

An Economical and Convenient Synthesis of Phenyl Vinyl Sulfone from Benzenethiol and 1,2-Dichloroethane

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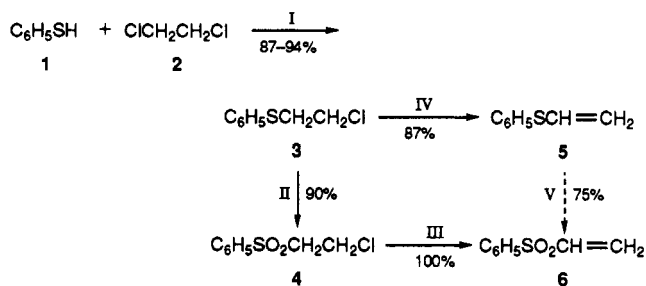
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Vinyl sulfones, and in particular *phenyl vinyl sulfone*, are useful synthetic tools and have a rich chemistry of their own.¹ A novel class of fluoroalkyl vinyl sulfones, [2-(F-alkyl)ethanyl vinyl sulfones, (R_FCH₂CH₂SO₂CH=CH₂)], useful for providing oil and water repellence to surfaces and as a reactive intermediate,² was synthesized analogously to that of alkyl or aryl vinyl sulfones,³⁻⁵ with one notable exception. In the first step, phase transfer catalyzed (PTC) alkylation of the congener thiol, R_FCH₂CH₂SH, by 1,2-dichloroethane (2) gave *monosubstitution* product R_FCH₂CH₂SCH₂CH₂Cl with high selectivity.^{2a,6} By contrast, attempted S_N2 alkylation *without a PTC agent* gave mostly *bis*-substitution product.⁷ Analogously, alkylation of benzenethiolate ion by 1,2-dibromoethane in alcohol solution without PTC gave chiefly 1,2-bis-(phenylthio)ethane; the *mono* substitution product C₆H₅SCH₂CH₂Br was isolated in only 40.6% yield.⁸ The purpose of this paper is to describe a practical, versatile, high-yield synthesis of phenyl vinyl sulfone and of vinyl sulfones as a class, utilizing as first step the novel PTC alkylation of an appropriate thiol.

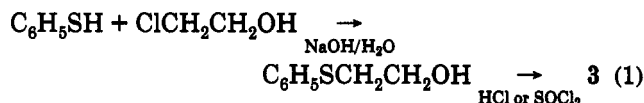
Results

In a biphasic system, alkylation of benzenethiol (1) with 1,2-dichloroethane (2) (molar ratio of 2:1 = 13.3) gave [(2-chloroethyl)thio]benzene (3) as undistilled product in 98-99% yield and purity or in 87-91% yield as distilled product (Scheme I, Step I). A probe sample showed by GC a greater than 50:1 molar ratio of mono to bis product. When 31.2 mol of 2:1 was employed, this product ratio was greater than 100:1. Thus, a large molar excess of 2 functions both as solvent and secondary reaction suppressant; unreacted 2 was recovered by distillation and was readily reused. The process employs standard laboratory equipment and has given 3 on a scale of 0.2-0.5 mol. The previous synthesis of [(2-chloroethyl)thio]benzene (3) from benzenethiol (1) was devised to avoid bis-alkylation by 1,2-dichloroethane but required two steps (eq 1), with an overall yield of 73-93%.³⁻⁵ Hopkins and

Scheme I. Phenyl Vinyl Sulfide, Sulfoxide, and Sulfone from [(2-Chloroethyl)thio]benzene^a



^a Key: I, room temperature, PTC (7), NaOH/water; II, H₂O₂, AcOH, 50-90 °C; III, 22 °C, Et₃N, THF; IV, reflux (80 °C), PTC (7), NaOH/water; V, H₂O₂, AcOH (ref 13).



Fuchs⁹ prepared 3 in 96% yield on a 2 mmol scale by addition of C₆H₅SCl to ethene. Benzenesulfonyl chloride was obtained by reaction of *N*-chlorosuccinimide and 1 on a half molar scale.⁹

Step II of Scheme I was accomplished by oxidation with hydrogen peroxide in acetic acid (87% yield)³⁻⁵ or by peracetic acid in acetic acid (93.8% yield).¹⁰ In earlier reports,³⁻⁵ this step was achieved in yields of 76-79%. Incomplete isolation of sulfone 4 is probably responsible for lower yields, as oxidation of 3 with either hydrogen peroxide or peracetic acid in stoichiometric amount gives 4 quantitatively. It was necessary to isolate and dry sulfone 4 for reaction with triethylamine in THF (step III). However, elimination of HCl from 4 occurred rapidly and (ethenylsulfonyl)benzene (6) was isolated quantitatively. The yields previously reported for step III were from 79 to 89%;³⁻⁵ the latter was achieved on a 1 mol scale.⁵

A biphasic PTC reaction of 4 with aqueous alkali on a 3 mmol scale *at room temperature* was recently reported.¹¹ This procedure provides vinyl sulfone 6 in 100% yield and may facilitate use of *wet* sulfone 4 in step III, thus rendering unnecessary the isolation of 4 before dehydrohalogenating to 6. When an excess of NaOH was employed, however, significant conversion of 4 to Michael addition product C₆H₅SO₂CH₂CH₂OH also occurred.¹²

Almost simultaneously with the present work,^{2a} Paquette and Carr developed an analogous synthesis of vinyl sulfone 6 which appeared also in *Organic Syntheses*.^{13,14} Controlled addition of benzenethiolate solution under nitrogen into 1,2-dibromoethane furnishes [(2-bromoethyl)thio]benzene, which with sodium ethoxide gives (ethenylthio)benzene (5) in 50-65% yield on a 1 molar scale.

(1) (a) Tompkins, N. S. *Tetrahedron* 1990, 46, 6951. (b) Fuchs, P. L.; Braish, T. F. *Chem. Rev.* 1986, 86, 903.

(2) (a) Brace, N. O. U. S. Patent 4,517,384 to CIBA-GEIGY Corp., May 14, 1985. Application was filed on Jan 21, 1983. *Chem. Abstr.* 1984, 101, 231193h. (b) A manuscript on the subject of 2-(perfluoroalkyl)-alkylene sulfides, sulfoxides, and sulfones, including vinyl and allyl derivatives and related compounds, is in preparation.

(3) Ford-Moore, A. H.; Peters, R. A.; Wakelin, R. W. *J. Chem. Soc.* 1949, 1754.

(4) Smith, L. I.; Davis, H. R., Jr. *J. Org. Chem.* 1950, 15, 824.

(5) Price, C. C.; Morita, J. *J. Am. Chem. Soc.* 1953, 75, 4747.

(6) In reaction of C₆F₁₇CH₂CH₂SH with 2 (1:30 mol, respectively) *without a PTC agent*, yield of *monosubstitution* product was 22% and *bis* product was 70% (example 11 in ref 2a).

(7) Brace, N. O. Phase Transfer Catalyzed Reactions. *10th International Fluorine Conference*, Vancouver, British Columbia, Aug 6, 1982. However, because of economic and other reasons, this part of the work on PTC reactions was not disclosed.

(8) Claisse, J. A.; Davies, D. I.; Alden, C. K. *J. Chem. Soc. C* 1966, 1498.

(9) Hopkins, P. B.; Fuchs, P. L. *J. Org. Chem.* 1978, 43, 1208.

(10) This method of oxidation (peracetic acid in acetic acid) gave 90-100% yield of sulfones with several analogous sulfides.⁹

(11) Shimizugawa, Y.; Takahashi, T.; Ishii, M.; Yamamoto, T. *Org. Prep. Proc. Int.* 1990, 22, 522.

(12) Conjugate addition of water or alcohols to sulfones 4 or 6 has been observed.^{1b,3} In dehydrohalogenation of sulfones R_FCH₂CH₂SO₂CH₂CH₂Cl, reaction with sodium methoxide in methanol gave a substantial amount of the β-methoxy product. This product was not found when acetonitrile was used as solvent.^{2b}

(13) Paquette, L. A.; Carr, V. C.; Kende, A. S., Eds. *Org. Synth.* 1985, 64, 157.

(14) (a) Carr, R. V. C.; Williams, R. V.; Paquette, L. A. *J. Org. Chem.* 1983, 48, 4976. (b) Carr, R. V. C.; Paquette, L. A. *J. Am. Chem. Soc.* 1980, 102, 853.

Hydrogen peroxide in acetic acid oxidizes **5** to (ethenylsulfonyl)benzene (**6**) in 74–78% yield. Unfortunately, the last step requires handling the unpleasant and easily decomposed^{5,9,13} (ethenylthio)benzene (**5**).

As shown in Scheme I (step IV), a biphasic PTC reaction of **3** in refluxing benzene solution with aqueous NaOH gave vinyl sulfide **5** in 87.8% yield.¹⁵ Then, oxidation of **5** (Scheme I, step V) affords a complementary route to vinyl sulfone **6**. It is more economical and convenient to oxidize undistilled **3** instead of the more volatile, somewhat unstable thioether **5**. Both **3** and **4** have vesicant properties, but no skin irritation was experienced in handling these materials in the manner described in the Experimental Section. Distilled vinyl sulfide **5**, prepared by PTC elimination reaction, decomposed to the extent of only 3–5% (GC) over a 6-year period, when kept tightly closed, cold, and dark. Samples of **3**, **4**, and **6** showed no signs of decomposition (GC; mp unchanged) when stored at ambient conditions for 6 years in closed containers.

The recently disclosed aqueous biphasic method¹¹ for converting sulfone **4** to vinyl sulfone **6**, if successfully scaled up, may further enhance the convenience and economy of this synthesis of **6** from benzenethiol and 1,2-dichloroethane. These procedures should be readily adapted to the synthesis of alkyl and aryl vinyl sulfones of many types from appropriate thiols, as already achieved for the fluoroalkyl vinyl sulfones and now with phenyl vinyl sulfone.

Experimental Section

Materials and Methods. Benzenethiol (**1**), 1,2-dichloroethane (**2**), hydrogen peroxide (30% in water), and acetic acid were the best commercial materials available. Tricaprylammonium chloride as Adogen 464 (**7**) is available from Aldrich Chemical Co. Peracetic acid (35.5%) in acetic solution was obtained from FMC Corp., Philadelphia, PA, and kept cold before and during use. Recommended precautions were carefully followed in its use. GC analyses: silicone oil "W-98", 15 wt % on 5-ft by 1/4-in. column; kept at 150 °C for 5 min, heated to 200 °C; 30 mL/min of helium carrier gas. Capillary GC: "DB-1", 15-m column, kept at 50 °C for 5 min, heated to 250 °C at 10 °C/min; 4 mL/min of helium carrier gas. Known mixtures of reactants and toluene (internal reference) were used to give response factors for quantitative estimation of reaction samples.

[(2-Chloroethyl)thio]benzene (3) from Benzenethiol (1) and 1,2-Dichloroethane (2). A 1-L, round-bottom flask was fitted with a paddle stirrer, reflux condenser, thermometer, and pressure-equalizing dropping funnel. Added successively were **2** (531 g, 5.37 mol, 430 cm³), methyltricaprylammonium bromide (**7**, 0.93 g, 2.1 mmol), and under nitrogen atmosphere to prevent oxidation, **1** (redistilled, bp 62–64 °C/18 mm; 44.64 g, 40.9 cm³; 0.405 mol). It was convenient to feed in nitrogen through the dropping funnel side arm. A bubbler tube with an oil seal that would permit release of excess pressure if necessary was attached to the condenser opening. This device monitored pressure change while maintaining a sealed system. The mixture was stirred vigorously, and a solution of NaOH (20.5 g, 0.500 mol) in water (250 cm³) was added at the rate of 33 cm³/h during 7.5 h at 23–25 °C, while cooling if necessary. Stirring of the biphasic mixture was continued for 16 h at 20–24 °C. A sample of the aqueous layer showed that none of **1** remained; GC of the organic layer showed product **3** and bis-adduct in a molar ratio of greater than 50:1. The upper, aqueous layer was removed by suction tube to a 1-L suction flask. The organic layer was washed by stirring with 1 M HCl (20 mL) and then with water (25 mL). The condenser was replaced by a distillation head and 10-in. Vigreux

column, and the liquid mixture was stirred to prevent bumping. An azeotrope of **2** with water distilled first, bp 71–82 °C, followed by **2**, bp 82–83 °C. The azeotrope (50 mL) was used to rinse the reaction flask and then to extract any product from the aqueous layer. The combined organic layer was dried (CaCl₂). Liquid product was decanted and the solid rinsed with dry dichloroethane into a distillation (pot) flask which was attached to the Vigreux distillation column and head. All of **2** was removed when the pot temperature reached 60 °C at a water pump pressure of 13 mm. The liquid residue (70.21 g, 0.406 mol; 100% conversion, by wt) was nearly pure [(2-chloroethyl)thio]benzene (**3**). A portion (17.3 g, 100 mmol as **3**) was oxidized to pure [(2-chloroethyl)sulfonyl]benzene (**4**) in 87.1% yield (see below). The remaining product liquid (57.79 g) was distilled (without Vigreux column) using an oil bath kept at 139–142 °C; this gave **3**, bp 122–124 °C/15 mm, 46.00 g (266 mmol; 91.5% yield) (lit.³ bp 123 °C/14 mm) (GC: **3**, 99.05%). The residue, 6.85 g, was a mixture of **3**, 1,2-bis(phenylthio)ethane (**8**), and diphenyl disulfide (**9**).

A similar experiment that employed **1** (0.200 mol), **2** (6.240 mol), NaOH (0.3385 mol in 250 mL of water), and **7** (0.60 g; 1.4 mmol) gave **3** (30.88 g, 89.4% distilled yield; GC homogeneous) and residue (2.61 g). The product mixture (before distillation) consisted of **2**, 40.58%; **3**, 57.92%; **9**, 0.40%; and **8**, 0.55% (determined by capillary column GC). Relative amounts were thus: **3**, 98.38%; **9**, 0.68%; and **8**, 0.94%.

(Ethenylthio)benzene (5) from [(2-Chloroethyl)thio]benzene (3). A 250-mL flask was fitted with reflux condenser, nitrogen inlet, magnetic stirrer bar, and thermometer. Distilled **3** (17.3 g, 100 mmol), NaOH (8.00g, 0.200 mmol) dissolved in water (50 mL), phase-transfer catalyst **7** (1.00g, 2.26 mmol), and benzene (50 mL) were charged to the flask under nitrogen purge. The mixture was heated in an oil bath kept at 80–82 °C. After 24 h at reflux a GC sample showed 85.0% of **5**, 5.0% of an unknown substance and 10.1% of unreacted **3**. After an additional 6 h, GC showed no **3**, the layers were separated, and the yellow organic layer was rinsed with 1 M HCl (10 mL) followed by water (10 mL, twice), and dried (CaCl₂). Benzene was removed at the water pump through a 10-in. Vigreux column, with a variable take off, total reflux head, operated at a 10/1 reflux ratio. The column was then removed and **5** distilled as a clear, colorless liquid, bp 84–87 °C/14 mm, 11.5 g (bath at 88–96 °C), *n*_D²⁵ 1.5836. GC: 95.2% of **5**, 3.96% of an unknown substance, and 0.84% of **3**. An additional 0.50 g of less pure **5**, bp 82–56 °C/14 mm (bath 116 °C, no reflux) was also obtained, giving a total yield of 87.8%. IR: bands identical with those reported.¹³ The residue was a dark liquid (2.72 g). A sample of **5**, kept cold and dark in a refrigerator, became only slightly colored during storage for 6 years, IR was unchanged, and GC gave **3**, 0.48%, **5**, 92.99%, **8**, 0.67%, and **9**, 0.47%, with unknowns of 2.24% and 1.65%.

[(2-Chloroethyl)sulfonyl]benzene (4) from [(2-Chloroethyl)thio]benzene (3). A solution of undistilled **3** (17.3 g, 100 mmol) and acetic acid (100 mL) was stirred by magnet bar in a 250-mL, two-neck flask and heated to 48 °C. A solution of hydrogen peroxide (31.7 g, 280 mmol, 27.5% aqueous solution) in acetic acid (50 mL) was added dropwise during 40 min at 40–49 °C, with cooling with a water bath as needed. The cloudy solution was heated to 70 °C and kept at 70 °C by a constant temperature oil bath for 4 h. The bath temperature was raised to 90 °C and held for 11 h. The white, cloudy mixture was cooled and water (200 mL) added to give a suspension of sulfone **4**. Diethyl ether (180 mL, and 40 mL) was added to extract the product and the ether layer washed in turn with brine and with water (50 mL, each) and dried (MgSO₄). The salt cake was extracted with ether and the solvent stripped by rotary evaporator (50 °C/13 mm, 2 h) to give sulfone **4**, 17.8 g. The solid melted incompletely and thus contained salt. The sulfone was washed with water by suspension and collected on a filter, dried at 25 °C, dissolved in warm benzene (75 mL), filtered, and evaporated to dryness (rotary evaporator), 16.10 g; mp 55–57.5 °C (lit.³ mp 55 °C, 78.5% yield). Additional **4** (1.73 g, mp 55–57 °C) was recovered by evaporating the aqueous extracts and the salt cake in a beaker followed by trituration with water (200 mL) and filtration. The total yield of **4** was 87.1%. In view of the difficulty in extraction by diethyl ether of pure product, it would have been preferable to filter the original aqueous suspension of **4** and remove salt by water washing.

(15) Vinyl sulfide R₂CH₂CH₂SCH=CH₂ was obtained from R₂CH₂CH₂SCH₂CH₂Cl with NaOMe in acetonitrile in a facile reaction,^{2b} and **5** was prepared in 88% yield from **3** by reaction with DBU.⁹

[(2-Chloroethyl)sulfonyl]benzene (4): Oxidation of [(2-Chloroethyl)thio]benzene (3) with Peracetic Acid in Chloroform Solution.¹⁰ A solution of distilled **3** (2.59 g, 15.0 mmol) in chloroform (10 mL) was stirred by magnetic bar in a 100-mL, two-neck flask and cooled to 1 °C with an ice-salt bath. A two-phase mixture of peracetic acid (7.2 g, 40 mmol, 35.5% solution in acetic acid) and chloroform (15 mL) was added dropwise during 1 h at 5–10 °C (bath at 1 °C). The stirred mixture was allowed to warm to 25 °C for 4 h, and the cloudy mixture was heated to 50 °C for 2 h. Following cooling, a sample tested strongly for peroxide with KI paper. Solid sodium bisulfite (1.0 g, 2.0 g, and 2.0 g) was added while the mixture was stirred at 25 °C (bath temperature); an exotherm occurred to 55 °C. The resulting clear solution tested negative for peroxide and was dried (MgSO₄)

and filtered. Removal of solvent gave **4**, 2.88 g (93.8% yield); mp 53–4 °C. IR spectra of product **4** from both preparations matched that of pure **4**.

(Ethenylsulfonyl)benzene (6) from Sulfone 4. A solution of sulfone **4** (2.04 g, 10.0 mmol) in THF (25 mL) was stirred at 30 °C, while triethylamine (1.52 g, 15 mmol) in THF (10 mL) was added during 1 min. The clear solution clouded and precipitate formed while the mixture was stirred for 24 h at 20–24 °C. Solid triethylamine hydrochloride (1.38 g, 100% yield) was filtered and the clear filtrate evaporated (rotary evaporator, to 42 °C/12 mm) to give solid **6** (1.69 g, 100% yield). Recrystallized from ligroin (10 mL) and benzene (5 mL) at 5 °C gave 0.76 g, mp 65–67.5 °C (lit.^{3,5,13} mp 66–7 °C). IR: bands identical to those reported.¹³

Additions and Corrections

Vol. 57, 1992

Mark S. Meier* and John P. Selegue . Efficient Preparative Separation of C₆₀ and C₇₀. Gel Permeation Chromatography of Fullerenes Using 100% Toluene as Mobile Phase .

Page 1925. Reference 18 should include the following. Separation on a JAIGEL HPLC column using benzene as eluant has also be used: Kikuchi, K.; Nakahara, N.; Honda, M.; Suzuki, S.; Saito, K.; Shiromaru, H.; Yamauchi, K.; Ikemoto, I.; Kuramochi, T.; Hino, S.; Achiba, Y. *Chem.*

Lett. 1991, 1607–1610. We thank Dr. Kikuchi for bringing this article to our attention and we regret the oversight.

Percy S. Manchand,* Peter S. Belica, Michael J. Holman, Tai-Nang Huang, Hubert Maehr, Steve Y.-K. Tam, Roxana T. Yang, John J. Partridge, Matthew J. Petrin, Anthony M. Pico, Anthony J. Laurenzano, Errol S. Schnurman, and Ronald C. West . Syntheses of the Anti-AIDS Drug 2',3'-Dideoxycytidine from Cytidine.

Page 3473. The following authors should be added: John J. Partridge, Matthew J. Petrin, Anthony M. Pico, Anthony J. Laurenzano, Errol S. Schnurman, and Ronald C. West.