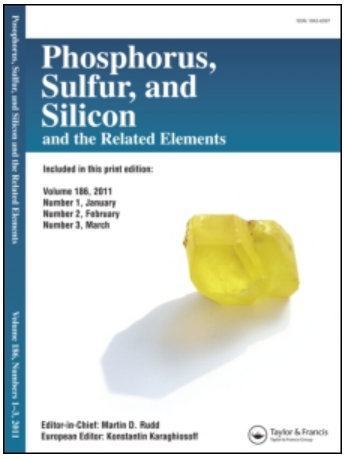

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SULFONYL DERIVATIVES OF 2,5-DIPHENYLFURAZAN

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SULFONYL DERIVATIVES OF 2,5-DIPHENYLFURAZAN

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2,5-Diphenylfurazan (**2**) was converted into the monosulfonyl chlorides (**3a**, **3b**) on treatment with chlorosulfonic acid (~7 moles). These products were identified by reaction with secondary amines when both 3'- and 4'-sulfonyl derivatives were isolated. Under more forcing conditions, using a much larger excess of the reagent (~25 moles), bis-substitution was achieved. Although TLC indicated the formation of two products, after reaction with secondary amines only 3',3''-disulfonyl derivatives could be isolated. These results are discussed in electronic terms.

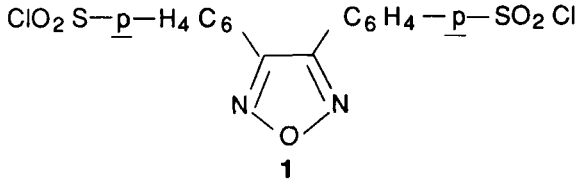
Key words: 2,5-Diphenylfurazan; chlorosulfonation; sulfonamides; bis(sulfonamides).

INTRODUCTION

We have previously reported[1] that the treatment of 3,4-diphenylfurazan with an excess of chlorosulfonic acid (~6 moles) gave the 4',4''-disulfonyl chloride (**1**). This product was identified by conversion into the bis(N,N-dimethylsulfonamide) derivative. The ^{1}H NMR spectrum of this compound contained a characteristic AA'BB' pattern in the aromatic region, indicative of *para*-disubstitution. These observations were contrary to our earlier report,[2] but they have been confirmed by repetition of this work.[3]

This reaction therefore demonstrated the dominance of the +M effect of the heterocyclic oxygen atom over the −M effect of the imino part of the ring.

It was therefore of interest to study the reaction of the isomeric substrate, 2,5-diphenylfurazan, with chlorosulfonic acid under similar conditions and to show whether the course of the reaction is determined in a similar way.



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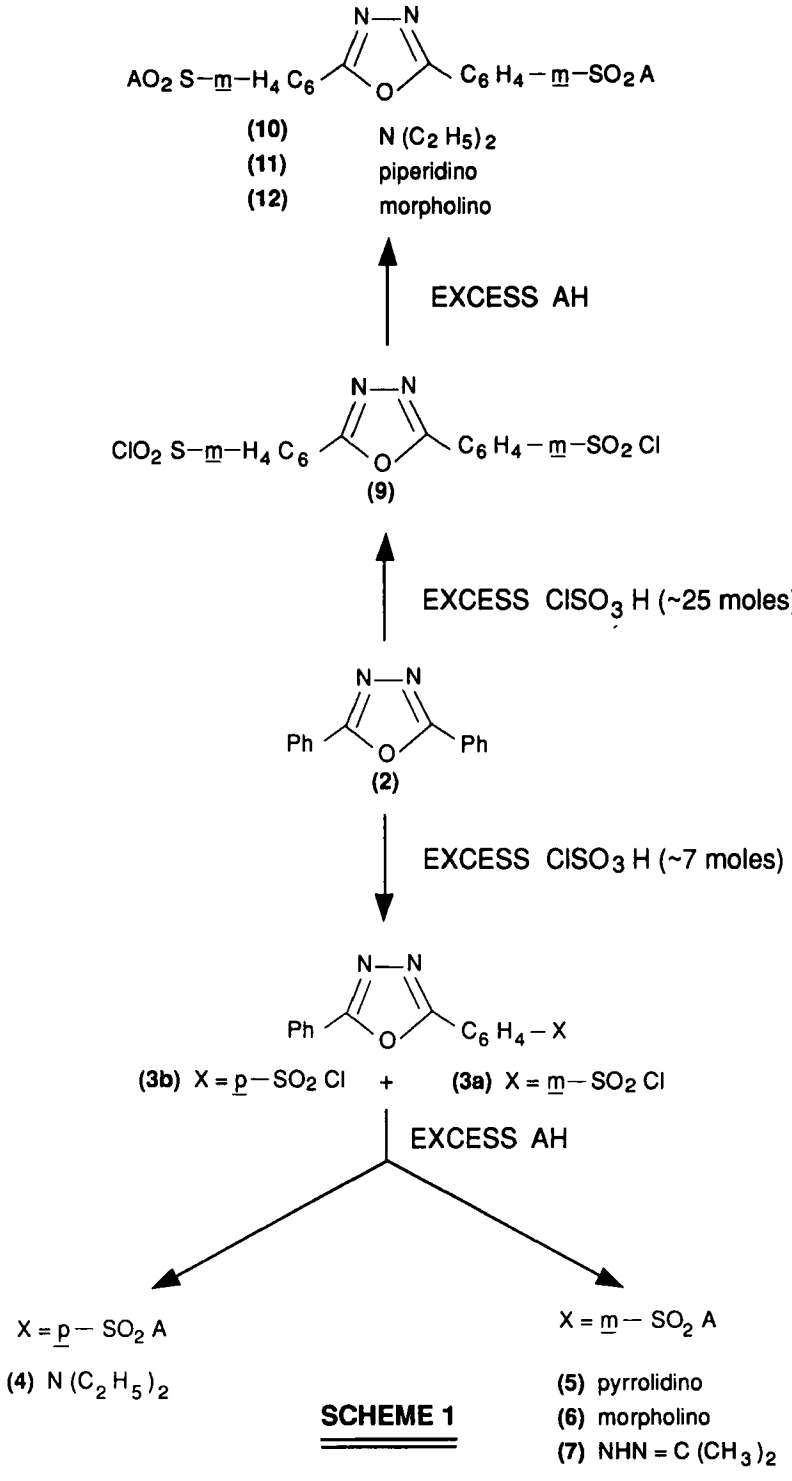
DISCUSSION

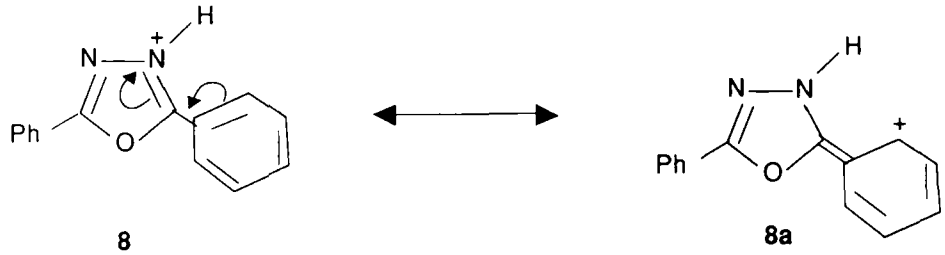
Treatment of 2,5-diphenylfurazan (**2**) with an excess of chlorosulfonic acid (~7 moles) under conditions similar to those used with the 3,4-diphenyl isomer, (85°, 3 hours), gave two products together with probably sulfonic acid (R_F 0.0) and



SCHEME 1

unreacted starting material. The mixture was therefore heated for a further 1½ hours at 110°. However, the product still contained sulfonic acid and starting material. It was possible to obtain derivatives of the sulfonyl chlorides (**3a**) and (**3b**), (Scheme 1). The mixture was reacted with an excess of diethylamine and after recrystallization the N,N-diethylsulfonamide (**4**) (M^+ 357) was obtained. Examination of the ^1H NMR spectrum showed that the aromatic region contained, in addition to other multiplets, an AA'BB' pattern characteristic of *para*-disubstitution. With an excess of pyrrolidine and morpholine, the corresponding sulfonamides (**5**, **6**) were obtained. The reaction with an excess of hydrazine hydrate followed by treatment with acetone gave the acetone hydrazone (**7**). In these instances, the ^1H NMR spectra of the purified derivatives did not show the AA'BB' pattern in the aromatic region.

Under the conditions of chlorosulfonation, the *meta*- and *para*-sulfonyl chlorides (**3a**, **3b**) are formed. The orientation of electrophilic substitution is affected by both the +M effect of the hetero atom and the −M effect of the ring. Unlike the reaction with 3,4-diphenylfurazan where the disulphonyl chloride (**1**) was obtained, with somewhat more forcing conditions only monosubstitution products could be obtained. This difference in reactivity can be attributed to more favourable protonation of 2,5-diphenylfurazan. The cation is resonance stabilized by the +M effect of the phenyl group as shown by the canonical structures **8** and **8b** below:



8 **8a**

On this basis one of the phenyl rings is more deactivated to electrophilic attack than the other.

In order to obtain the bis-product, more forcing conditions were required—a very much larger excess of chlorosulfonic acid (~25 moles), an increase in the temperature (120°) and a longer reaction time (14 hours) followed by treatment with thionyl chloride (3 hours). There was no evidence of monosubstitution products, (R_F 0.3, 0.4), but two new products were formed (R_F 0.6, 0.7), together with the probable formation of sulfonic acid which remained on the base line. The yield of product mixture was very high. Sulfonic acids are hydrophilic and no chloroform extraction was undertaken as with the previous reaction work-up. It is therefore possible that the high yield of product mixture using the larger excess of chlorosulfonic acid may be due to sulfonic acid hydrate formation.

In addition to the base-line product it seems likely that by analogy with the reaction involving less reagent both the bis-*meta*- and bis-*para*-products are formed. However, it was only possible to obtain derivatives of the disulfonyl chloride (**9**), (Scheme 1). Treatment of the mixture with an excess of diethylamine gave, after purification, the bis(N,N-diethylsulfonamide) (**10**) (M^+ 492). The reactions with excess quantities of piperidine and morpholine gave the corresponding bis(sulfon-

amides) (**11**, **12**). In each case the aromatic region of the ^1H NMR spectrum was unsymmetrical and included up to four multiplets. The pattern for the bis(N,N-diethylsulfonamide) (**10**) was amenable to first-order analysis. The failure to isolate any *para*-derivatives after treatment with excess amine, could be due to the greater solubility of each of these compounds in the recrystallization solvent (ethanol).

EXPERIMENTAL

Melting points were determined with a Gallenkamp electrically heated apparatus and are uncorrected. IR spectra were measured as nujol mulls on a Philips PU9706 spectrophotometer. ^1H NMR spectra were recorded with a Bruker WP80 spectrometer using tetramethylsilane as internal standard. Mass spectra were determined with a VG Micromass 16F instrument. The FAB mass spectrum was obtained using a VG70-250 SEQ instrument by courtesy of Smith, Kline and French Ltd., Welwyn, Hertfordshire. TLC was carried out on Camlab Polygram silica gel plates sensitized to UV 254 nm, using petroleum ether (60–80°)—ethyl acetate (3:2), as eluant for the monosubstitution products and petroleum ether (80–100°)—ethyl acetate (3:2), as eluant for the bis-substitution products. Microanalyses and the chemical ionisation mass spectrum were carried out by courtesy of Shell Research Ltd., Sittingbourne, Kent.

2,5-Diphenylfurazan. **2** was prepared by the method of Fitton and Smalley.[4]

2,5-Diphenylfurazan-3'-sulfonyl chloride **3a** *and 2,5-Diphenylfurazan-4'-sulfonyl chloride* **3b**. 2,5-Diphenylfurazan (**2**) (9.8 g, 0.044 mole) was added to cooled chlorosulfonic acid (0.324 mole) portionwise, while the temperature was kept below 10°. The mixture was heated at 85° for 3 hours, after which time the temperature was raised to 110° for 1½ hours. The mixture was cooled and poured onto ice (100 g) with vigorous stirring. The solid was filtered off, well washed with water and extracted with chloroform (100 ml). The solvent was removed by rotary film evaporation to give the product (9.6 g). TLC R_F 0.0, 0.30, 0.45.

General method for the preparation of mono- and bis-sulfonamides. The sulfonyl chloride (1.5 g) was dissolved in methanol (25 ml). The amine (at least 10 moles) was added at room temperature with stirring, which was continued for 2–3 hours. The product was filtered off and recrystallized from ethanol.

Compound **4**. (37%), m.p. 151–152°, TLC single spot R_F 0.51.
(Found: C, 60.3; H, 5.3; N, 11.7. Calc. for $C_{18}H_{19}N_3O_3S$: C, 60.5; H, 5.3; N, 11.8%). V_{MAX} 1340, 1160 (SO_2) cm^{-1}. ^1H NMR δ: 8.3–7.9 (6H, m, aromatic H), 7.7–7.5 (3H, m, aromatic H), 3.3 (4H, q, 2 × CH_2), 1.2 (6H, t, 2 × CH_3). MS m/Z 357 (M^+, ~17%), 342 (M^+-Me), 285 (M^+-NEt_2), 221 (M^+-SO_2NEt_2), 105 ($C_6H_5CO^+$), 77 ($C_6H_5^+$).

Compound **5**. (62%), m.p. 169–171°, TLC single spot R_F 0.10.
(Found: C, 60.8; H, 4.8; N, 11.8. Calc. for $C_{18}H_{17}N_3O_3S$: C, 60.8; H, 4.8; N, 11.8%). V_{MAX} 1345, 1150 (SO_2) cm^{-1}. ^1H NMR δ: 8.6–7.4 (9H, m, aromatic H), 3.3 (4H, m, 2 × NCH_2), 1.8 (4H, m, 2 × CH_2). MS m/Z 355 (M^+, ~34%), 286 (M^+-C_4H_7N), 222 (M^+-$SO_2NC_4H_7$), 105 ($C_6H_5CO^+$), 77 ($C_6H_5^+$).

Compound **6**. (35%), m.p. 181–183°, TLC single spot 0.60.
(Found: C, 56.9; H, 4.7; N, 11.3. Calc. for $C_{18}H_{17}N_3O_4.0.5H_2O$: C, 56.8; H, 4.7; N, 11.1%). V_{MAX} 1350, 1165 (SO_2) cm^{-1}. ^1H NMR δ: 8.6–7.3 (9H, m, aromatic H), 3.7 (4H, m, 2 × OCH_2), 3.1 (4H, m, 2 × NCH_2). MS m/Z 371 (M^+, ~10%), 285 (M^+-C_4H_8NO), 221 (M^+-$SO_2C_4H_8NO$), 105 ($C_6H_5CO^+$), 86 ($C_4H_8NO^+$), 77 ($C_6H_5^+$).

Compound **7**. The sulfonyl chloride (**3**) (1 g, 0.003 mole) was dissolved in methanol (25 ml). Hydrazine hydrate (0.017 mole) was added and the mixture was stirred at room temperature for 2 hours. The precipitate was filtered off and the dried product was added to acetone (40 ml). The mixture was heated under reflux for 30 minutes. The product was filtered off and recrystallized from ethanol (6%), m.p. 198–199°, TLC single spot R_F 0.0.
(Found: C, 56.9; H, 4.7; N, 16.0. Calc. for $C_{17}H_{16}N_4O_3S$: C, 57.3; H, 4.5; N, 15.7%). V_{MAX} 3220 (NH), 1330, 1180 (SO_2) cm^{-1}. ^1H NMR δ: 8.6–7.5 (10H, m, aromatic H), 1.8 (6H, s, 2 × CH_3). MS (CI) m/Z 357 (M + H^+), 223 (M + H^+-SO_2NNCMe_2).

2,5-Diphenylfurazan-3,3'-disulfonyl chloride **9**. 2,5-Diphenylfurazan (**2**) (2.22 g, 0.01 mole) was added to cooled chlorosulfonic acid (0.256 mole) portionwise, while the temperature was kept below 10°. The mixture was heated at 120° for 14 hours after which time thionyl chloride (0.14 mole) was added and the mixture heated for a further 3 hours. The mixture was poured onto ice (100 g) while stirring. The solid was filtered off, washed well with water and dried by suction, (8.1 g), TLC R_F 0.0, 0.60, 0.70.

Compound **10**. (37%), m.p. 151–152°, TLC single spot R_F 0.51.
(Found: C, 53.5; H, 5.9; N, 11.9. Calc. for $C_{22}H_{28}N_4O_5S_2$: C, 53.7; H, 5.7; N, 11.4%). V_{MAX} 1340, 1170 (SO_2) cm^{-1}. ^1H NMR δ: 8.8 (2H, td, aromatic H2', H2"), 8.6 (2H, dt, aromatic H4', H4"), 8.3 (2H, dt, aromatic H6', H6"), 8.1 (2H, td, aromatic H5', H5"), 3.3 (8H, q, 4 × CH_2), 1.2 (12H, t, 4 × CH_3). MS m/Z 492 (M^+, ~10%), 477 (M^+-Me), 356 (M^+-SO_2NEt_2).

Compound **11**. (24%), m.p. 180–181°, TLC single spot R_F 0.55. (Found: C, 55.9; H, 5.6; N, 10.9. Calc. for $C_{24}H_{28}N_4O_5S_2$: C, 55.8; H, 5.4; N, 10.9%). V_{MAX} 1340, 1170 (SO_2) cm^{-1}. ^1H NMR δ: 8.6–7.6 (8H, m, aromatic H), 3.2 (^1H, m, 4 × CH_2N), 2.0–1.3 (12H, m, 2 × $(CH_2)_3$). MS (FAB-) m/Z 515 (M^+-H), 432 (M^+-H-C_5H_9N).

Compound **12**. (6%), m.p. 222–223°, TLC single spot R_F 0.20. (Found: C, 51.0; H, 5.2; N, 11.4. Calc. for $C_{22}H_{24}N_4O_7S_2$: C, 50.8; H, 4.6: N, 10.8%). V_{MAX} 1350, 1170 (SO_2) cm^{-1}. ^1H NMR δ: 8.6–7.7 (8H, m, aromatic H), 3.8 (8H, m, 4 × CH_2O), 3.1 (8H, m, 4 × CH_2N). MS m/Z 520, (M^+, 35%), 371 (M^+-$SO_2NC_4H_7O$).

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