(d, $J$ = 10 Hz, 2 H), 4.56 (s, 2 H), 3.80 (s, OH), and 3.50 (s, 2 H).

Attempted purification of quinol **1d** by bulb-to-bulb distillation (120–155 °C (0.04 mm)) or by chromatography on silica gel, Florisil, and neutral alumina (Woehm, Activity Grade I) afforded varying amounts of a viscous oil identified as hydroquinone **7**: IR ($CH_2Cl_2$) 3570, 3390, and 1698 $cm^{-1}$; NMR ($CDCl_3$–acetone-$d_6$) $\delta$ 7.34 (s, 5 H), 7.00 (s, 2 OH), 6.73 and 6.67 (two m, 3 H), and 4.66 and 4.58 (two s, 4 H); $m/e$ ($M^+$) 230.

Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.02; H, 6.13. Found: C, 72.87; H, 6.28.

**Jacaranone (1e).** A 1.11-g sample of adduct **8** was subjected to deprotection conditions in 28 mL of THF–$H_2O$. The reaction mixture was diluted with 300 mL of $H_2O$; 100 mL of pentane was added, and the two-phase mixture was filtered. Unreacted starting material was isolated from the pentane layer. The aqueous phase was saturated with NaCl and extracted with five 100-mL portions of methylene chloride, which were combined, dried, and concentrated to afford 614 mg (89%) of jacaranone, mp 75.5–78 °C. Recrystallization from ether–hexane gave colorless crystals: mp 80–81 °C (lit.[2b] mp 76–77 °C); IR ($CH_2Cl_2$) 3560, 3480, 1738, 1720, 1675, and 1635 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 7.04 (d, $J$ = 10 Hz, 2 H), 6.21 (d, $J$ = 10 Hz, 2 H), 4.20 (s, OH), 3.77 (s, 3 H), and 2.74 (s, 2 H); $m/e$ ($M^+$) 182.

Anal. Calcd for $C_9H_{10}O_4$: C, 59.33; H, 5.53. Found: C, 59.47; H, 5.66.

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**Registry No. 1c**, 71316-87-5; **1d**, 71316-88-6; **1e**, 60263-07-2; **3**, 40861-57-2; **4**, 71316-89-7; *cis*-**5**, 71316-90-0; *trans*-**5**, 71316-93-3; **6**, 71316-91-1; **7**, 71316-92-2; **8**, 71316-94-4; 2-lithio-1,3-dithiane, 36049-90-8; [(phenylthio)methyl]lithium, 13307-75-0; [(benzyloxy)methyl]lithium, 71316-95-5; methyl lithioacetate, 57570-85-1.

## Optical Activity as a Probe in the Examination of Alkoxyaluminohydride Disproportionations

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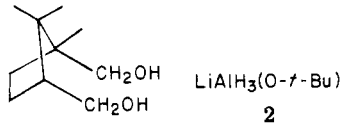
We recently described the effect of achiral alcohols upon the asymmetric reduction of acetophenone, using (+)-1,2,2-trimethyl-1,3-bis(hydroxymethyl)cyclopentane (**1**)–lithium aluminum hydride solutions.[1] It was apparent from this study that the disproportionation of intermediate alkoxyaluminohydrides was resulting in a decrease in the enantiomeric excess of methylphenylcarbinol.

There have been a variety of investigations into the alkoxyaluminohydride disproportionation process using stereochemical,[2,3] kinetic probes,[4] and direct chemical analysis.[5] In particular, the kinetic results of Wiegers and Smith[4] suggest that reducing solutions prepared from lithium aluminum hydride and methanol results in a disproportionation process which produces lithium aluminum hydride as the sole reducing agent. In contrast, their results suggest that reducing solutions prepared from lithium aluminum hydride and *tert*-butyl alcohol produce both lithium aluminum hydride and lithium *tert*-butoxyaluminotrihydride (**2**) as active reducing agents.




**1** **2**

We felt that optical activity could furnish a complementary third probe by which to investigate these disproportionation processes. If reducing solutions prepared from lithium aluminum hydride and methanol did produce lithium aluminum hydride as the sole reducing species, then the addition of **1** to this solution should produce the same reducing species as that obtained from lithium aluminum hydride and **1** prepared independently. We have previously shown[1] that this latter species gave a 7.7% enantiomeric excess of (+)-methylphenylcarbinol from the reduction of acetophenone.

Experimentally, this hypothesis was tested by adding a molar equivalent of methanol to lithium aluminum hydride in ether–THF (3:1).[6] After 1 h of reflux, a molar equivalent of **1** was added, and after an additional 1.5 h of reflux, a molar equivalent of acetophenone was added. This procedure resulted in a 70% reduction of acetophenone with a 7.4% enantiomeric excess of (+)-methylphenylcarbinol. This result is consistent with the Wiegers–Smith model for the alkoxyaluminohydride disproportionation where methoxide is the alkoxide species.

On the other hand, reducing solutions prepared from lithium aluminum hydride and *tert*-butyl alcohol which produce **2** and lithium aluminum hydride as the active reducing species, according to the Wiegers–Smith model, should produce two chiral reducing agents upon the addition of **1**. The chiral reagent derived from lithium aluminum hydride and **1** has just been described above. The effect of the other chiral reagent, derived from **2** and **1**, could be approximated from reducing solutions derived from lithium aluminum hydride and **1** followed by the addition of *tert*-butyl alcohol. We have previously described[1] this reducing solution and obtained a 13.1% enantimeric excess of (+)-methylphenylcarbinol in the reduction of acetophenone. Consequently, the addition of **1** to reducing solutions derived from lithium aluminum hydride and *tert*-butyl alcohol should give (+)-methylphenylcarbinol with an enantiomeric excess somewhere between 7.7% and 13.1% from the reduction of acetophenone. A theoretical value would be difficult to predict due to several factors: (1) the unknown molar ratio of lithium aluminum hydride to **2** under these conditions; (2) the difference in the rate reduction between the species derived from lithium aluminum hydride and **1** and the species derived from **2** and **1**; and (3) the former reducing species is a dihydride, whereas the latter species is a monohydride.

Experimentally, this hypothesis was tested by adding a molar equivalent of *tert*-butyl alcohol to lithium aluminum hydride in ether–THF (3:1).[7] After 1 h of reflux, a molar equivalent of **1** was added, and after an additional

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(6) This solvent system is identical with the one which resulted in the 7.7% enantiomeric excess described in the preceding paragraph and ref 1.
(7) This solvent is identical with the one which resulted in both the 7.7 and 13.1% enantiomeric excesses described in the preceding paragraph.

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1.5 h of reflux, a molar equivalent of acetophenone was added. This procedure resulted in a 62% reduction of acetophenone with an 8.3% enantiomeric excess of (+)-methylphenylcarbinol. This result is likewise consistent with the Wiegers–Smith model for reducing solutions derived from lithium aluminum hydride and *tert*-butyl alcohol.

Another aspect of reduction by alkoxyaluminohydride species involves the steric bulk imposed by the alkoxy unit. Numerous workers[2] have attested to the fact that such bulk imparts a slower rate of reduction for alkoxyaluminohydride species vs. their nonalkoxy counterpart. When Wiegers and Smith combined this feature with hindered ketone substrates, they found[4] that the kinetics describing such reductions pointed to a greater percentage of the reduction coming from lithium aluminum hydride rather than the alkoxyaluminohydride species. The most dramatic example was provided from the reduction of 2,4,6-trimethylbenzophenone by reducing solutions derived from lithium aluminum hydride and *tert*-butyl alcohol. The kinetics from this experiment suggest that the reduction was accomplished by lithium aluminum hydride.[4]

The production of chiral hydride reagents from lithium aluminum hydride and chiral alcohols is, of course, not immune to these disproportionation processes either. The low levels of enantiomeric excess[1] realized from the reducing solutions derived from lithium aluminum hydride and 1 implied that an appreciable amount of reduction was due to the achiral hydride species. We have previously reported[1] on experiments, involving excess hydride, which substantiated the disproportionation process. A further test of this contention would be the reduction of the hindered 2,4,6-trimethylbenzophenone by solutions composed of lithium aluminum hydride and 1. This reduction should give carbinol of low enantiomeric excess, and the overall yield, as well, should be predictably lower than when acetophenone was the substrate.

We found that the reduction of 2,4,6-trimethylbenzophenone by hydride solutions derived from lithium aluminum hydride and 1 was indeed quite different than that obtained when acetophenone was the substrate. The latter had given a 96% production of carbinol with a 7.7% enantiomer excess of the (+)-carbinol. The former gave only a 55% production of carbinol, and the resultant carbinol was optically inactive![8] The low level of reduction and the optical inactivity of the product are consistent with some disproportionation with reduction occurring via achiral lithium aluminum hydride.

Indeed, optical activity has proven to be a very useful probe for examining alkoxyaluminohydride disproportionations. The method is sensitive enough to distinguish between the different disproportionation modes obtained from lithium aluminum hydride and methanol solutions and those obtained from lithium aluminum hydride and *tert*-butyl alcohol. The probe is also sensitive enough to determine the major reducing species when hindered substrates such as 2,4,6-trimethylbenzophenone are used. The results are consistent with the stereochemical and kinetic results of previous workers.

## Experimental Section

**Acetophenone Reduction with Lithium Aluminum Hydride and Methanol Solutions.** To a 250-mL, three-necked, round-bottomed flask equipped with a mechanical stirrer, reflux condenser, and addition funnel were added 1.00 g (0.025 mol) of lithium aluminum hydride and 100 mL of anhydrous ether. To this stirred solution was added 0.8 g (0.025 mol) of methanol in 20 mL of ether. The reaction was heated to reflux for 1 h. Then, 4.3 g (0.025 mol) of 1 in 40 mL of THF was added dropwise, and the reaction was heated for another 1.5 h. The reaction was then cooled to room temperature, and 3.0 g (0.025 mol) of acetophenone in 20 mL of ether was added, dropwise. After 2 h of additional reflux, the reaction was cooled to room temperature and quenched by the dropwise addition of 1 mL of water, followed by 1 mL of 15% aqueous sodium hydroxide, and finally by 3 mL of water. The precipitate was filtered and washed with 25 mL of ether. The filtrate was dried quickly over anhydrous sodium sulfate, filtered, and evaporated in vacuo. The resultant residue was purified and analyzed as previously described.[1]

**Acetophenone Reduction with Lithium Aluminum Hydride and *tert*-Butyl Alcohol Solutions.** The reaction was carried out as described above except that 0.025 mol of *tert*-butyl alcohol was used in place of methanol.

**2,4,6-Trimethylbenzophenone Reduction with Lithium Aluminum Hydride and 1.** To a 250-mL, three-necked, round-bottomed flask equipped with a mechanical stirrer, reflux condenser, and addition funnel were added 0.76 g (0.02 mol) of lithium aluminum hydride and 100 mL of anhydrous ether. To this stirred solution was added, dropwise, 3.4 g (0.02 mol) of 1 in 40 mL of THF. The reaction was heated to reflux for 1 h after the addition of 1 had been completed. The reaction was then cooled to room temperature, and 8.9 g (0.04 mol) of 2,4,6-trimethylbenzophenone in 40 mL of ether was added, dropwise. After 2 h of additional reflux, the reaction was cooled and worked up as described above.

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**Registry No.** 1, 68510-42-9; acetophenone, 98-86-2; 2,4,6-trimethylbenzophenone, 954-16-5; lithium aluminum hydride, 16853-85-3; methanol, 67-56-1; *tert*-butyl alcohol, 75-65-0.

(8) An $\alpha$ value of 0.001 would have been detectable.

# Stereospecific Synthesis of $\alpha$-Amino-$\beta$-hydroxy Acids

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$\alpha$-Amino-$\beta$-hydroxy acids have been prepared by various different methods, including epoxidation of unsaturated carboxylic acids and subsequent amination,[2] condensation of isonitriles with aldehydes or ketones,[3] and base-catalyzed reactions of glycine (or its derivatives) with carbonyl compounds.[4] Most of these procedures suffer however from one or another limitation, requiring either scarce starting materials or drastic reaction conditions, or providing mixtures of stereoisomers. We wish to describe a promising new method for the synthesis of $\alpha$-amino-$\beta$-hydroxy acids which affords exclusively either the erythro or threo isomers in an efficient one-pot procedure. The procedures involve base-catalyzed condensation of glycine derivatives with carbonyl compounds: *N,N*-bis(trimethylsilyl)glycine trimethylsilyl ester (1) serving as

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