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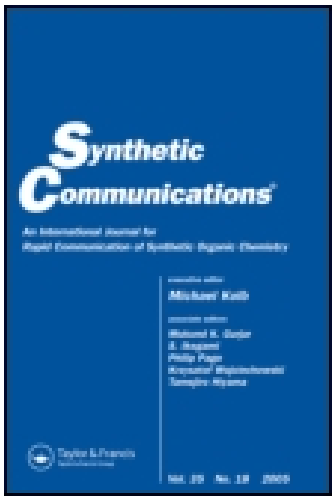

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Graham Walker [a] & Kishore K. Rana [a]

[a] GlaxoSmithKline , New Frontiers Science Park, Harlow, Essex, UK

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A Novel Preparation of 2-Naphthyl and 5-Benzo[B]thienyl Methanesulfonyl Chlorides

Graham Walker* and Kishore K. Rana

GlaxoSmithKline, New Frontiers Science Park,
Harlow, Essex, UK

ABSTRACT

Electron rich arylmethylsulfonyl chlorides can be prepared from arylmethyl bromides by phase transfer sulfonation and chlorination with PCl_5.

Key Words: Sulfonyl chlorides; Phase transfer sulfonation.

*Correspondence: Graham Walker, GlaxoSmithKline, Department of Medicinal Chemistry, New Frontiers Science Park, Coldharbour Road, Harlow, Essex, CM19 5AD, UK; Fax: 01279-622790; E-mail: graham_r_walker@gsk.com.

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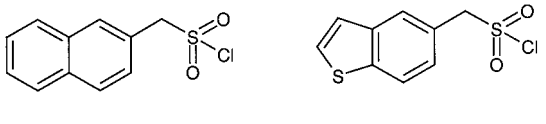
We recently required a preparation of naphthylmethylsulfonyl chloride **1** and benzothienylsulfonyl chloride **2** from the corresponding arylmethyl halides (Sch. 1).

A recent report of the synthesis of **1** by reaction of the sodium sulfonate **3a** with phosphorus oxychloride in acetonitrile–sulfolane at 70°C[1] in our hands was found to give a 2:1 mixture of **1** and the corresponding chloride **4**, which could only be separated with difficulty (Sch. 2).

Problems of this sort have been described previously in the preparation of benzylic and other electron rich sulfonyl chlorides,[2] and such sulfonyl chlorides are also known to easily be decomposed to the benzyl chloride.[3] Alternative routes have therefore been used in which benzylic sulfonyl chlorides are formed by oxidation of disulfides or thiols,[4] but such methods are unsuitable for easily oxidized systems such as **2**. More recently described methods use the reaction of tetrabutylammonium sulfonates with triphosgene or triphenylphosphine–sulfuryl chloride,[5] but these methods have not been applied to benzylic sulfonates.

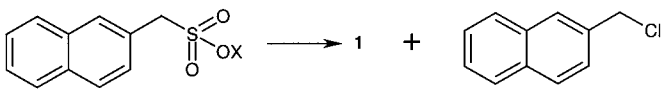
We therefore prepared the tetrabutylammonium salt **3b** and investigated its chlorination with the above reagents and also with phosphorous pentachloride. All three reagents gave mixtures of sulfonyl chloride **1** and benzyl chloride **4**, but by reducing the reaction temperature to −20°C or below the yield of benzyl chloride **4** could be reduced to less than 1%. Both triphosgene and phosphorous pentachloride cleanly converted **3b** to **1** in over 90% yield under these conditions.

We then turned to the benzothienyl derivative **2**. Unexpectedly, when bromide **5** was treated with sodium sulfite, alcohol **6** and aldehyde **7** were formed as well as the desired sulfonate **8a** (Sch. 3). In a typical example we obtained 37% of **6**, 7% of **7**, and 21% of **8a**, but these yields were



1 **2**

Scheme 1.



3 a X = Na
b X = $(C_4H_9)_4N$

4

Scheme 2.

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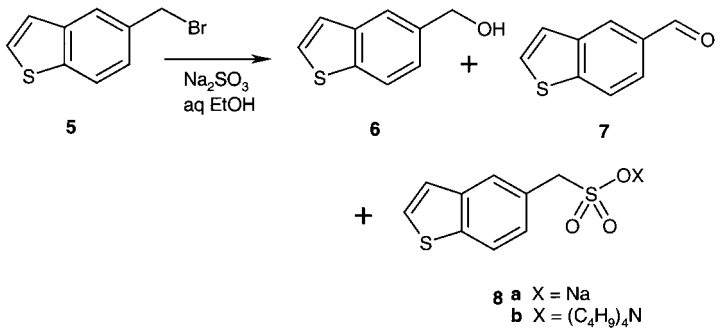

Scheme 3.

variable and in some instances none of the desired sulfonate was formed. Corresponding by-products were also formed in the preparation of the naphthylmethyl sulfonate **3a**, but in much smaller amounts, typically <10% total. We therefore investigated phase transfer conditions for the direct conversion of bromide **5** to tetrabutylammonium sulfonate **8b**. Normal phase transfer catalysis is not possible in this system however, since as soon as sulphonate and bromide ions begin to be formed they sequester the catalytic cation into the organic phase and reaction ceases. We have now found that complete reaction can take place provided that two equivalents of the phase transfer cation are used. Thus reaction of 1 mole of bromide **5** with 2 moles of sodium sulfite, 2 moles of tetrabutylammonium bisulfate and 2 moles of sodium hydroxide in dichloromethane–water gave full conversion to a 1:1 mixture of tetrabutylammonium bromide and **8b**. The use of only 1 equivalent of tetrabutylammonium bisulfate and sodium hydroxide led to the same product mixture in only 50% yield. **5** and 2-naphthylmethyl bromide were both converted to the corresponding tetrabutylammonium sulfonates in >80% yield during 16 h at room temperature.

Finally we have shown that although the tetrabutylammonium bromide present in these products cannot easily be removed, it does not interfere in the subsequent preparations of the sulfonyl chlorides. Best results were obtained using reverse addition to phosphorous pentachloride. The phase transfer derived products **3b** and **8b** were added to phosphorous pentachloride in dichloromethane at $-20^{\circ}C$ and the reaction worked up by subsequent filtration of the reaction mixture through silicagel. Sulfonyl chlorides **1** and **2** were produced in >70% yield with minimal formation of chloromethyl by-product.

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We have successfully used this route for the preparation of 5–10 g batches of sulfonyl chlorides **1** and **2**, and are investigating its utility for the preparation of other arylmethyl sulfonyl chlorides.

EXPERIMENTAL

Tetrabutylammonium Naphthalene-2-methanesulfonate 3b

Sodium naphthalene-2-methanesulfonate[1] (12.5 g, 50 mmol) was added to a mixture of tetrabutylammonium bisulfate (17.0 g, 50 mmol), sodium hydroxide (2.0 g, 50 mmol), water (100 mL), and dichloromethane (100 mL). After stirring for 15 min at room temperature the organic layer was separated, washed with water (100 mL), dried ($MgSO_4$), and evaporated. Recrystallization from ethyl acetate gave **3b** as rhombs, 17.5 g (76%). M.p. 115–118°C; ^{1}H NMR. (400 MHz, $CDCl_3$) 7.88 (s, 1H), 7.72–7.78 (m, 2H), 7.69 (m, 2H), 7.39–7.44 (m, 2H), 4.20 (s, 2H), 2.86–2.90 (m, 8H), 1.25–1.37 (m, 16H), and 0.89–0.92 (m, 12H); ^{13}C NMR (63 MHz, $CDCl_3$) 133.4, 132.2, 129.6, 129.1, 127.8, 127.4, 126.9, 125.5, 125.3, 58.0, 57.9, 23.9, 19.8, and 13.3; MS (ES^-): 221 (RSO_3^-) and 684 [$(RSO_3^-)_2B^+$]; Found C 69.77, H 9.79, N 3.01, $C_{27}H_{45}NO_3S$ requires C 69.93 H 9.78 N 3.02.

Also prepared as described below for **8b** in 76% yield.

Tetrabutylammonium Benzo[b]thiophene-5-methanesulfonate 8b

A mixture of 5-bromomethylbenzo[b]thiophene[6] (40 g, 0.18 mol), tetrabutylammonium bisulfate (122 g, 0.36 mol), sodium hydroxide (14.4 g, 0.36 mol), sodium sulfite (45.4 g, 0.36 mol), water (300 mL), and dichloromethane (300 mL) was stirred overnight at room temperature. The separated organic layer was washed with water (300 mL), dried ($MgSO_4$), and evaporated. Recrystallization from tetrahydrofuran–ether (1:1) gave an approximately 1:1 mixture of **8b** and tetrabutylammonium bromide, 123 g (88%). ^{1}H NMR (400 MHz, $CDCl_3$) 7.92 (s, 1H), 7.75 (d, 1H, $J = 8.4$ Hz), 7.50 (d, 1H, $J = 8.4$ Hz), 7.37 (d, 1H, $J = 5.6$ Hz), 7.27 (d, 1H, $J = 5.6$ Hz), 4.18 (s, 2H), 3.19–3.23 (m, 16H), 1.53–1.61 (m, 16H), 1.37–1.43 (m, 16H), and 0.96–1.00 (m, 24H); ^{13}C NMR (63 MHz, $CDCl_3$) 139.9, 137.8, 131.8, 127.6, 126.0, 125.6, 123.9, 121.5, 58.7, 57.6, 24.3, 19.7, and 13.7; MS (ES^-) 227 (RSO_3^- and 696 [$(RSO_3^-)_2B^+$].

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Benzo[b]thiophene-5-methanesulfonyl Chloride 2

Sulfonate **8b** produced as above (30 g, equivalent to 38 mmol) in dichloromethane (150 mL) was added over 10 min to phosphorous pentachloride (8.3 g, 40 mmol) in dichloromethane (150 mL) at −20°C. The reaction was warmed to +20°C during 25 min then filtered through silica (150 g) washing with ethyl acetate–hexane (1:1, 300 mL). Evaporation of the total eluate and recrystallization from hexane gave **2** as plates, 7.4 g (79%). M.p. 105–107°C; ^{1}H NMR (400 MHz, $CDCl_3$) 7.95 (d, 1H, $J = 8.4$ Hz), 7.93 (s, 2H), 7.53 (d, 1H, $J = 5.5$ Hz), 7.39 (d, 1H, $J = 8.4$ Hz), 7.36 (d, 1H, $J = 5.5$ Hz) and 4.99 (s, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) 141.6, 140.0, 128.7, 126.8, 126.5, 123.7, 123.3, 122.0, and 71.1; MS (ES^-): 227(RSO_3^-) only; Found C 43.91, H 2.76, $C_9H_7ClO_2S_2$ requires C 43.81, H 2.86.

Naphthalene-2-methanesulfonyl Chloride 1[1]

Prepared in the same way from **3b** in 71% yield.

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