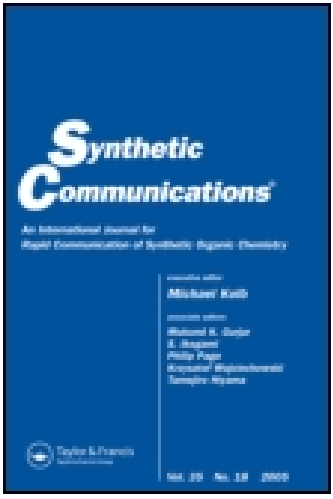

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An Efficient Preparative Route to Substituted Alkyl Benzenesulfenates. Versatile Reagents for Site-selective Sulfenylative Cyclizations.

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AN EFFICIENT PREPARATIVE ROUTE TO SUBSTITUTED ALKYL BENZENESULFENATES. VERSATILE REAGENTS FOR SITE-SELECTIVE SULFENYLATIVE CYCLIZATIONS.

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Abstract: A versatile procedure for the synthesis of alkyl benzenesulfenates possessing varied patterns of nuclear substitution is described.

Cationic cyclizations that proceed with the net incorporation of new heteroatom containing moieties have proven exceptionally useful for the synthesis of polycondensed natural products.[2] Studies in these laboratories have primarily focused on the use of methyl benzenesulfenate ($PhSOCH_3$), in combination with $BF_3 \bullet CH_3NO_2$ or Me_3SiOTf, for promoting sulfenylative carboannulations.[3] Although $PhSOCH_3 \bullet BF_3$ is capable of promoting efficient sulfenylative cascade cyclizations of a limited number of 9-aryl-2,6-nonadiene derivatives, several

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limitations associated with the use of this phenylsulfenium ion equivalent have been observed in the cyclization of a broader range of substrates in this category. We have recently described the development and utilization of a new class of arylsulfenium ion sources, as epitomized by 2-methoxyethyl 4'-chlorobenzensulfenate **4a**, that obviates many of the synthetic deficiencies of $PhSOCH_3$.[4] In this communication we describe an eminently practical method for the synthesis of **4a**, as well as a range of structurally varied sulfenylating reagents.

The preparative sequence which has proven efficacious for the synthesis of the requisite sulfenate esters consists simply of chlorinating the corresponding benzenethiol **1** via exposure to excess Cl_2 in CCl_4 at 0 °C followed by removal of the volitile components in-vacuo and subsequent exposure of the crude sulfenyl chloride to the alcohol of interest in the presence of Et_3N dissolved in Et_2O.[5] The succinimide derivative **5** was prepared in a related manner by treating 4-chlorobenzenesulfenyl chloride with sodium succinimide in CH_3CN at room temperature for 30 min. A series of sulfenate esters prepared by the above procedure is presented in **Table I**.

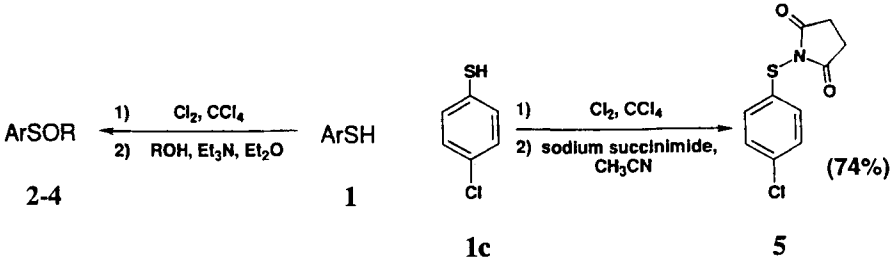
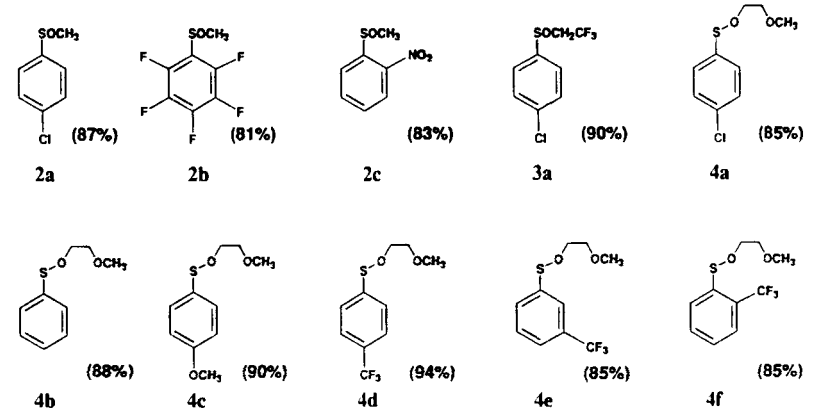


Table I. Synthesis of Benzenesulfenate Esters



The sulfenate esters synthesized by the present method possess a wide range of variability with regard to the electronic characteristics of the ionizable sulfur-oxygen bond. The utilization of these reagents as tunable episulfonium sources for the initiation of cationic cyclizations is described in a separate account from these laboratories.[4]

Experimental Section

General.

Nuclear magnetic resonance (NMR) spectra (^{1}H and ^{13}C) were recorded on a Bruker AC 300 MHz spectrometer. ^{1}H-NMR chemical shifts are reported in ppm relative to the residual proton in chloroform-d_1 assigned at 7.24 ppm. ^{13}C-NMR chemical shifts are reported in ppm relative to the center line in chloroform-

d_1 assigned at 76.90 ppm. The descriptors: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), dt (doublet of triplets), td (triplet of doublets), tt (triplet of triplets), m (multiplet), cm (complex multiplet), and br (broad) were used for assigning the multiplicities of ^{1}H-NMR spectra. Infrared spectra were obtained on a Perkin-Elmer Model 1800, dual beam, FT-IR spectrometer. Electron impact mass spectra (70-eV) were recorded with a VG Instruments MM16-F spectrometer. High resolution mass spectra were recorded on a VG Instruments 70E-HF spectrometer. Gas chromatographs were obtained with a Varian Model 3700 gas chromatograph equipped with a flame ionization detector and a Hewlett-Packard 3390A Reporting Integrator. Either an Alltech Econocap SE-54 bonded phase; 15 m lenghth, 0.54 mm id, and 1.2 m film size column or a J and W Scientific DB-5 bonded phase 15 m megabore, 0.53 mm id. column were utilized for obtaining GLC's. Melting points were determined with an Electrothermal melting point apparatus and are uncorrected.

1. General Procedure for Chlorinating Benzenethiols

A flame-dried, 1-L, three-necked flask equipped with a magnetic stirring bar, gas dispersion tube fitted through a rubber septum, gas outlet connected to a mineral oil bubbler, and a 125-mL pressure equalizing addition funnel was charged with CCl_4 (300 mL), freshly distilled from P_2O_5, and cooled to -5 - 0 °C. Chlorine gas was dried by passage through a column of conc. H_2SO_4, and slowly bubbled into the CCl_4 for ca. 5 min. A solution of the benzenethiol (0.25 mol) in dry CCl_4 (60 mL) was added dropwise from the addition funnel over 1 h while continuing to bubble Cl_2 through the solution. After complete addition of the benzenethiol, the excess chlorine and most of the solvent were removed in vacuo,

and the residual solvent was removed under high vacuum. The crude, deep red sulfenyl chloride was used without purification in the next step.

Chlorination of bis-(2-Nitrophenyl)disulfide was performed at 50-55 °C.

2. General Procedure for the Preparation of Sulfenate Esters

A flame-dried, 1-L, round-bottomed flask equipped with a magnetic stirring bar and 125-mL pressure equalizing addition funnel fitted with a rubber septum and N_2 inlet was charged with dry ether (500 mL), the appropriate ROH (0.30 mol), and Et_3N (0.30 mol), and the solution was cooled to 0 °C. Vigorous stirring was initiated, and a solution of the crude sulfenyl chloride (0.25 mol) in dry ether (25 mL) was added dropwise from the addition funnel. The reaction mixture was stirred for 30 min at 0 °C following the addition of the sulfenyl chloride. The solution was filtered, and the filter cake was washed with dry ether (3 x 100 mL). The solvent was evaporated in vacuo, and the crude product was purified by vacuum distillation to yield 80-95% of the sulfenate esters.

The succinimide derivative was prepared in an analogous fashion in 74% isolated yield from 4-chlorobenzenesulfenyl chloride and sodium succinimide in CH_3CN for 30 min at room temperature.

Methyl 4-chlorobenzenesulfenate (2a). For **2a** as a light yellow liquid: ^1H-NMR ($CDCl_3$) δ 7.49 (d, 2 H, J = 8.5 Hz, Ar*H*), 7.38 (d, 2 H, J = 8.5 Hz, Ar*H*), 3.86 (s, 3 H, OCH_3) ppm; ^{13}C-NMR ($CDCl_3$) δ 138.3 (*C*), 131.9 (*C*),

128.7 (2 *C*H), 125.0 (2 *C*H), 64.9 (O*C*H_3) ppm; IR (neat) 3082-2818 (CH envelope), 1474, 1092, 1010, 988, 814, 746, 720 cm^{-1}; HRMS calcd for C_7H_7ClOS: 173.9906. Found: 173.9902.

Methyl pentafluorobenzenesulfenate (2b). For **2b** as a light yellow liquid: ^{1}*H*-NMR ($CDCl_3$) δ 3.67 (s, 3 H, OC*H*$_3$) ppm; ^{13}*C*-NMR ($CDCl_3$) δ 147.7, 145.3, 144.3, 141.9, 139.3, 135.3 (m, 6 C, *C* and *C*F), 66.3 (O*C*H_3) ppm; IR (neat) 2971-2818 (CH envelope), 1638, 1514, 1486, 1094, 984, 704 cm^{-1}; HRMS calcd for $C_7H_3F_5OS$: 229.9825. Found: 229.9823.

Methyl 2-nitrobenzenesulfenate (2c). For **2c** as a yellow solid: mp 43-44 °C; ^{1}*H*-NMR ($CDCl_3$) δ 8.30-7.27 (cm, 4 H, Ar*H*), 3.80 (s, 3 H, OC*H*$_3$) ppm.

2,2,2-Trifluoroethyl 4-chlorobenzenesulfenate (3a). For **3a** as a light yellow liquid: ^{1}*H*-NMR ($CDCl_3$) δ 7.40 (d, 2 H, *J* = 8.7 Hz, Ar*H*), 7.36 (d, 2 H, *J* = 8.7 Hz, Ar*H*), 4.07 (q, 2 H, *J* = 8.4 Hz, C*H*$_2$) ppm; ^{13}*C*-NMR ($CDCl_3$) δ 136.4 (*C*), 134.7 (*C*), 129.4 (2 *C*H), 128.3 (2 *C*H), 123.1 (q, *C*F_3), 74.0 (*C*H_2) ppm; IR (neat) 3068-2880 (CH envelope), 1476, 1276, 1164, 1094, 1044, 1012, 962, 852, 818, 748 cm^{-1}; HRMS calcd for $C_8H_6ClF_3OS$: 241.9780. Found: 241.9783.

2-Methoxyethyl 4-chlorobenzenesulfenate (4a). For **4a** as a light yellow liquid: ^{1}*H*-NMR ($CDCl_3$) δ 7.26 (d, 2 H, *J* = 8.6 Hz, Ar*H*), 7.17 (d, 2 H, *J* = 8.6 Hz,

Ar*H*), 3.86 (t, 2 H, J = 4.5 Hz, CH_2), 3.48 (t, 2 H, J = 4.5 Hz, CH_2), 3.29 (s, 3 H, OCH_3) ppm; ^{13}C-NMR ($CDCl_3$) δ 138.7 (*C*), 131.8 (*C*), 128.7 (2 *C*H), 124.7 (2 *C*H), 77.1 (*C*H_2), 71.1 (*C*H_2), 58.5 (O*C*H_3) ppm; IR (neat) 3075-2811 (CH envelope), 1474, 1452, 1198, 1128, 1092, 1028, 1010, 896, 814 cm^{-1}; HRMS calcd for $C_9H_{11}ClO_2S$: 218.0168. Found: 218.0155.

2-Methoxyethyl benzenesulfenate (4b). For **4b** as a light yellow liquid: ^1H-NMR ($CDCl_3$) δ 7.37 (m, 5 H, Ar*H*), 4.04 (t, 2 H, J = 4.6 Hz, CH_2), 3.64 (t, 2 H, J = 4.6 Hz, CH_2), 3.44 (s, 3 H, OCH_3) ppm; ^{13}C-NMR ($CDCl_3$) δ 139.9 (*C*), 128.2 (2 *C*H), 125.7 (*C*H), 122.8 (2 *C*H), 76.6 (*C*H_2), 70.8 (*C*H_2), 58.0 (O*C*H_3) ppm; IR (neat) 3061-2811 (CH envelope), 1478, 1440, 1128, 1024, 896, 738, 692 cm^{-1}; HRMS calcd for $C_9H_{12}O_2S$: 184.0558. Found: 184.0557.

2-Methoxyethyl 4-methoxybenzenesulfenate (4c). For **4c** as a light yellow liquid: ^1H-NMR ($CDCl_3$) δ 7.52 (d, 2 H, J = 8.8 Hz, Ar*H*), 6.93 (d, 2 H, J = 8.8 Hz, Ar*H*), 3.84 (t, 2 H, J = 4.6 Hz, CH_2), 3.81 (s, 3 H, OCH_3) 3.50 (t, 2 H, J = 4.6 Hz, CH_2), 3.32 (s, 3 H, OCH_3) ppm; ^{13}C-NMR ($CDCl_3$) δ 160.0 (*C*), 132.2 (2 *C*H), 128.7 (*C*), 113.8 (2 *C*H), 75.4 (*C*H_2), 70.9 (*C*H_2), 58.0 (O*C*H_3), 54.6 (O*C*H_3) ppm; IR (neat) 3061-2832 (CH envelope), 1590, 1494, 1290, 1250, 1128, 1028, 892, 830 cm^{-1}; HRMS calcd for $C_{10}H_{14}O_3S$: 214.0664. Found: 214.0668.

4-Methoxyethyl 4-trifluoromethylbenzenesulfenate (4d). For **4d** as a light yellow oil: ^{1}H-NMR ($CDCl_3$) δ 7.58 (d, 2 H, J = 8.4 Hz, Ar*H*), 7.30 (d, 2 H, J = 8.4 Hz, Ar*H*), 4.00 (t, 2 H, J = 4.4 Hz, CH_2), 3.60 (t, 2 H, J = 4.4 Hz, CH_2), 3.38 (s, 3 H, OCH_3) ppm; ^{13}C-NMR ($CDCl_3$) δ 146.3 (*C*), 131.8 (*C*), 125.5 (2 *C*H), 124.1 (q, *C*F_3), 120.6 (2 *C*H), 77.7 (*C*H_2), 71.2 (*C*H_2), 58.6 (O*C*H_3) ppm; IR (neat) 3075-2818 (CH envelope), 1606, 1326, 1164, 1124, 1092, 1062, 1012, 896, 828 cm^{-1}; HRMS calcd for $C_{10}H_{11}F_3O_2S$: 252.0432. Found: 252.0424.

2-Methoxyethyl 3-trifluoromethylbenzenesulfenate (4e). For **4e** as a light yellow oil: ^{1}H-NMR ($CDCl_3$) δ 7.58 (app s, 1H, Ar*H*) 7.50-7.35 (m, 3 H, Ar*H*), 3.99 (t, 2 H, J = 4.4 Hz, CH_2), 3.59 (t, 2 H, J = 4.4 Hz, CH_2), 3.37 (s, 3 H, OCH_3) ppm; ^{13}C-NMR ($CDCl_3$) δ 142.5 (*C*), 129.5 (*C*), 129.1 (*C*H), 124.8 (*C*H), 123.9 (q, *C*F_3), (122.3 (*C*H), 118.6 (*C*H), 77.8 (*C*H_2), 71.2 (*C*H_2), 58.6 (O*C*H_3) ppm; IR (neat) 3061-2818 (CH envelope), 1323, 1168, 1128, 1104, 1072, 1026, 896, 698 cm^{-1}; HRMS calcd for $C_{10}H_{11}F_3O_2S$: 252.0432. Found: 252.0440.

2-Methoxyethyl 2-trifluoromethylbenzenesulfenate (4f). For **4f** as a light yellow oil: ^{1}H-NMR ($CDCl_3$) δ 7.70-7.20 (cm, 4 H, Ar*H*), 3.98 (t, 2 H, J = 4.4 Hz, CH_2), 3.61 (t, 2 H, J = 4.4 Hz, CH_2), 3.38 (s, 3 H, OCH_3) ppm; ^{13}C-NMR ($CDCl_3$) δ 140.9 (*C*), 132.3 (*C*), 131.9 (*C*H), 126.4 (*C*H), 124.9 (*C*H), 123.8 (q, *C*F_3), 122.2 (*C*H), 77.5 (*C*H_2), 71.2 (*C*H_2), 58.6 (O*C*H_3) ppm; IR (neat) 3068-

2825 (CH envelope), 1594, 1444, 1316, 1256, 1178, 1118, 1092, 1032, 896, 764 cm^{-1}; HRMS calcd for $C_{10}H_{11}F_3O_2S$: 252.0432. Found: 252.0430.

N-(4-Chlorophenyl)sulfenyl succinimide (5). For **5** as a white solid: mp 123-127 °C; ^1H-NMR ($CDCl_3$) δ 7.56 (d, 2 H, J = 8.5 Hz, Ar*H*), 7.28 (d, 2 H, J = 8.5 Hz, Ar*H*), 2.80 (s, 4 H, 2 CH_2) ppm; ^{13}C-NMR ($CDCl_3$) δ 176.1 (2 *C*=O), 136.2 (*C*), 133.9 (2 *C*H), 132.0 (*C*), 129.4 (2 *C*H), 28.4 (2 CH_2) ppm; IR (KBr) 3165-2811 (CH envelope), 1727 (C=O), 1694, 1476, 1302, 1190, 1142, 1090, 1006, 814, 805 cm^{-1}; HRMS calcd for $C_{10}H_8ClNO_2S$: 240.9964. Found: 240.9962.

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