pathlength (0.1 cm) matched quartz cuvettes were used in the measurements. No attempt was made to determine the extinction coefficient of the absorption band of the molecular complex at λ_{max}.

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A One-Pot Synthesis of α-Ester Sulfones

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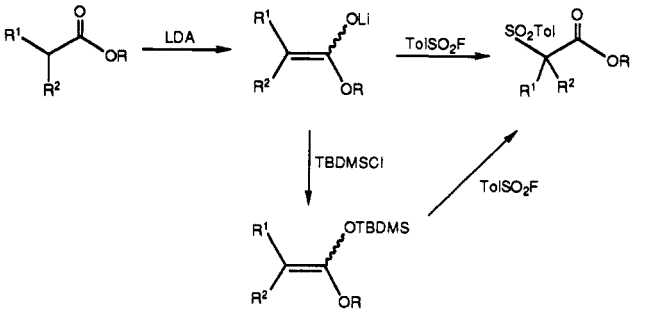
The sulfonyl group is increasingly attracting attention as a useful functionality in organic synthesis. Of particular interest are the applications of the sulfonyl group as a temporary transformer of chemical reactivity in the synthesis of eventually sulfur-free compounds.[1] As part of our research program on the synthesis of ambruticin,[2] we required a method to introduce the sulfone functionality α to an ester group. α-Ester sulfones are generally prepared by oxidation of the corresponding sulfides or sulfoxides,[3,4] or by alkylation of benzenesulfinate salts with α-halo esters.[5]

In this paper we present an alternate and a very facile procedure which enables the one-pot preparation of α-ester sulfones under mild conditions. This new route involves the direct sulfonylation of esters by reaction of the ester lithium enolate or the silyl ketene acetal with *p*-toluenesulfonyl fluoride[6] (Scheme I).

The silyl ketene acetal is prepared[7] by treating the ester with 1.2 equiv of LDA in dry tetrahydrofuran at −78 °C. The resulting solution is stirred for 1 h, after which *tert*-butyldimethylchlorosilane in THF is added dropwise to the anion. The reaction mixture is stirred at −78 °C for 30 min and at 0 °C for an additional 30-min period. The *p*-toluenesulfonyl fluoride is added all at once to the silyl ketene acetal at −78 °C and then warmed to room temperature. Our method is experimentally simple, and yields range from moderate to good (Table I).

Scheme I



Reaction of *p*-toluenesulfonyl fluoride with either the ester enolate or the silyl ketene acetal derived from α,α′-disubstituted esters gave good yields of the corresponding α-ester sulfones (entries 1 and 3). On the other hand, reaction of *p*-toluenesulfonyl fluoride with the ester enolate derived from α-monosubstituted esters gave only moderate yields of the sulfonylated product. Under these conditions once the α-ester sulfone is formed, it presumably is deprotonated by any unreacted ester enolate.

When the ester enolate derived from ester **5** was treated in a comparable manner with *p*-toluenesulfonyl chloride, no sulfonylation occurred. Instead the α-chloro ester was formed as the sole product, as observed earlier for ketone enolates by Hünig.[6c]

Experimental Section

Melting points are uncorrected. ^{1}H NMR spectra were recorded on a Nicolet QE-300 spectrometer, and chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane. ^{13}C NMR spectra were recorded on a Nicolet QE-300 spectrometer at 75.5 MHz and are reported in ppm from the center line of the chloroform-*d* triplet (77.0 ppm). Infrared spectra were recorded on a Perkin-Elmer 1310 spectrophotometer. Nominal and accurate mass spectra were obtained by electron impact on a VG-7035 mass spectrometer. Elemental analyses were performed by Galbraith Laboratories, Inc.

All reactions were run in flame-dried flasks under an atmosphere of nitrogen. Tetrahydrofuran was distilled from sodium and benzophenone prior to use. Unless otherwise mentioned, the chemicals were used as received from commercial sources.

General Procedure. Two general procedures were employed for the formation of α-ester sulfones. The following experimental procedures are representative.

Method A. Preparation of 2-Methyl-2-[(4-methylphenyl)sulfonyl]propanoic Acid Methyl Ester (2). A solution of diisopropylamine (4.8 mmol, 0.67 mL) in THF (4.0 mL) was treated with *n*-butyllithium (2.5 M in *n*-hexane, 4.8 mmol, 1.92 mL), at 0 °C, under nitrogen, with stirring. After 20 min at 0 °C, the solution was cooled to −78 °C, and a solution of 2-methylpropanoic acid methyl ester (**1**) (4.0 mmol) in THF (3.0 mL) was slowly added. After 1.0 h at −78 °C, *tert*-butyldimethylchlorosilane (4.8 mmol) in THF (2.0 mL) was added dropwise. After 30 min at −78 °C, the mixture was warmed to 0 °C, stirred for 30 min, and then cooled again to −78 °C, and *p*-toluenesulfonyl fluoride (5.74 mmol) in THF (3.0 mL) was added all at once. The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The reaction was cooled to 0 °C, quenched with saturated ammonium chloride solution (5.0 mL) and then water (5.0 mL), and extracted with ethyl acetate several times. The combined organic extracts were washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was recrystallized from ethyl acetate–hexane to give 0.891 g (87%) of **2** as colorless crystals: mp 70–71 °C; IR ($CHCl_3$) 2960, 1735, 1600, 1470, 1440, 1315, 1302, 1270, 1160, 1130 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.70 (2 H, d, J = 8.1 Hz), 7.33 (2 H, d, J = 8.1 Hz), 3.68 (3 H, s), 2.44 (3 H, s) 1.59 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 169.05,

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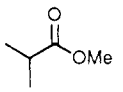
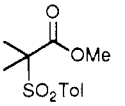
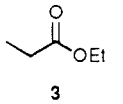
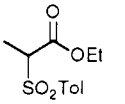
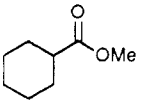
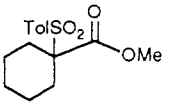
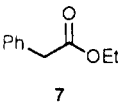
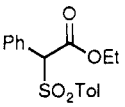
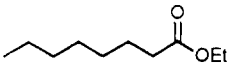
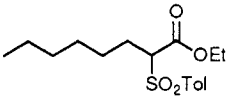
Table I

entry	ester	product	method	yield,[a] %
1	 1	 2	A	87
2	 3	 4	A	44
3	 5	 6	A B	84 80
4	 7	 8	B	36
5	 9	 10	B	51

[a] Yields were not optimized. All yields refer to purified compounds.

145.19, 132.43, 130.16, 129.70, 68.79, 52.82, 21.47, 20.06; MS (70 eV) m/e (relative intensity) 256 (M^+, 2.4), 225 (2.4), 155 (7.3), 139 (14.5), 101 (100.0), 91 (43.5), 73 (48.8), 69 (41.1), 65 (24.6). Anal. Calcd for $C_{12}H_{16}O_4S$: C, 56.25; H, 6.25. Found: C, 56.26; H, 6.46.

Method B. Preparation of 1-[(4-Methylphenyl)-sulfonyl]cyclohexanecarboxylic Acid Methyl Ester (6). A solution of diisopropylamine (4.8 mmol, 0.67 mL) in THF (6.0 mL) was treated with *n*-butyllithium (2.5 M in *n*-hexane, 4.8 mmol, 1.92 mL), at 0 °C, under a nitrogen atmosphere. After 20 min at 0 °C, the solution was cooled to −78 °C, and a solution of cyclohexanecarboxylic acid methyl ester (**5**) (4.0 mmol) in THF (4.0 mL) was slowly added. After 1.0 h at −78 °C, *p*-toluenesulfonyl fluoride (5.74 mmol) in THF (3.0 mL) was added all at once. The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The reaction was cooled to 0 °C, quenched with saturated ammonium chloride solution (5.0 mL) and then water (5.0 mL), and extracted with ethyl acetate several times. The combined organic extracts were washed with water and brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was recrystallized from ethyl acetate–hexane to give 0.947 g (80%) of **6** as colorless crystals: mp 149–150 °C; IR ($CHCl_3$) 3020, 2945, 1735, 1600, 1410, 1305, 1220, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.65 (2 H, d, J = 7.9 Hz), 7.34 (2 H, d, J = 7.9 Hz), 3.71 (3 H, s), 2.45 (3 H, s), 2.40 (1 H, br s), 2.36 (1 H, br s), 1.83 (4 H, m), 1.64 (1 H, m) 1.20 (3 H, br s); ^{13}C NMR ($CDCl_3$) δ 167.95, 145.13, 132.39, 130.03, 129.28, 74.01, 52.77, 28.08, 24.45, 23.03, 21.59; MS (70 eV) m/e (relative intensity) 265 (M^+ − 31, 1.7), 155 (1.7), 141 (49.5), 110 (4.2), 91 (23.4), 82 (6.9), 81 (100.0). Anal. Calcd for $C_{15}H_{20}O_4S$: C, 60.81; H, 6.76. Found: C, 60.75; H, 6.80.

2-[(4-Methylphenyl)sulfonyl]propanoic acid ethyl ester (4): purified by chromatography on SiO_2 (90% hexane/10% ethyl acetate), 44% yield as a clear oil;[5b] IR ($CHCl_3$) 3020, 2990, 1735, 1600, 1455, 1325, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.74 (2 H, d, J = 8.0 Hz), 7.34 (2 H, d, J = 8.0 Hz), 4.10 (2 H, q, J = 7.3 Hz), 4.01 (1 H, q, J = 7.1 Hz), 2.44 (3 H, s), 1.54 (3 H, d, J = 7.1 Hz), 1.16 (3 H, t, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 166.20, 145.30, 133.95, 129.60, 129.20, 65.30, 62.05, 21.58, 13.77, 11.70; MS (70 eV) m/e (relative intensity) 256 (M^+, 0.7), 226 (0.5), 211 (2.4), 155 (34.2), 139 (8.7), 101 (1.5), 91 (100.0), 65 (30.2), 56 (20.2); exact mass calcd for $C_{12}H_{16}O_4S$ 256.0769, obsd 256.0752.

α-[(4-Methylphenyl)sulfonyl]benzeneacetic acid ethyl ester (8): purified by chromatography on SiO_2 (90% hexane/10% ethyl acetate), 36% yield as a white solid; mp 112–113 °C (ether–hexane); IR ($CHCl_3$) 3020, 1740, 1600, 1330, 1310, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.48 (2 H, d, J = 8.1 Hz), 7.38 (5 H, m), 7.22 (2 H, d, J = 8.1 Hz), 5.09 (1 H, s), 4.22 (2 H, m), 2.42 (3 H, s), 1.25 (3 H, t, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 164.83, 145.29, 133.48, 130.25, 129.84, 129.56, 129.21, 128.50, 127.99, 75.18, 62.40, 21.64, 13.87; MS (70 eV) m/e (relative intensity) 318 (M^+, 6.0), 163 (94.4), 118 (13.9), 107 (58.6), 91 (100.0), 90 (28.6). Anal. Calcd for $C_{17}H_{18}O_4S$: C, 64.15; H, 5.66. Found: C, 64.26; H, 5.68.

2-[(4-Methylphenyl)sulfonyl]octanoic acid ethyl ester (10): purified by chromatography on SiO_2 (90% hexane/10% ethyl acetate), 51% yield as a clear oil; IR ($CHCl_3$) 2920, 1730, 1600, 1320, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.76 (2 H, d, J = 8.2 Hz), 7.36 (2 H, d, J = 8.2 Hz), 4.14 (2 H, q, J = 7.1 Hz), 3.90 (1 H, dd, J_1 = 11.02, J_2 = 4.04 Hz), 2.47 (3 H, s), 1.97 (2 H, m), 1.27 (8 H, m), 1.19 (3 H, t, J = 7.1 Hz), 0.86 (3 H, t, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 166.04, 145.18, 134.36, 129.53, 129.30, 70.97, 61.95, 31.25, 28.56, 26.75, 22.33, 21.57, 13.83, 13.81; MS (70 eV) m/e (relative intensity) 326 (M^+, 0.4), 281 (2.7), 242 (31.5), 171 (19.5), 155 (43.3), 139 (13.3), 91 (100.0). Anal. Calcd for $C_{17}H_{26}O_4S$: C, 62.58; H, 7.98. Found: C, 62.49; H, 7.99.

Registry No. **1**, 547-63-7; **2**, 124358-21-0; **3**, 105-37-3; **4**, 95314-82-2; **5**, 4630-82-4; **6**, 124358-22-1; **7**, 101-97-3; **8**, 104368-08-3; **9**, 106-32-1; **10**, 124358-23-2; *p*-toluenesulfonyl chloride, 455-16-3.