

## Synthesis of Methanesulfonyl Derivatives of 2,2-Bis(4-chlorophenyl)-1,1-dichloroethylene (*p,p'*-DDE), Present in Seal from the Baltic

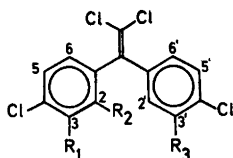
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The low and declining reproduction of the seal in the Baltic<sup>1</sup> has made urgent a thorough characterisation of foreign compounds accumulating in this species. Already known are representatives of compounds related to DDT [2,2-bis(4-chlorophenyl)-1,1,1-trichloroethane] and PCB (polychlorinated biphenyls).<sup>2</sup> In connection with such studies Jensen and Jansson<sup>3</sup> recently detected a series of compounds which, from their physicochemical and mass spectral properties, were characterized as methyl sulfones derived from *p,p'*-DDE and from PCB, respectively.

This paper describes the synthesis and structural elucidation of three methanesulfonyl derivatives of *p,p'*-DDE. The work was performed in order to make available reference compounds for analytical and toxicological studies.

Simple aryl methyl sulfones are generally accessible by Friedel-Crafts type acylations of arenes, under mild conditions, with methanesulfonyl anhydride.<sup>4</sup> In the case of *p,p'*-DDE it proved necessary to perform the reaction over an extended period in a melt of a large excess of the anhydride. Chromatography on silica gel of the crude product gave a fair yield of a methanesulfonyl derivative of DDE (*1*). Traces of an isomeric methyl sulfone (*2*) and larger amounts of a more polar bis-methanesulfonyl derivative (*3*) were also obtained.



1  $R_1 = \text{SO}_2\text{CH}_3$   $R_2 = R_3 = \text{H}$

2  $R_1 = R_3 = \text{H}$   $R_2 = \text{SO}_2\text{CH}_3$

3  $R_1 = R_3 = \text{SO}_2\text{CH}_3$   $R_2 = \text{H}$

The structure of the main methyl sulfone was indicated by its oxidation by chromium(VI) oxide to the corresponding benzophenone; the latter compound proved to be identical to 4,4'-

dichloro-3-methanesulfonylbenzophenone (*4*) as prepared from 4,4'-dichlorobenzophenone by reaction with methanesulfonyl anhydride. The expected formation of the 3-methanesulfonyl derivative in the latter reaction was borne out by the reported formation of the 5,3'-dinitro derivative as a single bisnitration product from 2,4'-dichlorobenzophenone.<sup>5</sup>

From these results, the main methyl sulfone was formulated as 2-(4-chloro-3-methanesulfonylphenyl)-2-(4-chlorophenyl)-1,1-dichloroethylene (*1*). The structure is also in accordance with observed <sup>1</sup>H NMR spectral properties.

The minor isomer was tentatively formulated as 2-(4-chloro-2-methanesulfonylphenyl)-2-(4-chlorophenyl)-1,1-dichloroethylene (*2*). Due to very low amounts of the pure compound *2* the analytical data are in certain parts incomplete.

The two isomers gave characteristic mass spectra, which were qualitatively and partly quantitatively similar; the relative intensities of certain common fragments did, however, show pronounced differences. Both compounds thus gave rise to strong fragments  $m/e = 280$ , interpreted as fluorene type ions.<sup>6</sup> This view was supported by the presence of a metastable ion at  $m^* = 201$ , as expected in the case of simultaneous loss of  $\text{CH}_3\text{SO}_2 + \text{Cl}$  (114 m.u.) from the molecular ion. Furthermore, in both spectra the ion  $m/e = 210$  was prominent, indicating a loss of 2 Cl from the fluorene ion. However, *1* showed the molecular ion (M)  $m/e = 394$  with the base peak  $m/e = 396$  whereas *2* exhibits the base peak  $m/e = 125$  which according to the high resolution mass spectrum was interpreted as a tropylium ion  $\text{C}_7\text{H}_6\text{Cl}$ . In the case of *1* the intensity of this fragment was only 8 % of the base peak. Further *2* gave an intense fragment at  $m/e = 359$  (M - Cl) which was of almost negligible importance in the case of *1*. It is tempting to postulate that, in support of the proposed structure of sulfone *2*, these two major fragmentation routes both reflect the sterically crowded situation caused by the methanesulfonyl group in the *ortho*-position to the bridge carbon.

It is noteworthy that the isomerisation to a sulfinate with subsequent fragmentation, a route typical for alkyl aryl sulfones,<sup>6</sup> was observed only in the case of *2*,  $m/e = 331$  (M -  $\text{SOCH}_3$ ).

The above-mentioned bis-methanesulfonyl derivative of *p,p'*-DDE, should, from its formation in as much as ca. 20 % yield, be formulated as 2,2-bis(4-chloro-3-methanesulfonylphenyl)-1,1-dichloroethylene (*3*). This symmetrical structure was fully confirmed by its <sup>1</sup>H NMR spectrum which contained signals from three types only of aromatic protons.

The methyl sulfone *1* prepared here has recently been shown to have a retention time and mass spectral properties in full agreement with those of the sulfone obviously derived from DDE and detected as an essential metabolite in grey seal from the Baltic.<sup>3</sup> Likewise *2* is apparently identical with a trace metabolite

also derived from DDE in the same species.<sup>8</sup>

**Experimental.** <sup>1</sup>H NMR spectra (100 MHz) were obtained on a Varian XL-100 instrument in CDCl<sub>3</sub>. High resolution mass spectrometry was carried out on a Varian-MAT SM 1 instrument. Combined gas chromatography-mass spectrometry (GLC-MS) was performed as described by Jensen and Jansson.<sup>8</sup> Chromatography was performed on silica gel plates (DC-Fertigplatten, Kieselgel 60 F-254, Merck). Hexane-ethyl acetate (2:1) was used as eluent.

**Synthesis of mono- and bis-methanesulfonyl derivatives of p,p'-DDE.** Freshly distilled methanesulfonic anhydride<sup>7</sup> (12.2 g, 70 mmol) was added to p,p'-DDE (0.45 g, 1.4 mmol) [synthesised from p,p'-DDT (Merck) and crystallised from ethanol until free from o,p'-DDE (GLC)].<sup>8</sup> The mixture was heated with magnetic stirring to 140 °C (bath temp.) for 38 h. The reaction mixture was dissolved in chloroform and stirred with ice water for 3 h. The water phase was extracted with chloroform and the combined chloroform phases were washed with water and evaporated to dryness. The crude product was fractionated on a silica gel column (3 × 45 cm) and the separation was followed by TLC. The appropriate fractions were combined to give compound 2 (R<sub>f</sub>-value 0.46), 1 (0.36), 4 (0.22) and 3 (0.08). Unreacted starting material and traces of 4,4'-dichlorobenzophenone were eluted before the sulfones.

Compound 1, 2-(4-chloro-3-methanesulfonylphenyl)-2-(4-chlorophenyl)-1,1-dichloroethylene, yield 290 mg (52 %), was crystallised from methanol-water to give prisms, m.p. 160–162 °C. Anal. C<sub>15</sub>H<sub>10</sub>O<sub>2</sub>Cl<sub>4</sub>S: C, H, Cl, S. IR (CHCl<sub>3</sub>): 1150, 1325 cm<sup>-1</sup>. UV [abs. ethanol (ε)]: 243 (16 000) and 213 (23 000) nm. MS [EE 70 eV; m/e (rel.int %)]: 396 (100, M+2), 394 (78, M), 359 (3), 314 (36), 280 (56), 210 (74) and 125 (8). m\* 396 → 282, obs. 200, calc. 201. <sup>1</sup>H NMR: δ 3.26 (3 H, s), 8.07 (H<sub>2</sub>, d, J 2 Hz), 7.53 (H<sub>5</sub>, d, J 8 Hz), 7.41 (H<sub>6</sub>, dd, J 8 and 2 Hz), 7.18 (H<sub>2',6'</sub>, dd, J 8.5 and 2 Hz), 7.36 (H<sub>2',6'</sub>, dd, J 8.5 and 2 Hz).

Compound 2, 2-(4-chloro-2-methanesulfonylphenyl)-2-(4-chlorophenyl)-1,1-dichloroethylene, yield 12 mg (2 %), was analysed by high resolution mass spectrometry: Mol.wt., obs. 395.9126, calc. for C<sub>15</sub>H<sub>10</sub>O<sub>2</sub><sup>35</sup>Cl<sub>3</sub><sup>37</sup>ClS 395.9140. Base peak obs. 125.0157, calc. for C<sub>7</sub>H<sub>5</sub><sup>35</sup>Cl 125.0159. Prisms from hexane, m.p. 144–145 °C. UV [abs. ethanol (ε)]: 256 (16 000) and 212 (26 000) nm. MS [EE 70 eV; m/e (rel.int %)]: 394, (32, M), 359 (44), 331 (12), 314 (2), 280 (56), 210 (62) and 125 (100). <sup>1</sup>H NMR: δ 2.48 (s), 7.88 (H<sub>2</sub>, d, J 2 Hz), 7.53 (H<sub>5</sub>, dd, J 8 and 2 Hz), 7.29 (H<sub>6</sub>, d, J 8 Hz), 7.13 (H<sub>2',6'</sub>, d, J 7.5 Hz), 7.22 (H<sub>2',6'</sub>, d, J 7.5 Hz).

Compound 3, 2,2-bis(4-chloro-3-methanesulfonylphenyl)-1,1-dichloroethylene, was crystallised from methanol-water to give two crystalline forms m.p. 183–185 and 208.5–209.5 °C, respectively. Anal. C<sub>16</sub>H<sub>12</sub>O<sub>4</sub>Cl<sub>4</sub>S<sub>2</sub>: C, H, S. IR (CHCl<sub>3</sub>): 1150, 1320 cm<sup>-1</sup>. UV [abs. ethanol

(ε)]: 260 (14 000) and 216 (26 000) nm. MS [EE 70 eV; m/e (rel.int %)]: 474 (100, M+2), 472 (75, M), 392 (7), 358 (8), 314 (40) and 244 (81). <sup>1</sup>H NMR: δ 3.28 (6H, s), 8.03 (H<sub>2,2'</sub>, d, J 2 Hz), 7.58 (H<sub>5,5'</sub>, d, J 8 Hz), 7.47 (H<sub>6,6'</sub>, dd, J 8 and 2 Hz).

**Synthesis of 4,4'-dichloro-3-methanesulfonylbenzophenone(4).** 4,4'-Dichlorobenzophenone (200 mg, 0.80 mmol) was prepared from p,p'-DDE in analogy with the oxidation procedure described below. It was treated with methanesulfonic anhydride (7.1 g, 40.8 mmol) as above for 120 h. The crude reaction product, containing large amounts of starting material was purified on a silica gel column (3 × 35 cm). The sulfone was isolated and crystallised from methanol to give 4, yield 29 mg, m.p. 192.5–193.5 °C. Anal. C<sub>14</sub>H<sub>10</sub>O<sub>2</sub>Cl<sub>2</sub>S: C, H, Cl, S. IR (CHCl<sub>3</sub>): 1147, 1325, 1665 cm<sup>-1</sup>. UV [abs. ethanol (ε)]: 262 (19 000) and 219 (20 000) nm. MS [EE 70 eV, m/e (rel. int. %)]: 328 (12, M), 293 (1), 217 (13), 139 (100) and 111 (37). <sup>1</sup>H NMR: δ 3.31 (3 H, s), 8.48 (H<sub>2</sub>, d, J 2 Hz), 7.69 (H<sub>5</sub>, d, J 8 Hz), 7.98 (H<sub>6</sub>, dd, J 8 and 2 Hz), 7.72 (H<sub>2',6'</sub>, dd, J 8.5 and 2 Hz), 7.48 (H<sub>2',6'</sub>, dd, J 8.5 and 2 Hz).

**Oxidation of the sulfone 1 by chromium(VI) oxide.** The sulfone 1 (109 mg, 0.28 mmol) was treated with chromium(VI) oxide (Merck) (275 mg, 2.75 mmol) in acetic acid (14 ml) for 1 h at 100 °C. Water was added and the reaction product was isolated by chloroform extraction. The crude product (100 %) was crystallised from methanol to give scales, m.p. 192.5–193.5 °C. The identity of the oxidation product with 4,4'-dichloro-3-methanesulfonylbenzophenone (4) was proved by mixed m.p. determination and by comparison of IR, <sup>1</sup>H NMR and mass spectra.

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