A Novel Cyclisation Reaction of Benzil

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Benzil reacts with chlorosulphonic acid to give 3-chloro-2-phenylbenzofuran-6,4'-disulphonyl dichloride. The product was characterised as the corresponding bis-dimethylsulphonamide (1), and a mechanism has been proposed for the chlorosulphonation reaction. The chlorosulphonation of 2,3-diphenylpyrazine and 3,4-diphenylfurazan is also reported.

Biocidal activity has been reported for a variety of sulphonyl derivatives, *e.g.* amides,[1] azides,[2] and hydrazides.[3-6] These compounds can be obtained by the chlorosulphonation of the appropriate substrate, followed by nucleophilic displacement of the chlorine atom. The present investigation forms part of the programme concerned with the chlorosulphonation of aromatic ketones; this has been successful with benzophenone,[7] and a range of derivatives have been obtained for biological assay. The reaction of benzil with chlorosulphonic acid has not been reported previously, and in view of its known biological activity, *e.g.* an insecticide in the protection of seeds [8] and use in the control of schistomiasis,[9] and of the high activity of 4,4'-dichlorobenzil as an antibacterial drug,[10] it seemed to be an excellent compound for study. In addition, benzil can be converted into 2,3-diphenylpyrazine [11] and 3,4-diphenylfurazan.[12] As heterocyclic compounds have proved to be a fertile source of pesticides,[13] the chlorosulphonation of these compounds was also studied.

Experimental

M.p.s were determined with a Kofler hot-stage apparatus and are uncorrected. I.r. spectra were determined with a Unicam SP-300 spectrophotometer. U.v. spectra were determined with a Unicam SP-1800 spectrophotometer. N.m.r. spectra were recorded with a Bruker WP 80 spectrometer using tetramethylsilane as internal standard. Mass spectra were obtained with a VG Micromass V15 instrument. Microanalyses were by Butterworth's Microanalytical Consultancy Ltd., Teddington.

3-*Chloro*-2-*phenylbenzofuran*-6,4'-*disulphonyl Dichloride*.—Benzil (5 g, 0.023 mol) was added to chlorosulphonic acid (16 g, 0.14 mol) at 0 °C. The mixture was heated on a steam bath at 40 °C for 2 h, and then poured onto ice. The precipitate was filtered off, washed with water (2 × 100 ml) and then air-dried to give the sulphonyl chloride as yellow crystals (6 g, 60%), m.p. 194—196 °C, t.l.c. [ethyl acetate–light petroleum (40—60 °C) as eluant], one spot, R_F 0.4; $\nu_{max.}$ (Nujol) 1 600 (Ar C=C), and 1 340, and 1 160 cm^{-1} (SO_2); *m/z* 430, 428, 426, and 424.

3-*Chloro*-N,N-*dimethyl*-2-*phenylbenzofuran*-6,4'-*disulphonamide* (1).—A mixture of the sulphonyl chloride (2 g, 0.0047 mol) and dimethylamine (1.3 g, 0.028 mol) in methanol (100 ml) was heated under reflux for 2 h. The mixture was cooled, triturated with water, and after recrystallisation from chloroform gave fluffy white crystals of the *dimethylamide* (1) (1.3 g, 62%), m.p. 208—209 °C, t.l.c. (ethyl acetate–cyclohexane, 2 : 1, as eluant), one spot, R_F 0.6 (Found: C, 48.5; H, 4.3; Cl, 8.2; N, 6.1; S, 14.5. $C_{18}H_{19}N_2ClO_5S_2$ requires C, 48.8; H, 4.3; Cl, 8.0; N, 6.3; S, 14.5%); $\nu_{max.}$ (Nujol) 1 600 (Ar C=C), 1 340 and 1 160 cm^{-1} (SO_2); $\delta(C^2HCl_3)$ 8.4—7.8 (m, 7 H, Ar H) and 2.75 (s, 12 H NMe_2); *m/z* 444 and 442; $\lambda_{max.}$ 320 and 330 nm (log ε 4.3 and 4.0).

2,3-*Diphenylpyrazine*-3',3''-*disulphonyl Dichloride* (2).—2,3-Diphenylpyrazine (10 g, 0.043 mol) was added to chlorosulphonic acid (32 g, 0.27 mol) at room temperature. The mixture was heated at 170 °C for 0.75 h, and then poured onto ice. The precipitate was filtered off, washed with water (2 × 100 ml), and then air-dried to give white crystals of the sulphonyl chloride (2) (15.3 g, 83%), m.p. 90—92 °C; $\nu_{max.}$ (KBr) 1 600 (Ar C=C), 1 360 and 1 140 cm^{-1} (SO_2); *m/z* 432, 430, and 428.

N,N-*Dimethyl*-2,3-*diphenylpyrazine*-3',3''-*disulphonamide*.—The disulphonyl dichloride (2 g, 0.0047 mol) was heated with dimethylamine (1.5 g, 0.033 mol) in methanol (100 ml) for 6 h. The mixture was cooled, triturated with ice, and gave, after recrystallisation from methanol, the *diamide* (1.8 g, 85%), m.p. 69—71 °C (Found: C, 52.8; H, 5.0; N, 12.2. $C_{20}H_{22}N_4O_4S_2 \cdot \frac{1}{2}H_2O$ requires C, 52.75; H, 5.1; N, 12.3%); $\nu_{max.}$ (KBr) 1 600 (Ar C=C), 1 340 and 1 160 cm^{-1} (SO_2); δ [$(C^2H_3)_2SO$] 8.8 (s, 2 H, pyrazolyl H), 7.9—7.5 (m, 8 H, Ar H), and 2.8—2.4, (d, 12 H NMe_2); *m/z* 446.

3,4-*Diphenylfurazan*-3',3''-*disulphonyl Dichloride* (3).—3,4-Diphenylfurazan (10 g, 0.045 mol) was added to chlorosulphonic acid (32 g, 0.27 mol) at 0 °C. The mixture was heated at 100 °C for 2 h, and then poured onto ice. The precipitate was filtered off, washed with water (2 × 100 ml) and air-dried to give the sulphonyl chloride (3) (5.4 g, 30%), m.p. 132—138 °C; $\nu_{max.}$ (Nujol) 1 600 (Ar C=C), 1 340 and 1 160 cm^{-1} (SO_2).

N,N-*Dimethyl*-3,4-*diphenylfurazan*-3',3''-*disulphonamide*.—The disulphonyl dichloride (3) (2 g, 0.0049 mol) was heated with dimethylamine (1.5 g, 0.033 mol) in methanol (100 ml) for 2 h. The mixture was cooled, triturated with water, and gave after recrystallisation from methanol the *dimethylamide* (0.3 g, 15%), m.p. 159—161 °C (Found: C, 48.2; H, 4.8; N, 12.3. $C_{18}H_{20}N_4O_5S_2$ requires C, 49.5; H, 4.6; N, 12.8%); $\nu_{max.}$ (KBr) 1 600 (Ar C=C), 1 360 and 1 120 cm^{-1} (SO_2); $\delta(C^2HCl_3)$ 8.2—7.8 (m, 8 H, Ar H) and 2.8—2.6 (d, 12 H, NMe_2); *m/z* 436.

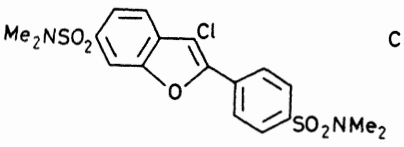
Discussion

The behaviour of benzil with chlorosulphonic acid is very different to that of benzophenone, which gave the expected 3,3'-disulphonyl dichloride under forcing conditions (6 mol; 120 °C; 6 h).[7] In contrast, careful control of the reaction conditions was particularly important with benzil, in order to avoid degradation. The optimum yield of the product was obtained when the reaction temperature was kept below 50 °C (see the Table). Above this temperature the reaction mixture charred. The use of a solvent to moderate the reaction did not improve the yield, although an identical product was obtained in boiling chloroform. The significantly milder reaction

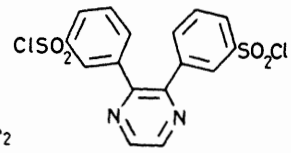
Table. Conditions used in the reaction of benzil with chlorosulphonic acid

$ClSO_3H$ (mol)	Temp. (°C)	Solvent	Reaction time	Reagent	Yield (%)
6	40		2 h		62
6	Room temp.		2 weeks [a]		58
6	65	$CHCl_3$	2 h		45
8	65	$CHCl_3$	2 h		45
12	65	$CHCl_3$	2 h		Charred
6	Room temp.		2 weeks	PCl_5	60
4	65		10 min		Charred

[a] In the dark.



(1)



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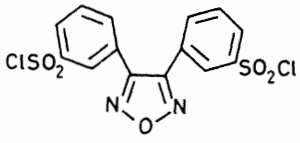


(3)

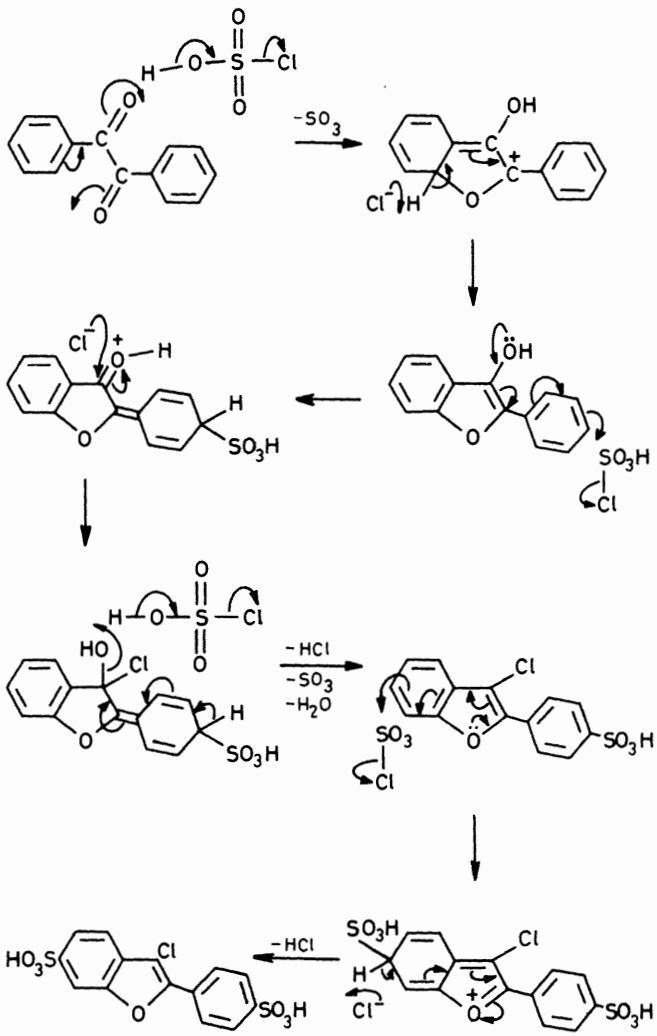
conditions required with benzil are surprising in view of the deactivation towards electrophilic attack imposed by the carbonyl group, which clearly determines the reaction conditions in the case of benzophenone. The presence of the α-carbonyl group must therefore influence the reactivity.

The product was characterised as the bis-dimethylamide, and chemical and spectral evidence showed that the original carbonyl groups were absent, and that an unreactive chlorine atom was present. The u.v. spectrum showed two maxima ($\lambda_{max.}$ 320, 330; $\varepsilon_{max.}$ *ca.* 10^4), and it was similar to that of 2-phenylbenzofuran.[14] *X*-Ray crystallography was used to determine the positions of the substituents, and showed that the product was 3-chloro-*N*,*N*-dimethyl-2-phenylbenzofuran-6,4′-disulphonamide (1). A full account of the *X*-ray work will be reported separately.[15]

2-Phenylbenzofuran was prepared by the method of Davies and Middleton,[16] and it was then treated with chlorosulphonic acid under conditions identical with those used in the reaction with benzil, in order to determine whether it was an intermediate in the reaction sequence. However, the product was water soluble and t.l.c. showed that it was a mixture; none of the R_F values corresponded with that of the product from the benzil reaction.

The influence of an alternative reagent was investigated using concentrated sulphuric acid and also oleum. With the former the starting material was recovered, but on using more forcing conditions with oleum, the compound was largely degraded.

The mechanism proposed for the formation of the benzofuran derivative is given in the Scheme. Initial protonation,



Scheme. Proposed mechanism for the reaction of benzil with chlorosulphonic acid

followed by ring-closure as the result of the participation of the α-carbonyl group is suggested. The intermediate 3-hydroxy-2-phenylbenzofuran is activated to chlorosulphonation in both the phenyl and benzo rings. With concentrated sulphuric acid and oleum it is probable that both carbonyl groups are protonated, which would remove the possibility of neighbouring group participation and cause increased resistance to electrophilic attack.

Benzil was converted into 2,3-diphenylpyrazine by heating with an ethanolic solution of ethylenediamine,[11] and into 3,4-diphenylfurazan by conversion into the dioxime followed by heating with acetic anhydride.[12] In each case the phenyl rings were deactivated by the heterocyclic moiety, as reaction temperatures of 170 and 100 °C respectively together with an excess of chlorosulphonic acid were required to obtain the 3′,3″-disulphonyl dichlorides (2) and (3). The chlorides were converted into the bis-dimethylamides, and the lack of symmetry in the aromatic resonances in the ^1H n.m.r. spectra confirmed the positions of substitution.

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Received 18*th February* 1983; *Paper* 3/251