

## Sulfones in Horner-Wittig Synthesis of Alkenes

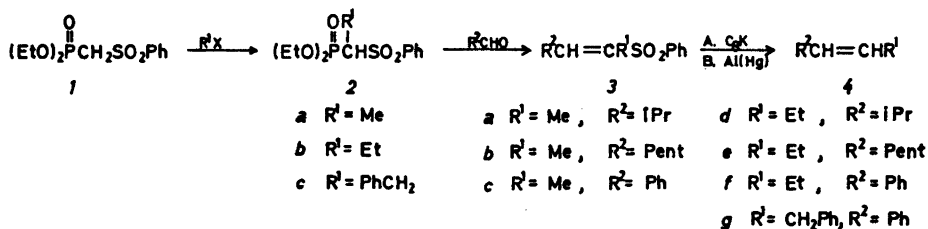
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Alkenyl sulfones and phenyl derivatives are reductively cleaved to corresponding olefins by potassium graphite and aluminium amalgam, respectively. The sulfones were prepared by the Horner–Wittig reaction using phenylsulfonylethylphosphonates. The latter were prepared from diethyl phenylsulfonylethylphosphonate and alkyl halides with phase-transfer catalysis by tetrabutylammonium salts.

Sulfones are valuable synthons in formation of new carbon–carbon bonds.<sup>1</sup> After bond formation the sulfone group can be removed by reductive cleavage of the carbon–sulfur bond. Reagents such as alkali metals in liquid amines,<sup>2,3</sup> aluminium amalgam [Al(Hg)]<sup>4</sup> and sodium amalgam [Na(Hg)]<sup>5</sup> as well as cathodic reduction<sup>6</sup> have been reported to cleave *sp*<sup>3</sup>-hybridized C–S bonds. The reductive cleavage of  $\alpha,\beta$ -unsaturated sulfones appears to depend largely on the nature of the substrate; success has been reported in some cases using the reagents Al(Hg),<sup>7,8</sup> LiAlH<sub>4</sub>-CuCl<sub>2</sub>,<sup>7</sup> lithium ethylamine<sup>9</sup> and potassium graphite (C<sub>8</sub>K)<sup>9</sup> and by the use of cathodic reduction.<sup>10</sup> Since  $\alpha,\beta$ -unsaturated sulfones are readily available,<sup>3,4,8–13</sup> their use as intermediates for the preparation of some alkenes has been studied. Direct coupling between sulfones and ketones or aldehydes, as in the reaction with 1,1-

dilithio salts of alkyl phenyl sulfones, will yield  $\alpha,\beta$ -unsaturated sulfones.<sup>8,13</sup> The reaction with sulfone is more conveniently run in aqueous systems using catalysis by quaternary ammonium salts. This reaction is limited to aromatic or  $\alpha,\beta$ -unsaturated aldehydes, however, since aliphatic aldehydes and ketones readily undergo self-condensation.<sup>11</sup> We, therefore, have used the Horner–Wittig coupling between phenylsulfonylethylphosphonates **2** and carbonyl compounds in successful syntheses of  $\alpha,\beta$ -unsaturated sulfones. The reactions are shown in Scheme 1. C-Alkylation of diethyl phenylsulfonylethylphosphonate **1** gave the synthons **2**. Alkyl halides reacted with **1** and sodium hydride in aprotic solvents with formation of mono- and dialkylated products. Alkylation in a two-phase system of sodium hydroxide solution and dichloromethane and quaternary ammonium salts as reported for the alkylation of related phosphonates,<sup>14</sup> however, gave 65–90% yields of monoalkylated products using primary halides, but the reaction failed with secondary halides. The Horner–Wittig reaction between **2** and the aldehydes proceeded readily in methanolic sodium methoxide to yield the  $\alpha,\beta$ -unsaturated sulfones **3**. Preliminary studies showed that simple ketones reacted very slowly and these reactions were



Scheme 1.

not further pursued. The Horner–Wittig reaction in a two-phase system catalyzed by tetrabutylammonium hydroxide proceeded equally well. The products **3** from either method were stereoisomeric mixtures. In methanolic sodium methoxide formation of the (*E*)-isomer was favoured, the relative yield of the (*E*)-isomer varying from 50% (**3g**) to 100% (**3f**). Under conditions of phase-transfer catalysis, however, formation of the (*Z*)-isomer was favoured; **3a** (65%), **3b** (54%), **3d** (90%) and **3e** (79%). The yields were about the same, in the region 70–95%. The isomer ratios were analyzed by GLC and the isomers identified by <sup>1</sup>H NMR; the (*Z*)-isomer has the vinyl proton at the higher field.<sup>9,11,15</sup>

The 6% Na(Hg) reagent, which has been recommended for the reductive cleavage of  $\alpha$ -benzenesulfonylcarboxylates,<sup>5</sup> did not cleave the C–S bond in the alkenyl sulfones **3** in a preparative manner. Reductive cleavage with Al(Hg) was satisfactory for the styrene derivatives **3c**, **3f** and **3g** in accordance with related reactions of other styrene derivatives using this reagent.<sup>7</sup> Its reactions with the other non-aromatic derivatives, however, were not satisfactory. Potassium graphite<sup>8</sup> appears to be a superior reagent for this purpose. All the non-aromatic  $\alpha,\beta$ -unsaturated sulfones were reduced to the corresponding alkenes by this reagent in 65–85% yield. Either method for reductive cleavage led to stereoisomerization of the double bond. The (*E*)-isomer is favoured in most cases, the relative yield being ca. 90%. Both reagents [Al(Hg), C<sub>6</sub>K] probably work as electron sources in which case the reaction mechanism may be related to the mechanism for the electrochemical reduction of vinylic sulfones in aprotic medium.<sup>10</sup>

## EXPERIMENTAL

**Preparation of phosphonates 2.** A solution of diethyl phenylsulfonylethylmethylphosphonate<sup>16</sup> (5.0 g, 17 mmol) and alkyl halide (68 mmol; for MeI 17 mmol) in dichloromethane (80 ml) was added to an aqueous solution from tetrabutylammonium bromide (5.6 g, 17 mmol) in 0.5 M NaOH (34 ml). The mixture was stirred at 45°C for 20 h before separation of the organic layer. The latter was evaporated, the residue extracted with ether, the combined ether extracts evaporated, and the residual oily material distilled as described below.

**2a:** From methyl iodide in 90% yield, b.p. 165°C/0.05 Torr. Anal. C<sub>12</sub>H<sub>18</sub>PO<sub>3</sub>S: C, H.  
**2b:** From ethyl iodide in 80% yield, b.p. 168°C/0.01 Torr. Anal. C<sub>13</sub>H<sub>21</sub>PO<sub>3</sub>S: C, H.  
**2c:** From benzyl bromide in 85% yield, b.p. 192°C/0.03 Torr. Anal. C<sub>15</sub>H<sub>23</sub>PO<sub>3</sub>S: C, H.

**Preparation of  $\alpha,\beta$ -unsaturated sulfones 3.**  
**Method A.** The phosphonate (**2**, 5 mmol) and the aldehyde (5 mmol) were dissolved in methanol (5 ml) and 1 M methanolic sodium methoxide (5 ml) added with cooling. The mixture was stirred at room temperature for 20 h before water (20 ml) was added. The resultant mixture was extracted with ether, and the ether extracts washed and dried before evaporation of the solvent. The residual material was distilled or recrystallized as described for the individual compounds below.

**Method B.** A mixture of the phosphonate (**2**, 3.3 mmol), the aldehyde (4 mmol) and tetrabutylammonium bromide (3.3 mmol) in dichloromethane (5 ml) was added dropwise to a stirred two-phase system consisting of dichloromethane (35 ml) and 50% aq. NaOH (20 ml). The organic phase was separated after 20 h at room temperature and washed with aq. NaHSO<sub>3</sub> and water. The further work up follows the procedure above.

The analyses of the isomer ratios were performed on the crude products by GLC using a 10% OV-17 column (240 cm); the instrument was programmed for +7°C/min from injection temperature at 80°C and up to 250°C. The retention time was in the range 22–25 min; the (*Z*)-isomer has the shorter retention time (ca. 1 min shorter). **3a:** Meth. A; (*E*)/(*Z*) 65:35. Meth. B; (*E*)/(*Z*) 35:65 yield 90–95%, b.p. 138°C/0.05 Torr. Anal. C<sub>11</sub>H<sub>16</sub>O<sub>2</sub>S: C, H. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  for (*E*) 1.82 (MeC=), 6.70 (HC=); for (*Z*) 1.95 (MeC=), 5.75 (HC=). **3b:** Meth. A; (*E*)/(*Z*) 60:40. Meth. B; (*E*)/(*Z*) 46:54; yield 90%, b.p. 132°C/0.01 Torr. Anal. C<sub>14</sub>H<sub>20</sub>O<sub>2</sub>S: C, H. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  for (*E*) 1.80 (MeC=), 6.87 (HC=); for (*Z*) 1.97 (MeC=), 6.00 (HC=). **3c:** Meth. A; (*E*)/(*Z*) 85:15; yield 90%, m.p. 94°C (benzene:hexane). Anal. C<sub>15</sub>H<sub>18</sub>O<sub>2</sub>S: C, H. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  for (*E*) 2.20 (MeC=); for (*Z*) 2.10 (MeC=). The vinyl protons were not resolved. **3d:** Meth. A; (*E*)/(*Z*) 75:25. Meth. B; (*E*)/(*Z*) 10:90; yield 80–90%, b.p. 142°C/0.01 Torr. Anal. C<sub>13</sub>H<sub>18</sub>O<sub>2</sub>S: C, H. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  for (*E*) 6.72 (HC=); for (*Z*) 5.75 (HC=). **3e:** Meth. A; (*E*)/(*Z*) 60:40. Meth. B; (*E*)/(*Z*) 21:79; yield 90–95%, b.p. 144°C/0.01 Torr. Anal. C<sub>15</sub>H<sub>22</sub>O<sub>2</sub>S: C, H. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  for (*E*) 6.87 (HC=); for (*Z*) 5.98 (HC=). **3f:** Meth. A; (*E*)/(*Z*) 100:0; yield 80%, m.p. 64°C (benzene:hexane). Anal. C<sub>14</sub>H<sub>16</sub>O<sub>2</sub>S: C, H. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  7.8–8.1 and 7.4–7.7 (PhSO<sub>2</sub>), 7.55 (HC=), 7.35 (Ph), 2.50 and 1.10 (Et). **3g:** Meth. A; (*E*)/(*Z*) 50:50; yield 70%, m.p. 142°C (benzene:hexane). Anal. C<sub>21</sub>H<sub>18</sub>O<sub>2</sub>S: C, H. <sup>1</sup>H NMR (CHCl<sub>3</sub>):  $\delta$  8.05 (HC=), 4.00 (–CH<sub>2</sub>C=); otherwise the spectra were not resolved.

*Preparation of alkenes 4 by reductive desulfurylation. Method A.* A 3-necked flask was charged with graphite (0.6 g; 50 mg atom) and the flask heated at 100 °C (oil-bath) under argon. Potassium (0.24 g, 6.2 mg atom), which had been washed with anhydrous hexane, was added into the flask in small portions with stirring over ca. 10 min.<sup>9</sup> After the addition of potassium was completed, the sulfone (3, 0.5 mmol) in anhydrous THF (5 ml) was added dropwise to the potassium-graphite reagent at room temperature. After stirring for 1 h, crushed ice and ether were added carefully to the mixture, and the graphite was removed by filtration. The organic phase was separated, washed and dried, and the solvent evaporated off. The alkenes were isolated by distillation of the residual material.

*Method B.* Al(Hg) was prepared from Al in 2 % aq. HgCl<sub>2</sub> and washed well with ethanol and ether.<sup>4</sup>

Al(Hg) (0.27 g, 0.01 g atom) was added to a solution of the sulfone (3, 0.05 mmol) in 10 % aq. THF under nitrogen and the mixture heated under reflux. The progress of the reaction was monitored by GLC. When the reaction had been completed the mixture was filtered, and the filtrate concentrated to a small volume at reduced pressure before being extracted with ether. The further work-up of the reaction follows Method A.

The analysis of the isomer ratios were performed on the crude products by GLC as described above. *4-Methyl-2-pentene*<sup>17</sup> 4a: Meth. A; (E)/(Z) 70:30; yield 85 % after 1 h. *Octene*<sup>18</sup> 4b: Meth. A; (E)/(Z) 95:5; yield 75 % after 1 h. *1-Propenylbenzene*<sup>19</sup> 4c: Meth. B; (E)/(Z) 95:5; yield 90 % after 10 h. *2-Methyl-3-hexene*<sup>20</sup> 4d: Meth. A; (E)/(Z) 92:8; yield 80 % after 1 h. *3-Nonene*<sup>21</sup> 4e: Meth. A; (E)/(Z) 84:16; yield 50 % after 10 h. *1-Butenylbenzene*<sup>22</sup> 4f: Meth. B; (E)/(Z) 95:5; yield 80 % after 18 h. *1,3-Diphenylpropene*<sup>23</sup> 4g: Meth. B; (E)/(Z) 90:10; yield 65 % after 18 h.

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