norbornadiene-2-carboxylic acid derivatives. Since even the sterically hindered tertiary butyl compound **1c** reacts readily at room temperature, this reaction should be of general applicability.

Experimental Section

General Procedures. Infrared spectra were recorded on a Beckman Acculab 1 IR spectrophotometer. ^1H NMR spectra were taken in carbon tetrachloride on a JEOL JNM-C-60-HL spectrometer, and mass spectra were recorded on a Varian MAT CH 4 spectrometer.

Methyl 3-Phenylbicyclo[2.2.1]hepta-2,5-diene-2-carboxylate (4a). Cyclopentadiene (2.70 g, 40.9 mmol) was added to precooled (0 °C) phenylpropynoyl chloride (**1a**;[7] 6.00 g, 36.5 mmol) in a nitrogen atmosphere and the mixture was allowed to warm to 20 °C within 4 h. After 10 h, more cyclopentadiene (2.70 g, 40.9 mmol) was added. After the mixture was stirred for 24 h, **1a** was consumed completely (monitoring by NMR) and the mixture was added slowly to a suspension of $NaHCO_3$ (3.5 g) in 50 mL of methanol. After 1 h, the mixture was filtered and the solvent evaporated. The residue was dissolved in 20 mL of ether and filtered, the ether evaporated, and the residue distilled: 6.93 g (84%) of **4a**; bp 109–110 °C (0.2 mmHg) [lit.[4] bp 111–116 °C (0.6 mmHg)]; IR (neat) 3050, 2980, 2940, 2870, 1705, 1605, 1590, 1485, 1425, 1330, 1290, 1230, 1185, 1145, 1095, 1080, 1070, 755, 715, 690 cm^{-1}; ^1H NMR (CCl_4) δ 2.03, 2.23 (br AB system, J = 7 Hz, 2 H), 3.60 (s, 1 H), 3.82 (br s, 1 H), 4.03 (br s, 1 H), 6.94 (br s, 2 H), 7.1–7.7 (m, 5 H); mass spectrum (70 eV), m/e (relative intensity) 226 (100, M^+), 195 (24), 167 (63), 166 (21), 165 (39), 161 (69), 152 (15), 129 (47).

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.50; H, 5.96.

Methyl 3-Methylbicyclo[2.2.1]hepta-2,5-diene-2-carboxylate (4b). 2-Butynoyl chloride (**1b**; from 2-butynoic acid[8] and $SOCl_2$;[9] 4.00 g, 39.0 mmol) and cyclopentadiene (2.70 g, 40.9 mmol) were combined at room temperature (N_2 atmosphere). After 48 h at ambient temperature more cyclopentadiene (2.70 g, 40.9 mmol) was added, and the mixture was left for another 48 h and worked up as above. The crude material was purified by filtration over silica gel. After elution of dicyclopentadiene with petroleum ether, **4b** was eluted with ether, the ether evaporated, and the residue distilled: 5.0 g (78%) of **4b**; bp 67–70 °C (4 mmHg) [lit.[6] bp 85–90 °C (15 mmHg)]. For spectral data, see ref. 6.

Methyl 3-*tert*-Butylbicyclo[2.2.1]hepta-2,5-diene-2-carboxylate (4c). 4,4-Dimethyl-2-pentynoyl chloride (**1c**; from 4,4-dimethyl-2-pentynoic acid[10] and $SOCl_2$;[9] 9.00 g, 62.2 mmol) and cyclopentadiene (5.00 g, 75.6 mmol) were combined at 20 °C (N_2 atmosphere). After 30 h more cyclopentadiene (4.10 g, 62.0 mmol) was added, and the mixture was stirred for 5 days at room temperature and worked up as described for **4a**: 10.5 g (82 %) of **4c**; bp 62–64.5 °C (1 mmHg); IR (neat) 3070, 2950, 2870, 1720, 1600, 1560, 1480, 1460, 1435, 1365, 1300, 1235, 1195, 1160, 1090, 1050, 725 cm^{-1}; ^1H NMR (CCl_4) δ 1.16 (s, 9 H), 1.88 (m, 2 H), 3.67 (s and m, 5 H), 6.82 (m, 2 H); mass spectrum (70 eV), m/e (relative intensity) 206 (58, M^+), 191 (21), 175 (22), 174 (40), 159 (24), 147 (80), 141 (51), 131 (100).

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 76.00; H, 9.05.

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Registry No. **1a**, 7299-58-3; **1b**, 39753-54-3; **1c**, 52324-03-5; **4a**, 24161-43-1; **4b**, 85894-25-3; **4c**, 85894-26-4; cyclopentadiene, 542-92-7.

(7) Bergmann, F.; Haskelberg, L. *J. Am. Chem. Soc.* **1941**, *63*, 2243.
(8) Simmross, F.-M.; Weyerstahl, P. *Synthesis* **1981**, 72.
(9) General procedure: "Organikum", 7th ed.; VEB Deutscher Verlag der Wissenschaften: Berlin, 1967; p 409.
(10) Moreu, C.; Delange, R. *Bull. Soc. Chim.* **1903**, *29*, 648.

Sulfinic Acids and Related Compounds. 14. Derivatives of 3-Sulfinopropanoic Acid[1,2]

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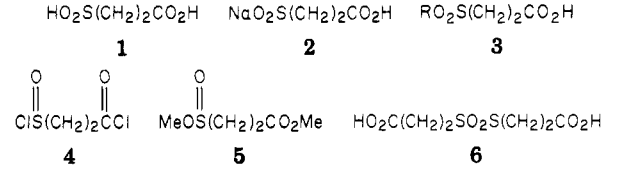
Sulfinate salts containing di- or trisulfide linkages have shown promise as antiradiation drugs.[3] An attractive alternative to long sequential syntheses of such structures would be convergent syntheses in which separately synthesized sulfinic acid derivatives and di- or trisulfides become connected by a carboxylate ester linkage involving CO_2H on one of the synthons and OH on the other. For such purposes, 3-sulfinopropanoic acid (**1**), as its sulfinate salt (**2**) or ester (**3**), is an attractive synthon both per se and as a model. This paper reports studies of several compounds related to **1**: the salt **2**, the diacid dichloride **4**, the diester **5**, the thiolsulfonate **6**, and various related compounds.



A reported method for oxidizing thiols to sulfinic acids, in which *m*-chlorobenzoic acid precipitates,[6] was unsatisfactory with 3-mercaptopropanoic acid (**7**) because **1** coprecipitated. However, when an alkaline solution of the products was adjusted to pH 3, the acid **1** (pK_a probably of ~2 for SO_2H)[7] remained in solution as its salt, while *m*-chlorobenzoic acid could be extracted (pK_a = 3.8,[8] sparingly soluble). The spectra of **2** obtained by evaporating the aqueous phase met expectation and showed a negligible amount of *m*-chlorobenzoic acid. Titration for sulfinic acid content by the method of Marvel and Johnson, by using nitrous acid,[9] indicated a content in the salt **2** of ~94% of sulfinate (with allowance for NaCl, which could not readily be separated and usually would be inconsequential); this titration is selective for sulfinic acids in the presence of sulfonic or carboxylic acids and related materials.[9b] The identity of the **2** was confirmed by conversion to a bis(benzylthiuronium) salt. Efforts to condense the carboxy salt **2** with bis(2-hydroxyethyl) disulfide have been unpromising so far because of solubility problems,[2] however, and we therefore turned to a study of the diacid dichloride **4**.

Douglass and Farah prepared **4** by chlorinating the mercapto acid **7**,[10] and others also have encountered no

(1) For paper 13, see Eswarakrishnan, V.; Field, L. *J. Org. Chem.* **1981**, *46*, 4182–4187.
(2) Abstracted from part of the M.S. Thesis of J. Mark Hoch, Vanderbilt University, Nashville, TN, Dec 1982, which can be consulted for further details.
(3) For leading citations, see ref 1, 4, and 5.
(4) Klayman, D. L.; Copeland, E. S. In "Drug Design"; Ariëns, E. J., Ed.; Academic Press: New York, 1975; Vol. 6, pp 81–142.
(5) Sweeney, T. R. "A Survey of Compounds from the Antiradiation Drug Development Program of the U.S. Army Medical Research and Development Command"; Walter Reed Army Institute of Research: Washington, DC, 1979; see especially pp 5, 672, 688, 689, 769, and 770.
(6) Filby, W. G.; Günther, K.; Penzhorn, R. D. *J. Org. Chem.* **1973**, *38*, 4070–4071.
(7) Cf. Oae, S.; Kunieda, N. In "Organic Chemistry of Sulfur"; Oae, S., Ed.; Plenum Press: New York, 1977; p 612.
(8) Davis, M. M. "Acid–Base Behavior in Aprotic Organic Solvents"; U.S. Government Printing Office: Washington, DC, 1968; p 33.
(9) (a) Marvel, C. S.; Johnson, R. S. *J. Org. Chem.* **1948**, *13*, 822–829. (b) Cf. also Kice, J. L.; Bowers, K. W. *J. Am. Chem. Soc.* **1962**, *84*, 605–610.

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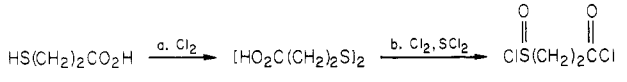
problem in such chlorinations of the thiol 7 or its disulfide(8).[11,12] To our surprise, however, we could effect oxidation of 7 only to the stage of the disulfide 8 (eq 1a);



7 8 4 (1)

8 precipitated and underwent no significant change. Since it seemed likely that trace impurities had catalyzed the earlier successful chlorinations, we tried iodine as a possible Lewis-type catalyst. The course of the reaction was altered, but (although 4 evidently was produced) the only product actually evidenced by derivatization was the diacid dichloride corresponding to 8. On the other hand, addition of 5 mol % of sulfur dichloride resulted in a smooth chlorination that led to 4 (eq 1b). In view of a previous misinterpretation of results in chlorination of 8,[11] later corrected,[12] we characterized the 4 extensively by spectra, by titration with use of both nitrous acid[9] and aqueous potassium permanganate,[13] and by preparation of three known derivatives.

Attempts to obtain selective reaction of the acyl chloride function of 4 were unsuccessful. Reaction with 1 mol of methanol led to about a 60:40 reaction of the COCl and SOCl groups, as estimated by nitrous acid titration (partial reaction of the SO_2CH_3 function in the titration precluded a clear distinction). Isolation of some of the diester 5 and IR spectra of products confirmed the lack of much selectivity.

Formation of the diester 5 could be achieved by reaction of the diacid dichloride 4 with excess methanol. The diester could not be obtained quite analytically pure because it decomposes fairly readily during distillation or chromatography (at least on silica gel or magnesium silicate). However, the identity and near purity were confirmed by elemental analysis, spectra (IR, ^1H, and ^{13}C NMR), nitrous acid titration, and saponification equivalent. This reaction provided a model for the reaction of 4 with bis(2-hydroxyethyl) disulfide to give what appeared to be a substantial amount of macrolide that will be tested for antiradiation properties but is insufficiently well-defined to warrant report in detail here.[2]

In the course of the work, the thiolsulfonate 6 was produced. It has interesting possibilities as a sulfinic acid counterpart in convergent syntheses of potential antiradiation drugs, but the method of the Kaspareks[12] (with use of SCl_2), or H_2O_2–AcOH oxidation,[14] may afford better preparative results than that described in the Experimental Section. Efforts to synthesize the cyclic anhydride of 1 by a variety of approaches were unavailing,[2] which came as no surprise in view of comment about the "inherent instability of carboxylic–sulfinic acid anhydrides".[15]

Experimental Section

Melting points were determined with a Thomas-Hoover stirred-liquid apparatus and are corrected. ^1H NMR spectra were obtained by using a JEOL Model JNM-MH-100 spectrometer with Me_4Si or (in D_2O) $Me_3Si(CH_2)_3SO_3Na$ as internal standards, and ^{13}C spectra were obtained by using a JEOL FX90Q spectrometer operating at 22.64 MHz with Me_4Si as an internal reference; data are reported in ppm (δ). IR spectra were obtained with a Perkin-Elmer Model 727 spectrometer and KBr pellets or neat liquids. Elemental analyses were done by Galbraith Laboratories. Moist extracts were dried with Na_2SO_4 or $MgSO_4$, and solvents then were removed with a rotary-flask evaporator under reduced pressure. TLC was performed on Eastman Chromagram silica gel plates (catalog no. 13181), with visualization by I_2 vapor or UV, and preparative TLC was done on 1000-μM Whatman PLK5F silica gel plates. Sodium nitrite used in nitrous acid titrations was standardized with aqueous $KMnO_4$ according to Scott.[16] Titration for sulfinate content was carried out as described by Marvel and Johnson;[9] since p-$CH_3PhSO_2Na{\cdot}2H_2O$ gave a titer only of 85%, values reported have been corrected by 100/85.

Monosodium Salt of 3-Sulfinopropanoic Acid (2). The procedure was based on one reported.[8] At intervals of 0.5 h during 10 h, 10 mL of a well-slurried suspension of 17.26 g (101 mmol) of m-chloroperoxybenzoic acid in 200 mL of CH_2Cl_2, kept meanwhile at −30 °C, was added to a vigorously stirred solution of 5.31 g (50.0 mmol) of 3-mercaptopropanoic acid (7) in 10 mL of CH_2Cl_2 at −30 °C. The mixture was kept at −20 °C for 20 h more, and 100 mL of 2 N NaOH then was shaken with it; virtually no material was left in the CH_2Cl_2. Acidification to pH 3 with 3 N HCl gave m-chlorobenzoic acid, which was extracted into three 50-mL portions of EtOAc. Attempted freeze-drying led to melting, so H_2O was removed at ~3 torr with periodic adjustment of the pH to 3, using small amounts of dilute aqueous NaOH (to preclude disproportionation of the free sulfinic acid); yield of 2 as a gummy syrup, 13.87 g [after subtracting NaCl, 5.10 g of 2 (64%)]. Efforts to dissolve salt 2 in MeOH to separate it from 150 mmol of NaCl presumed present led to changes in the IR spectrum and to extensive loss of the reducing power for $KMnO_4$ (which might be precluded under an inert atmosphere, although facile oxidation seems characteristic of sodium alkanesulfinates):[13] IR (neat) 3600–2900, 1720, 1400, 1260, 1200, 1190, 1140, 1050, 980, 920, 800, 750 cm^{-1} (expected for RSO_2Na, "~1070 and perhaps ~1180 and/or ~1020 cm^{-1}");[17] ^1H NMR (D_2O) δ 3.38 (t, 2 H), 2.96 (t, 2 H); ^{13}C NMR (CD_3OD) δ 175.23 (CO_2H), 34.75, 34.43. Titration for sulfinic acid of 2 indicated a (corrected) content of ~94%,[9] if one takes the NaCl present into account.

The identity of salt 2 was confirmed by isolation of the bis(*S*-benzylthiuronium salt), $[(H_2NC{=}NH_2^+)SCH_2Ph]_2^-O_2S(CH_2)_2CO_2^-$: *S*-benzylthiuronium chloride (Fluka A.G., 0.526 g, 2.59 mmol) in a minimum of H_2O was added to 0.378 g (2.36 mmol if pure) of 2 dissolved in a minimum of warm water (to which 2 drops of 1 N HCl then had been added). A white precipitate formed immediately. The mixture was chilled at 0 °C, and the solid was removed and washed with ice water; yield, 0.292 g (48%, based on the thiuronium chloride), mp 154–157 °C. Recrystallization from MeOH and 3:1 EtOH–hexane gave the bis(*S*-benzylthiuronium) salt corresponding to 2: mp 166–167 °C; IR (KBr) 3200, 3100–2900, 1680 (CO_2^-), 1575, 1500, 1450, 1425, 1400, bands at 1040, 1000, and 970 some or all of which signify SO_2^-, 710, and 695 cm^{-1}.[17] IR spectra indicated no oxidation of the bis(thiuronium) salt during the recrystallizations.

Anal. Calcd for $C_{19}H_{26}N_4O_4S_3$: C, 48.49; H, 5.57; S, 20.44. Found: C, 48.32; H, 5.60; S, 20.32.

3-(Chlorosulfinyl)propanoyl Chloride (4). When the chlorination procedure of Douglass and Farah was followed exactly,[10] using 10.6 g of 3-mercaptopropanoic acid (7) in 50 mL of CH_2Cl_2 at −10 °C, a precipitate of 3,3′-dithiodipropanoic acid (8) appeared that clogged the gas-inlet tube, hampered stirring, and showed no indication of disappearance as Cl_2 was passed to a faint yellow color; filtration of 8 after 4 equiv of Cl_2 had been passed and the temperature allowed to rise to ~25 °C gave 16.3 g of 8, evidently still containing CH_2Cl_2; mp (recrystallized) 155–156 °C; lit.[18] mp 157–159 °C; IR congruent with that of authentic 8. Another attempt using rigorously dried glassware and reagents led to 12 g of 8; mp (recrystallized) 154–155 °C.

(10) Douglass, I. B.; Farah, B. S. *J. Org. Chem.* **1961**, *26*, 351–354.
(11) Chiang, Y. H.; Luloff, J. S.; Schipper, E. *J. Org. Chem.* **1969**, *34*, 2397–2401.
(12) Kasperek, J. G.; Kasperek, G. J. *J. Org. Chem.* **1978**, *43*, 3393–3394.
(13) Allen, P., Jr. *J. Org. Chem.* **1942**, *7*, 23–30.
(14) Dickinson, W. B. U.S. Patent 3 328 452, 1967; *Chem. Abstr.* **1967**, *67*, 99, 652.
(15) Kohn, H.; Charumilind, P.; Simonsen, S. H. *J. Am. Chem. Soc.* **1979**, *101*, 5431–5432.
(16) "Scott's Standard Methods of Chemical Analysis", 5th ed.; N. H. Furman, Ed.; Van Nostrand: New York, 1939; Vol. 1, pp 653–655.
(17) Field, L.; Eswarakrishnan, V. *J. Org. Chem.* **1981**, *46*, 2025–2029.
(18) "Catalog/Handbook of Fine Chemicals"; Aldrich Chemical Co.: Milwaukee WI, 1982–1983; p 519.

Repetition of the original chlorination with 0.25 g (1 mol %) of I_2 as catalyst still led to a copious precipitate of 8, but when the temperature was increased to ~15 °C, the precipitate dissolved to give a clear red solution. Oil obtained by evaporation did not give a satisfactory sulfinanilide, but use of *n*-butylamine gave the diamide of the disulfide (5% yield), i.e., $[S(CH_2)_2CONH\text{-}n\text{-}Bu]_2$, which had consistent IR and NMR spectra and a melting point of 125–128 °C (lit.[11] mp 130–131 °C); since the yield of oil would have amounted to 130% for 3,3'-dithiodipropanoyl chloride, considerable 4 probably was present.

For the successful preparation of 4, a solution of 10.6 g (100 mmol) of 3-mercaptopropanoic acid (7) in 50 mL of CH_2Cl_2 was chilled at −20 °C with protection from H_2O by $CaCl_2$, and 0.51 g (5 mmol, 5 mol %) of SCl_2 (Matheson Coleman and Bell) was added. Cl_2 (Matheson High Purity, 99.5% minimum) was passed through 3A molecular sieves and then below the surface of the solution at 1–2 bubbles/s for ~1 h with good stirring below −10 °C; a clear solution with a persistent yellow color resulted. Some precipitate formed immediately but rapidly dissolved. The temperature was allowed to rise to ~25 °C, and the mixture then was warmed for 15 min at ~35 °C to expel additional HCl. Removal of solvent left 18.3 g (105%) of 4 as an oil, reported to be undistillable;[10] titration with alkaline $KMnO_4$ by the colorimetric method of Allen gave 115% of the theoretical value (presumably owing to oxidation of impurities, such as the SCl_2);[13] addition of 0.5 g of 4 to 10 mL of H_2O, followed by titration with nitrous acid, gave a (corrected) content of 100% of RSO_2H:[9] IR (neat) 3000, 2950, 1800, 1410, 1380, 1340, 1220, 1180–1120, 1040, 960 cm^{-1} [lit.[10] IR 1800, 1152]; ^1H NMR ($CDCl_3$) δ 3.6 (m).

N-*n*-Butyl-3-[(*n*-butylamino)sulfinyl]propanamide was prepared as a derivative of 4 (21% yield): mp 80–82.5 °C (lit.[11] mp 83–84 °C); ^1H NMR ($CDCl_3$) δ 6.5 (s, 1 H), 4.6 (t, 1 H), 3.1 (m, 6 H), 2.6 (q, 2 H), 1.4 (m, 8 H), 0.9 (t, 6 H); IR (KBr) 3300, 3200, 2950–2850, 1640, 1540, 1460, 1410, 1070, 1020–990 cm^{-1}. 4 also was converted to 3-(benzylsulfonyl)propanoic acid as a derivative by placing 2.0 g (11.4 mmol) in 25 mL of deoxygenated (Ar flushed) 1 N NaOH and adding the solution to 1.30 g (10.3 mmol) of benzyl chloride in 30 mL of EtOH. The solution was heated under reflux under N_2 for 6 h, concentrated to ~15 mL, and acidified to pH 1. Extraction, washing, drying, and removal of solvent gave the crude sulfone. Recrystallization from MeOH gave 0.3 g (13%) of the sulfone with mp 150–155 °C, and further recrystallization ($BrCH_2CH_2Br$) gave 0.14 g (6%): mp 176–178.5 °C (lit.[10] mp 177–178 °C); ^1H NMR ($CDCl_3$) δ 7.45 (s, 5 H), 4.4 (s, 2 H), 3.3 (t, 2 H), 2.7 (t, 2 H); IR (KBr) 3250–2950, 1700 (br), 1480, 1430, 1400, 1330, 1300, 1160, 1140, 1115, 780, 685 cm^{-1}.

Anal. Calcd for $C_{10}H_{12}O_4S$: C, 52.62; H, 5.30; S, 14.05. Found: C, 52.52; H, 5.49; S, 13.94.

Diacid dichloride 4 could be converted to the pure corresponding thiolsulfonate 6 only in low yield. A solution of 100 g (0.57 mol) of 4 in THF was cooled to 0 °C, and H_2O (20.5 mL, 1.14 mol) was added. THF was removed, 250 mL of glacial AcOH was added, and the solution was heated at 70 °C for 15 min, as recommended for *p*-toluenesulfinic acid.[9b] Slow cooling to −10 °C gave 6, which after recrystallization from EtOAc gave a pasty solid that amounted to 21.0 g (46%, based on eq 1 of ref 9b); two recrystallizations from EtOAc–CCl_4 gave 5.0 g (11%): mp 135–136.5 °C dec (lit.[12] mp 149–150 °C dec). A third recrystallization raised the melting point to 142–143 °C dec, but even brief drying at 75 °C (2 torr) caused decomposition to begin; after a fourth recrystallization and drying at ~25 °C (2 torr), 2.2 g (5% overall yield) remained, mp 139–140 °C dec. The IR spectrum agreed with reported values.[12]

Methyl 3-(Methoxysulfinyl)propanoate (5). A solution of MeOH (60 mL, 1.5 mol) in 50 mL of CH_2Cl_2 was added with stirring during 1 h to one of the dichloride 4 (100 g, 0.57 mol) in 15 mL of CH_2Cl_2 at −35 °C. The resulting solution was stirred and allowed to warm to ~25 °C during ~1.5 h. Removal of solvent then left 93.1 g (98%) of 5 as a light-yellow oil (n^{23}_D 1.4667), 57 g of which was dissolved as two portions in Et_2O and treated with 0.5 g of recrystallized *p*-toluidine each, as recommended,[19] to remove any sulfonyl chloride. Precipitate was removed by filtration, and each solution was washed once with 50 mL of ice water and dried ($MgSO_4$). Removal of Et_2O left a total of 27.4 g (47% yield; n^{23}_D 1.4641), 20.0 g of which was distilled in an oil bath preheated to 120 °C from ~0.1 g of K_2CO_3 in 5-g portions, using a 4-cm short-path head; combination of fractions gave 3.4 g (8%) of diester 5 with bp 92–94 °C (0.6–1.5 torr) and n^{23}_D 1.4575–1.4606. A sample (n^{23}_D 1.4605) of the combined fractions was analyzed: IR (neat) 3000, 2950, 1740, 1440, 1370, 1240, 1180, 1120, 1000, 960 cm^{-1} (we have reported ranges of 1153–1099 and 990–889 cm^{-1} for esters of arenesulfinates,[20] and these ranges seem to hold for three esters of alkanesulfinates as well);[1] ^1H NMR ($CDCl_3$) δ 3.8 (s, 3 H), 3.75 (s, 3 H), 3.00 (m, 2 H), 2.8 (m, 2 H). Treatment of this 5 with aqueous NaOH and titration with nitrous acid gave a (corrected) percent content of sulfinic acid of 99%.[9]

Anal. Calcd for $C_5H_{10}O_4S$: C, 36.14; H, 6.06; S, 19.29. Found: C, 34.45; H, 5.64; S, 18.49.

An earlier product (98% yield, n^{23}_D 1.4758) was reduced by 56% after one distillation (n^{24}_D 1.4545–1.4574; saponification equiv 158, calcd 166) and by an additional 90% after a second distillation (n^{24}_D 1.4580), thus testifying to thermal instability of the 5; no K_2CO_3 was used in these distillations. The product of the second distillation had no better analysis than that reported. A third product with essentially identical spectra (n^{23}_D 1.4574) had the following ^{13}C NMR spectrum ($CDCl_3$): 171.26 ($\mathbf{C}O_2Me$), 54.14 (OCH_3), 51.65 (OCH_3), 51.00 ($\mathbf{C}H_2SO_2Me$), 25.26 ($\mathbf{C}H_2CO_2Me$).

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Registry No. 2, 85939-96-4; 2·bis(*S*-benzylthiuronium), 85939-97-5; 4, 77711-00-3; 5, 85939-98-6; 6, 18365-80-5; 7, 107-96-0; 8, 1119-62-6.

(19) Douglass, I. B. *J. Org. Chem.* **1965**, *30*, 633–635.

(20) Field, L.; Hoelzel, C. B.; Locke, J. M. *J. Am. Chem. Soc.* **1962**, *84*, 847–850.

Use of 4-Biphenylmethanol, 4-Biphenylacetic Acid, and 4-Biphenylcarboxylic Acid/Triphenylmethane as Indicators in the Titration of Lithium Alkyls. Study of the Dianion of 4-Biphenylmethanol†

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The fast development of carbanion chemistry in the past years is due in great measure to the commercial availability of alkyllithiums such as the butyllithiums and methyllithium.[1] These reagents deteriorate with time, through their reaction with moisture and oxygen, and it is, therefore, very important to know the actual concentration of alkyllithium in anticipation of its use in synthesis.

Recently, Kofron and Baclawski[2] reported a convenient method for the determination of alkyllithium concentration based on the use of diphenylacetic acid (1) as reagent–indicator. (Scheme I). This method eliminates the

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