methylene chloride, yielded anthrone (0.031 g, 3%) and 10-(dimethoxymethyl)-9-anthrone (0.064 g, 0.239 mol, 5%), mp 144–146 °C (from hexane–benzene). Its NMR spectrum showed signals at δ 8.3 (2 H, m), 7.55 (6 H, m), 2.35 (1 H, d, J = 3.0 Hz), 2.40 (1 H, d, J = 3.0 Hz), and 3.15 (6 H, s). Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.13; H, 5.98. Found: C, 75.79; H, 6.06.

10-(Diethoxymethyl)-9-hydroxy-9-methyl-9,10-dihydroanthracene (6). A 1.56 M solution of methyllithium in ether (3 mL, 4.68 mmol) was added to a solution of 10-(diethoxymethyl)-9-anthrone (0.50 g, 1.68 mmol) in 15 mL of anhydrous ether. The solution was stirred, allowed to stand at room temperature for 5 min, and then poured into water. The organic layer was separated and dried over magnesium sulfate, and the solvent evaporated under vacuum to yield 10-(diethoxymethyl)-9-hydroxy-9-methyl-9,10-dihydroanthracene as a yellow oil (0.53 g, 1.69 mmol) which crystallized on standing overnight in the refrigerator. Its NMR spectrum showed peaks at δ 7.90–7.65 (m, 2 H), 7.50–7.15 (m, 6 H), 4.31 (1 H, d, J = 5 Hz, proton at acetal carbon), 4.05 (1 H, d, J = 5 Hz, proton at C-10), 3.80–2.85 (m, 4 H) 2.45 (s, 1 H, hydroxy proton), 1.63 (s, 3 H), and 1.00 (6 H, t, J = 7 Hz). Attempted recrystallization from warm hexane converted the product to 9-methylanthracene (0.39 g).

In another run, 0.27 g of the alcohol was dissolved in anhydrous ether, cooled to −78 °C, and filtered to give 0.09 g of pale yellow powder, which decomposed on melting to yield 9-methylanthracene. The NMR spectrum of the recrystallized material was essentially identical with that of the unrecrystallized reaction product.

Reaction of methyllithium with 10-(diethoxymethyl)-9-anthrone-*10-d* gave **6**-*10-d*. Its NMR spectrum showed a 0.14-H doublet at δ 4.05 and a singlet (together with a small doublet) at δ 4.3 (1 H).

Reaction of 10-(Diethoxymethyl)-9-methyl-9,10-dihydroanthracene with Acid. Hydrochloric acid solution (1.2 M, 1 mL) was added to a solution of 10-(diethoxymethyl)-9-hydroxy-9-methyl-9,10-dihydroanthracene (0.25 g, 0.80 mmol) in 10 mL of acetone. The solution was shaken for 1 min, diluted with water, and extracted with methylene chloride. The methylene chloride solution was washed with water, dried over magnesium sulfate, and filtered, and the solvent evaporated to give 0.15 g (0.78 mmol, 98%) of 9-methylanthracene. IR, NMR, and vapor-phase chromatographic analyses showed no evidence for the presence of 10-methylanthracene-9-carboxaldehyde.

10-(Diethoxymethyl)-9-hydroxy-9-phenyl-9,10-dihydroanthracene (5). A 1.90 M solution of phenyllithium in ether (2.3 mL, 4.37 mmol) was added to a solution of 10-(diethoxymethyl)-9-anthrone (0.60 g, 2.03 mmol) in 20 mL of ether. The dark phenyllithium color disappeared in about 5 min. The solution was then poured into water, the layers were separated, the ether layer was washed with water, dried over magnesium sulfate, and filitered, and the solvent was evaporated to give 0.72 g of yellow oil which crystallized on standing at room temperature. The product was recrystallized from benzene–hexane to give 0.43 g of 10-(diethoxymethyl)-9-hydroxy-9-phenyl-9,10-dihydroanthracene (1.15 mmol, 57%) as yellow needles, mp 149–151 °C. The NMR spectrum showed signals at δ 8.17–7.95 (m, 2 H), 7.7–7.2 (m, 6 H), 7.20 (s, 5 H), 4.05 (d, J = 8 Hz, 1 H, proton at C-10), 3.45 (d, J = 8 Hz, 1 H, diethoxymethyl proton), 2.43–4.05 (m, 4 H), 1.52 (s, 1 H, hydroxy proton), and 0.87 (t, J = 8 Hz, 6 H). Anal. Calcd for $C_{25}H_{26}O_3$: C, 80.18; H, 7.00. Found: C, 80.30; H, 7.17.

Reaction of 10-(diethoxymethyl)-9-anthrone-*10-d* with phenyllithium gave 10-(diethoxymethyl)-10-hydroxy-10-phenyl-9,10-dihydroanthracene-*10-d*. Its NMR spectrum showed a reduced intensity for the doublet at δ 4.05 and a singlet (together with a small doublet) at δ 3.45.

Reaction of 10-(Diethoxymethyl)-9-hydroxy-9-phenyl-9,10-dihydroanthracene with Acid. Hydrochloric acid solution (1.2 M, 1 M) was added to a solution of 10-(diethoxymethyl)-9-hydroxy-9-phenyl-9,10-dihydroanthracene (0.20 g, 0.54 mmol) in 5 mL of acetone. The mixture was shaken for 1 min, diluted with 20 mL of water, and extracted with methylene chloride, the organic layer washed with water, dried over magnesium sulfate and filtered, and the solvent evaporated to give 0.17 g of yellow gum which solidified on scratching and trituration with petroleum ether. Vapor-phase chromatography at 235 °C showed two peaks with retention times of 3.3 and 7.9 min. These products were isolated and identified as 9-phenylanthracene and 10-phenylanthracene-9-carboxaldehyde.[9]

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Registry No. 1, 77224-36-3; *trans*-**5**, 77224-37-4; *trans*-**6**, 77224-38-5; *trans*-**6**-*10-d*, 77224-39-6; anthrone, 90-44-8; triethyl orthoformate, 122-51-0; anthrone-*10,10-d*$_2$, 77224-40-9; 10-(diethoxymethyl)-9-anthrone-*10-d*, 77224-41-0; 10-(dimethoxymethyl)-9-anthrone, 77224-42-1; 9-methylanthracene, 779-02-2; 10-(diethoxymethyl)-9-hydroxy-9-phenyl-9,10-dihydroanthracene-*10-d*, 77224-43-2; 9-phenylanthracene, 602-55-1; 10-phenylanthracene-9-carboxaldehyde, 54458-81-0.

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A Chiral Ligand for Lithium

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Our continuing interest in the area of asymmetric induction[1] has led naturally to the design and construction of chiral ligands for synthetically important alkali metals such as lithium and mangesium. Such cations certainly play a significant role in the addition of organometallic reagents to ketones and aldehydes,[2] and relatively recent evidence implicates the cation as being intimately involved in the transition state of the reduction of carbonyl compounds by complex metal hydrides.[3] Chiral ligands for the cation would provide for diastereoselection between the otherwise enantiotopically related faces of a ketone or aldehyde. The report of a rather extensive effort in this area by Mukaiyama[4] serves as the impetus for this publication of our research with a similar ligand.

Our approach to the design of a ligand for lithium was predicated on two considerations: the ligand should be bidentate so as to afford, at the minimum, two additional binding sites to the metal—one for the carbonyl system and the other for a nucleophilic group such as the carbon chain of an alkyl lithium; while a tertiary amine would be desirable as a ligand, the carbon trisubstitution at nitrogen would afford less freedom in design for stereodifferentiation than a disubstituted oxygen or sulfur ligand site. The ligand **1** (Figure 1) was one outcome of these deliberations, and its preparation in enantiomerically enriched form proceeded as outlined. The tetrahydrofuryl amine used was outlined by resolution of racemic material by a known procedure.[5] The optical rotation for the starting amine was within experimental error the same as that previously reported. We were also able to prepare **1** by the reaction of pyrrolidine with the methanesulfonate ester to tetrahydrofurfuryl alcohol, and in greatly superior yield.

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(2) For a leading reference see: Ashby, E. C.; Buhler, J. D.; Lopp, I. G.; Wiesemann, T. L.; Bowers, J. S., Jr.; Laemmle, J. T., *J. Am. Chem. Soc.* **1976**, *98*, 6561.
(3) Ashby, E. C.; Boone, J. R. *J. Am. Chem. Soc.* **1976**, *98*, 5524; Handel, H.; Pierre, J.-L. *Tetrahedron Lett.* **1976**, 2029.
(4) Mukaiyama, T.; Soai, K.; Sato, T.; Shimizu, H.; Suzuki, K. *J. Am. Chem. Soc.* **1979**, *101*, 1455. See also citations in this reference to previous research in the area.
(5) Newman, P. "Optical Resolution Procedures for Chemical Compounds"; Optical Resolution Information Center: Riverdale, NY, 1978; Vol. 1, p 45.

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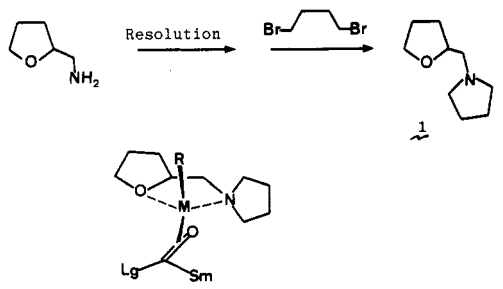

Figure 1.

Table I

$$PhCHO \xrightarrow[2.\ H_2O]{1.\ RM} PhCHR(OH)$$

RM	time, h/ temp, °C	solvent	% yield chemical	% yield optical
MeLi	1.5/−78	pentane	38	19
n-BuLi	1.5/−78	pentane	36	17
MeMgCl	14/25	ether	18	0

Table II

$$PhCOCH_3 \xrightarrow[2.\ H_2O]{1.\ [H^-]} PhCHCH_3(OH)$$

[H⁻]	time, h/ temp, °C	solvent	% yield chemical	% yield optical
$LiAlH_4$	2/−78	pentane	56	3
$LiAlH_4$		ether	52	2
$LiBH_4$	2/reflux	THF	51	15
$NaBH_4$	23/reflux	THF	52	3

However, we were unable to find a convenient system for the direct resolution of 1.

A number of systems involving nucleophilic addition to the carbonyl groups of benzaldehyde and acetophenone was examined, and these results are summarized in Tables I and II. In all cases, a slight excess (~20%) of the ligand 1 relative to the metal was employed. In the case of both methyllithium and methylmagnessium chloride, the use of nonether solvents led to the relatively rapid reaction between the ligand and the nucleophile (the yields reported are for highly purified material and do not represent the true level of conversion). It is interesting to note that, in contrast to the results with the ligand system described by Mukaiyama, no overall enantioselectivity was observed with magnesium as the cation. Relatively little induction was also obtained with sodium as the counterion and with the relatively more reactive lithium aluminum hydride.

Experimental Section

All reagents were commercial materials and were used without further purification except for ether solvents which were obtained immediately prior to use by distillation from blue solutions of the anion radical from benzophenone and sodium. Melting and boiling points are uncorrected. Varian HA-100 and FT-80 spectrometers were used to obtain ^1H and ^{13}C spectra with tetramethylsilane as internal standard. Optical rotations were obtained by using a Perkin-Elmer 141 polarimeter, and all samples measured were homogeneous by spectral and GLC (SE-30 and/or Carbowax 20M) analyses. Elemental analysis was performed by Chemalytics, Tempe, Az. HPLC refers to the use of two 0.95 × 60 cm columns packed with Porasil A.

(−)-*N*-(Tetrahydrofurfur-2-yl)methylpyrrolidine (1). Resolution of tetrahydrofurfurylamine was carried out by repeated crystallization of the tartartic acid salt according to the literature procedure.[5] Five recrystallizations afforded 72% (based on one enantiomer) of the salt with mp 96–98.5 °C. The free base obtained from this salt after distillation [bp 60 °C (15 mm)] had $[\alpha]^{25}_D$ −8.69° (H_2O) (lit.[5] $[\alpha]^{27}_D$ −8.57°).

The amine obtained above (11.3 g, 0.11 mol) was added dropwise to a refluxing solution of 26.4 g (0.12 mol) of 1,4-dibromobutane and 31.6 g (0.25 mol) of *N,N*-diisopropylethylamine in 250 mL of THF. After 48 h at reflux, the reaction was cooled and then extracted with 350 mL of 6 N aqueous sodium hydroxide. The aqueous layer was extracted with three 500-mL portions of ether and the combined organic layers were dried and concentrated in vacuo. The crude oil was fractionated by distillation to afford 4.0 g (23%) of 1: bp 90 °C (15 mm); $[\alpha]^{25}_D$ −61.7° (*c* 4.1, 0.67 N aqueous HCl); ^{13}C NMR (acetone-d_6) δ 78.0, 67.8, 61.1, 54.8, 30.3, 25.6, 23.6. Anal. Calcd for $C_9H_{17}NO$: C, 69.68; H, 10.97; N, 9.03. Found: C, 69.52; H, 10.71; N, 9.00.

Representative Procedure for Addition of Alkyllithium to Benzaldehyde in the Presence of 1. To a solution of 250 mg (1.61 mmol, 1.2 equiv) of 1 in 10 mL of pentane under nitrogen at −78 °C was added 1.34 mmol (by titration) of *n*-butyllithium solution in pentane. The solution was stirred at −78 °C for 1 h. A solution of 129 mg (1.22 mmol, 0.9 equiv) of benzaldehyde in 2 mL of pentane was introduced dropwise via syringe. The reaction was quenched after 1.5 h at low temperature by the addition of 0.25 mL of methanol. The reaction solution was diluted with ether and extracted with 15 mL of saturated aqueous ammonium chloride. Concentration gave an oil that was further purified by HPLC (2:1 hexane–ethyl acetate, $k' = 2$) to afford 71 mg (36%) of 1-phenyl-1-butanol, $[\alpha]^{25}_D$ +5.42° (*c* 3, benzene) [lit.[6] $[\alpha]^{24}_D$ 31.3° (benzene)].

For 1-phenylethanol obtained by the addition of methyllithium to benzaldehyde: $[\alpha]^{25}_D$ +9.69° (*c* 3, toluene) [lit.[7] $[\alpha]_D$ 50.6 (*c* 3, toluene)]; HPLC $k' = 2.5$, 2:1 hexane–ethyl acetate.

Reduction of Acetophenone with $LiBH_4$ in the Presence of 1. To a solution of 38 mg (1.66 mmol) of lithium borohydride in 6 mL of THF at −78 °C under nitrogen was added 344 mg (2.2 mmol) of 1 in 1 mL of THF. After 1 h, 199 mg (1.66 mmol of acetophenone in 2 mL of THF was added dropwise. The solution was warmed slowly to room temperature and then heated at reflux for 2 h. The product, 103 mg (51%) of 1-phenylethanol, was isolated as described above, $[\alpha]^{25}_D$ −7.48° (*c* 2.1, toluene).

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Registry No. (−)-1, 77224-35-2; (−)-tetrahydrofurfurylamine D-tartrate, 33002-00-5; (−)-tetrahydrofurfurylamine, 7202-43-9; 1,4-dibromobutane, 110-52-1; benzaldehyde, 100-52-7; (+)-1-phenyl-1-butanol, 22144-60-1; (+)-1-phenylethanol, 1517-69-7; acetophenone, 98-86-2; (−)-1-phenylethanol, 1445-91-6.

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Regiospecific Total Synthesis of (±)-11-Deoxycarminomycinone

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The recent discovery of naturally occurring antitumor anthracyclines related to 11-deoxydaunorubicin (1)[1] and the favorable spectrum of antitumor activity and reduced

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