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 (CO_2Me), 54.14 (OCH_3), 51.65 (OCH_3), 51.00 (CH_2SO_2Me), 25.26 (CH_2CO_2Me).

Acknowledgment. This investigation was supported by the U.S. Army Medical Research and Development Command, Department of the Army, under Research Contract No. DAMD17-79-C-9039; this paper has been designated as Contribution No. 1664 to the Army Drug Development Program. We thank Prof. N. E. Heimer of the University of Mississippi for helpful suggestions.

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.

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(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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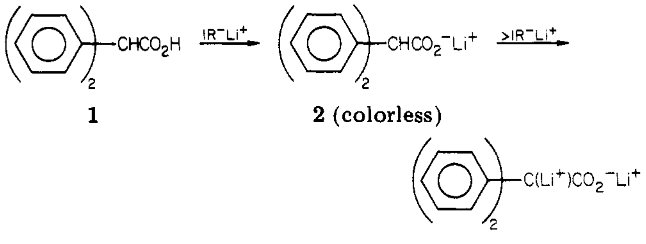
[†] Presented in part at the 181st National Meeting of the American Chemical Society, Atlanta, GA, March 1981: Juaristi, E.; Cruz, J. S.; Martínez-Richa, A. "Abstracts of Papers", 181st National Meeting of the American Chemical Society, Atlanta, GA, March 1981; American Chemical Society: Washington, DC, 1981; ORGN 236.

0022-3263/83/1948-2603\$01.50/0

Scheme I

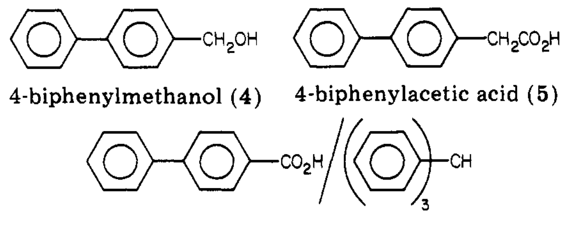


1

2 (colorless)

3 (yellow)

Scheme II



4-biphenylmethanol (4) 4-biphenylacetic acid (5)

4-biphenylcarboxylic acid (6)/triphenylmethane (7)

Table I. Titration of Alkyllithium Solutions

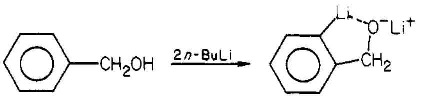
R^-Li^+	method	concn,[a] M
n-BuLi	Gilman[b]	1.43 ± 0.01
	K & B[c]	1.43 ± 0.03
	4	1.42 ± 0.02
	5	1.43 ± 0.01
	6/7	1.44 ± 0.01
sec-BuLi, lot no. 1	Gilman[b]	0.77 ± 0.15
	K & B[c]	0.83 ± 0.05
	4	0.82 ± 0.02
sec-BuLi, lot no. 2	K & B[c]	1.18 ± 0.01
	5	1.18 ± 0.01
	6/7	1.19 ± 0.01
t-BuLi, lot no. 1	Gilman[b]	2.08 ± 0.02
	4	2.06 ± 0.04
t-BuLi, lot no. 2	Gilman[b]	2.17 ± 0.01
	K & B[c]	2.17 ± 0.01
	5	2.16 ± 0.01
	6/7	2.15 ± 0.02
MeLi	Gilman[b]	0.45 ± 0.03
	4	0.44 ± 0.02

[a] At least three measurements were made in each case. [b] See ref 3. [c] Kofron and Baclawski in ref 2.

need for a double titration[3] because only the strong base is able to abstract the benzylic proton, and, therefore, the colored dianion **3** forms after the consumption of 1 equiv of the strong base, R^-Li^+.[4]

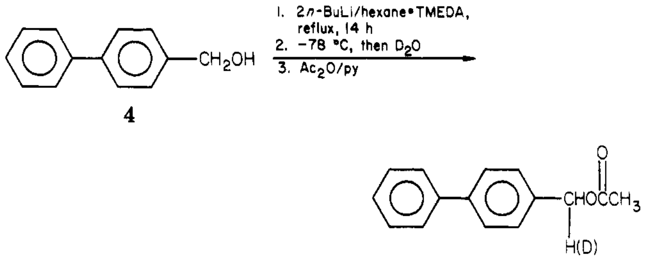
We have now examined the title compounds, **4**, **5**, and **6/7**, (Scheme II) as potential alternatives to **1** in the estimation of organolithiums. It was considered that because of their highly delocalized nature, the resulting anions would provide easy-to-observe titration end points. In addition, some comment is made on the nature of the interesting dianion derivative of **4**.

Scheme III



11 12

Scheme IV



4

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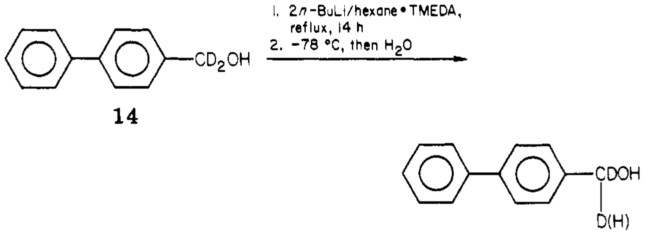
Scheme V



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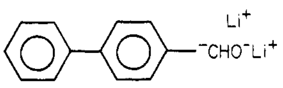
Results and Discussion

Table I shows the results obtained in the estimation of several samples of *n*-butyllithium, *sec*-butyllithium, *tert*-butyllithium, and methyllithium by using 4-biphenylmethanol (**4**), 4-biphenylacetic acid (**5**), and a 2:1 mixture of 4-biphenylcarboxylic acid (**6**) and triphenylmethane (**7**).

It is obvious from these results that each of the reagents (**4**, **5**, and **6/7**) offers an alternative method for the quantitation of alkyllithium concentration. Nevertheless, indicator **4** is the reagent of choice since the color change at the titration end point is sharper (colorless to orange-red) than with **1**[2] or **5** (colorless to yellow) or with the pair **6/7** (unexpectedly, the originally colorless solution becomes yellow or green before it turns red at the end point).[5]

Structure of the Dianion of 4-Biphenylmethanol (4). While there is no doubt about the benzylic nature of the anions responsible for the color changes at the titration end points when **5** and **7** are used as indicators,[6] the dianion of **4** could be the benzylic species **8** or the ortho-metalated derivative **9**.[7] Actually, carbinol **4** was studied



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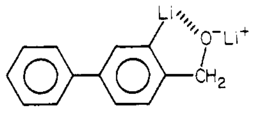

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(1) Stowell, J. C. "Carbanions in Organic Synthesis"; Wiley: New York, 1979.

(2) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879–1880.

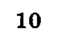
(3) Ziegler, K.; Crossmann, F.; Kleiner, H.; Schafer, O. *Justus Liebigs Ann. Chem.* **1929**, *473*, 31. Gilman, H.; Haubein, A. H. *J. Am. Chem. Soc.* **1944**, *66*, 1515–1516.

(4) Other analytical procedures for the assay of organolithium reagents have been reported: Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165. Lipton, M. F.; Sorensen, C. M.; Sadler, A. C.; Shapiro, R. H. *Ibid.* **1980**, *186*, 155–158. Winkle, M. R.; Lansinger, J. M.; Ronald, R. C. *J. Chem. Soc., Chem. Commun.* **1980**, 87–88. Bergbreiter, D. E.; Pendergrass, E. *J. Org. Chem.* **1981**, *46*, 219–220.

(5) Similar results are reported when a mixture of benzoic acid and triphenylmethane is used: Eppley, R. L.; Dixon, J. A. *J. Organomet. Chem.* **1967**, *8*, 176–178.

(6) Ivanov, D.; Vassilev, G.; Panayotov, I. *Synthesis* **1975**, 83–98.

(7) A better representation for the benzylic dianion could be **10**. Apparently, the electrostatic stabilization in this quadrupolar structure more than compensates for entropic and other effects.[8]



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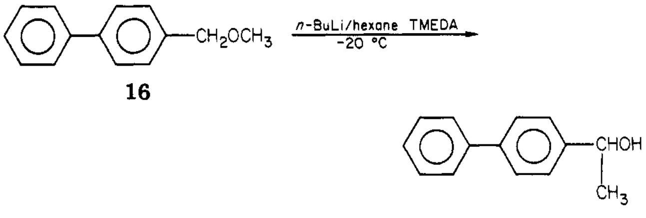
Scheme VI



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17

as a potential substitute for 1 on the assumption that the strong base would abstract a benzylic proton to afford a delocalized, highly colored dianion. Indeed, the orange-red color obtained upon treatment of 4 with alkyllithium appears as an argument against the localized species 9. However, Seebach and Meyer observed ortho metalation of benzyl alcohol 11 upon treatment with 2 equiv of n-BuLi[9,10] (Scheme III). On the other hand, the p-phenyl substituent in 4 should increase the acidity of the methylenic protons by at least 2 or 3 orders of magnitude.[11] The following experimental evidence supports structure 8 for the dianion of 4:[7]

(1) When carbinol 4 was treated with 2 equiv of n-BuLi, under the conditions reported by Seebach for the preparation of 12,[9] and quenched at −78 °C with D_2O, the recovered material showed up to 50% deuterium incorporation at the benzylic position, as measured by integration of the proton NMR spectrum of the acetate 13 (Scheme IV) and confirmed by mass spectrometry.

(2) When the deuteriated derivative 14 (prepared by $LiAlD_4$ reduction of 6) was metalated under the same conditions used above and quenched with H_2O, ca. 20% of hydrogen incorporation was observed (Scheme V).

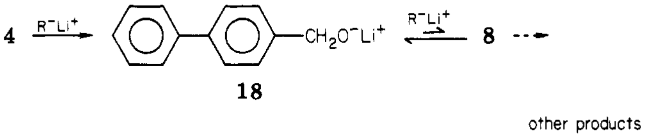
(3) The visible spectrum of the orange-red solution obtained when 4 was treated with 2 equiv of n-BuLi (in THF, at room temperature) shows a bell-shaped absorption with λ_{max} = 483 nm. By comparison, p-phenylbenzylcesium's λ_{max} = 474 nm in cyclohexylamine.[12]

(4) When the methyl ether derivative 16 was treated with 1 equiv of n-BuLi, an orange-red solution is again observed, and the rearranged (Wittig) product 17 was produced, in a clean reaction (Scheme VI). Despite some controversy as to the mechanism of the Wittig rearrangement, the initial involvement of the benzylic carbanion appears inescapable.[13]

Stability of Dianion 8. Several observations indicate that although the alkoxide 18 may be fairly acidic in a kinetic sense (the instantaneous deprotonation to afford 8 allows its use as indicator in the evaluation of alkyllithiums, Table I), its *thermodynamic* acidity is low (Scheme VII).

(1) The ca. 50% D incorporation at the benzylic carbon of 4 described above (Scheme IV) was the *highest* observed, despite several attempts to increase deuterium incorporation. Similarly, addition of chlorotrimethylsilane, methyl iodide, n-propyl bromide, or benzaldehyde to the orange-red solution of 4, previously treated with 2 equiv of n-BuLi, did not provide the expected alkylation products but led instead to complex reaction mixtures.

Scheme VII



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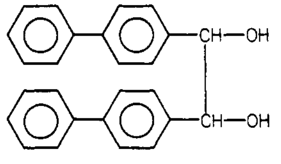
(2) The extinction coefficient measured for 8 is only 510 ± 10, much smaller that the observed value for p-phenylbenzylcesium; ϵ = 39 200.[11]

(3) Diol 19 was isolated in up to 20% yield from the reaction media when 4 was treated with 2 equiv of n-BuLi. We consider it likely that 19 arises from radical 20, produced by [single-electron transfer (SET)] oxidation of 8.[14,15]



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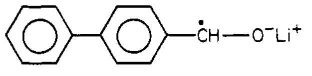

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Experimental Section[16]

Commercial samples[18] of 4-biphenylmethanol (4), 4-biphenylacetic acid (5), 4-biphenylcarboxylic acid (6), and triphenylmethane (7) were recrystallized [4, hexane–chloroform (8:2); 5, methanol; 6, benzene; 7, hexanes] and dried under vacuum before use.

(a) With 4-Biphenylmethanol (4). In a dry, 25-mL Erlenmeyer flask was placed 200–300 mg of 4-biphenylmethanol (4) and a dry magnetic bar. The flask was capped with a rubber septum and flushed with nitrogen before the introduction of ca. 10 mL of dry THF. From a graduated syringe was then added dropwise the alkyllithium solution, until the appearance of an orange-red color. The amount consumed contains 1 equiv of alkyllithium, relative to 4.

(b) With 4-Biphenylacetic Acid (5). The same procedure was followed, but the equivalence point is apparent by a colorless to bright yellow change.

(c) With 4-Biphenylcarboxylic Acid/Triphenylmethane (6/7). Approximately 200 mg of the acid and ca. 100 mg of the indicator were used, following the same procedure described in a. The appearance of a deep-red color indicates the consumption of 1 equiv of alkyllithium, relative to the amount of carboxylic acid employed.

Dianion of 4-Biphenylmethanol. The procedure described by Seebach and Meyer[9] for the preparation of the dianion of benzyl alcohol (11 → 12) was followed.

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(8) Streitwieser, A., Jr. 183rd National Meeting of the American Chemical Society, Las Vegas, NV, March 1982; American Chemical Society: Washington, D.C., 1982; ORGN 4. Streitwieser, A., Jr.; Swanson, J. T. *J. Am. Chem. Soc.* **1983**, *105*, 2502–2503. Schleyer, P. v. R. *Pure Appl. Chem.* **1983**, *55*, 355–362.

(9) Meyer, N.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 521–522; *Chem. Ber.* **1980**, *113*, 1304–1319.

(10) We thank Prof. V. Snieckus, University of Waterloo, for bringing this work to our attention.

(11) Streitwieser, A., Jr.; Juaristi, E.; Nebenzahl, L. L. In "Comprehensive Carbanion Chemistry"; Buncel, E., Durst, T., Eds.; Elsevier: Amsterdam 1980; p 323.

(12) Hafelinger, G.; Streitwieser, A., Jr. *Chem. Ber.* **1968**, *101*, 672–680.

(13) See, for example: Yeh, M. K. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1652–1653.

(14) A related example of dimer formation from a benzylic carbanion via SET has been recently reported: d'Orchymont, H.; Goeldner, M. P.; Biellmann, J. F. *Tetrahedron Lett.* **1982**, *23*, 1727–1730.

(15) The most likely e⁻ acceptor is alkoxide 18, whose reduction potential should be fairly similar to that of biphenyl itself.

(16) Melting points, determined with a Mel-Temp or an Electrothermal apparatus, are uncorrected. Infrared (IR) spectra were recorded with a Pye Unicam SP 1000 or a Nicolet MX-1-FT spectrometer calibrated against the 1601-cm^{-1} band of styrene. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Varian EM-360 or EM-390 spectrometer. Chemical shifts are expressed in δ units relative to 1% tetramethylsilane as an internal standard; coupling constants (J values) are given in hertz. Mass data were obtained on a Hewlett-Packard 5985-A spectrometer. Visible spectra were recorded on a Cary 17D spectrometer. Flasks, stirring bars, and hypodermic needles used for the generation and reactions of alkyllithiums were dried for ca. 12 h at 120 °C and allowed to cool in a desiccator over anhydrous calcium sulfate. Anhydrous solvents were obtained by distillation from benzophenone ketyl (ethers), or calcium hydride (amines or hydrocarbons).[17]

(17) Brown, H. C. "Organic Synthesis via Boranes"; Wiley: New York, 1975; p 256.

(18) Aldrich Chemical Co.

Monoanion of the Methyl Ether of 4-Biphenylmethanol (Wittig Rearrangement). The general procedure of Geissman[19] was followed. A dry, 25-mL flask containing 1 g (5 mmol) of ether **16** was capped with a rubber septum and flushed with nitrogen before the addition, via canula, of 10 mL of dry hexane. One equivalent (0.58 g) of TMEDA was then syringed, and the mixture was cooled to -20 °C and then treated with 1 equiv (3.36 mL of a 1.5 M hexane solution) of *n*-butyllithium. The orange-red solution was stirred at room temperature for 6 h and then quenched with 2 N HCl. The aqueous layer was extracted with ether and worked up the usual way. Column chromatography [silica gel, hexane-benzene (50:50) as the eluant] afforded ca. 500 mg of recovered starting material and ca. 400 mg of carbinol **17**: mp 97-98 °C (lit.[20] mp 96.4-97.3 °C); ^{1}H NMR δ 1.50 (d, J = 6, 3, CH_3), 2.10 (s, 1, OH), 4.84 (q, J = 6, 1, CH), 7.2-7.6 (m, 9, aromatic).

4-Biphenylmethanol-α,α-d_2 (14). In a slight modification of the procedure of Brown et al.,[21] 200 mg (ca. 1 mmol) of **6** in 25 mL of dry ethyl ether, at 0 °C, was treated with 76 mg (2 mmol) of lithium aluminum deuteride. The ice-water bath was removed and the reaction mixture heated to reflux for 1 h. Product **14** was then extracted and purified. ^{1}H NMR and MS spectra indicated ca. 100% deuterium present at the benzylic carbon.

1,2-Di-4-biphenyl-1,2-ethanediol (19). 4-Biphenylmethanol (**4**, 278 mg, 1.5 mmol) was dissolved in 25 mL of dry THF and 348 mg (3 mmol) of freshly distilled tetramethylethylenediamine (TMEDA) and treated with 2.2 equiv (2.2 mL of a 1.5 M solution) of *n*-butyllithium. The resulting orange-red solution was heated to reflux for 6 h and then cooled to room temperature (the reaction mixture had turned purple after 4-5 h of reflux). Twenty five milliliters of 1 N HCl was added, and the organic material extracted with ethyl acetate. The usual workup procedure was followed by preparative TLC, with ethyl acetate-chloroform (50:50) as the eluant. Diol **19** (50 mg, 20% yield) was isolated from the lower band, R_f 0.24, and was crystallized from chloroform: mp 217-218 °C; IR (KBr) 3100-3600 (OH) cm^{-1}; ^{1}H NMR δ 3.85 (s, 2, OH), 4.77 (s, 2, CH), 7.2-7.7 (m, 18, aromatic); MS, m/e 348 (M^+ - 18), 184 (M^+ - 182), 183 (M^+ - 183), 181 (M^+ - 185).

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Oxidation of 2-Methyl-4,5,6,7-tetrahydrobenzofuran with *m*-Chloroperbenzoic Acid

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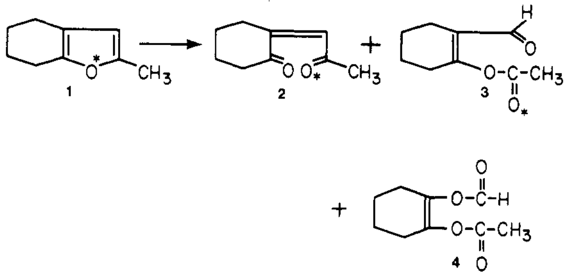
The peracid oxidation of 3-methyl-4,5,6,7-tetrahydrobenzofuran and perhydrodibenzofuran has been reported earlier.[1] In these systems, a facile reaction occurred at 0 °C to form an ϵ-lactone in nearly quantitative yield. In this article, we report on the *m*-chloroperbenzoic acid (mCPBA) oxidation of 2-methyl-4,5,6,7-tetrahydrobenzofuran (**1**), which has provided yet another interesting and unique set of products. Further, use of ^{18}O-labeled **1** has provided evidence for its oxidative pathway.

Results and Discussion

Synthesis and Reaction of Compound 1. Compound **1** was readily synthesized in five steps (48% yield) by using standard reactions that were slightly modified as noted in the Experimental Section. It reacted more vigorously than the 3-methyl analogue at 0 °C to form products **2**-**4** as is shown in eq 1. A higher yield of **2** (70%) was obtained when 1 equiv of mCPBA was added slowly to a dilute solution of **1** in CH_2Cl_2 at 25 °C. Furthermore, compounds **3** and **4** were also obtained from **1** in higher yields under the proper conditions (see Experimental Section).



(1)

Compound **2** was characterized as an enedione by spectral data. Its infrared spectrum indicated carbonyl functionality with a broad absorption at 1690 cm^{-1}, which was further corroborated by ^{13}C NMR spectroscopy with resonances at 204.9 and 200.1 ppm. From the gated decoupled spectra, both of these resonances were shown to be singlets. Specific proton decoupling experiments showed that the ^{13}C resonance at 200.1 ppm was coupled to the methyl hydrogens by 4 Hz and to the olefinic proton by 6 Hz. Another resonance at 150.3 ppm, which was also shown to be a singlet by gated decoupling experiments, was assigned to the olefinic carbon in the six-membered ring. Finally, the resonance at 129.4 ppm, which is a doublet in the gated decoupled spectrum, was assigned to the olefinic carbon bonded to a single hydrogen and the acetyl function. There were five aliphatic carbon resonances at 43.2 (t), 36.3 (t), 29.7 (q), 26.2 (t), and 26.2 (t) ppm, which justifies the methyl group and the four carbons of the cyclohexyl group.

The structure of compound **3** was also justified by spectral data. The aldehydic carbon (1680 cm^{-1}) resonated at 189.1 ppm in the ^{13}C NMR spectrum and was coupled to a single proton by 177 Hz, which is typical. The ester carbonyl carbon and the two olefinic carbons, which were all singlets, had resonances at 168.5, 164.1, and 126.6 ppm, respectively. Further oxidation of compound **3** gave formate **4**, which exhibited ^{13}C NMR shifts of 168.5 (s), 158.5 (d, $^1J_{C-H}$ = 231 Hz), 137.2 (s), and 136.1 (s) ppm. These are consistent with the acetyl ester carbonyl, the formate carbonyl, and the olefinic carbons of **4**. The formation of **4** from compound **3** is extremely facile.

In order to determine the reaction paths for the formation of enedione **2** and ester **3**, we decided to label **1** with ^{18}O. This was readily accomplished by an $H_2{}^{18}O$ exchange reaction with a ketonic intermediate in the synthesis of **1**. The label was located and quantized by NMR and mass spectral methods.[2]

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