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# A Simplified Method for the Preparation of Ethynyl P-Tolyl Sulfone and Ethynyl Phenyl Sulfone

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## A SIMPLIFIED METHOD FOR THE PREPARATION OF ETHYNYL P-TOLYL SULFONE AND ETHYNYL PHENYL SULFONE

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Abstract: Silica gel mediated desilylation of aryl 2-(trimethylsilyl)ethynyl sulfones was found to greatly simplify the synthesis of the acetylenic sulfones, ethynyl ptolyl sulfone 1 and ethynyl phenyl sulfone 2. Each were easily prepared in good yield and high purity on a multigram scale from bis(trimethylsilyl)acetylene 3.

The acetylenic sulfones, ethynyl p-tolyl sulfone 1 and ethynyl phenyl sulfone 2 have long been used as acetylene equivalents in organic synthesis.<sup>1</sup> Most recently these and related aryl sulfones have proven to be useful in cycloaddition reactions with pyrroles for the construction of 7-azabicyclo[2.2.1]heptadiene<sup>2</sup> and 7-azabicyclo[2.2.1]heptane systems<sup>3</sup>, the latter characteristic of the epibatidine alkaloids.<sup>4</sup> Our interest in the synthesis of these and related bicyclic ring systems resulted in the need for synthetically useful quantities of the aryl ethynyl sulphones 1 and 2.

A survey of the literature revealed that several methods exist for the preparation of these acetylenic sulfones. These methods include elimination<sup>5</sup> and

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oxidation<sup>6</sup> procedures as well as a recent strategy which employs ethynyliodonium triflates in sulfonylation reactions.<sup>7</sup> However of all these methods, the sulfonylation procedure originally developed by Bhattacharya *et al* seemed to be the most conducive to multigram synthesis.<sup>8</sup> This method and several recent modifications of the method<sup>9,10</sup> employ a two-step reaction sequence which uses commercially available bis(trimethylsilyl)acetylene (BTMSA) **3** as the starting material. These two-step procedures provide acetylenic sulphones from BTMSA **3** in overall yields of 60 - 65%. Herein we wish to report a further modification which greatly simplifies the synthesis of ethynyl p-tolyl sulfone **1** and ethynyl phenyl sulfone **2** (Scheme I) by reducing the entire synthetic sequence to a single reaction step with a single purification step.



Our initial attempts to synthesize ethynyl p-tolyl sulfone 1 employed a slightly modified procedure of the aluminium chloride mediated sulfonylation of BTMSA 3.<sup>11</sup> This provided the p-tolyl-2-(trimethylsilyl)ethynyl sulfone 4a in 80% yield after purification. However, hydrolysis of the trimethylsilyl group of 4a in basic buffered media according to literature procedures proved to be less straightforward.<sup>8,9</sup> This method was plagued by erratic and sometimes low yields, incomplete hydrolysis and formation of the side product, p-tolyl 2-methoxyethenyl sulfone 5.<sup>12</sup> The side product 5 was always present and in varying concentration, depending upon the concentration of buffer employed for the hydrolysis reaction. As an impurity, 5 could not be easily removed from the product 1 by column chromatography, distillation or recrystallization. In an effort to avoid these problems an investigation into an alternative method for the removal of TMS group was pursued in order that the ethynyl p-tolyl sulfone 1 might be obtained more directly and in a higher degree of purity.



During the course of studying the hydrolysis reaction of **4a**, it was observed from TLC (SiO<sub>2</sub>) analysis of the reaction that a significant portion of a pure sample of **4a**, spotted independently on the TLC plate, had been desilylated during elution. This observation prompted an investigation to explore the possibility of silica gel mediated desilylation of **4a**. A sample of pure p-tolyl 2-(trimethylsilyl)ethynyl sulfone **4a** was passed through a flash silica gel column<sup>13</sup> (25 equivalents by weight) and eluted with an ethyl acetate-petroleum ether (3:7) mixture. This resulted in clean desilylation of **4a** and provided the ethynyl p-tolyl sulfone 1 in 80% yield as a white crystalline material of exceptionally high purity. Subsequently it was discovered that the silica gel mediated desilylation was found to be equally successful for the direct conversion of the crude **4a** into pure ethynyl p-tolyl sulfone **1** (62% yield based on BTSMA **3**). The silica gel mediated desilylation eliminates the need for purification of **4a** and greatly simplifies the synthesis by effectively making the conversion of BTMSA **3** into **1** a one-pot transformation with a single purification step. In addition, the yield of this procedure was no less than the overall yield of other two-step procedures which provide **1** in equal quantity and purity.<sup>8-10</sup>

The silica gel mediated desilylation has also been found to be equally efficient for the preparation of ethynyl phenyl sulfone 2 (Scheme I). BTMSA 3 when treated with a preformed complex of benzenesulfonyl chloride-aluminium chloride afforded phenyl 2-(trimethylsilyl)ethynyl sulfone 4b. Following workup, flash chromatography of the crude reaction product 4b furnished ethynyl phenyl sulfone 2 in 65% yield.

In summary the synthesis of ethynyl p-tolyl sulfone 1 and ethynyl phenyl sulfone 2 from aluminum chloride mediated sulfonylation of BTMSA 3 has been greatly simplified with the development of the silica gel mediated desilylation of the intermediate aryl 2-(trimethylsilyl)ethynyl sulfones. This one-pot reaction sequence provides the desired aryl ethynyl sulfones in good yields of very high purity and allows for the rapid preparation of multigram quantities of these synthetically important acetylene equivalents.

#### **Experimental Section**

All chemicals and reagents not otherwise noted were purchased from Aldrich Chemical Co. Dichloromethane (E.M. Science) was dried over P<sub>2</sub>O<sub>5</sub> and distilled under nitrogen before use. Chromatography solvents ethyl acetate (E.M. Science) and 30-60°C petroleum ether (E.M. Science) were distilled prior to use. Flash silica gel (Silica Gel 60, E.M. Science, 230 - 400 mesh) was used as purchased from Curtin-Matheson Scientific. Silica gel TLC plates (E.M. Science, Kieselgel 60, F<sub>254</sub>, 0.2 mm layer, plastic and/or glass back) were purchased from Curtin-Matheson Scientific. NMR spectra were recorded using a Varian Gemini 300 MHz spectrometer. IR spectra were recorded on a Perkin-Elmer 2000 FT-IR spectrometer. Melting points were recorded on a Buchi melting point apparatus and are corrected.

#### p-Tolyl ethynyl sulfone (1).

p-Toluenesulfonyl chloride (12.30 g, 65 mmol ) was added to powdered aluminum chloride (8.6 g, 65 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (50 mL). The pale yellow solution was maintained at room temperature for 30 minutes, then slowly transferred by cannula (30 min) under nitrogen to an ice-cold solution of bis-(trimethylsilyl)acetylene 3 (10 g, 58 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (50 mL). The color of the solution changed from colorless to red then to dark red. The reaction mixture was allowed to stir at room temperature for 24 hours and was then added to a mixture (1:1) of dilute 1 N HCl (50 mL) with crushed ice (50 g). The organic layer was separated, washed twice with water and dried (Na<sub>2</sub>SO<sub>4</sub>). The solvent was removed under reduced pressure to furnish a dark brown solid. The solid residue was dissolved in 15 mL of 30% EtOAc/petroleum ether and applied to the top of a solvated prepacked column of silica gel (300 g). The sample was eluted with 30% EtOAc/petroleum ether by flash chromatography (N2).13 Concentration of the corresponding fractions under reduced pressure afforded p-tolyl ethynyl sulfone 1 (6.5 g, 62%) as white crystalline solid. mp 74-75°C (Lit. 74-75°C)<sup>8</sup>. FT-IR (CH<sub>2</sub>Cl<sub>2</sub>) 3232.2, 2068.5, 1349.7, 1168.8 cm<sup>-1</sup> <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.89 (d, J = 8.2 Hz, 2H), 7.38 (d, J = 8.2 Hz, 2H), 3.43 (s, 1H), 2.41 (s, 3H).  $^{13}C$  NMR (CDCl<sub>3</sub>) δ 145.9, 137.7, 130. 0, 127.8, 81.1, 80.4, 21.8.

#### Phenyl ethynyl sulfone (2).

The sulfonylation of **3** (8.5 g, 50 mmol) was performed in similar fashion to that described for **1** with benzenesulfonyl chloride (9.7 g, 55 mmol ) and powdered aluminum chloride (7.4 g, 55 mmol). Upon work-up, the resultant liquid residue was applied to the top of a solvated prepacked column of silica gel (300 g). The sample was eluted with 20% EtOAc/petroleum by flash chromatography (N<sub>2</sub>).<sup>13</sup> Concentration of the corresponding fractions under reduced pressure afforded phenyl ethynyl sulfone **2** (5.4 g, 65%) as a yellowish liquid. bp 84-85°C/0.09 torr (Lit. 98°C/0.1 torr)<sup>8</sup>. FT-IR (CH<sub>2</sub>Cl<sub>2</sub>) 3281.5, 2072.9, 1342.3, 1167.3 cm-<sup>1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  8.02 (m, 2H), 7.71 (m, 1H), 7.60 (m, 2H), 3.47 (s, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  140.2, 136.5, 128.3, 127.2, 82.2, 79.7.

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- Pure p-tolyl 2-(trimethylsilyl)ethynyl sulfone 4a was prepared in similar fashion to that described in the experimental section. However, the crude material was purified by bulb-to-bulb vacuum distillation followed by recrystallization from light petroleum ether. bp 125-126°C/ 0.1 torr (Lit. 130°C/0.6 torr)<sup>8</sup> mp 65-66°C. (Lit. 65-66°C)<sup>8</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.88 (d, J = 8.2 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 2.46 (s, 3H), 0.20 (s, 9H).
- p-Tolyl 2-methoxyethenyl sulfone 5 <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 7.84 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 6.41 (d, J = 6.5 Hz, 1H), 5.51 (d, J = 6.6 Hz, 1H), 3.81 (s, 3H), 2.42 (s, 2H).
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