The alumina-B was prepared as described previously,[6] and graded (20–40 mesh) before being impregnated with chromia.[6]

II. Chemicals.—Naphthalene, biphenyl, and the terphenyls were provided by commercial sources, and were checked for purity before use.

1,1-Diphenylcyclohexane.—Following reported procedures[17,18] 4,4-diphenylcyclohexanone was prepared from benzoin in an over-all yield of 30%. The product was recrystallized from *n*-heptane and melted at 142–144° (lit.[17] mp 143–144°).

The 4,4-diphenylcyclohexanone (4.55 g, 0.019 mole) was heated under reflux with 5.6 ml of 85% hydrazine hydrate solution and 37 ml of triethylene glycol. After 20 min solid sodium hydroxide (3.7 g, 0.093 mole) was added. The reflux condenser was removed and the mixture was heated to 220° to allow the water to evaporate. The mixture was then kept at 180° for 3 hr, poured onto ice, and extracted with *n*-hexane (three 50-ml portions). The organic solution was washed with water until neutral and then dried over anhydrous magnesium sulfate. Removal of the solvent gave a crude product, which was purified by using a 20-ml alumina column with *n*-pentane as eluent. Recrystallization of the solid from 95% ethanol gave white, needlelike crystals of 1,1-diphenylcyclohexane (3.52 g, 0.016 mole, 82% yield), mp 45–46.5° (lit.[19] mp 47°).

1,2-Diphenylcyclohexane was prepared from a Grignard reaction (56% yield) of 2-phenylcyclohexanone and phenylmagnesium bromide, followed by dehydration (29% yield) over 85% phosphoric acid,[20] and subsequent hydrogenation over 5% palladium–carbon. During the dehydration, a substantial amount (47%) of rearranged products was also obtained, having mp 65–66° after hydrogenation, which was not reported by Parmerter.[20] The 1,2-diphenylcyclohexane, *cis*/*trans* = 3.3 ($n^{20}{}_{D}$ 1.5695), was isolated by preparative vpc using a 5 ft × $^3/_8$ in. 15% GE-SE-52 on 60–80 WAB column, and gave *o*-terphenyl when aromatized over chromia–alumina-B[6] at 377 ± 2°. Unreacted 1,2-diphenylcyclohexane was partly epimerized with *cis*/*trans* = 0.87.

1,3-Diphenylcyclohexane was prepared according to the procedure described by Abdun-Nur.[21] Interaction of phenylmagnesium bromide (0.08 mole) and 3-phenylcyclohex-2-enone[22] (0.027 mole) gave 1,3-diphenylcyclohexadiene-1,3 (63%), mp 89–100° (lit.[22] mp 98–99°). This diene was hydrogenated in acetic acid using 10% palladium–carbon under 40 psi. The product was distilled [bp 140–145° (0.2 mm)], and then a small sample was further purified by preparative vpc on a 2-m column, packed with 15% Carbowax 20 M on 40–60 Chromosorb P at 200° and a helium flow of 75 ml/min. The compound had a retention time of 14 min.

1,4-Diphenylcyclohexane was prepared by the same procedure as described for 1,2-diphenylcyclohexane, but using 4-phenylcyclohexanone in the Grignard reaction. Here, no rearranged product was observed. The final product was recrystallized from benzene (70%), mp 159–173°, and was a mixture of *cis* and *trans* isomers. It yielded *p*-terphenyl on aromatization over chromia–alumina-B.[6]

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[17] F. G. Bordwell and K. M. Wellman, *J. Org. Chem.*, **28**, 2544 (1963).

[18] H. E. Zimmerman and D. I. Schuster, *J. Am. Chem. Soc.*, **84**, 4527 (1962).

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[20] S. M. Parmerter, *J. Am. Chem. Soc.*, **71**, 1127 (1949).

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Phenylthiomethyllithium and Bis(phenylthio)methyllithium

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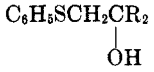
Efficient procedures are described for the generation of the functionally substituted organolithium derivatives cited in the title. Several characteristic reactions which indicate the synthetic applicability of these reagents are presented.

Gilman and Webb have reported that thioanisole is metalated by *n*-butyllithium at the methyl group to form phenylthiomethyllithium (I), in contrast to anisole, which is converted under the same conditions to *o*-methoxyphenyllithium.[1,2] This discovery, while of definite theoretical significance, has not led to practical application in synthesis because of the fact that the maximum yield of I which was obtained in many experiments was only *ca.* 35%.[1,2] After numerous unsuccessful attempts to develop a satisfactory method for the generation of this potentially useful reagent, an excellent procedure was finally found which depends on a catalysis of metalation with *n*-butyllithium, which is produced from its interaction with 1,4-diazabicyclo[2.2.2]octane (Dabco).[3–5] Reaction of equimolar amounts of *n*-butyllithium, Dabco, and thioanisole in tetrahydrofuran at 0° for 45 min produces I in *ca.* 97% yield, as determined by subsequent quenching with deuterium oxide and quantitative nmr analysis. Reaction of the lithio derivative I, so produced with an equivalent amount of benzophenone, affords the β-hydroxysulfide II, R = C_6H_5, in 93% yield, confirming the nmr analytical result. Further, addition of I to acetone produces the carbinol II, R = CH_3 (75%), and alkylation of I with isopropyl iodide leads to phenyl isobutyryl sulfide III in 55% yield.

$C_6H_5SCH_2Li$

I


$C_6H_5SCH_2C(OH)R_2$

II

$C_6H_5SCH_2CH(CH_3)_2$

III

It has also been found that I can be generated from thioanisole efficiently, using phenyllithium without the assistance of Dabco with tetrahydrofuran as solvent at 25°; this process is slow, however, and a 15-hr reaction period was required to give good conversion to I (shown by formation of II, R = C_6H_5, in 90% yield).

The benzophenone adduct II, R = C_6H_5, could be dehydrated to the vinyl sulfide IV, X = H, which underwent facile metalation using *n*-butyllithium in tetrahydrofuran at −30° without assistance from Dabco to form IV, X = Li.[6] Vinyl lithio derivatives such as IV, X = Li, are of interest as "masked"

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[1] H. Gilman and F. J. Webb, *J. Am. Chem. Soc.*, **62**, 987 (1940).

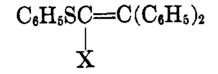
[2] H. Gilman and F. J. Webb, *ibid.*, **71**, 4062 (1949).

[3] W. A. Butte, *J. Org. Chem.*, **29**, 2928 (1964).

[4] C. G. Screttas and J. F. Eastham, *J. Am. Chem. Soc.*, **87**, 3276 (1965).

[5] "Dabco" has been used to precipitate a variety of organolithium compounds from solutions, in form of crystalline complexes containing 1 mole of diamine and 4 moles of the organometallic compound.[4]

[6] Organolithium derivatives of this type have been described previously; see, for instance, J. F. Arens, *et al.*, *Rec. Trav. Chim.*, **85**, 31, 560 (1966).



$C_6H_5S\underset{X}{C}=C(C_6H_5)_2$

IV

$(C_6H_5S)_2CHLi$

V

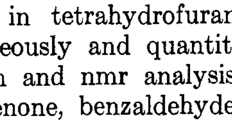
$(C_6H_5S)_2CHR$

VI

nucleophilic acylating agents, similar to the recently described anions derived from 1,3-dithianes[7] and the anions from mercaptals.[8,9]

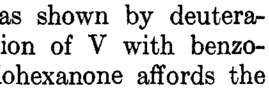
The lithio derivative V is expected to be more stable than I and hence more readily formed using organolithium reagents. This anticipation has been confirmed by the finding that the reaction of *n*-butyllithium with bis(phenylthio)methane (VI, R = H) at 0° in tetrahydrofuran generates V almost instantaneously and quantitatively, as shown by deuteration and nmr analysis. Reaction of V with benzophenone, benzaldehyde, or cyclohexanone affords the corresponding carbonyl adducts (VIIa–c) in 80, 87, and 90% yield, respectively. Alkylation of V with methyl iodide and *n*-butyl iodide proceeds readily to give the phenylmercaptals of acetaldehyde (VI, R = CH_3) and *n*-valeraldehyde (VI, R = n-C_4H_9) in yields of 70% and 96%, respectively. Attempts to metalate the mercaptals VI, R = alkyl, using *n*-butyllithium under the conditions which suffice for VI, R = H, were not successful. This result is hardly surprising in view of the tendency of alkyl groups to destabilize carbanions relative to hydrogen. At the other extreme are cases such as VI, R = C_6H_5, in which the substituent R stabilizes the carbanion and renders its formation facile under conditions which are not effective with unstabilized systems.[10,11]

Interestingly, metalation of VI, R = CH_3, *can* be achieved with *n*-butyllithium in the presence of Dabco, as shown by the isolation of the carbonyl adduct VIII with benzophenone. The yield is only fair with VI, R = CH_3 (74%), and drops off with the larger alkyl groups. It is clear from these results that these lithio derivatives, stabilized by two α-phenylthio substituents, are far less satisfactory as synthetic reagents than the recently reported 1,3-dithiane systems.[7]



$(C_6H_5S)_2CH\overset{R_1}{\underset{OH}{C}}-R_2$

VIIa, $R_1 = H$; $R_2 = C_6H_5$
b, $R_1 = R_2 = C_6H_5$
c, $R_1 = R_2 = (CH_2)_5$



$(C_6H_5S)_2\underset{CH_3}{C}-\underset{OH}{C}(C_6H_5)_2$

VIII

Experimental Section

Preparation of a Solution of Phenylthiomethyllithium (I).—To a solution of 3.369 g (30 mmoles) of Dabco and 3.726 g (30 mmoles) of thioanisole in 45 ml of tetrahydrofuran, stirred under nitrogen at 0°, was added 32 mmoles of *n*-butyllithium (Foote Mineral Co.) in *n*-hexane within 12 min. A complex[4,5] precipitated which dissolved upon warming to room temperature to give a pale yellow solution of the reagent. After 45 min an aliquot was hydrolyzed with deuterium oxide (>99%) to give 90% yield of thioanisole, the integrated nmr spectrum of which showed a ratio of aromatic to aliphatic protons of 5.00–2.015, indicating 98.5% deuteration. The peak due to the CH_2D group, centered at τ 7.76, was no longer a sharp singlet but a triplet with J = *ca.* 2 cps.

Phenyl (2,2-Diphenyl-2-hydroxy)ethyl Sulfide (II, R = C_6H_5).—A solution containing 25.7 mmoles of I in 30 ml of tetrahydrofuran at 0° was treated with a cold solution of 4.00 g (22.0 mmoles) of benzophenone in 10 ml of tetrahydrofuran. The cold bath was removed, and the colorless mixture was stirred at room temperature for 2 hr. The reaction mixture was poured into a fourfold volume of water and extracted. The combined organic layers from three extractions with chloroform were washed five times with water and dried over potassium carbonate. The colorless, crystalline material obtained after evaporation of the solvent was recrystallized from a 4:1 mixture of petroleum ether (bp 40–50°)–cyclohexane, furnishing 6.26 g (93.3%) of heavy, clustered needles, mp 73.5–75°; nmr spectrum (CCl_4): singlets at τ 6.59 and 6.29 and multiplet centered at 2.8, ratio 1:2:15; no carbonyl absorption in the infrared spectrum, absorption due to hydroxyl at 2.74 μ.

Anal. Calcd for $C_{20}H_{18}OS$: C, 78.41; H, 5.92; S, 10.45. Found: C, 78.49; H, 5.90; S, 10.41.

Phenyl (2,2-Diphenyl)vinyl Sulfide (IV, X = H).—A vigorously stirred solution of 1.645 g (5.37 mmoles) of the carbinol II, R = C_6H_5, and 73 mg of *p*-toluenesulfonic acid monohydrate in 85 ml of benzene was refluxed for 10 min using a water take-off head. The benzene solution was washed twice with 7% potassium hydroxide solution and twice with water, dried over potassium carbonate, and evaporated to give 1.506 g (97.1%) of IV, X = H; melting point of the analytical sample, recrystallized from pentane, 71.3–71.7°; nmr spectrum ($CDCl_3$): vinylic proton at τ 3.26, aromatic protons as two peaks with broad bases at 2.9 and 2.7, ratio 1:15; infrared spectrum ($CHCl_3$): 3.20, 5.10, 5.30, 5.52, 6.30, 6.75, 6.94, 7.49, 9.18, 9.30, 9.72, 10.60, 10.98, and intensive broad absorption between 12 and 15 μ.

Anal. Calcd for $C_{20}H_{16}S$: C, 83.31; H, 5.59; S, 11.10. Found: C, 83.18; H, 5.70; S, 11.26.

n-Butyllithium (3.2 mmoles) was added to a solution of 0.40 g (1.39 mmoles) of IV, X = H, in 10 ml of tetrahydrofuran at −30° with stirring under nitrogen. An orange solution of IV, X = Li, was obtained. Hydrolysis with deuterium oxide after 10 min and isolation gave rise to 0.35 g (87%) of colorless crystals, the nmr spectrum of which showed aromatic and vinylic protons in a ratio of 40:1, indicating 60% H–D exchange of the vinylic proton.

1-Phenylmercapto-2-hydroxy-2-methylpropane (II, R = CH_3).—To a solution of 64.4 mmoles of the lithium compound I and Dabco, stirred at 0°, was added 3.71 g (64.0 mmoles) of neat acetone (Fisher reagent). The cold bath was removed, and after 1.6 hr the colorless mixture was poured into three times its volume of water. The product was extracted with five 70-ml portions of ether. After washing the combined ether layers successively three times each with 10% aqueous acetic acid and 8% aqueous potassium hydroxide, and drying over potassium carbonate, the solvent was removed to furnish 10.891 g of a colorless liquid containing, according to quantitative nmr analysis, 25 mole % of thioanisole and 75 mole % of II, R = CH_3, the yield of which was 76.6%; nmr spectrum (CCl_4): singlets at τ 8.78 (CH_3), 7.02 (CH_2), and 6.80 (OH), ratio 6:2:1; infrared spectrum (neat): no carbonyl absorption, hydroxyl absorption at 2.79 μ.

Phenyl Isobutyryl Sulfide (III).—A solution containing 16.4 mmoles each of I and Dabco was stirred at 0° and combined with 2.74 g (16.5 mmoles) of 2-iodopropane. The mixture, which became very thick after 5 min, was stored at 25° under a nitrogen atmosphere for 3 days. Water was added to give a clear solution, which was extracted with three 30-ml portions of ether. The combined ethereal layers were washed five times with water and dried over sodium sulfate. It was shown by quantitative nmr analysis that the colorless oil, obtained after evaporation of the solvent, contained thioanisole and the desired compound as the only components, ratio 4:5, yield of phenyl isobutyryl sulfide 55%; nmr spectrum (CCl_4): doublets of CH_3 at τ 9.03 (J = 6.5 cps) and of CH_2 at 7.33 (J = 7.0 cps), multiplet of CH centered at 8.3 (alkylations of I should be carried out in the absence of Dabco, using phenyllithium to generate I).

Bis(phenylthio)methane (VI, R = H).[12]—The soduim salt of thiophenol was prepared by adding 16 g of sodium hydroxide to 43 g (0.39 mole) of thiophenol in 200 ml of absolute ethanol.

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[7] E. J. Corey and D. Seebach, *Angew. Chem.*, **77**, 1134, 1135 (1965); *Angew. Chem. Intern. Ed. Engl.*, **4**, 1075, 1077 (1965).

[8] J. F. Arens, M. Fröling, and A. Fröling, *Rec. Trav. Chim.*, **78**, 663 (1959).

[9] A. Fröling and J. F. Arens, *ibid.*, **81**, 1009 (1962).

[10] W. E. Truce and F. E. Roberts, *J. Org. Chem.*, **28**, 961 (1963).

[11] H. Normant and T. H. Cuvigny, *Bull. Soc. Chem. France*, 1881 (1965).

[12] E. Fromm, *Ann.*, **253**, 161 (1889).

The solution obtained was stirred under nitrogen, and 16.0 ml (53.2 g, 0.199 mole) of diiodomethane was added at such a rate that the temperature of the reaction mixture did not exceed 60°. After heating at reflux for 1 hr, most of the solvent was evaporated, the semisolid residue was dissolved in 300 ml of water and 300 ml of ether, and the aqueous layer was extracted twice with 50 ml of ether. After washing the combined ethereal layers twice with 7% potassium hydroxide solution and three times with water, drying over potassium carbonate, evaporating the solvent, and recrystallizing the solid so obtained from petroleum ether (bp 40–50°), 36.0 g (80%) of colorless needles was obtained, mp 39.5–40.5° (lit.[9] mp 39.5–40°); CH_2 protons in the nmr spectrum (CCl_4) at τ 5.84.

Preparation of a Solution of Bis(phenylthio)methyllithium (V).—To a solution of 2.324 g (10 mmoles) of VI, R = H, in 20 ml of tetrahydrofuran, stirred under nitrogen at 0°, was added 10 mmoles of *n*-butyllithium within 7 min to afford a clear, yellow solution of the lithium compound, which can be used for reactions after 10 min and which is stable at 0° for at least 12 hr. Hydrolysis of an aliquot containing the lithium compound from 500 mg of VI, R = H, gave 389 mg (77.8%) of colorless, crystalline VI, R = D; nmr spectrum (CCl_4): CH_2 peak at τ 5.82 as a triplet (J = *ca.* 2 cps), ratio of aromatic to aliphatic protons 1:10.0, indicating 100% deuteration.

α,α-Diphenyl-α-hydroxyacetaldehyde Diphenylthioacetal[9] (VIIb).—A solution of 1.80 g (9.9 mmoles) of benzophenone in 7 ml of tetrahydrofuran was added dropwise within 5 min to a solution of 10 mmoles of V stirred at 0°. After 30 min the ice bath was removed, and stirring was continued for 60 min at 25°. The reaction mixture was worked up as described for II, R = C_6H_5, using ether rather than chloroform as solvent. By evaporating the solvent, 4.01 g (97.2%) of an oil was obtained. It crystallized at 0° and was recrystallized from a 1:1 mixture of methanol–cyclohexane to give 3.28 g of V (80%) as fine needles; mp 103–104° (lit.[9] 102.5–103°); nmr spectrum (CCl_4): singlets at τ 6.37 and 5.09 and multiplet at 2.9, ratio 1:1:20; hydroxyl absorption in the infrared spectrum (CCl_4) at 2.78 μ.

Anal. Calcd for $C_{26}H_{22}OS_2$: C, 75.35; H, 5.35; S, 15.44. Found: C, 75.41; H, 5.31; S, 15.49.

α-Phenyl-α-hydroxyacetaldehyde Diphenylthioacetal (VIIa).—The reaction and isolation were conducted as described above for VIIb. Compound V (8.65 mmoles) and 0.88 g (8.30 mmoles) of neat benzaldehyde were allowed to react for 10 min at 0° and for 20 min at 25°; 2.53 g (87%) of an oily product was obtained; nmr spectrum (CCl_4): doublets at τ 6.54 (J = 3.3 cps) and 5.51 (J = 4.5 cps) and multiplets at 5.22 (with splittings of 3.3 and 4.5 cps) and 2.8, ratio 1:1:1:15; infrared spectrum (neat): no carbonyl absorption, hydroxyl absorption at 2.82 μ.

α-Hydroxycyclohexanecarboxaldehyde Diphenylthioacetal (VIIc).—Following the procedure given for VIIb, 6.56 g (92.4)% of crude, crystalline VIIc was obtained from 21.5 mmoles of the lithium compound V and 2.13 g (21.65 mmoles) of neat cyclohexanone after a reaction time of 30 min at 0° and 30 min at 25°. The product was obtained as massive prisms from cyclohexane–pentane (4:1), mp 47.5–48.5°; nmr spectrum (CCl_4): multiplets due to cyclohexane protons and aromatic protons, singlets at τ 7.59 and 5.71, ratio 1:1; hydroxyl absorption in the infrared (CCl_4) at 2.75 μ.

Anal. Calcd for $C_{19}H_{22}OS_2$: C, 69.07; H, 6.71; S, 19.38. Found: C, 69.07; H, 6.70; S, 19.28.

Acetaldehyde Diphenylthioacetal (VI, R = CH_3) and α,α-Diphenyl-α-hydroxyacetone Diphenylthioketal (VIII).—To a solution of 7.55 mmoles of the lithium compound V, stirred at 0°, was added 1.08 g (7.60 mmoles) of neat methyl iodide. The cold bath was removed, and after 45 min at 25° an aliquot containing product from 500 mg (2.16 mmoles) of VI, R = H, was withdrawn and worked up following the procedure described for VIIb; 355 mg (67%) of methylation product VI, R = CH_3, was obtained as a colorless oil; nmr spectrum (CCl_4): doublet at τ 8.47 (J = 7 cps), quartet at 5.59 (J = 7 cps) and multiplet at 2.8, ratio 3:1:10.

To the rest of the solution containing 5.4 mmoles of VI, R = CH_3, was added a solution of 650 mg (5.8 mmoles) of Dabco in 5 ml of tetrahydrofuran, causing a precipitate. The mixture was stirred at 0° and combined with 6.4 mmoles of *n*-butyllithium. After 10 min 0.945 g (5.2 mmoles) of benzophenone in 1 ml of tetrahydrofuran was added, and stirring was continued for 70 min at 27°. The isolation procedure was the same as described for VIIb. The crude product (1.865 g, oily crystals) was washed with ice-cold methanol to give 1.65 g (74%) of dry, colorless material, mp 148–153°. The analytical sample (from methanol, 100 ml/g) had mp 153–155°; nmr spectrum ($CDCl_3$): singlets at τ 8.84 and 6.29 in addition to the multiplets of the aromatic protons, ratio 3:1:20; infrared absorption due to hydroxyl appeared at 2.77 μ ($CHCl_3$).

Anal. Calcd for $C_{27}H_{24}OS_2$: C, 75.68; H, 5.65; O, 3.73; S, 14.94. Found: C, 75.85; H, 5.48; O, 3.90; S, 15.17.

Pentanal Diphenylthioacetal (VI, R = *n*-C_4H_9).—A solution of 42.5 mmoles of V was stirred at 0° and combined with 7.67 g (56 mmoles) of neat *n*-butyl bromide. The bath was removed and stirring was continued at 25° for 2.5 hr. The solution was poured into three times its volume of water, the layers were separated, and the aqueous layer was extracted four times with 40 ml of ether. The combined organic extracts were washed twice with 5% potassium hydroxide and four times with water and dried over magnesium sulfate. Evaporation of the solvent gave 11.70 g (96%) of a slightly yellow oil; nmr spectrum: no starting VI, R = H, present, triplet due to methine proton at τ 5.67, aromatic and aliphatic protons as multiplets, ratio 1:10:9. A mixture of 2.56 g of crude VI, R = *n*-C_4H_9, 5 g of mercuric chloride, 4 g of mercuric oxide, 10 ml of water, and 100 ml of methanol was stirred vigorously and heated at reflux for 12 hr. After filtration and concentration of solvent to 30 ml, a solution of 2 g of 2,4-dinitrophenylhydrazine in 7 ml of concentrated sulfuric acid, 8 ml of water, and 25 ml of ethanol was added. The hydrazone separated immediately; yield 1.52 g (65%) after recrystallization from ethanol, mp 97–99° (lit.[13] 98°).

Acknowledgments.—This work was supported by the National Institutes of Health. We are indebted to Dr. George T. Kwiatkowski for the experimental procedure for the generation of I with phenyllithium.

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[13] "Tables for Identification of Organic Compounds," Chemical Rubber Publishing Co., Cleveland, Ohio, 1960, p 69.