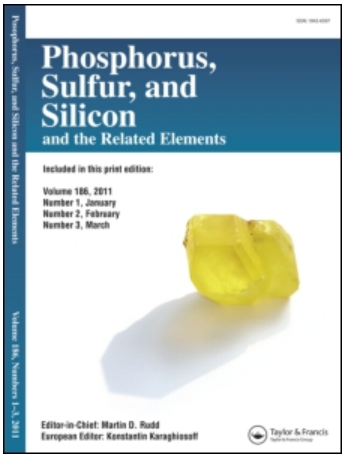


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

THE REACTION OF CHLOROSULFONIC ACID WITH BENZALACETONE AND BENZALPINACOLONE

Richard J. Cremlyn[a]; Frederick J. Swinbourne[a]; Peter A. Carter[a]; Linda Ellis[a]
[a] Division of Chemical Sciences, Hatfield Polytechnic, Hertfordshire, England

To cite this Article Cremlyn, Richard J. , Swinbourne, Frederick J. , Carter, Peter A. and Ellis, Linda(1990) 'THE REACTION OF CHLOROSULFONIC ACID WITH BENZALACETONE AND BENZALPINACOLONE', Phosphorus, Sulfur, and Silicon and the Related Elements, 47: 3, 267 — 272
To link to this Article: DOI: 10.1080/10426509008037978
URL: http://dx.doi.org/10.1080/10426509008037978

Phosphorus, Sulfur, and Silicon, 1990, Vol. 47, pp. 267–272
Reprints available directly from the publisher
Photocopying permitted by license only

THE REACTION OF CHLOROSULFONIC ACID WITH BENZALACETONE AND BENZALPINACOLONE

RICHARD J. CREMLYN, FREDERICK J. SWINBOURNE, PETER A. CARTER and MRS. LINDA ELLIS

Division of Chemical Sciences, Hatfield Polytechnic, Hatfield, Hertfordshire, England

(Received May 3, 1989; in final form May 29, 1989)

Freshly prepared benzalacetone (**1**) can be converted into styrene-4,β-disulfonyl dichloride (**3**) on treatment with an excess of chlorosulfonic acid. The yield is influenced by the work-up conditions. A number of derivatives have been prepared from **3**, by reaction with nitrogen nucleophiles. Benzalpinacolone (**5**), which precludes enolisation—a key step in the conversion of **1** into **3**, was also converted into **3** on treatment with an excess of chlorosulfonic acid. The identity of the product was confirmed by reaction with dimethylamine and morpholine, which gave the bis-sulphonamides (**4**) and (**16**) respectively. A reaction mechanism for the conversion of (**5**) into (**3**) has been proposed.

Key words: Chlorosulfonic acid and benzalacetone; styrene-4,β-disulfonyl dichloride; reaction with nucleophiles.

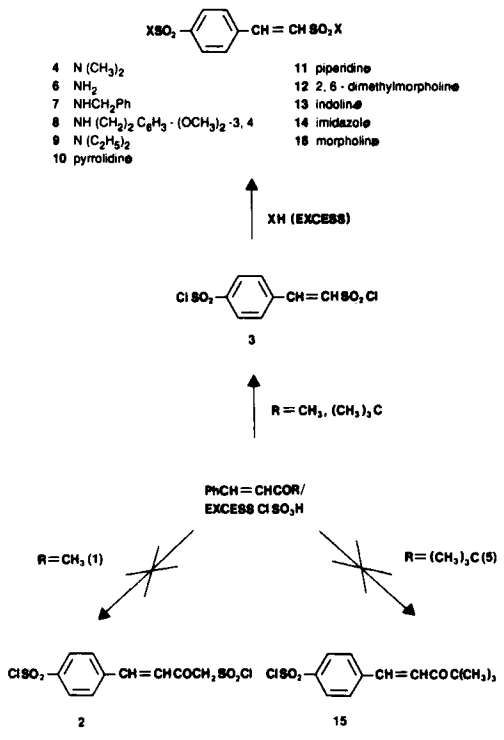
INTRODUCTION

As part of our program concerned with the synthesis and biocidal evaluation of sulfonyl compounds, we are investigating the chlorosulfonation of ketones.[1–4] We reported previously[5] the novel reaction of benzalacetone (**1**) with an excess of chlorosulfonic acid. The product of this reaction was not the expected 4,ω-disulfonyl dichloride (**2**), by analogy with the conversion of acetophenone into the 2,ω-disulfonyl dichloride,[6] but styrene-4,β-disulfonyl dichloride (**3**), which was characterised as the bis(*N*,*N*-dimethylsulfonamide) (**4**, X = $N(CH_3)_2$, Scheme 1).

In view of the unusual structure of the product obtained by chlorosulfonation of benzalacetone (**1**) in which the sulfonyl group is directly bonded to the alkenic group, we have prepared several other derivatives for biological evaluation as pesticides and medicinal agents. In addition, we have extended the investigation to the reaction of benzalpinacolone (**5**) with chlorosulfonic acid.

DISCUSSION

Benzalacetone (**1**) was converted into styrene-4,β-disulfonyl dichloride (**3**) by the method previously described.[5] However, the starting material must be freshly prepared and the following modifications made to the work-up procedure, in order to achieve a satisfactory yield (56%), which was lower than that previously



SCHEME 1

reported:

(a) addition of salt to the aqueous phase and filtration through Highflo Supercel in order to assist separation of the phases;

(b) addition of large quantities of $MgSO_4$ to the organic phase and drying for at least 1 hour.

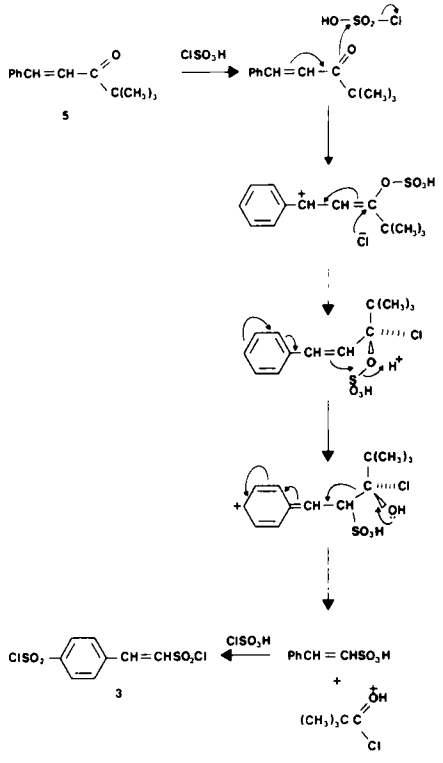
The crude disulfonyl dichloride (**3**) was converted into a number of derivatives (**6–14**, Scheme 1) by reaction with ammonia and primary and secondary amines. The products were generally obtained in comparatively low yields (<40%). Their identities were confirmed by microanalysis and spectral data. With one exception, compound **7**, each mass spectrum contained the molecular ion. Those observed were, as expected, of low intensity (≤20%), due to the fragmentation of the N-substituted groups. Consequently, it is not surprising that the ion from the bis-sulfonamide (**6**) was significantly more stable (~50%). The ^{1}H NMR spectra showed the presence of the *para*-disubstituted aromatic ring together with the E-disubstituted alkenic bond in most cases. The IR spectra confirmed the presence of the SO_2 group and supported the presence of the alkenic bond and the *para*-disubstituted aromatic ring.

The formation of styrene-4,β-disulfonyl dichloride (**3**) from benzalacetone (**1**) was thought to involve enolisation of the acetyl group, favoured by the acidic reaction conditions.[5] It was therefore considered that the use of benzalpinacolone

(**5**), which precludes enolisation, should therefore lead to the formation of benzalpinacolone-4-sulfonyl chloride (**15**). Treatment of benzalpinacolone (**5**) with a substantial excess of chlorosulfonic acid gave a product, which on the basis of the ^{1}H NMR spectrum contained no alkyl hydrogen atoms. In addition, the product contained a *para*-disubstituted aromatic ring and an E-disubstituted alkenic bond. The IR spectrum demonstrated that the product contained a SO_2 group and the mass spectrum the presence of 2 chlorine atoms (M^+). It therefore seemed likely that the product was styrene-4,β-disulfonyl dichloride (**3**). This was confirmed by reaction with dimethylamine and morpholine, which gave the corresponding derivatives, **4** and **16** respectively.

The formation of the disulfonyl dichloride (**3**) from benzalpinacolone (**5**) is interpreted by the reaction mechanism given in Scheme 2. Although enolisation is no longer possible, attack by chlorosulfonic acid at the oxygen atom of the carbonyl group is directly analogous to the β-attack on the enol in the transformation of benzalacetone (**1**). The remainder of the mechanism in Scheme 2 also parallels the other transformation.

Our work demonstrates that substrates containing an alkyl ketone group are clearly subject to decomposition and lead to a novel intermediate sulfonyl chloride, when treated with chlorosulfonic acid.



SCHEME 2

EXPERIMENTAL

Melting points were determined with a Gallenkamp electrically heated apparatus and are uncorrected. IR spectra were measured as nujol mulls on a Perkin Elmer 781 spectrophotometer or Unicam SP1800 spectrophotometer. NMR spectra were recorded with a Bruker WP80 spectrometer using tetramethylsilane as internal standard. An asterisk indicates a resonance signal removed after addition of D_2O. Mass spectra were determined with a VG Micromass V15 instrument. TLC was carried out on Camlab Polygram silica gel plates sensitized to UV 254 nm, using cyclohexane-ethyl acetate 1:1 as eluant unless otherwise stated. Microanalyses were carried out by the courtesy of ICI (Pharmaceuticals Division) plc, Macclesfield, Cheshire.

Benzalacetone **1** was prepared by the method of Vogel.[7]

General procedure for bis-sulphonamide preparation. The crude disulfonyl dichloride **3** (0.02 mole) in acetone (20 ml) was gradually added to a stirred solution of the appropriate amine (0.08 mole) in acetone (20 ml) at 0°. The mixture was left for a week at room temperature and was added to ice-water (100 ml). The precipate was filtered off with suction, washed with water (2 × 25 ml) and dried. The products were purified by recrystallisation from acetone or methanol to give the bis-sulfonamides (**4**, **6–14**, **16**). Compound **6** was prepared by using concentrated aqueous ammonia (4 mole equivs).

Styrene-4,β-disulfonyl dichloride **3**. Benzalpinacolone (**5**) (5 g, 0.027 mole) was added to chlorosulfonic acid (17.6 ml, 0.27 mole) at 0° portionwise with stirring. The reaction mixture was allowed to warm to room temperature and stirred for one week. The reaction mixture was added slowly to ice-water and the resulting sticky solid extracted with chloroform (3 × 100 ml). The chloroform layer was separated, washed with water (100 ml), dried (Na_2SO_4) and evaporated under reduced pressure to give a brown residue (5.5 g, 68%). TLC major spot R_F 0.65. ν_{max} 1610 (C=C), 1390–1360, 1200–1160 (SO_2), 800 (*para*-disubstitution) cm^{-1}. MS *m/z* 304, 302, 300 (M^+), 267, 265 (M^+—Cl), 203, 201 (267, 265 —SO_2), 102 ($C_6H_4CH{=}CH$).

Compound **4**. (6%), m.p. 208–209° (lit.[5] 208–210°). (Found: C, 45.1; H, 5.7; N, 8.6. Calc. for $C_{12}H_{18}N_2O_4S_2$: C, 45.3; H, 5.7; N, 8.8%). ν_{max} 1620 (C=C), 1350–1320, 1190–1160 (SO_2), 795 (*para*-disubstitution) cm^{-1}.
^1H NMR ($CDCl_3$) δ: 7.85–7.60 (4H, AA'BB', aromatic H, *para*-disubstitution), 7.50 (1H, ½AB, E—CH=CH, $J \sim 16$ Hz), 6.85 (1H, ½AB, E—CH=CH, $J \sim 16$ Hz), 2.75 (6H, s, NMe_2), 2.69 (6H, s, NMe_2). MS *m/z* 318 ($M^+ \sim 10\%$), 254 (M^+—SO_2), 146 (M^+—Me_2NSO_2), 102 ($C_6H_4CH{=}CH$), 44(Me_2N).

Benzalpinacolone **5**. A mixture of 3,3-dimethylbutan-2-one (50 g, 0.5 mole) and benzaldehyde (60 g, 0.565 mole) in ethanol (190 ml), water (65 ml) and 10% sodium hydroxide (50 ml) was stirred at room temperature for one week. The mixture was diluted with water (300 ml) and extracted with toluene (3 × 150 ml). The combined extracts were washed with water until the washings were neutral, a saturated solution of sodium bisulfite (100 ml) and finally with water (2 × 100 ml). Toluene was removed by rotary film evaporation and a yellow oil was obtained. The crude product was distilled at reduced pressure, b.p. 100–112° (0.4 mm Hg). On standing the oil solidified to give benzalpinacolone as a yellow solid (78 g, 83%), m.p. 41–42° (lit.[8] 42–43°).

Compound **6**. (12%), m.p. 208°, TLC (chloroform-methanol, 3:7) one spot R_F 0.78. (Found: C, 35.8; H, 4.0; N, 10.0. Calc. for $C_8H_{10}N_2O_4S.\frac{1}{2}H_2O$: C, 35.4; H, 4.1; N, 10.3%). ν_{max} 3330, 3240 (N—H), 1620 (C=C), 1330, 1140 (SO_2), 800 (*para*-disubstitution) cm^{-1}. MS *m/z* 262 (M^+, ~50%), 198 (M^+—SO_2), 181 (M^+—HSO_2NH_2), 101 (181 —SO_2NH_2).

Compound **7**. (36%), m.p. 208°, TLC one spot R_F 0.58. (Found: C, 60.3; H, 5.1; N, 6.3. Calc. for $C_{22}H_{22}N_2O_4S_2$: C, 59.7; H, 5.0; N, 6.3%). ν_{max} 3270 (N—H), 1626 (C=C), 1330, 1150 (SO_2), 800 *para*-disubstitution) cm^{-1}.
^1H NMR ($(CD_3)_2SO$) δ: 8.25*, 8.00* (2H, 2 × t, 2 × NH), 7.85 (4H, s, *para*-disubstituted ring), 7.50–7.15 (12H, 2 × phenyl H, CH=CH), 4.20, 4.05 (4H, 2 × d, 2 × CH_2). MS *m/z* M^+ (not observed), 378 (M^+—SO_2), 272 (M^+—$PhCH_2NHSO_2$), 106 ($PhCH_2NH$), 102 ($C_6H_4CH{=}CH$).

Compound **8**. (21%), m.p. 140°, TLC one spot R_F 0.11. (Found: C, 57.2; H, 5.9; N, 4.8. Calc. for $C_{28}H_{34}N_2O_8S_2$: C, 56.9; H, 5.8; N, 4.7%). ν_{max} 1610 (C=C), 1350, 1150 (SO_2), 800 (*para*-disubstitution). ^1H NMR ($CDCl_3$) δ: 7.50–6.72 (5H, AA'BB', aromatic H, *para*-disubstitution, ½AB,

CH=CH), 6.48–6.00 (7H, 2 × ABC, aromatic H, ½AB, CH=CH), 4.00* (2H, m, 2 × NH), 3.50 (12H, s, 4 × OCH_3), 3.10–2.60 (4H, m, 2 × NCH_2), 2.50–2.13 (4H, m, 2 × CH_2 aryl). MS *m/z* 590 (M^+ ~ 10%), 152 ($C_9H_{12}O_2$), 137 ($C_8H_9O_2$).

Compound **9**. (13%), m.p. 136°, TLC one spot R_F 0.64. (Found: C, 51.1; H, 7.0; N, 7.4. Calc. for $C_{16}H_{26}N_2O_4S_2$: C, 51.3; H, 7.0; N, 7.5%). ν_{max} 1620 (C=C), 1340, 1160–1140 (SO_2), 800 (*para*-disubstitution) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.00–7.25 (5H, AA'BB', aromatic H, *para*-disubstitution, ½AB, E—CH=CH, J ~ 16 Hz), 6.70 (1H, ½AB, E—CH=CH, J ~ 16 Hz), 3.28 (8H, 2 × q, 4 × NCH_2), 1.25 (6H, t, 2 × CH_3), 1.17 (6H, t, 2 × CH_3). MS *m/z* 374 (M^+, ~10%), 359 (M^+—CH_3), 310 (M^+—SO_2), 302 (M^+—NEt_2), 238 (M^+—SO_2NEt_2), 166 (238—NEt_2), 102 (C_6H_4CH=CH).

Compound **10**. (32%), m.p. 154°, TLC one spot R_F 0.43. (Found: C, 52.3; H, 6.0; N, 7.5. Calc. for $C_{16}H_{22}N_2O_4S$: C, 51.9; H, 6.0; N, 7.6%). ν_{max} 1615 (C=C), 1335, 1160–1140 (SO_2), 800 (*para*-disubstitution) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.00–7.33 (5H, AA'BB', aromatic H, *para*-disubstitution, ½AB, E—CH=CH, J ~ 16 Hz), 6.85 (1H, ½AB, E—CH=CH, J ~ 16 Hz), 3.50–3.00 (8H, m, 4 × NCH_2), 2.20–1.50 (8H, m, 2 × $(CH_2)_2$). MS *m/z* 370 (M^+, ~10%), 306 (M^+—SO_2), 236 (306—C_4H_8N), 172 (306—$C_4H_8NSO_2$), 102 (C_6H_4CH=CH), 70 (C_4H_8N).

Compound **11**. (32%), m.p. 228°, TLC one spot R_F 0.55. (Found: C, 54.4; H, 6.7; N, 7.0. Calc. for $C_{18}H_{26}N_2O_4S_2$: C, 54.3; H, 6.5; N, 7.0%). ν_{max} 1620 (C=C), 1340–1320, 1170–1140 (SO_2), 795 (*para*-disubstitution) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.00–7.30 (5H, AA'BB', aromatic H, *para*-disubstitution, ½AB, E—CH=CH, J ~ 16 Hz), 6.80 (1H, ½AB, E—CH=CH, J ~ 16 Hz), 3.40–2.87 (8H, m, 4 × NCH_2), 1.90–1.20 (12H, m, 2 × $(CH_2)_3$). MS *m/z* 398 (M^+, ~10%), 334 (M^+—SO_2), 250 (M^+—$C_5H_{10}N$), 102 (C_6H_4CH=CH), 84 ($C_5H_{10}N$).

Compound **12**. (28%), m.p. 210°, TLC one spot R_F 0.58. (Found: C, 52.9; H, 6.7; N, 6.1. Calc. for $C_{20}H_{30}N_2O_6S_2$: C, 52.4; H, 6.6; N, 6.1%). ν_{max} 1623 (C=C), 1370–1320, 1170–1130 (SO_2), 795 (*para*-disubstitution) cm^{-1}. ^1H NMR ($(CD_3)_2SO$) δ: 8.25–7.65 (4H, AA'BB', aromatic H, *para*-disubstitution; 2H, s, CH=CH), 3.90–3.40 (4H, m, 4 × OCH), 2.65–1.65 (8H, m, 4 × NCH_2), 1.15, 1.05 (12H, 2 × d, 4 × CH_3). MS *m/z* 458 (M^+, ~10%), 280 (M^+—$C_6H_{12}NO$), 102 (C_6H_4CH=CH).

Compound **13**. (34%), m.p. 178°, TLC one spot R_F 0.06. (Found: C, 61.8; H, 4.7; N, 6.0. Calc. for $C_{24}H_{22}N_2O_4S_2.0.2H_2O$: C, 61.3; H, 4.8; N, 6.0%). ν_{max} 1350, 1150 (SO_2), 800 (*para*-disubstitution) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.50–6.10 (14H, AA'BB', aromatic H, *para*-disubstitution, 2 × ABCD indolino, AB, E—CH=CH, J ~ 16 Hz), 3.70–3.25 (4H, m, 2 × NCH_2), 2.80–2.25 (4H, m, 2 × CH_2). MS *m/z* 466 (M^+, ~20%), 284 (M^+—$C_8H_8NSO_2$), 118 (C_8H_8N), 102 (C_6H_4CH=CH).

Compound **14**. (34%), m.p. 206°, TLC one spot R_F 0.04. (Found: C, 46.3; H, 3.4; N, 15.3. Calc. for $C_{14}H_{12}N_4O_4S_2$: C, 46.2; H, 3.3; N, 15.4%), ν_{max} 1620 (C=C), 1350, 1160 (SO_2), 820 (*para*-disubstituted) cm^{-1}. ^1H NMR ($(CD_3)_2SO$) δ: 8.50–7.05 (6H, 2 × ABC, imidazolo H; 4H, AA'BB', aromatic H, *para*-disubstitution; 2H, s, CH=CH). MS *m/z* 364 (M^+, <10%), 233 (M^+—$C_3H_3N_2SO_2$), 102 (C_6H_4CH=CH).

Compound **16**. (16%), m.p. 259°. (Found: C, 47.4; H, 5.4; N, 6.7. Calc. for $C_{16}H_{22}N_2O_6S_2$: C, 47.7; H, 5.5; N, 7.0%). ν_{max} 1615 (C=C), 1350–1320, 1180–1160 (SO_2), 795 (*para*-disubstitution) cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.85–7.60 (4H, AA'BB', aromatic H, *para*-disubstitution), 7.50 (1H, ½AB, E—CH=CH, J ~ 16 Hz), 6.75 (1H, ½AB, E—CH=CH, J ~ 16 Hz), 3.90–3.60 (8H, m, 4 × OCH_2), 3.35–2.90 (8H, m, 4 × NCH_2). MS *m/z* 402 (M^+, ~10%), 338 (M^+—SO_2), 86 (C_4H_8NO).

REFERENCES

1. R. J. Cremlyn, O. O. Shode and F. J. Swinbourne, *J. Chem. Soc. Perkin Trans. I*, 2181 (1983).
2. R. J. Cremlyn, O. O. Shode, F. J. Swinbourne and J. L. Lynch, *J. Heterocyclic Chem.* **24**, 117 (1987).
3. R. J. Cremlyn, F. J. Swinbourne, N. Godfrey, P. Hedges, J. Lapthorne and C. Mizon, *Indian J. Chem.* **23B**, 962 (1984).
4. R. J. Cremlyn, F. J. Swinbourne and O. O. Shode, *J. Chin. Chem. Soc.*, **31**, 383 (1984).

5. R. J. Cremlyn, F. J. Swinbourne and L. Goodman, *Phosphorus and Sulfur*, **28**, 395 (1986).
6. A. Weston and C. M. Suter, *J. Am. Chem. Soc.*, **61**, 389 (1939).
7. A. I. Vogel, A Textbook of Practical Organic Chemistry, Longmans, London and New York, 3rd. Edn. 716 (1957).
8. G. A. Hill and G. M. Bramann, Organic Syntheses, Collected Volume V, (Wiley, Chichester, 1941), 2nd Ed., p 81.