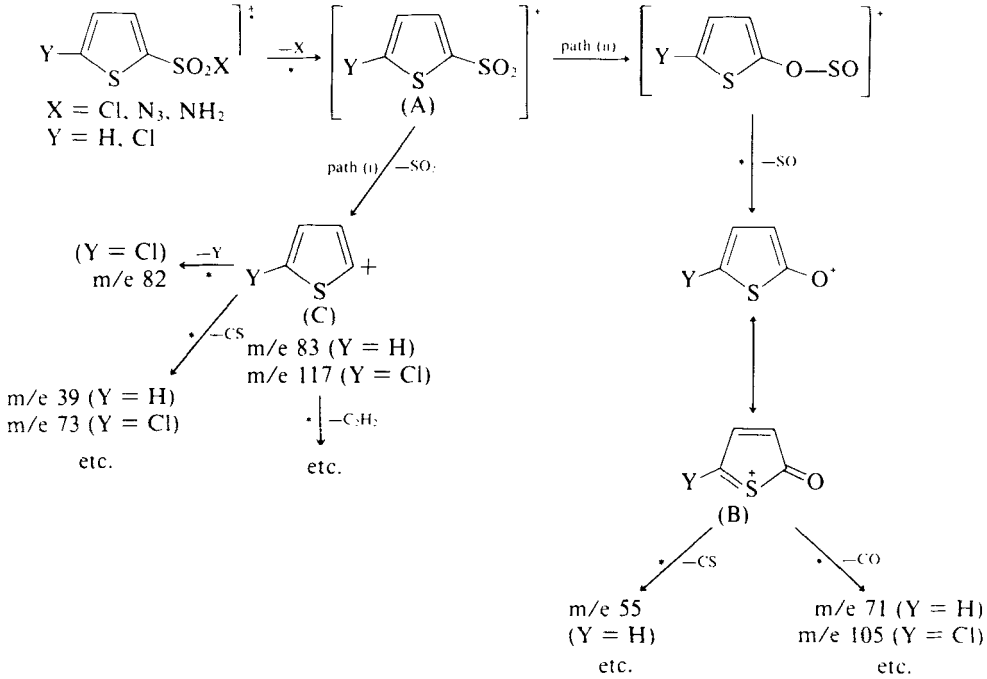
hibit ions resulting from chlorine atom migration from sulfur to carbon, with concomitant loss of SO_2, as a minor pathway: $ArSO_2Cl]^{+\cdot} \xrightarrow{-SO_2} ArCl]^{+\cdot}$

This fragmentation pathway is completely absent in all the substituted 2-thiophenesulfonyl chlorides studied under electron-impact so far.

As was observed previously[6] in the electron-impact induced fragmentation of some unsubstituted 2-thiophenesulfonyl derivatives, the mass spectra of compounds (**2**), (**3**) and (**5**) are dominated by the cleavage of the S—X bond (X = Cl, N_3 and NH_2) to give the 5-chloro-2-thiophenesulfonyl cation at m/e 181 (ion A in Scheme 4), which is the base peak in all the spectra, unlike in the unsubstituted 2-thiophenesulfonyl derivatives where the base peaks occur at m/e 39.[6] Further fragmentation of the chloro-thiophenesulfonyl cation then takes place by two routes: (i) by loss of SO_2 and subsequent fragmentation of the chlorothiophene ring. (ii) by thiophene—S--→ thiophene—O rearrangement with concomitant loss of SO to give a 2-ketosulfonium ion (B) in a one-step process (metastable peak evidence) (Scheme 4).

In contrast to the two major pathways described above, for further fragmentations of the thiophenesulfonyl cations, the 4-nitrothiophenesulfonyl derivatives (**28**) and (**29**) fragment first by loss of Cl or N_3 but the resulting nitro-substituted thiophenesulfonyl cation fragment further mainly by loss of SO_2 (path (i) of Scheme 4). The thiophene—S → thiophene—O rearrangement process, with the concomitant loss of SO (path (ii) of Scheme 4) becomes only a minor process. Such a thiophene—S → thiophene—O rearrangement, followed by loss of SO, would lead to the 4-nitro-2-thiophene oxide cation (ion A, m/e 178 in Scheme 5) which is low in abundance in both compounds (the intensity of this ion is less than 3% in both compounds). The low abundancy of this ion may be explained by its lesser stability due to the presence of electron-withdrawing nitro substituent, making the C—S → C—O rearrangement process a less favorable pathway. The possible fragmentation pathways of the 4-nitro-2-thiophenesulfonyl derivatives are shown in Scheme 5, supported in some cases by metastable peaks.

In the *N*-methyl-*N*-phenylsulfonamide (**7**), the mass spectrum is dominated by loss of sulfur dioxide to give an ion at m/e 223 (49.5%), which then looses the chlorothiophene ring giving rise to the amine moiety PhNMe (m/e 106, 100%) as the base peak. The relative intensity of the ion corresponding to the chloro-thio-



SCHEME 4 Fragmentation route of 2-thiophenesulfonyl derivatives.

phenesulfonyl group or those arising from its further fragmentation are very small in contrast to what was observed in the fragmentation of *N*-substituted-*p*-toluenesulfonamides where the ions corresponding to the *p*-toluenesulfonyl group are abundant.[18]

EXPERIMENTAL

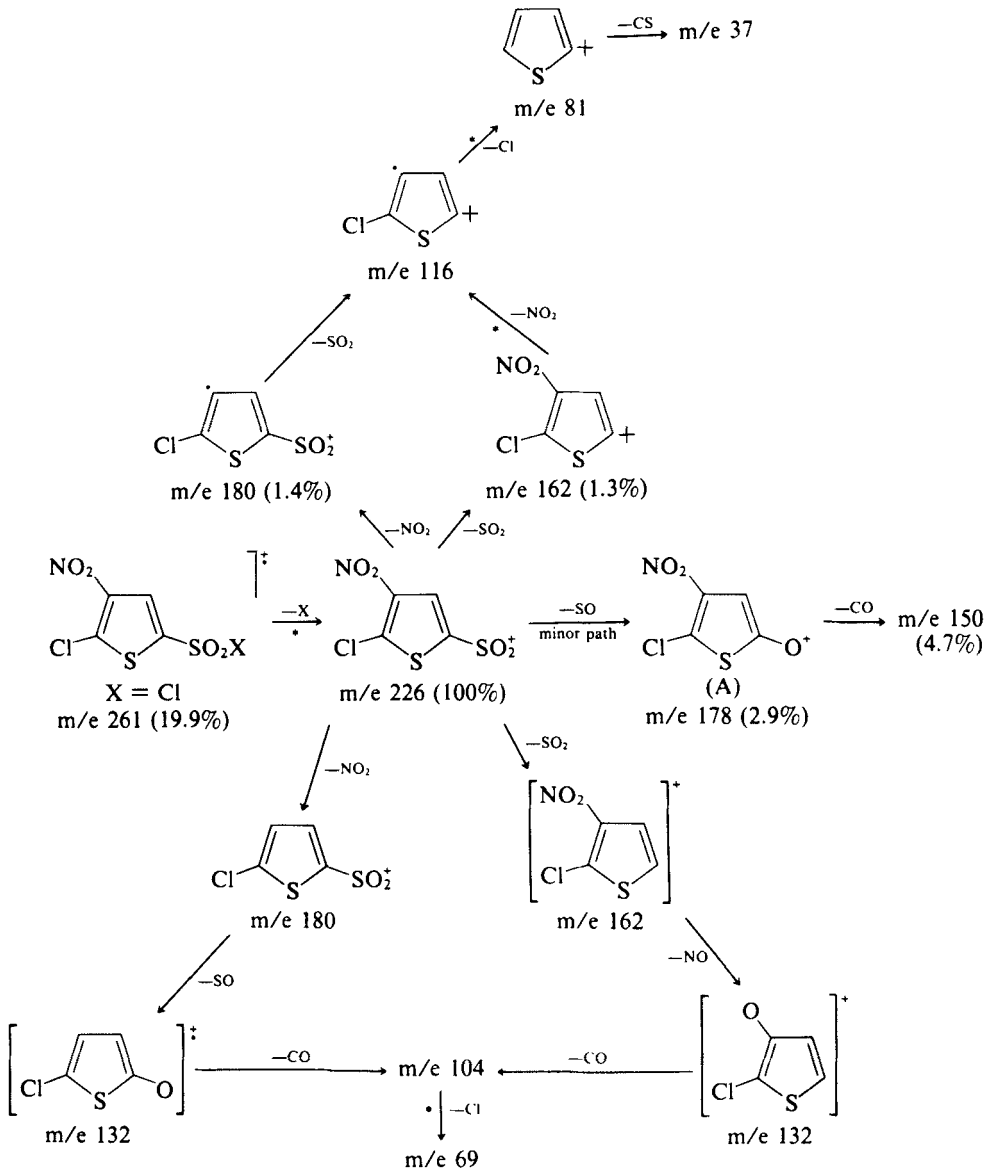
All melting points were taken on a Gallenkamp melting point apparatus and are uncorrected. Ir absorption spectra were measured with a Perkin-Elmer 237 spectrometer, using KBr discs or as neat films. The mass spectra were determined on an AEI MS12 and Micromass 7070F spectrometers at 70 ev. Nmr spectra were determined with a Varian T60 spectrometer in chloroform-d or acetone-d_6 as appropriate using tetramethylsilane as internal standard.

5-chloro-2-thiophenesulfonyl chloride (2):

This was prepared according to a literature procedure[8] from the reaction of 2-chlorothiophene (obtained from thiophene and sulfuryl chloride)[7] with a mixture of chlorosulfonic acid and phosphorus pentachloride. Mp 27° (lit.[20] 28°). Nmr ($CDCl_3$): δ 7.63, (d, 1H, thiophene-3H), 7.03 (d, 1H, thiophene-4H), $J_{3,4}$ = 4 Hz. ν_{max} 1380, 1168 (SO_2) cm^{-1}.

5-Chloro-2-thiophenesulfonamide (5):

Compound (**5**) was prepared from compound (**2**) and excess ammonium hydroxide. Mp 114–116° (lit.[19] 115–116°). Nmr (Acetone-d_6): δ 7.27 (d, 1H, thiophene-3H), 6.80 (d, 1H, thiophene-4H), 6.60 (br, 2H, NH_2). The signal at δ 6.60 was removed by D_2O treatment. ν_{max} (Table II).



SCHEME 5 The possible fragmentation pathways of 4-nitro-2-thiophenesulfonyl derivatives.

5-Chloro-2-thiophenesulfonamides (**6**)–(**25**):

The thiophenesulfonamides (**6**)–(**25**) were synthesized by refluxing the 5-chloro-2-thiophenesulfonyl chloride (4.6 mmole) with the appropriate amine (9.2 mmole) in acetonitrile for 4 h. The solvent was evaporated and the residue washed three times with water and then recrystallized from aqueous ethanol.

N-Phenyl—(**6**): Nmr ($CDCl_3$): δ 7.47–7.07 (m, 6H, C_6H_5 + thiophene-3H), 6.87 (d, 1H, thiophene-4H).

N-methyl-*N*-phenyl—(**7**): Nmr ($CDCl_3$): δ 7.33–6.90 (m, 6H, C_6H_5 + thiophene-3H), 6.79 (d, 1H, thiophene-4H), 3.22 (s, 3H, N—CH_3).

N-4-bromophenyl—(**8**): Nmr (acetone-d_6): δ 9.47 (s, br, 1H, NH), 7.63–6.93 (m, 6H, aromatic protons). The signal at δ 9.47 removed by D_2O treatment.

N-4-chlorophenyl—(**9**): Nmr (acetone-d_6): δ 9.50 (s, br, 1H, NH), 7.57–7.33 (m, 5H, C_6H_4 + thiophene-3H), 7.08 (d, 1H, thiophene-4H). The signal at δ 9.50 was removed by D_2O treatment.

N-Cyclohexyl—(**10**): Nmr ($CDCl_3$): δ 7.40 (d, 1H, thiophene-3H), 6.90 (d, 1H, thiophene-4H), 4.83 (s, br, 1H, NH), 3.20 (m, poorly resolved, 1H, cyclohexyl-C-1 proton), 2.07–0.97 (m, 10H, cyclohexyl). The signal at δ 4.83 was removed by D_2O treatment.

N-2-methoxyphenyl—(**13**): Nmr (acetone-d_6): δ 7.80–6.67 (m, 6H, aromatic), 3.73 (s, 3H, OCH_3).

N-4-methoxyphenyl—(**14**): Nmr (acetone-d_6): δ 9.0 (s, br, 1H, NH), 7.37–6.73 (m, 6H, aromatic), 3.77 (s, 3H, OCH_3). The signal at δ 9.0 disappeared on treatment with D_2O.

N-3-methylphenyl—(**16**): Nmr (acetone-d_6) δ 9.24 (s, br, 1H, NH), 7.40 (d, 1H, thiophene-3H), 7.27–6.97 (m, 5H, aromatic), 2.27 (s, 3H, CH_3).

N-4-methylphenyl—(**17**): Nmr ($CDCl_3$): δ 7.30 (d, 1H, thiophene-3H), 7.13 (s, 4H, aromatic), 6.83 (d, 1H, thiophene-4H), 2.30 (s, 3H, CH_3).

N-B-napthyl—(**20**): Nmr (acetone-d_6): δ 9.67 (s, br, 1H, NH), 8.10–7.73, 7.71–7.37 (2m, 8H, aromatic), 7.03 (d, 1H, thiophene-4H). The signal at δ 9.67 removed by D_2O treatment.

N-4-dimethylaminophenyl—(**22**): Nmr ($CDCl_3$): δ 7.27–6.47 (m, 6H, aromatic), 2.93 (s, 6H, NMe_2).

1-(5-chloro-2-thiophenesulfonyl)imidazole (**26**):

Imidazole (310 mg, 4.6 mmole) was dissolved in dimethylsulfoxide together with powdered potassium hydroxide (0.3 g). The resulting solution was cooled with ice-water and the 5-chloro-2-thiophene-sulfonyl chloride (1.0 g, 4.6 mmole) added dropwise, stirred at room temperature for 1 h. and then poured into water (15 ml) and extracted with chloroform. The chloroform extract was washed with water, dried over anhydrous magnesium sulfate and the chloroform evaporated to give an oil. Cooling with scratching gave a crystalline product which was recrystallized from chloroform-light petroleum (40–60°) (0.4 g, 32%), mp 64–66°C. Mass spectrum showed the molecular ion at m/e 248 (3.9%).

1-(5-chloro-2-thiophenesulfonyl)indole (**27**):

This was prepared as described for compound (**26**) above (45% yield), mp 58–59°C. Mass spectrum gave the molecular ion at m/e 297.

Attempted chlorination of 5-chloro-2-thiophenesulfonyl chloride (**2**):

Compound (**2**) (1.0 g) and sulfuryl chloride (2.0 g) in benzene (5 ml) was refluxed for 12 h. to afford the starting sulfonyl chloride (**2**) (ir, nmr and mass spec.).

5-Chloro-2-thiophenesulfonyl azide (**3**):

5-Chloro-2-thiophenesulfonyl chloride (10.0 g, 0.046 mole) was treated at room temperature with sodium azide (6.0 g, 0.092 mole) in aqueous acetone for 6 h. to give the sulfonyl azide (**3**) (7.7 g, 75%); mp 34–36° (petroleum-ether, bp 40–60°); (Found: C, 21.29; H, 0.91; N, 18.92; $C_4H_2ClN_3O_2S_2$ requires: C, 21.48; H, 0.90; N, 18.79). Nmr ($CDCl_3$): δ 7.72 (d, 1H, thiophene-3H), 7.10 (d, 1H, thiophene-4H). ν_{max} 3110 (C—H); 2130 (N_3), 1375, 1170 (SO_2) cm^{-1}.

Attempted bromination of 5-chloro-2-thiophenesulfonyl azide (**3**):

5-Chloro-2-thiophenesulfonyl azide (1.0 g) was heated with pyridinium bromide perbromide (2 molar equiv.) in methanol under reflux conditions for 2 h. to give back the unreacted sulfonyl azide (**3**) (ir, nmr and ms evidences).

5-Chloro-4-nitro-2-thiophenesulfonyl chloride (**28**):

5-Chloro-2-thiophenesulfonyl chloride (**2**) (15.0 g, 0.069 mole) was added dropwise to a vigorously stirred fuming nitric acid (52 ml) at room temperature. It was then stirred for a further 3 h. at 40–60° and then poured into large volume of crushed ice when an oil separated. The oily product was extracted with chloroform, dried with anhydrous $MgSO_4$ and the chloroform removed. The resulting oil was cooled in the fridge to give a crystalline product. Recrystallization from petroleum-ether (bp 40–60°)—

chloroform (5:1, v/v) gave the pure sulfonyl chloride (**28**) (13.4 g 74%), mp 50–52°. (Found: C, 18.21; H, 0.40; N, 5.33. $C_4HCl_2NO_4S_2$ requires: C, 18.33; H, 0.38; N, 5.34). Nmr ($CDCl_3$): δ 8.37 (s, thiophene-3H). ν_{max} 1540, 1330 (NO_2), 1380, 1170, 1150 (SO_2) cm^{-1}.

5-Chloro-4-nitro-2-thiophenesulfonyl azide (**29**):

5-Chloro-4-nitro-2-thiophenesulfonyl chloride (10.0 g, 0.038 mole) was stirred with sodium azide (2 molar equiv.) in aqueous acetone for 8 h. to give the sulfonyl azide as brown oil which did not crystallize upon cooling. The brown oil was extracted with light petroleum (40–60°) and the oil from the petroleum extract was used for analysis and further reactions. Found: C, 17.69; H, 0.36; N, 20.94; $C_4HClN_4O_4S_2$ requires: C, 17.88; H, 0.38; N, 20.86). ν_{max} 2142 (N_3), 1535, 1330 (NO_2), 1378, 1160 (SO_2) cm^{-1}.

Reactions of 5-chloro-2-thiophenesulfonyl azide (**3**) *and 5-chloro-4-nitro-2-thiophenesulfonyl azide* (**29**):

(i). With phosphorus compounds.

(a). Triphenyl (5-chloro-2-thiophenesulfonylimino)phosphorane (**30**).

The azide (**3**) (1.0 g, 4.5 mmole) in ether (15 ml) was added dropwise to triphenylphosphine (1 molar equiv.) in ether (20 ml) and the mixture refluxed for 5 h. The ether was removed and the solid recrystallized from EtOH/$CHCl_3$ to give (**30**) (1.3 g, 65%), mp 145–146°. (Found: C, 57.65; H, 3.58; N, 3.10; $C_{22}H_{17}ClNO_2PS_2$ requires: C, 57.70; H, 3.74; N, 3.06). Ms (457, M^+). ν_{max} 1440 (P=N), 1340, 1165 (SO_2) cm^{-1}.

(b). Triethoxy(5-chloro-4-nitro-2-thiophenesulfonylimino)-phosphorane (**31**).

Compound (**31**) was prepared as described above for compound (**30**), from equimolar amounts of 5-chloro-4-nitro-2-thiophenesulphonyl azide (**29**) and triethylphosphite, obtained as an oil. (Found: C, 29.66; H, 4.11; N, 6.70. $C_{10}H_{16}ClN_2O_7PS_2$ requires: C, 29.53; H, 3.96; N, 6.89). Nmr ($CDCl_3$): δ 8.32 (s, 1H, thiophene-3H), 1.35 (t, 9H), 4.10 (q, 6H). ν_{max} 1535, 1330 (NO_2), 1438 (P=N), 1370, 1150 (SO_2) cm^{-1}. Mass spectrum showed $(M-15)^+$ at m/e 391.

(ii). With norbornene.

(a). The azide (**3**) (1.0 g, 4.5 mmole) was treated with norbornene (1 molar equiv.) under reflux in ether (15 ml) for 12 h. Recrystallization from ethanol gave the aziridine (**32**) (0.58 g, 45%), mp 59–61°. (Found: C, 45.63; H, 3.91; N, 4.87. $C_{11}H_{12}ClNO_2S_2$ requires: C, 45.59; H, 4.17; N, 4.83). ν_{max} 1370, 1155 (SO_2) cm^{-1}. Mass spectrum showed the molecular ion at m/e 289.

(b). The azide (**29**) was reacted with norbornene as described above to give the aziridine (**33**) in 38% yield; mp 125–127°. (Found: C, 39.37; H, 3.30; N, 8.29. $C_{11}H_{11}ClN_2O_4S_2$ requires: C, 39.46; H, 3.31; N, 8.37). ν_{max} 1530 (NO_2), 1340, 1145 (SO_2) cm^{-1}.

(iii). With cyclohexene.

(a). 5-Chloro-2-thiophenesulfonyl azide (1.0 g) was heated with cyclohexene (20 ml) under reflux at 130–140° for 24 h. Excess cyclohexene was removed to give an oil. ν_{max} 3285 (NH), 2945 (CH_2), 1610 (s, br, $C{=}NSO_2$)[1], 1330, 1140 (SO_2) cm^{-1}. The oil was cooled in the fridge and the resulting solid dissolved in aqueous ethanol and left to stand when the 5-chloro-2-thiophenesulfonamide crystallized out (0.60 g, 68%), identical (nmr, ms, ir and mmp) to compound (**5**) obtained from reaction of 5-chloro-2-thiophenesulfonyl chloride with excess aqueous ammonia.

(b). 5-chloro-4-nitro-2-thiophenesulfonyl azide (1.0 g) was similarly treated with cyclohexene as in (a) above to give an oil. ν_{max} 3290 (NH), 2950 (CH_2), 1605 ($C{=}NSO_2$)[1], 1538 (NO_2), 1345 (s, br, SO_2, NO_2), 1145 (SO_2) cm^{-1}. Recrystallization from aqueous ethanol gave the sulfonamide (**37**), (75% yield), mp 155–157°. (Found: C, 19.88; H, 1.29; N, 11.31. $C_4H_3ClN_2O_4S_2$ requires: C, 19.80; H, 1.25; N, 11.54). Nmr (acetone-d_6): δ 8.43 (s, 1H, thiophene-3H), 6.97 (s, br, NH_2, removed by D_2O treatment). ν_{max} 3355, 3265 (NH_2), 1530, 1330 (NO_2), 1370, 1150 (SO_2) cm^{-1}.

(iv). With indole and *N*-methylindole.

(a). 2-(5-Chloro-2-thiophenesulfonylimino)indoline (**34**).

Indole (1.10 g, 9.0 mmole) and 5-chloro-2-thiophenesulfonyl azide (2.0 g, 9.0 mmole) were mixed and heated to 50 C. After 20 min., the reaction suddenly went violent leaving a black tar. The reaction was then repeated at room temperature and left at that temperature for 24 h. Methanol was added and the solid residue was collected and recrystallized from chloroform or acetic acid-propanol to give compound (**34**) as white feathers. (2.1 g, 75%) mp 207–209° (dec.). (Found: C, 45.98; H, 2.86; N, 8.74. $C_{12}H_9ClN_2O_2S_2$ requires: C, 46.08; H, 2.90; N, 8.96). Nmr ($CDCl_3$-DMSO-d_6, 5:1): δ 11.92 (s, br, NH),

7.77–7.07 (m, 6H, aromatic), 4.23 (s, 2H, indoline C-3(H_2)[1]). The signal at δ 11.92 was removed by treatment with D_2O. ν_{max} 1580 (s, br, C=NSO_2),[1] 1320, 1132 (SO_2) cm^{-1}.

(b). 2-(5-Chloro-2-thiophenesulfonylimino)-1-methylindoline (**35**).

1-methylindole (1.2 g, 9.2 mmole) and 5-chloro-2-thiophenesulfonyl azide (2.0 g, 9.0 mmole) were mixed and warmed to 50 for 30 min. and then left at room temperature for 24 h. and worked-up as above to give compound (**35**) (2.2 g, 76%), mp 197–199° (dec.). (Found: C, 47.64; H, 3.20; N, 8.60. $C_{13}H_{11}ClN_2O_2S_2$ requires: C, 47.78; H, 3.39; N, 8.57). Nmr ($CDCl_3$-DMSO-d_6): δ 7.72–6.90 (m, 6H, aromatic), 4.19 (s, 2H, indoline-C-3(H_2)), 3.40 (s, 3H, NCH_3). ν_{max} 1562 (s, br, C=NSO_2)[1], 1360, 1160 (SO_2) cm^{-1}.

(c). 2-(5-chloro-4-nitro-2-thiophenesulfonylimino)indoline (**36**).

A mixture of indole (2.0 g, 17 mmole) and 5-chloro-4-nitro-2-thiophenesulfonyl azide (4.6 g, 17 mmole) is explosive and should not be mixed without an inert solvent. An equimolar amounts of indole and the azide, in acetonitrile, were left at room temperature for 48 h., the solvent removed and the solid residue recrystallized from propanol-acetic acid after being treated with activated charcoal to give (**36**), mp 199° (dec. black residue). (Found: C, 40.30; H, 2.41; N, 11.36. $C_{12}H_8ClN_3O_4S_2$ requires: C, 40.28; H, 2.25; N, 11.74). ν_{max} 1585 (s, br, C=NSO_2), 1530, 1330 (NO_2), 1365, 1155 (SO_2) cm^{-1}.

5-Chloro-2-thiophenesulfonohydrazide (**4**):

5-Chloro-2-thiophenesulfonyl chloride (5.0 g, 23 mmole) was added dropwise to hydrazine hydrate (4.1 g, 85%, 69 mmole) in tetrahydrofuran (20 ml) kept at 0°, after which it stirred at room temperature overnight. Ice-water was added and the organic layer extracted with ethyl acetate, and the extract dried over anhydrous magnesium sulfate and the solvent evaporated in vacuo to give a white solid product. Recrystallization from aqueous methanol gave the pure hydrazide (4.1 g, 85%), mp 81–82°C. ν_{max} 3323, 3220, 3198 (NH), 3120 (CH), 1340, 1150 (SO_2) cm^{-1}. (Found: C, 22.54; H, 2.49; N, 12.96. $C_4H_5ClN_2O_2S_2$ requires: C, 22.59; H, 2.37; N, 13.17).

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