Configuration Determination of (R)-(+)-1,1,2-Triphenylpropane. Configuration Inversion

of (R)-(+)- α -Phenylethyltrimethylammonium Iodide by Benzhydryllithium

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The absolute configuration of (R)-(+)-1,1,2-triphenylpropane (2) has been determined by its synthesis from (S)-(+)-hydratropic acid (1a). The reaction of benzhydryllithium with (R)-(+)- α -phenylethyltrimethylammonium iodide occurs 100% stereospecifically with inversion of configuration forming 2. High yields (>90%) of polyphenylethanes are secured in reactions of benzylic organolithiums with benzylic quaternary ammonium iodide salts.

We were interested in the stereochemistry of the coupling reactions of benzhydryllithium with α -phenylethyltrimethylammonium iodide salts to form 1,1,2-triphenylpropane derivatives. This reaction is related to the work of Sommer and Korte¹ and Sauer and Braig,² who have shown that charge-delocalized carbanions in organolithium reagents couple stereospecifically with chiral secondary halides with inversion of configuration. In the reaction of benzhydryllithium with 47% optically pure (-)- α -phenylethyl chloride to give (+)-1,1,2-triphenylpropane, a value of 100% for the stereospecificity of the inversion process was estimated, but caution was recommended since optically pure hydrocarbon of known configuration was unavailable.¹

Now we are able to assign the absolute configuration of (+)-1,1,2-triphenylpropane as the R stereoisomer based on its synthesis from (S)-(+)-2-phenylpropanoic acid [(S)-(+)-hydratropic acid, 1a]. We also can report that benzhydryllithium reacted with (R)-(+)- α -phenylethyltrimethylammonium iodide stereospecifically with >98.2% inversion of configuration to give (R)-(+)-1,1,2-triphenylethane (2). In addition we have secured uniformly high yields of ethane coupling products from reactions of charge-delocalized organolithium compounds with benzylic trimethylammonium quaternary salts (see Table I) in harmony with the stereochemical results reported earlier for reactions of secondary halides with allylic² or benzylic¹ organolithium reagents.

Results

(S)-(+)-Hydratropic acid, 98.2% optically pure 1a, was converted with diazomethane into methyl (S)-(+)-hydratropate, 95% 1b. Ester 1b reacted with 2 mol of phenylmagnesium bromide to give 46.4% of (S)-(-)-1,1,2-triphenyl-1propanol (1c). Alcohol 1c was reduced with sodium in liquid ammonia to give 50% of (R)-(+)-1,1,2-triphenylpropane (2). See Scheme I.

Scheme I



When benzhydryllithium was treated with (R)-(+)- α phenylethyltrimethylammonium iodide of 97.5% minimum optical purity, **2** was obtained in 65% yield. See eq 2. Since the sample of **2** obtained by displacement of trimethyl-

$$(C_{6}H_{5})_{2}CH:^{-} + H_{3}C \xrightarrow{H} N(CH_{3})_{3} \longrightarrow (R) \cdot (+) \cdot 2$$

$$C_{6}H_{5} I^{-} \qquad [\alpha]^{23}D + 30.99^{\circ}$$

$$(R) \cdot (+) \cdot 3$$

$$[\alpha]^{22}D + 10.72^{\circ} \qquad (2)$$

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amine from 3 has a slightly higher rotation than the authentic sample of Scheme I, its optical purity is higher, indicating that the stereospecificity of reaction 2 is quite high, if not 100%. As the arrangement of groups in (R)-(+)-3 is opposite to that in (R)-(+)-2, reaction 2 occurs stereospecifically with inversion of configuration.³

The reactions of trityl-, benzhydryl-, and benzyllithium with benzhydryl- (4) and benzyltrimethylammonium iodides (5) to give polyphenylethane coupling products in greater than 90% yields are summarized in Table I. No evidence for Sommelet-Hauser rearrangement products could be detected, although such products are the predominant ones in reactions of 4 and 5 with alkyllithium reagents.⁴

Discussion

Early work reported failure to convert 1b into 1c but described the reaction of (+)- α -chloroethylbenzene, $[\alpha]D$ +19.5°, to (+)-2, $[\alpha]D$ +6.67°, with benzhydrylsodium.⁵ That the starting material and product were of low optical purity can be seen from the data on the later conversion of (-)- α -chloroethylbenzene (6, 47% optically pure, $[\alpha]^{25}D$ -59.3°, neat) into (-)-2 $([\alpha]^{24}D \ 21.7^\circ)$.¹

The conclusion¹ that benzhydryllithium reacted with (-)-6 with inversion of configuration is correct, although the percent stereospecificity using the rotation value from this work is 70%. No doubt benzhydryllithium reacts with 6 not only by displacement but also to establish a halogenmetal interconversion⁶ equilibrium forming α -lithioethylbenzene, which upon reversion to 6 suffers racemization.

An alternate mechanistic explanation of stereochemistry involving electron transfer to form radicals⁸ would conflict with the general view proposed by Sauer and Braig² that organolithiums containing allylic or benzylic groups react with halides by SN2 mechanisms while alkyllithiums react with halides to form products intelligible only if radical intermediates were formed.

In the present study, halogen-metal interconversion is not a serious possibility and if the coupling product of eq 2 is forming by an electron-transfer process, then a geminate radical pair in a cage tight enough to prevent racemization is required. That radical intermediates form in reactions of charge-delocalized organolithiums with halides was shown recently⁹ by the electron detachment oxidation of triphenylmethyl carbanion by triphenylmethyl halide which undergoes dissociative electron attachment.¹⁰ Quaternary

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Coupling Reactions of Charge-Delocalized Organolithium Reagents with Trimethylammonium Quaternary Salts

RLi reagent	$R'N(CH_3)_3^+I$ reactant		RR' product	Yield, ^c %
(C ₆ H ₅) ₃ CLi ^a	(C ₆ H ₅) ₂ CH	4	$(C_{g}H_{5})_{3}CCH(C_{g}H_{5})_{2}$	91
$(C_6H_5)_3CLi^a$	$C_6H_5CH_2$	5	$(C_6H_5)_3CCH_2C_6H_5$	93
$(C_6H_5)_2$ CHLi ^a	$(C_6H_5)_2CH$	4	$(C_{g}H_{5})_{2}CHCH(C_{g}H_{5})_{2}$	95
$(C_6H_5)_2$ CHLi ^a	C ₆ H ₅ CH ₂	5	$(C_{g}H_{5})_{2}CHCH_{2}C_{g}H_{5}$	92
$C_6H_5CH_2Li^b$	$(\check{\mathbf{C}}_{6}\check{\mathbf{H}}_{5})_{2}\check{\mathbf{C}}\mathbf{H}$	4	$(C_{6}H_{5})_{2}CHCH_{2}C_{6}H_{5}$	91
$C_6H_5CH_2Li^b$	$C_6H_5CH_2$	5	C ₆ H ₅ CH ₂ CH ₂ C ₆ H ₅	90

^a Prepared by metalation of the hydrocarbon in tetrahydrofuran with *n*-butyllithium. ^b Prepared by cleavage of benzylmethyl ether with lithium metal. ^c Isolated yields. Gas chromatographic analysis of mother liquors indicated additional amounts of material for all compounds except pentaphenylethane, which cannot be gas chromatographed.

ammonium halide salts are known to oxidize potassium in liquid ammonia¹¹ or lithium naphthalenide in tetrahydrofuran¹² by electron transfer processes to produce radical species of finite lifetime as judged by trapping products formed through intermolecular processes. If such pathways are being followed during the present coupling reactions, they do not produce radicals of sufficient lifetime to allow diffusion followed by reduction, coupling, or disproportionation reactions. Since the quaternary ammonium salts of Table I are the same as those which formed radical intermediates upon treatment with lithium naphthalenide,¹² the displacement of trimethylamine from salt by a chargedelocalized organolithium occurs by a polar process without chemical evidence for an electron transfer component.¹³

Our results should be contrasted with those obtained during a study of the stereochemistry of free-radical recombination reactions after thermal decomposition of (S)-(-)azobis- α -phenylethane to produce α -phenylethyl radicals.¹⁴ The results showed that the principal products were derived from α coupling to produce meso and nonmeso 2,3-diphenylbutanes. Thus a substantial loss of stereochemistry through randomization or turnover occurs in the loose radical cages which are required for departing nitrogen in such systems.

Experimental Section

All reactions were performed under an argon atmosphere, and solvents were evaporated on a rotary evaporator under vacuum. Melting points were taken on a Fisher-Johns or Mel-Temp apparatus and are uncorrected. NMR spectra were recorded on Varian T-60 and A-60A 60-MHz instruments and except where noted, in CDCl₃ solvent. Chemical shift values are reported in parts per million relative to TMS as internal standard. Ir spectra were recorded on a Perkin-Elmer Model 267 spectrophotometer. Organolithium reagents were obtained from Alfa Inorganics and were titrated using the procedure of Eastham.¹⁵

All compounds were dried thoroughly before use. Optical rotation measurements were determined with a Rudolph polarimeter (Model 70). Elemental analyses were by Schwarzkopf Microanalytical Laboratory, Woodside, N.Y.

Preparation of Hydratropic Acid via Hydratroponitrile.¹⁶ Racemic hydratropaldehyde (159 g, 1.17 mol in 480 ml of ethanol) and hydroxylamine hydrochloride (99.0 g, 1.41 mol in 120 ml of H₂O) was treated with 96 ml of 19 N aqueous NaOH to give 135 g (76%) of hydratropaldoxime, a colorless oil: bp 110° (3.5 mm) [lit. bp 133° (11 mm)]; ir v_{max} (neat) 3220 and 1500 (bonded OH) and 1670 cm⁻¹ (C=N).

The oxime (135 g, 0.90 mol) was refluxed for 0.5 hr with 200 ml of acetic anhydride following the literature procedure to yield 84 g (71%) of hydratroponitrile: bp 74° (0.5 mm) [lit. bp 106° (12 mm)]; ir $\nu_{\rm max}$ (neat) 2245 cm⁻¹ (C=N).

If ν_{max} (neat) 2245 cm⁻¹ (C=N). Hydrolysis of the nitrile (84 g, 0.63 mol) with aqueous NaOH, followed by acidification (HCl), ether extraction, and distillation, provided (±)-hydratropic acid: 72 g, 76%, bp 113° (1.0 mm) [lit.¹⁶ bp 147° (11 mm)]; ir ν_{max} (neat) 2960 and 1701 cm⁻¹; NMR (DCCl₃) δ 1.4 (3 H, d), 3.1 (1 H, q), 7.35 (5 H, s), 12 (1 H, s).

Resolution of Hydratropic Acid. Hydratropic acid (48 g) and

strychnine (88 g) were dissolved in 200 ml of 75% (v/v) aqueous ethanol. After 3 days at 0°, the crystallized strychnine hydratropate was collected and crystallized five additional times to constant mp $176-177^{\circ}$ of dried salt.

Treatment of the salt with 6 N HCl liberated the free acid which was extracted into ether, dried, and distilled to produce 9.0 g of (S)-(+)-hydratropic acid: bp 101-103° (0.4 mm); $[\alpha]^{22}D$ +97.00° (neat, l = 1.0 dm) [lit.¹⁷ $[\alpha]^{21}D$ 98.8° (neat, l = 1.0 dm)]; optical purity 97.5%; NMR (DCCl₃) δ 1.4 (3 H, d), 3.1 (1 H, q), 7.35 (5 H, s), 12 (1 H, s).

Preparation of Methyl (S)-(+)-Hydratropate (1b). Aldrich Chemical Co. Diazald (21.5 g, 0.1 mol of N-methyl-N-nitroso-ptoluenesulfonamide in 130 ml of ether) was added dropwise to KOH (5 g in 8 ml of H₂O, 25 ml of ethanol) at 65° to produce diazomethane (ca. 0.01 mol) as a distillate in ether. Addition of this solution to an ether solution of (+)-hydratropic acid (7.5 g, 0.05 mol) until the yellow color of CH₂N₂ persists and N₂ gas is no longer evolved was followed by distillation of excess reagent, solvent, and methyl ester, bp 60-65° (2 mm), to furnish 7.80 g of methyl (S)-(+)-hydratropate (95%): NMR (DCCl₃) δ 1.2 (3 H, d), 3.5 (3 H, s), 3.6 (1 H, q), 7.35 (5 H, m); $[\alpha]^{22}D$ +103.50° (neat, l = 1 dm).

Preparation of (S)-(-)-1,1,2-Triphenyl-1-propanol (1c). Phenylmagnesium bromide was prepared from bromobenzene (23.4 g, 0.149 mol) and singly sublimed Dow Chemical Co. Mg (3.2 g, 0.13 mol) in 50 ml of THF at the boiling point of the solvent. To this Grignard solution was added dropwise methyl (S)-(+)-hydratropate (5.0 g, 0.03 mol). The reaction mixture was refluxed for 2 hr, decomposed with 100 ml of ammonium chloride, and extracted with ether. After drying of the ether solution and evaporation of the solvent, the oil was distilled to afford 4.0 g of (S)-(-)-1,1,2-triphenyl-1-propanol: bp 180–182° (3.0 mm); NMR (DCCl₃) δ 1.4 (3 H, d), 2.4 (1 H, s), 4.0 (1 H, q), 7.3 (15 H, m); $[\alpha]^{22}D$ -142° (CH₃OH, c 1.717 g/25 ml, l = 2 dm).

Anal. Calcd for $C_{21}H_{20}O$; C, 87.50; H, 6.94. Found: C, 87.60; H, 7.20.

Reduction of (S)-(-)-1,1,2-Triphenyl-1-propanol (1c) to (R)-(+)-1,1,2-Triphenylpropane (2), with Sodium in Liquid Ammonia. The carbinol 1c (5.76 g, 0.02 mol) and ethanol (2.02 g, 0.044 mol) were dissolved in a mixture of 50 ml of THF and 200 ml of liquid ammonia. Sodium (1.01 g, 0.044 mol) was added in small pieces during 45 min. After all the sodium dissolved, ammonia was evaporated and the residue was treated with crushed ice. The product was extracted with ether; the ether was dried (MgSO₄), and evaporated and the product was distilled in vacuo to give (R)-(+)-1,1,2-triphenylpropane (2.72 g, 50%). Upon addition of petroleum ether, the oil solidified, mp 63-65°, $[\alpha]^{22}D$ +30.15° (acetone, l = 2 dm, c 0.5998 g/25 ml). This material was identical with the sample secured as described below in all of its physical and spectral properties.

(+)-1,1,2-Triphenylpropane (2) from Reaction of Benzhydryllithium with (R)-(+)-N,N,N-Trimethyl- α -phenylethylammonium Iodide (3). To approximately 0.04 mol of benzhydryllithium in 100 ml of THF (see below) at 0° was added 11.64 g of (R)-(+)-N,N,N-trimethyl- α -phenylethylammonium iodide (0.04 mol). The reaction mixture was stirred for 1.0 hr, after which the red color of the carbanion had disappeared. After acidification with HCl, extraction with ether, drying of the ether (CaCl₂), and removal of the solvent in a rotary evaporator, the remaining oil was fractionally distilled in vacuo to give a middle fraction of bp 165° (1 mm). Treatment of this oil with cold methanol caused crystallization of 7.02 g (65%) of crude (+)-1,1,2-triphenylpropane, mp $60-64^{\circ}$, $[\alpha]^{23}D + 29.56^{\circ}$ (acetone, l = 2 dm). Five recrystallizations

Configuration of (R)-(+)-1,1,2-Triphenylpropane

from methanol afforded the analytical sample, mp 64-66°, $[\alpha]^{23}$ D +30.99° (acetone, $l = 2 \text{ dm}, c \ 0.6061 \text{ g}/25 \text{ ml}$).

Anal. Calcd for C₂₁H₂₀: C, 92.64; H, 7.35. Found: C, 92.51; H, 7.41

NMR (DCCl₃) δ 1.20 (3 H, d), 3.6 (1 H, m), 4.1 (1 H, d), 7.3 (15 H. m).

The literature¹⁸ melting point (73-75°) is for racemic hydrocarbon. It thus appears that the individual enantiomers melt lower than the racemates, as was found in the 2,3-diphenylbutanes.¹

Preparation of (-)-1,1,2-Triphenylpropane. The reaction of benzhydryllithium (0.04 mol) in THF at 0° under argon with (S)-(-)-N,N,N-trimethyl- α -phenylethylammonium iodide produced (-)-1,1,2-triphenylpropane, mp 65-67°, $[\alpha]^{22}$ D -28.74° (acetone, l $= 2 \text{ dm}, c \ 0.6096 \text{ g}/25 \text{ ml}).$

Anal. Calcd for C₂₁H₂₀: C, 92.64; H, 7.35. Found: C, 92.58; H, 7.23.

The NMR and ir spectral properties were indistinguishable from those for (+)-2.

Resolution of (\pm)-\alpha-Phenylethylamine. α -Phenylethylamine was resolved according to the method of Theilacker and Winkler.¹⁹ The specific rotation for the (R)-(+) amine is $[\alpha]^{22}D$ +39.60° (neat), optical purity 98.2% using the best literature value²⁰ $[\alpha]^{25}$ D +40.60° (neat). The specific rotation for the (S)-(-) amine is $[\alpha]^{22}$ D -39.30° (neat), 98.0% optically pure.

NMR (CD₃CN) δ 1.3 (3 H, d), 1.4 (2 H, s), 4.0 (1 H, q), 7.5 (5 H, m). The spectra were identical for the two isomers.

(R)-(+)-N,N-Dimethyl- α -phenylethylamine. (R)-(+)- α -phenylethylamine (12.1 g, 0.1 mol) was added with cooling to 90% formic acid (25.5 g, 0.5 mol). Formaldehyde (19 g, 0.22 mol of a 35% H_2O solution) was added and the system was heated on a steam bath for 4 hr. Concentrated HCl (9 ml, 0.1 mol) was added and the formic acid and excess formaldehyde were removed with the rotary evaporator. The cold reaction mixture was made alkaline with 25% NaOH and extracted $(3 \times 15 \text{ ml})$ with ether and the organic layer was dried over KOH. Distilling of the solvent and the product produced 11.90 g (80%) of (R)-(+)-N,N-dimethyl- α -phenylethylamine: bp 92–94° (30 mm); $[\alpha]^{22}$ D +60.50° (neat, l = 1 dm) [lit.²¹ $[\alpha]^{26}$ D 61.76° (neat), l = 1 dm)]; optical purity 98.0%; NMR (CD₃CN) δ 1.0 (3 H, d), 1.95 (6 H, s), 2.8 (1 H, q), 7.1 (5 H, m).

(S)-(-)-N,N-Dimethyl- α -phenylethylamine. This amine was prepared as described above for the (R)-(+) isomer, $[\alpha]^{22}D$ -60.48° (neat, l = 1 dm). The NMR and ir spectra were indistinguishable from those for the (+) isomer: NMR (CD₃CN) δ 1.0 (3 H, d), 1.95 (6 H, s), 2.8 (1 H, q), 7.1 (5 H, m).

(R)-(+)-N,N,N-Trimethyl- α -phenylethylammonium Iodide (3). To a solution of (R)-(+)-N,N-dimethyl- α -phenylethylamine (14.9 g, 0.1 mol) in ether (100 ml) was added slowly 21.3 g (0.15 mol) of methyl iodide. After 15 min the mixture solidified. The flask was cooled in an ice bath for 2 hr and allowed to stand at 25° for 16 hr and the product was collected by filtration, washing with ether (50 ml) and drying in vacuo for 24 hr to give 27.64 g (95%) of the title salt, mp 155–156° (lit.²² mp 157–157.5°), $[\alpha]^{22}D$ 10.72° (H₂O, l = 2 dm, c 0.6184 g/25 ml), $[\alpha]^{20}D$ +23.28° (95% C₂H₅OH, l= 2 dm, c 0.9393 g/25 ml). The literature value²² is $[\alpha]^{20}$ D +19.60° (C₂H₅OH). NMR (CDCl₃) δ 1.8 (3 H, d), 3.2 (9 H, s), 4.9 (1 H, q), 7.8 (5 H, s).

(S)-(-)-N,N,N-Trimethyl- α -phenylethylammonium Iodide. This solid was prepared as described for the (R)-(+) isomer, $[\alpha]^{22}D$ -12.03° ($l = 2 \text{ dm}, c \ 0.6749 \text{ g}/25 \text{ ml H}_2\text{O}$), $[\alpha]^{20}\text{D} -22.95^{\circ}$ (95%) C_2H_5OH , l = 2 dm, c 0.8568 g/25 ml) [lit.²² [α]²⁰D -19.60° $(C_2H_5OH)].$

Preparations of Triphenylmethyllithium and Diphenylmethyllithium. To a solution of triphenylmethane (4.88 g, 0.02 mol) or diphenylmethane (3.3 g, 0.0196 mol) in 100 ml of THF under argon at 0° was added 19.4 ml of n-butyllithium (0.021 mol of 1.13 M in hexane from Alfa Inorganics). The solutions were allowed to stir for 1.0 hr (3.0 hr in the case of Ph₂CH₂) before use. The coupling reactions shown in Table I demonstrate that metalation yields exceeded 90% while the 65% yield of 2 secured in eq 2 shows the lower yields sometimes secured in metalating diphenylmethane.

Preparation of Benzyllithium. Benzyl methyl ether (17.0 g, 0.085 mol) and lithium wire (6.0 g, Alfa Inorganics) in diethyl ether solvent were allowed to react according to a published procedure.²⁴

Preparation of N-Diphenylmethyl-N,N,N-trimethylammonium Iodide. Benzhydryltrimethylammonium iodide was pre-pared as described in the literature,²⁴ mp 175° dec (lit. mp 174– 175° dec), NMR (DCCl₃) δ 3.2 (9 H, s), 6.3 (1 H, s), 7.4 (10 H, m).

Preparation of N-Benzyl-N,N,N-trimethylammonium Iodide. Benzyltrimethylammonium iodide was prepared as described previously,²⁵ mp 178-179° dec (lit. mp 179°), NMR (D₂O) δ 3.2 (9 H, s), 4.6 (2 H, s), 7.7 (5 H, m).

Pentaphenylethane from Triphenylmethyllithium and N-Diphenyl-methyl-N,N,N-trimethylammonium Iodide. To a solution of trityllithium (0.02 mol) in THF at 0° under argon was added 7.06 g of solid benzhydryltrimethylammonium iodide (0.02 mol). After 25-30 min the red color of the lithium reagent disappeared completely. After work-up using ether and water, the ether layer was washed with 5% HCl, neutralized with 5% NaOH, and dried over MgSO₄. The ether was removed in the rotary evaporator to give a light yellow powder which was dissolved quickly in the minimum amount of hot benzene and precipitated by adding excess absolute ethanol, 6.54 g (80%), mp 156-161°. Concentration under reduced pressure gave 1.22 g (10%) additional pentaphenylethane which was identical with a sample described recently in this laboratory,⁹ NMR (DCCl₃) δ 5.8 (1 H, s), 7.2 (25 H, m).

unsym-Tetraphenylethane from Triphenylmethyllithium and Benzyltrimethylammonium Iodide. To a solution of trityllithium (0.02 mol) in 100 ml of THF at 0° under argon was added solid benzyltrimethylammonium iodide (5.54 g, 0.02 mol) with stirring for 4 hr. Using the work-up procedure described for pentaphenylethane, 6.01 g (90%) of unsym-tetraphenylethane, mp 143-145° (lit.²⁶ mp 144°) was obtained, NMR (DCCl₃) δ 3.95 (2 H, s), 7.2 (20 H, m).

sym-Tetraphenylethane from Diphenylmethyllithium and N-Diphenylmethyl-N,N,N-Trimethylammonium Iodide. To a solution of benzhydryllithium (0.01 mol in THF) was added 3.53 g of solid benzhydryltrimethylammonium iodide (0.01 mol) with stirring for 1 hr. Using the procedure described for pentaphenylethane above with recrystallization of the crude product from benzene-alcohol (5:1), a 3.01-g yield of sym-tetraphenylethane was secured, mp 214-215° (lit ¹⁸ mp 214-215°).

1,1,2-Triphenylethane from Benzyllithium and N-Benzhydryl-N.N.N-trimethylammonium Iodide (4). The title salt (3.53 g, 0.01 mol) and benzyllithium (0.01 mol) in ether at 0° were stirred until disappearance of the carbanion color. Hydrolysis with 100 ml of 5% HCl, extraction into 100 ml of ether, and drying with MgSO₄ was followed by removal of solvent to give 2.34 g (91%) of 1,1,2-triphenylethane (needles from alcohol), mp 55-56° (lit.¹⁸ mp 55-56°), NMR (DCCl₃) δ 3.5 (2 H, d), 4.3 (1 H, t) 7.2 (15 H, m).

1,2-Diphenylethane from Benzyllithium and N-Benzyl-N,N,N-trimethylammonium Iodide (5). Using the procedure described above, benzyltrimethylammonium iodide (2.77 g, 0.01 mol) reacted with benzyllithium (0.01 mol) to give 1.63 g of 1,2-diphenylethane, mp 50-51° (lit.²⁷ mp 52.0-52.5°), NMR (DCCl₃) & 2.9 (4 H.s). 7.1 (10 H.s).

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Registry No.-1a, 7782-24-3; 1b, 28645-07-0; 1c, 54667-59-3; (R)-(+)-2, 54667-60-6; (S)-(-)-2, 54667-61-7; (R)-(+)-3, 54712-34-4; (S)-(-)-3, 17279-33-3; 4, 6338-76-7; 5, 4525-46-6; (±)-hydratropaldehyde, 34713-70-7; hydroxylamine hydrochloride, 5470-11-1; hydratropaldoxime, 54667-62-8; hydratroponitrile, 42253-96-3; (±)-hydratropic acid, 2328-24-7; strychnine, 57-24-9; strychnine hydratropate, 54667-63-9; benzhydryllithium, 881-42-5; (\pm) - α phenylethylamine, 618-36-0; (R)-(+)- α -phenylethylamine, 3886-69-9; (S)-(-)- α -phenylethylamine, 2627-86-3; (R)-(+)-N,N-dimethyl- α -phenylethylamine, 19342-01-9; formaldehyde, 50-00-0; (S)-(-)-N,N-dimethyl- α -phenylethylamine, 17279-31-1; triphenylmethyllithium, 733-90-4; benzyllithium, 766-04-1; pentaphenylethane, 19112-42-6; unsym-tetraphenylethane, 2294-94-2; symtetraphenylethane, 632-50-8; 1,1,2-triphenylethane, 1520-42-9; 1,2-diphenylethane, 103-29-7.

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The Chemistry of Carbanions. XXVII. A Convenient Precursor for the Generation of Lithium Organocuprates¹

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To avoid side reactions resulting from the presence of Cu(II) compounds and other metal salt impurities in the Cu(I) salts used to form lithium organocuprate reagents, use of the easily prepared, crystalline complex, Me₂S-CuBr(2), is recommended. This complex 2 is readily soluble in mixtures of Me₂S and ethereal solvents, and the sulfide ligand, Me₂S (bp 37°), is easily separated from reaction products. This procedure is illustrated with several additional reactions involving the cuprate reagents, Me₂CuLi and (CH₂=CH)₂CuLi. The difficultly reduced enone 22 and the moderately acidic saturated ketones 32 and 37 undergo a relatively slow reaction with Me₂CuLi at 25° to form enolate anions that are inert to further reaction with the cuprate. The saturated ketones 32, 37, and 40 are also slowly converted to alcohol products by a solution of Me₂CuLi at 25°; this latter reaction may involve a small concentration of MeLi present in equilibrium with the cuprate reagent.

From various studies of the preparation and use of lithium organocuprate reagents,² it has become apparent that two practical problems complicating the general use of these reagents are inadvertent thermal decomposition³ and inadvertent oxidation leading to coupling of the organic residues.⁴ Both of these initial side reactions often lead to the formation of Cu(0), which usually appears as a black colloidal suspension in the reaction mixture and is believed to catalyze the decomposition of still more copper reagent.⁵

The most common preparative procedure for lithium dialkylcuprates consists of addition of 2 molar equiv of an alkyllithium solution to an ethereal slurry of one of the commercially available Cu(I) salts, CuI, CuBr, or CuCl. As noted previously,⁶ use of this procedure may be accompanied by partial decomposition, especially if the reagent is one of the relatively thermally unstable cuprates, such as a vinyl derivative or a derivative with alkyl substituents that have β H atoms. Among the causes of this decomposition are the presence of other transition metal impurities in the commercial Cu(I) salts and the occurrence of local overheating during the exothermic reaction of alkyllithium with insoluble Cu(I) salts.⁶ Another cause of decomposition is the presence of significant amounts of Cu(II) salts, which are effective oxidants for cuprates,^{4,6b} in many commercial samples of Cu(I) halides. Other Cu(I) compounds that have been used to form cuprate reagents include the insoluble derivatives $CuCN^7$ and $n-C_3H_7C \equiv CCu^8$ and the more soluble derivatives t-BuOCu,⁹ PhSCu,⁹ and t-BuC=CCu.^{6a} The latter, soluble Cu(I) acetylide offers the advantage of being a scavenger for oxidizing agents such as Cu(II) salts, undergoing oxidation to form the volatile diyne, t-BuC=CC=CBu-t.6 Unfortunately, the advantages of ether solubility and "protection" from oxidants offered by

t-BuC \equiv CCu are offset by the fact that the precursor, t-BuC=CH, is not presently available commercially at a reasonable cost. This fact has led us to examine other possible Cu(I) derivatives that might offer the advantages of both ether solubility and easy purification to separate unwanted Cu(II) impurities. In earlier work,^{6,10} we have noted the solubility advantages offered by several Cu(I) halide complexes such as n-Bu₃PCuI, (MeO)₃PCuI,(MeO)₃PCuBr, and especially, the liquid complexes $(n-Bu_2S)_2CuI$ and $(n-Bu_2S)_2CuBr$. The use of these complexes in synthetic work is made less attractive by the relatively high boiling points of the ligands, n-Bu₂S (bp 189°), n-Bu₃P [bp 150° (50 mm)], and (MeO)₃P (bp 112°) that complicate their removal from reaction products and by the persistent disagreeable odor associated with phosphine and phosphite ligands. We were attracted by reports indicating that complexes of certain Cu(I) salts with the ligand Me_2S (bp 37°) were both soluble in ether¹¹ and could be obtained as crystalline solids.¹² Upon exploring the reaction of Me₂S with Cu(I) halides, we found that each of the 1:1 complexes 1, 2, and 3 (Scheme I) could easily be obtained as a colorless, crystalline solid that was readily separated from Cu(II) contaminants. Since Cu(II) salts form solutions of highly colored complexes with Me₂S (dark green solution with $CuCl_2$ and dark red solution with $CuBr_2$), the absence of these Cu(II) impurities in the colorless Cu(I) complexes is readily discerned. Although the iodide complex 3 spontaneously lost Me₂S on standing, the bromide complex 2 proved to be both convenient to prepare in pure form and stable to storage. Thus, by conversion to the complex 2, commercial samples of CuBr are readily purified to remove Cu(II) salts and other impurities.

Although none of the complexes 1–3 was soluble in ether,