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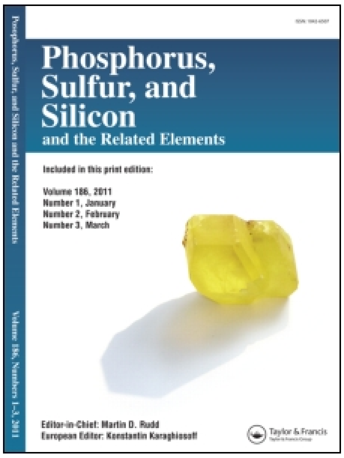

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Chlorosulfonation of 2-Styrylbenzothiazole, 2-Styryl- and 2-Phenylbenzoxazole

Richard J. Cremlyn[a]; Stephen Graham[a]; David Saunders[a]
[a] Division of Chemical Sciences, University of Hertfordshire, Hatfield, Hertfordshire, AL, England

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CHLOROSULFONATION OF 2-STYRYLBENZOTHIAZOLE, 2-STYRYL- AND 2-PHENYLBENZOXAZOLE

RICHARD J. CREMLYN, STEPHEN GRAHAM and DAVID SAUNDERS
Division of Chemical Sciences, University of Hertfordshire, Hatfield, Hertfordshire AL 10 9AB, England

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2-Styrylbenzothiazole (**1**), 2-styryl (**2**)- and 2-phenylbenzoxazole (**3**) reacted with excess chlorosulfonic acid (6 equivalents) to give the sulfonyl chlorides (**8, 14, 20**). The pure sulfonyl chlorides were not isolated and were characterised by conversion into 14 sulfonamides (**9–13, 15–19, 21–24**) the hydrazide (**25**) and acetone hydrazone (**26**). 2-Styrylbenzothiazole (**1**) by heating with a larger amount of chlorosulfonic acid (12 equivalents) afforded a chlorinated bis-sulfonyl chloride (**27**), which was characterised by formation of the bis-morpholidate (**28**). The NMR and MS spectral data are briefly discussed.

Key words: 2-Styrylbenzothiazole, 2-styryl- and 2-phenylbenzoaxazole, chlorosulfonation, sulfonamides.

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The work described in this paper forms part of our general research programme on the chemistry and biological activity of aromatic sulfonyl derivatives.[1–3] In particular, it extends previous work on the chlorosulfonation of heterocyclic compounds[4–8] by examining the chlorosulfonation of 2-styrylbenzothiazole (**1**) together with 2-styryl (**2**)- and 2-phenyl (**3**)-benzoxazole.

DISCUSSION

The starting materials (**1**) and (**2**) were obtained by condensation of 2-methylbenzothiazole (**4**) and 2-methylbenzoxazole (**5**) with benzaldehyde as previously described.[9–10] Compound (**3**) was prepared from *o*-nitrophenol (**6**) by benzoylation giving (**7**) and subsequent heating with triethyl phosphite (Scheme I).[11]

When 2-styrylbenzothiazole (**1**) was reacted with excess chlorosulfonic acid (6 molar equivalents) for one week at room temperature, the major product appeared to be the sulfonic acid rather than the desired sulfonyl chloride (**8**) (Chart I). This result may be due to failure of the initial sulfonic acid to be chlorinated by the excess reagent, indeed when the acid was subsequently refluxed with thionyl chloride and the product treated with morpholine, a low yield of the sulfonyl morpholidate (**9**) was isolated, but the product was contaminated with chlorine-containing compounds. An alternative and more likely explanation of the failure to obtain the sulfonyl chloride (**8**) may be facile hydrolysis during the work up procedure which involved pouring the reaction mixture onto ice. In view of this possibility, it was decided not to attempt isolation of the pure sulfonyl chloride (**8**), but after precipitation and rapid filtration to immediately react the crude product with the appropriate amines to obtain the sulfonamides. By this procedure, (**8**) was condensed with morpholine, diethylamine, piperidine, benzylamine and isopro-

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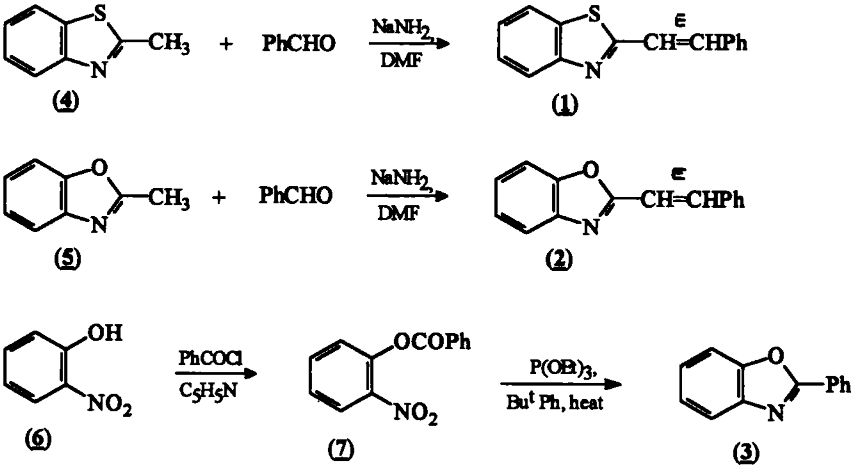
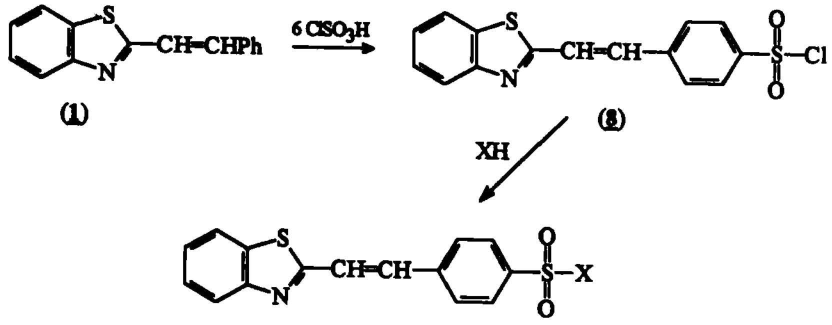


SCHEME I



X
(9) morpholino
(10) NEt_2
(11) piperidino
(12) $NHCH_2Ph$
(13) $NHCHMe_2$

CHART I Sulfonyl derivatives of 2-styrylbenzothiazole (**1**)

pylamine to give the derivatives (**9**–**13**) in modest yields (20–45%) (Chart I and Table I).

One problem with this method was that the product was contaminated with some of the corresponding sulfonic acid which had comparatively low aqueous solubility, hence the product needed to be washed with dilute sodium hydroxide solution to remove the impurity. With weakly acidic sulfonamides (**12**, **13**), containing the SO_2NH moiety, a weaker base (dilute sodium hydrogen carbonate) was used to avoid dissolution of the sulfonamide as well as the sulfonic acid. With benzothiazole

TABLE I

Physical data for sulfonyl derivatives of 2-styrylbenzothiazole and 2-styryl- and 2-phenylbenzoxazole

				Microanalysis found (Calc) %			MS
Comp No.	Yield %	m.p. °C	Molecular formula	C	H	N	(M^+)
2	41	80-82	$C_{15}H_{11}NO$	80.8 (81.4)	5.1 (5.0)	6.3 (6.3)	221
3	47	104-106	$C_{13}H_9NO$	80.2 (80.0)	4.8 (4.6)	7.0 (7.2)	195
9	20	275-278	$C_{19}H_{18}N_2O_3S_2$	58.5 (59.0)	4.6 (4.7)	7.0 (7.3)	386
10	43	182-185	$C_{19}H_{20}N_2O_2S_2$	60.8 (61.3)	5.2 (5.4)	7.2 (7.5)	372
11	39	210-212	$C_{20}H_{20}N_2O_2S_2$	62.0 (62.5)	5.1 (5.2)	7.5 (7.3)	384
12	45	166-168	$C_{22}H_{18}N_2O_2S_2$	64.6 (65.0)	4.1 (4.5)	6.5 (6.9)	406
13	30	160-163	$C_{18}H_{18}N_2O_2S_2$	59.9 (60.3)	5.0 (5.1)	7.5 (7.8)	358
15	68	232-234	$C_{19}H_{18}N_2O_4S$	61.3 (61.6)	4.8 (4.9)	7.2 (7.6)	370
16	41	226-228	$C_{20}H_{20}N_2O_3S$	64.8 (65.2)	5.4 (5.5)	7.6 (7.6)	368
17	49	184-186	$C_{19}H_{20}N_2O_3S$	63.7 (64.0)	5.4 (5.7)	7.6 (7.9)	356
18	50	187-188	$C_{18}H_{18}N_2O_3S$	62.6 (63.1)	5.2 (5.3)	7.9 (8.2)	342
19	66	202-204	$C_{22}H_{18}N_2O_3S$	67.8 (67.7)	4.7 (4.7)	7.3 (7.2)	390
21	7	158-161	$C_{17}H_{16}N_2O_4S$	58.6 (59.3)	4.7 (4.7)	7.8 (8.1)	344
22	63	144-146	$C_{18}H_{18}N_2O_4S$	62.8 (63.1)	5.4 (5.3)	8.0 (8.2)	342
23	39	90-92	$C_{17}H_{18}N_2O_3S$	62.3 (61.8)	5.3 (5.5)	8.3 (8.5)	330
24	72	128-130	$C_{20}H_{16}N_2O_3S$	65.7 (65.9)	4.6 (4.4)	7.4 (7.7)	364
25	68	161-162	$C_{13}H_{11}N_3O_3S$	54.5 (54.0)	3.5 (3.8)	14.2 (14.5)	289
26	66	184-185	$C_{16}H_{15}N_3O_3S$	58.1 (58.3)	4.6 (4.6)	12.7 (12.8)	329

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and 2-methylbenzothiazole previous work[5] demonstrated that chlorosulfonation of the aromatic nucleus required prolonged heating with excess chlorosulfonic acid. It does not occur with the reagent at room temperature which clearly shows that in the present work, the chlorosulfonation occurs only on the styryl moiety and there is no attack on the benzothiazole ring.

When 2-styrylbenzoxazole (**2**) was reacted with chlorosulfonic acid (6 molar equivalents) at room temperature (1 week), the intermediate sulfonyl chloride (**14**) was very difficult to filter which allowed more time for partial hydrolysis to the sulfonic acid. It also appeared to be more reactive than the benzothiazole analogue (**8**), as a consequence the yields of the sulfonamides (**15**, **19**) obtained by this procedure were very low (7–15%) (Chart II).

However, by using a modified procedure in which the reaction mixture, after pouring onto ice, was made alkaline by addition of triethylamine and was then reacted with the appropriate amine afforded improved yields (41–68%) of the sulfonamides (Chart II and Table I). This method avoided isolation of the sensitive sulfonyl chloride (**14**) and hence appeared to reduce side reactions.

When 2-phenylbenzoxazole (**3**) was reacted with chlorosulfonic acid under similar conditions (6 molar equivalents, room temperature, 1 week) and the crude mixture condensed with morpholine using the modified procedure adopted for the preparation of the 2-styrylbenzoxazole sulfonamides (**15**–**19**). The yield of the desired morpholidate (**21**) was very low (≈5%) with some 35% of unreacted starting material as estimated from the observed aliphatic-aromatic proton ratio in the ^{1}H-NMR spectrum (Chart III). The rest of the product was probably lost as the water-soluble sulfonic acid derivative during the aqueous work up procedure. The result clearly suggested that more vigorous chlorosulfonation conditions were required.

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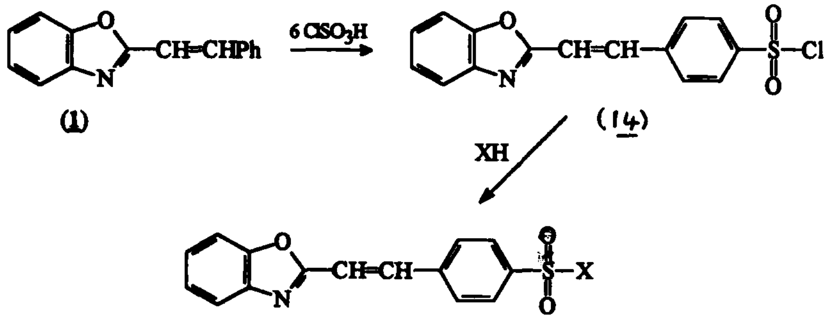
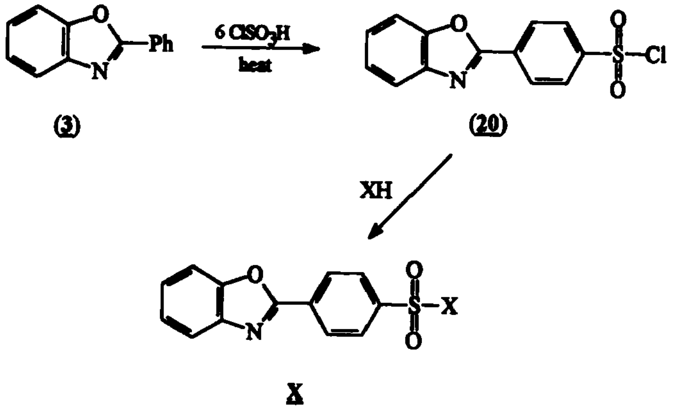


X

(15) morpholino
(16) piperidino
(17) NEt_2
(18) $NHCHMe_2$
(19) $NHCH_2Ph$

CHART II Sulfonyl derivatives of 2-styrylbenzoxazole (2)



(21) morpholino
(22) piperidino
(23) NEt_2
(24) $NHCH_2Ph$
(25) $NH\text{-}NH_2$
(26) $NH\text{-}N{=}CMe_2$

CHART III Sulfonyl derivatives of 2-phenylbenzoxazole (3)

2-Phenylbenzoxazole (**3**) was therefore heated at 100°C for 3 hours and left at room temperature (5 days) and the product reacted with morpholine to give ≈30% yield of a mixture of the morpholidate (**21**) and the sulfonyl chloride (**20**) based on mass spectral data. It therefore appeared that the conversion of the sulfonic acid to the sulfonyl chloride (**20**) was comparatively slow and also that the latter compound (**20**) was much less reactive towards amines than the styrylbenzoxazole analogue (**14**). The yield of the morpholidate obtained by this procedure was very low (≈7%) and in the synthesis of the other sulfonamides (**22–24**) (Chart III). In an effort to increase the yields, 2-phenylbenzoxazole (**3**) was heated with chlorosulfonic acid as previously described then thionyl chloride-DMF (3 drops) was added and the mixture refluxed for a further 2 hours. This modification ensured an improved conversion of the initially formed sulfonic acid to the sulfonyl chloride (**20**).

The mixture was added to crushed ice and the precipitated sulfonyl chloride was collected and immediately added to a solution of the appropriate amine. In this way, reasonable yields (39–68%) of the sulfonamides (**22–24**) were realised. A similar procedure in which hydrazine hydrate was employed rather than an amine afforded the sulfonyl hydrazide (**25**) which was characterised as the acetone hydrazone derivative (**26**).

When 2-styrylbenzothiazole (**1**) was reacted with a larger quantity of chlorosulfonic acid (12 molar equivalents) at 50°C, followed by treatment with thionyl chloride-DMF, a product was formed which was concluded to be the chlorinated bis-sulfonyl chloride (**27**). This was characterised by formation of the dimorpholidate derivative (**28**) (Scheme II).

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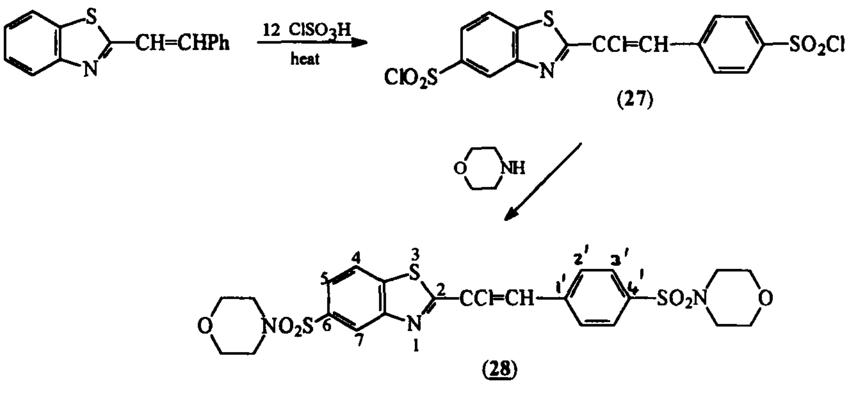

SCHEME II

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The ^{1}H NMR spectrum of **28** indicates 8 aromatic and alkenic protons rather than 9 which would be expected for the unchlorinated product. The aromatic proton resonances showed an unsymmetrical 1,2,4-substitution pattern confirming sulfonation of the benzothiazole nucleus. There was a clear AA^{1}BB^1 pattern (δ7.94, 7.71) indicative of *p*-sulfonation in the benzylidene ring. The remaining aromatic proton appeared as a broad singlet (δ8.25) with no AB pattern, therefore, the alkenic hydrogens are no longer present. It was concluded that addition of hydrogen chloride to the alkenic bond did not occur but rather one of the alkenic hydrogens had been substituted by a chlorine atom. The product showed a positive Beilstein test for halogen, and in the mass spectrum the molecular ion (M^+) appeared at 571, 569 and M^+-H at 570, 568, the characteristic isotropic peaks for a mono-chloro compound. The UV spectra of 2-styrylbenzothiazole (**1**), the mono-sulfonyl morpholidate (**9**) and the bis-morpholidate (**28**) showed that the position of the absorption maximum (λ_{max}) remained virtually unchanged (λ_{max} 330, 335 and 330 nm respectively). Addition of hydrogen chloride would reduce the extent of conjugation and hence the position of the absorption maximum. Previous work[5] indicated that 2-methylbenzothiazole is chlorosulfonated in the 5- and 6-positions and purification of the sulfonyl piperidate derivative gave the pure 6-substituted product.

The chemical shifts reported[5] for the sulfonylpiperidate were similar to those observed for the morpholidate (**28**) which was therefore also shown to be the 6-sulfonyl derivative.

With regard to the position of the chlorine atom in compound (**28**); the structure of the product was concluded to be as shown in (**28**) with the chlorine atom adjacent to the benzothiazole ring from a study of the fully proton-coupled C^{13} NMR spectrum because this showed the 2′-carbon resonance as a doublet of triplets (δ130.85). If compound **28** had possessed the alternative structure in which the chlorine atom was attached to the carbon atom adjacent to the phenyl ring, then there would be no coupling with the alkenic proton and hence the 2′-carbon resonance would appear as a doublet of doublets.

The aromatic proton resonances of the benzothiazole and benzoxazole sulfonyl derivatives appeared as complex multiplets. In compounds **17**, **18**, **22–26** an AA^{1}BB^1

pattern could be identified in the aromatic region indicative of *p*-sulfonation; this orientation would be in agreement with stereoelectronic predictions. In the ^1H NMR spectra of the two starting materials, namely 2-styrylbenzothiazole (**1**) and 2-styrylbenzoxazole (**2**), the resonances of the *trans* alkenic hydrogens were identified as two doublets resonating at δ7.53, 7.40 (*J* 15.6 H_z) and δ7.85, 7.35 (*J* 16.8 H_z) respectively.

On the other hand, in the ^1H NMR spectra of the derived sulfonyl compounds, it was generally difficult to clearly identify the resonances due to the alkenic protons probably because they had moved downfield due to the deshielding influence of the sulfonyl moiety; however, in compound **18**, the alkenic protons appeared at δ7.80, 7.20. The proton NMR spectra of the relevant sulfonamides showed the correct aliphatic-aromatic proton ratios and in the ^{13}C NMR spectra use of DEPT 135 and 90 techniques identified the different types of carbons which were in accord with the proposed structures.

The electron impact mass spectra showed that all the sulfonamides exhibited the molecular ions (M^+) (Table I); the fragmentation pattern involved successive loss of the hydrogen, amino and sulfamoyl moieties in general agreement with our previous observations.[12]

The hydrazide (**25**) and hydrazone (**26**) also showed the molecular ions which was surprising, since in previous work[12–14] hydrazides and hydrazones suffered extensive decomposition under electron impact conditions. The various sulfonamide derivatives have been submitted for biological evaluation for fungicidal, herbicidal and insecticidal activity.

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EXPERIMENTAL

Melting points were determined with a Gallenkamp electric apparatus and are uncorrected. NMR spectra were recorded with a Bruker AC 250 spectrometer using tetramethylsilane as internal standard; resonances marked with an asterisk were reduced by D_2O treatment. In the ^{13}C NMR spectra double height indicates two carbon atoms (2C) and CR_4 a quaternary carbon atom. Electron impact mass spectra were determined with a VG micromass V15 spectrometer operating at 70eV.

2-Styrylbenzothiazole (**1**): A mixture of 2-methylbenzothiazole (**4**) (10 g, 0.067 mole) and benzaldehyde (7.1 g, 0.067 mole) was added all at once to a suspension of sodamide (4 g, 0.1 mole) in dry DMF (70 ml); the mixture was refluxed (1 hour) cooled and poured onto ice-water (500 ml) to give a buff-coloured emulsion and gum.

After standing for 2 days, the product had hardened and the solid was filtered off and dried into a vacuum desiccator to give a solid (14.46 g), m.p. 92–95°C. A sample (1 g) was recrystallised three times from ethanol to give 2-styrylbenzothiazole (0.34 g, 91%), m.p. 109–112°C (lit[10] 111–112°C). MS showed the molecular ion (M^+, 237).

^1H NMR ($CDCl_3$) δ7.92–7.32 (m, 11H, ArH and alkenic H). (7.53, 7.40, 2H, alkenic H, *J*, 15.6 H_z).

^{13}C NMR ($CDCl_3$) DEPT 135 and 90 δ167.0, 153.9, 135.4, 134.4 (4 × CR_4), 137.7, 129.4, 128.9 (2C), 127.4 (2C), 126.3, 125.4, 123.0, 122.1, 121.5 (11CH groups).

2-Styrylbenzoxazole (**2**): A mixture of 2-methylbenzoxazole (**5**) (17.8 g, 0.134 mole) and benzaldehyde (14.2 g, 0.134 mole) was refluxed for 1 hour with sodium amide (8 g, 0.2 mole) in dry DMF (140 ml). The mixture was added to crushed ice (600 g) and the yellow gummy emulsion was left at room temperature for 4 days. The hardened product was ground up, washed with water, collected and dried in a vacuum desiccator to give a yellowish-brown powder (17.3 g, 72%), m.p. 60–62°C.

Recrystallisation from ethanol afforded (**2**), (12.14 g, 41%), m.p. 80–82°C (lit.[7] 81–82°C).

^1H NMR (DMSO-d_6) δ7.92–7.32 (m, 11H, alkenic H and ArH) (7.85 , 7.35 (2H, alkenic H, *J* 16.8 H_z).

^{13}C NMR (DMSO-d_6) δ162.3, 149.7, 141.6, 134.7 (4 × CR_4), 139.3, 129.8, 127.8 (2C), 127.8 (2C), 125.3, 124.6, 119.5, 113.7, 110.4 (11CH groups).

2-Phenylbenzoxazole (**3**)[6]: 2-Nitrophenol (**6**) (50 g, 0.36 mole) was dissolved in pyridine (100 ml) and benzoyl chloride (46 ml, 55 g, 0.39 mole) was added all at once. The solution became hot and an oily precipitate formed; the suspension was left at room temperature for 4 hours and was poured onto water (1 l). The mixture was stirred until a white solid had formed, this was filtered off, washed with water and dried (vacuum desiccator) to give (**7**) as pale yellow crystals (84.32 g, 96%), m.p. 54–57°C.

2-Nitrophenylbenzoate (**7**) (14.58 g, 0.06 mole) was refluxed with triethyl phosphite (31.5 g, 0.19 mole) in *t*-butylbenzene (186 ml) for 2 hours. The solvent and triethyl phosphite were distilled off and the brown residual solid extracted with boiling ethanol (3 × 60 ml). The extract was reheated and filtered hot to remove tar; water (20 ml) was added to the filtrate and the solution allowed to cool to give brown crystals (6.63 g, 57%), m.p. 100–103°C. The mother liquor by concentration afforded a second crop (0.41 g), m.p. 97–100°C; the combined products were recrystallised from 40% aqueous ethanol (140 ml) to yield (**3**) as light brown needles (5.48 g, 47%), m.p. 104–106°C.

^{1}H NMR (DMSO-d_6) δ8.30–7.39 (m, 9H, ArH).

^{13}C NMR (DMSO-d_6) DEPT 135 and 90 δ162.1, 150.1, 141.4, 126.3 (4 × CR_4), 131.8, 129.2 (2C), 127.1 (2C), 125.4, 124.7, 119.7, 110.8 (9CH).

2-(p-Amidosulfonylstyryl) benzothiazoles (**9–13**): 2-Styrylbenzothiazole (**1**) was gradually added, with swirling, to chlorosulfonic acid (6 molar equivalents) at 0°C over 45 minutes. The solution was left at room temperature for 1 week and was poured onto crushed ice and the precipitated sulfonyl chloride (**8**) was immediately collected and reacted with the appropriate amine (3 molar equivalents) in acetone. After 3 days, the mixture was poured into dilute hydrochloric acid and the resultant precipitate filtered off and stirred with 1 M sodium hydroxide solution, the solid was recollected, washed with water and dried in a vacuum desiccator over $CaCl_2$. In the case of the sulfonamides (**12, 13**) from primary amines, 5% aqueous sodium hydrogen carbonate was substituted for the sodium hydroxide solution. By this procedure, the following sulfonamide derivatives were prepared:

The morpholidate (**9**). MS: 386 (M^+), 385 (M^+-H), 300 (M^+-morpholino), 236 (M^+-$SO_2NC_4H_8O$).

^{1}H NMR (DMSO-d_6) δ8.16–7.37 (m, 10H, alkenic H, ArH), 3.64–2.94 (m, 8H, morpholino H).

The diethylamine derivative (**10**). MS: 372 (M^+), 371 (M^+-H), 357 (M^+-Me), 300 (M^+-NEt_2), 236 (M^+-$SO_2N\ Et_2$).

^{1}H NMR ($CDCl_3$) δ8.12–7.30 (m, 10H, alkenic H, ArH; AA^{1}BB^1 δ7.85, 7.68). 3.29 (q, 4H, $\underline{CH_2}Me$), 1.18 (t, 6H, $CH_2\underline{Me}$).

The piperidino derivative (**11**). MS: 384 (M^+) 383 (M^+-H), 300 (M^+-piperidino), 236 (M^+-$SO_2NC_5H_{10}$), 235 (M^+-$SO_2NHC_5H_{10}$).

^{1}H NMR ($CDCl_3$) δ8.36–7.30 (m, 10H, alkenic H, ArH AA^{1}BB^1 δ8.04, 7.90), 3.17–2.92 (m, 4H $\underline{CH_2}$-N), 1.76–1.20 (m, 6H, CH_2X3).

The benzylamine derivative (**12**). MS: 406 (M^+), 405 (M^+-H), 300 (M^+-$NHCH_2Ph$), 236 (M^+-SO_2NHCH_2Ph), 235 (M^+-$SO_2NH_2CH_2Ph$).

^{1}H NMR (DMSO-d_6) δ8.40–7.04 (m, 15H, alkenic H and ArH); AA^{1}BB^1 8.0, 7.82, 4.85* (s, 1H, NH), 4.01 (d, 2H, CH_2).

The isopropylamine derivative (**13**). MS: 358 (M^+), 357 (M^+-H), 315 (M^+-$CHMe_2$), 300 (M^+-$NHCHMe_2$), 236 (M-$SO_2NHCHMe_2$) 235 (M^+-$SO_2NH_2CHMe_2$).

^{1}H NMR ($CDCl_3$) δ8.11–7.30 (m, 10H, alkenic H, ArH, AA^{1}BB^1 δ7.85, 7.70), 4.97* (d, 1H, NH), 3.74–3.30 (m, 1H, $\underline{CH}Me_2$), 1.10 (d, 6H, Me).

2-(p-Amidosulfonylstyryl) benzoxazoles (**15–19**): 2-Styrylbenzoxazole (**2**) was added portionwise to chlorosulfonic acid (6 molar equivalents) at 0°C over 20 minutes. After 1 week at room temperature, the solution was poured onto ice, triethylamine (17 molar equivalents) and the appropriate amine (14 equivalents) in acetone (20 ml) were added. The mixture was stirred in ice-water for 30 minutes, the solid product was filtered off, washed successively with water, 1M hydrochloric acid, water and dried in a vacuum desiccator over $CaCl_2$. In the case of the benzylamine derivative (**19**), the bulk of the precipitated solid was so fine that it passed through the filter paper; however, it was coagulated by acidification (dilute hydrochloric acid) so that after this treatment the derivative could be collected.

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The morpholidate (**15**). MS: 370 (M^+), 369 (M^+-H), 284 (M^+-morpholino), 220 (M^+-$SO_2NC_4H_8O$), 219 (M^+-$SO_2NHC_4H_8O$).

^{1}H NMR ($CDCl_3$) δ7.92–7.20 (m, 10H, alkenic H, ArH), 3.76–3.04 (m, 8H, morpholino H).

^{13}C NMR ($CDCl_3$) DEPT 135 and 90 δ161.8, 150.5, 142.0, 139.7, 135.7 ($5CR_4$ groups), 136.9, 128.5 (2C), 127.9 (2C), 125.9, 124.8, 120.2, 117.3, 110.5 (10CH groups), 66.1 (2C), 46.0 (2C) (4 CH_2 groups).

The piperidino derivative (**16**). MS: 368 (M^+), 367 (M^+-H), 284 (M^+-piperidino), 220 (M^+-$SO_2NC_5H_{10}$), 219 (M^+-$SO_2NHC_5H_{10}$).

^{1}H NMR ($CDCl_3$) δ7.86–7.16 (m, 10H, alkenic H, ArH), 3.02–1.46 (m, 10H, CH_2).

^{13}C NMR ($CDCl_3$) DEPT 135 and 90 δ161.9, 150.4, 142.0, 139.2, 136.9 ($5CR_4$), 137.2, 128.3 (2C), 127.8 (2C), 125.8, 124.8, 120.1, 117.0, 110.5 (10CH), 46.9 (2C), 25.1 (2C), 23.4 ($5CH_2$).

The diethylamine derivative (**17**). MS: 356 (M^+), 355 (M^+-H), 341 (M^+-Me), 328 (M^+-C_2H_4), 284 (M^+-NEt_2), 220 (M^+-SO_2NEt_2), 219 (M^+-SO_2NHEt_2).

^{1}H NMR ($CDCl_3$) δ7.96–7.14 (m, 10H, alkenic H, ArH; AA^{1}BB^1 δ7.88, 7.68), 3.24 (q, 4H, $\underline{CH_2}Me$), 1.16 (t, 6H, $CH_2\underline{Me}$).

^{13}C NMR ($CDCl_3$) DEPT 135 and 90 δ161.9, 150.3, 141.9, 140.8, 138.8 ($5CR_4$), 137.2, 128.0 (2C), 127.5 (2C), 125.7, 124.7, 119.9, 116.7, 110.5 (10CH), 42.1 (2 × CH_2), 14.2 (2 × CH_3).

The isopropylamine derivative (**18**). MS: 342 (M^+), 341 (M^+-H), 327 (M^+-Me), 299 (M^+-$CHMe_2$), 284 (M^+-$NHCHMe_2$), 220 (M^+-$SO_2NHCHMe_2$), 219 (M^+-$SO_2NH_2CHMe_2$).

^{1}H NMR ($CDCl_3$) δ7.94–7.16 (m, 10H, ArH, alkenic H; AA^{1}BB^1 δ7.94, 7.72), 7.80, 7.20 (2H, alkenic H, *J* 16.3 H$_z$), 4.71* (d, 1H, NH), 3.70–3.41 (m, H, $\underline{CH}Me_2$), 1.11 (d, 6H, Me).

^{13}C NMR (DMSO-d_6) DEPT 135 and 90 δ161.9, 149.8, 142.4, 141.6, 138.3 ($5CR_4$), 137.6, 128.4 (2C), 126.8 (2C), 125.8, 124.8, 119.8, 116.4, 110.6, 45.3 (11CH), 23.2 (2 × CH_3).

The benzylamine derivative (**19**). MS: 390 (T), 389 (M^+-H), 229 (M^+-CH_2Ph), 284 (M^+-$NHCH_2Ph$), 220 ($M^{\bullet}$-SO_2NHCH_2Ph), 219 (M^+-$SO_2NH_2CH_2Ph$).

^{1}H NMR (DMSO-d_6) δ8.31–7.20 (m, 15H, alkenic H and ArH), 4.51* (s, 1H, NH), 4.03 (d, 2H, CH_2).

^{13}C NMR (DMSO-d_6) DEPT 135 and 90 δ161.8, 149.8, 141.6, 141.2, 138.5, 137.5 ($6CR_4$), 137.6, 128.4 (2C), 128.2 (2C), 127.5 (2C), 127.0 (2C), 126.1, 125.8, 124.8, 119.8, 116.5, 110.6 (15CH), 46.1 ($1CH_2$).

2-(p-Morpholinosulfonylphenyl) benzoxazole (**21**): 2-Phenylbenzoxazole (**3**) (1.95 g, 0.01 mole) was added to chlorosulfonic acid (4.2 ml, 0.063 mole), the reaction was exothermic and the resultant solution was heated on the steam bath for 3 hours, cooled and poured onto ice. Triethylamine (17.5 g, 0.17 mole) and morpholine (12.5 g, 0.15 mole) were added and the mixture stirred in ice-water (100 ml) for 30 minutes. The precipitate was collected, washed successively with water, 1M hydrochloric acid, water and dried in a vacuum desiccator over $CaCl_2$. Recrystallisation from ethanol afforded the morpholidate (**21**) as greyish crystals (0.25 g, 7%).

MS: 344 (M^+), 258 (M^+-morpholino), 194 (M^+-$SO_2NC_4H_8O$), 166 (M^+-$SO_2NC_4H_8$,-CO). ^{1}H NMR (DMSO-d_6) δ8.31–7.10 (m, 8H, ArH), 3.66–2.91 (m, 8H, morpholino H).

^{13}C NMR (DMSO-d_6) DEPT 135 and 90 δ165.3, 149.8, 145.3, 131.2, 125.6 (5 CR_4), 132.8, 129.4 (2C), 127.7 (2C), 124.5, 120.4, 111 (8CH), 65.2 (2 × CH_2), 45.9 (2 × CH_2).

General method for preparation of 2-(p-amidosulfonylphenyl) benzoxazoles (**22–24**) *and the hydrazide* (**25**)

2-Phenylbenzoxazole (**3**) was added all at once to chlorosulfonic acid (6 molar equivalents), the reaction was exothermic and all the solid dissolved; the solution was heated on the steam bath for 3 hours. Thionyl chloride (7 molar equivalents) and DMF (3 drops) were then added and the solution heated for a further 2 hours. The cold solution was carefully poured onto crushed ice and the precipitate was collected and immediately added to a solution of the amine (7.5 molar equivalents) in acetone. The mixture was left at room temperature for 4 days and then poured into 5% aqueous sodium hydrogen carbonate solution. The precipitate was filtered off, stirred with 1M hydrochloric acid, washed with water and dried in a vacuum desiccator. The same procedure was used for the preparation of the sulfonyl hydrazide (**24**), except that hydrazine hydrate was substituted for the amine and ethanol was used as solvent instead of acetone and the treatment with hydrochloric acid was omitted.

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The piperidino derivative (**22**). MS: 342 (M^+), 341 (M^+-H), 258 (M^+-piperidino), 194 (M^+-$SO_2NC_5H_{10}$), 166 (M^+-$SO_2NC_5H_{10}$,-CO).

^{1}H NMR (Me_2CO-d_6) δ8.34–7.59 (m, 8H, ArH; AA^{1}BB^1 δ8.30, 7.68), 3.03 (m, 4H, $\underline{CH_2}$-N), 1.63–1.43 (m, 6H, CH_2).

^{13}C NMR (Me_2CO-d_6) DEPT 135 and 90 δ166.5, 151.2, 146.4, 134.4, 127.3 (5CR_4), 133.4, 130.1 (2C), 128.7 (2C), 125.3, 121.1, 111.6 (8CH), 47.8 (2C), 26.0 (2C), 24.1 (5CH_2 groups).

The diethylamine derivative (**23**). MS: 330 (M^+), 315 (M^+-Me), 258 (M^+-NEt_2), 194 (M^+-SO_2NEt_2), 166 (M^+-SO_2NEt_2,-CO).

^{1}H NMR (DMSO-d_6) δ8.30–7.38 (m, 8H, ArH; AA^{1}BB^1 δ8.26, 7.68), 3.23 (q, 4H, CH_2), 1.07 (t, 6H, Me).

^{13}C NMR (DMSO-d_6) DEPT 135 and 90 δ165.1, 149.7, 144.6, 136.6, 125.7 (5CR_4), 132.6, 129.3 (2C), 127.6 (2C), 123.6, 120.3, 110.1 (8CH), 41.9 (2CH_2), 14.0 (2CH_3).

The benzylamine derivative (**24**). MS: 364 (M^+), 299 (M^+-SO_2H) 259 (M^+-NCH_2Ph), 258 (M^+-$NHCH_2Ph$), 194 (M^+-SO_2NHCH_2Ph).

^{1}H NMR (DMSO-d_6) δ8.28–7.12 (m, 13H, ArH; AA^{1}BB^1 δ8.27, 7.68), 4.90* (s, 1H, NH), 4.06 (m, 2H, $\underline{CH_2}$Ph).

^{13}C NMR (DMSO-d_6) DEPT 135 and 90 δ164.9, 149.5, 144.4, 137.7, 137.4, 125.7 (6CR_4), 132.6, 129.4, (2C), 128.1 (2C), 127.6 (2C), 127.4 (2C), 127.0, 123.4, 120.2, 109.9 (13CH), 46.2 (CH_2).

The hydrazide (**25**). MS: 289 (M^+), 274 (M^+-NH), 259 (M^+-N_2H_2), 258 (M^+-N_2H_3) 195 (M^+-SO_2NHNH_2).

^{1}H NMR (DMSO-d_6) δ8.56* (s, 1H, NH), 8.30–7.38 (m, 8H, ArH; AA^{1}BB^1 δ8.40, 7.69), 4.23* (s, 2H, NH_2).

^{13}C NMR (DMSO-d_6) DEPT 135 and 90 δ164.9, 149.5, 144.7, 135.0, 125.7 (5CR_4 groups), 132.6, 129.4 (2C), 127.6 (2C), 124.5, 120.0, 111.0 (8CH groups).

The acetone hydrazone (**26**). 2-(p-Hydrazinosulfonylphenyl)benzoxazole (**25**) (2 g, 0.007 mole), was dissolved in boiling acetone (50 ml) and the solution evaporated to approximately 25 ml and left at room temperature (12 hours). The solution by cooling (0°C) afforded the hydrazone (**26**) as buff crystals (1.5 g). MS: 329 (M^+), 274 (M^+-N=CMe_2), 260 (M^+-NHN=CMe_2).

^{1}H NMR (DMSO-d_6) δ10.24* (s, 1H, NH), 8.27–7.59 (m, 8H, ArH; AA^{1}BB^1 δ7.88, 7.68), 1.86 (d, 6H, Me).

^{13}C NMR (DMSO-d_6) DEPT 135 and 90 δ165.1, 157.4, 149.4, 144.8, 136.1, 125.7 (6CR_4), 132.6, 129.3 (2C), 127.7 (2C), 124.4, 120.0, 110.8 (8CH), 24.8, 17.7 (2CH_3).

Chlorosulfonation of 2-styrylbenzothiazole (**1**) *using more forcing conditions*

2-Styrylbenzothiazole (**1**) (2 g, 0.0073 mole) was slowly added to chlorosulfonic acid (10.2 g, 0.088 mole) at 0°C; the solution was then heated on a water bath at 50°C for 5 hours. The mixture was treated with thionyl chloride (30 ml) and DMF (2 drops) at room temperature (1 hour) until the evolution of gas ceased. Addition of ice-water (200 ml) gave a yellow precipitate of the bis-sulfonyl chloride (**27**) (66%, m.p. 95–100°C). The product was immediately reacted with a large excess of morpholine to give the disulfonyl morpholidate (**28**) (65%, m.p. 288–290°C).

(Found: C, 48.4; H, 4.2; N, 2.0. $C_{23}H_{24}ClN_3O_6S_3$ requires C, 48.5; H, 4.2; N, 7.4%). IR ν_{max} 1610 (arom C=C), 1340, 1160 (SO_2) cm^{-1}.

MS: 571, 569 (M^+), 570, 568 (M^+-H).

^{1}H NMR (DMSO-d_6) δ8.4 (d, 1H, Ar-H_7; $J_{7,5}$ 1.9H_z), 8.25 (s, 1H, alkenic H), 8.20 (d, 1H, Ar-H_4; $J_{4,5}$ 9.3H_z), 8.08–7.85 (m, 4H, benzylic H, AA^{1}BB^1 pattern), 7.9 (dd, 1H, Ar-H_5;$J_{5,4}$ 9.3H_z, $J_{5,7}$ 1.9H_z), 3.8–3.1 (m, 8H, morpholino H).

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