SHORT PAPER

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Preparation of 3-chloro-1,2-benzisothiazole 1,1-dioxide (*pseudo*-saccharyl chloride)†

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Reasons are given for the formation of two different products from the chlorination of saccharin with phosphorus pentachloride: initially 2-chlorosulfonylcyanobenzene is formed which, under appropriate conditions, cyclises to give 3-chloro-1,2-benzisothiazole 1,1-dioxide, an important derivatising agent for alcohols.

Keywords: 3-chloro-l, 2-benzisothiazole 1,1-dioxide

The preparation of the useful intermediate, 3-chloro-1,2-benzisothiazole 1,1-dioxide (*pseudo*-saccharyl chloride **1**; reaction (1)) has already been described.[1] Unfortunately, the literature description for the preparation of the isomeric 2-chlorosulfonylcyanobenzene (**2**; reaction (2)) is identical to that for the preparation of *pseudo*-saccharyl chloride.[2] In our hands, the descriptions for making the chloride **1** proved to be inadequate in that mixtures of products were formed on using the apparently pure chloride to make derivatives with phenols. Thus, in the synthesis of 3-(4-methoxyphenoxy)-1,2-benzisothiazole 1,1-dioxide **3** (reaction (1)) from 4-methoxyphenol **4** and *pseudo*-saccharyl chloride **1** in the presence a of base, the required compound was frequently difficult to isolate because of major contamination with an isomer, which was eventually shown to be 4-methoxyphenyl 2-cyanobenzenesulfonate **5** (reaction (2)) by X-ray crystallographic analysis (Fig. 1). The crystallographic structure of the isomeric compound **3** has been previously reported.[3]

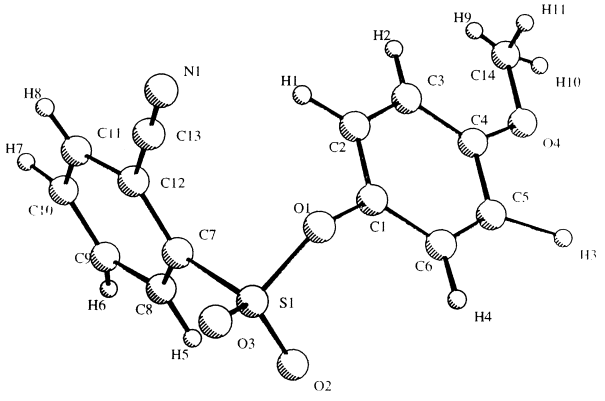
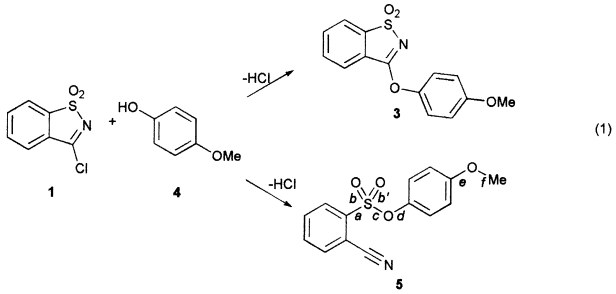
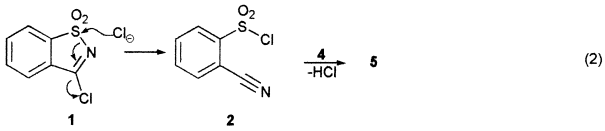


Fig.1 The molecular structure of 4-methoxyphenyl 2-cyanobenzene sulfonate **5** with atom labels.

Results and discussion

It was not clear whether or not compound **5** had been formed from compound **3** by isomerisation or through initial reaction of 4-methoxyphenol **4** at the sulfonyl group rather than at the chloro group (reaction (1)). Such a reaction would be unusual for 1,2-benzisothiazole 1,1-dioxides but not for 1,2-benzisothiazoles themselves.[4] A further possibility would be ring-opening of *pseudo*-saccharyl chloride 1 by chloride ion, followed by reaction with the phenol (reaction (2)).





In fact, the sulfonyl chloride **2** appears to be the first compound formed by the reaction of PCl_5 with saccharin (reaction (3)). At lower reaction temperatures or with shorter reaction times, the crude product of chlorination of saccharin showed an infrared absorption band at 2235 cm^{-1}, characteristic of a cyano group and, on reaction with 4-methoxyphenol, gave a mixture of the isomers **3** and **5**. For the same time of reaction, 2 hours, as the temperature for the chlorination of saccharin was increased, reaction of the subsequent chloride with 4-methoxyphenol **4** gave **3** and **5** but the proportion of isomer **5** decreased and eventually became zero. At the same time, the infrared absorption at 2235 cm^{-1}, corresponding to a cyano group, also disappeared in the crude chlorination product from saccharin. These results indicate that PCl_5 with saccharin first yields the sulfonyl chloride **2**, which then isomerises to *pseudo*-saccharyl chloride 1 if the reaction temperature is sufficiently high (reaction 3).

Electronic structure calculations at HF/6-31G level of theory were performed[5] to test this hypothesis. Structural minimisations indicate that isomer **1** is 36 kJ/mol more stable than its cyano-isomer **2**. It is, therefore, reasonable to assume that, once formed, isomer **1** will not be converted back into isomer **2**. The chlorine attack on the phosphorus intermediate **6**, leading to the formation of isomer **2**, seems to be easier to occur on sulfur, which exhibits a positive partial charge (1.6898) of greater magnitude than the partial charge exhibited by carbon atom in position 3 (0.0094). Once formed, the cyclisation of isomer **2** to give **1** requires the attack of chlorine on the carbon atom of the cyano group (reaction (3)), which has a low

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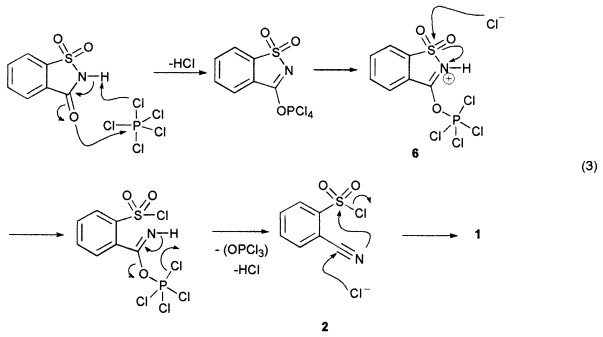
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*



nucleophilic susceptibility. This is in good agreement with the experimental observation that cyclic *pseudo*-saccharyl chloride is preferentially formed at higher temperatures.

Recommended best conditions for making *pseudo*-saccharyl chloride are given in the experimental section. When recrystallised from toluene, the *pseudo*-saccharyl chloride was found to be quite stable over a period of several months. This suggests that previous reports of instability were probably due to the presence of its isomer **2**.

Table 1 shows selected bond lengths and bond angles for compound **5**. Full crystallographic details have been deposited with the Cambridge Crystallographic Data Centre and allocated deposition number CCDC 176240.

Table 1 Selected bond lengths and angles for the structure **5**

Bond[a]	Length/Å	Bond angle	m.p./°
a	1.755	*ab*	108.95[c]
b	1.4195[b]	*ac*	104.6
c	1.590	*bc*	106.3[d]
d	1.416	*cd*	120.0
e	1.359	*ef*	117.7
f	1.440		

[a]See **5**, reaction (1).

[b]Average bond lengths *b* and *b'*.

[c]Average bond angles *ab* and *ab'*.

[d]Average bond angles *bc* and *b'c*.

Experimental

Preparation and full characterisation of isomer **3** has been reported.[3] Preparation of *pseudo*-saccharyl chloride **1** has been reported with a few variations.[1,2]

Preferred synthesis of 3-chloro-1,2-benzisothiazole 1,1-dioxide **1**: Saccharin (5.1 g; 2.8×10^{-2} mol) was thoroughly mixed with phosphorus pentachloride (7 g; 3.3×10^{-2} mol) and heated at 220°C. The mixture was refluxed for 2 h until liberation of hydrogen chloride had ceased. Phosphorus oxychloride was distilled under vacuum at 180°C and the residue crystallised from the reaction medium on cooling to room temperature. After filtration under pressure, recrystallisation of the product from trichloromethane afforded the desired product as colourless needles (4.1 g; 72 % yield), m.p. 144–145°C (lit[1] 143–145°C). Found C, 41.7; H, 2.0; N, 6.9%. Calculated for $C_7H_4NO_2SCl$, C, 41.7; H, 2.0; N, 7.0%. ^{1}H-NMR: δ 7.85 (4H, m, Ar–H); ν_{max}: 1726, 1654, 1604 (C=C), 1346 (SO_2), 775 (Ar–H) and 692 (C-Cl) cm^{-1}; ms (EI): *m*/*z* 201.

The above procedure was repeated at two lower temperatures (140 and 85°C); at 140°C: saccharin (2.49 g; 1.4×10^{-2} mol) and phosphorus pentachloride (4.7 g; 2.25 x 10^{-2} mol), were heated for 2 h. After distillation of the excess of phosphorus oxychloride, the crude product, consisting of a mixture of compounds **3** and **5** was obtained. ν_{max} 2235 (–C≡N) 1331 (–SO_2); 771 (Ar–H); 1605 and 1550 (C=C) cm^{-1}; at 85°C: saccharin (2.49 g; 1.4×10^{-2} mol) and phosphorus pentachloride (4.7 g; 2.25×10^{-2} mol), were heated for 2 h. Infrared spectroscopy of the crude material showed a mixture of compound 2 and the starting material saccharin. ν_{max}: 2235 (–C≡N) and 1795 (–C=O) cm^{-1}.

Synthesis of 4-methoxyphenyl 2-cyanobenzenesulfonate **5:** 4-Methoxyphenol (1.00 g; 8×10^{-3} mol) and potassium *tert*-butoxide (1.16 g; 9.5×10^{-3} mol) were stirred in dry dimethylformamide (10 ml) for 30 min at room temperature. The crude product from chlorination of saccharin at 140°C, containing isomeric compounds **1** and **2** (mostly *o*-cyanobenzenesulfonyl chloride; 1.60 g; 8×10^{-3} mol) was then added. After 20 min, the reaction mixture was poured into ice water (10 ml). The solid formed was filtered off and, after being air-dried at room temperature for 30 min, was dissolved in trichloromethane (20 ml). The solution was washed with saturated aqueous sodium hydrogen carbonate (2×20 ml), then with aqueous HCl (1 M; 2×20 ml) and finally with water (3×10 ml). The organic phase was dried (Na_2SO_4), filtered, and the solvent evaporated under vacuum. The residual solid was recrystallised from ethanol to give colourless crystals of 4-methoxyphenyl 2-cyanobenzenesulfonate (0.519 g), m.p. 110–111°C. Found C, 58.58; H, 3.90; N, 4.99%. $C_{14}H_{11}O_4SN$ requires C, 58.12; H, 3.83, N, 4.84%. ^{1}H-NMR δ 3.75 (3H, s, -OCH_3); 6.79 (2H, d, *J* = 10 Hz, Ar–H); 7.05 (2H, d, *J* = 10 Hz, Ar–H) 7.75 (2H, m, Ar–H) 7.92 (1H, m, Ar–H), 8.03 (1H, m, Ar–H); ν_{max}: 2233 (-C≡N)) 1331 (-SO_2); 771 (Ar-H); 1603, 1550, 1503, 1612 and 1618 (C=C) cm^{-1}; ms (EI): *m*/*z* 289.

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