Alkylmetal Asymmetric Reduction. 9.[1] Asymmetric Reduction of Alkyl Phenyl Ketones by Sterically Hindered Chiral Organoaluminum Compounds

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Optically active aliphatic organoaluminum compounds, containing groups of different steric requirements on the β-chiral carbon atom, have been prepared via an alkyl exchange reaction from the corresponding trialkylboranes. The organoaluminum compounds were allowed to react with alkyl phenyl ketones to yield optically active alkylphenylcarbinols. The extent of asymmetric reduction and the absolute configuration of the predominant enantiomeric carbinol were found to depend both on the structure of the alkyl substituent on the aluminum atom and on the experimental conditions adopted. The stereoselectivity of the reduction process is discussed and rationalized in terms of the previously suggested stereochemical approach.

Recently we have investigated the reduction of alkyl phenyl ketones by optically active aliphatic Grignard reagents containing an isopropyl or a *tert*-butyl group on the chiral carbon atom.[2] The data obtained have shown an anomalous trend in the asymmetric reduction of ketones by these sterically hindered Grignard reagents.[2] In fact, simple considerations of conformational analysis do not correctly predict the absolute configuration of the predominant enantiomeric carbinol in all the cases investigated, although the general trend may be rationalized in terms of the effective sizes of the groups being compressed in the transition states.

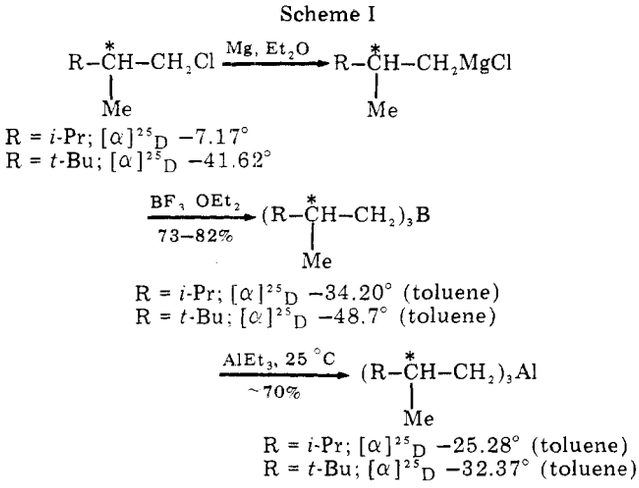
Therefore, taking into account the ability of chiral organoaluminum compounds to reduce carbonyl compounds asymmetrically,[3,4] we have undertaken this research to further check the stereochemical picture previously proposed[3-5] by using tris[(*R*)-2,3-dimethylbutyl]aluminum [(*R*)Al2,3DMB] and tris[(*R*)-2,3,3-trimethylbutyl]aluminum [(*R*)-Al2,3,3TMB].

Results and Discussion

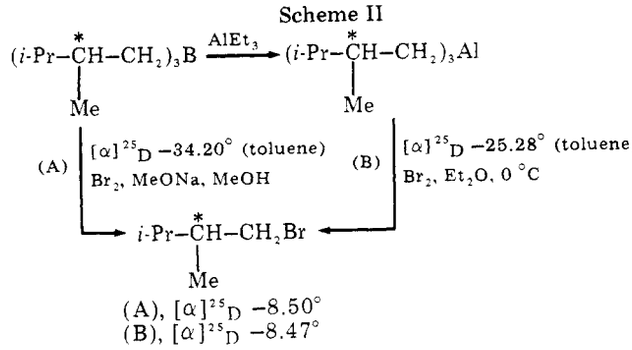
Synthesis of the Organometallic Compounds. The preparation of the optically active trialkylaluminum compounds was carried out via the corresponding trialkylboranes (Scheme I). Tris[(*S*)-2,3-dimethylbutyl]boron [(*S*)B2,3DMB] and tris[(*S*)-2,3,3-trimethylbutyl]boron [(*S*)B2,3,3TMB] were obtained by the reaction of (*R*)-2,3-dimethylbutyl- and (*R*)-2,3,3-trimethylbutylmagnesium chloride, respectively, with a slight excess of boron trifluoride diethyl etherate.[6] The boron compounds were isolated in a good yield by simple distillation at reduced pressure and characterized through quantitative determination of the boron.[6]

The trialkylboranes were then converted into the corresponding trialkylaluminum compounds by an alkyl exchange reaction with $AlEt_3$ (Scheme I), according to a known procedure.[7] Purification of the aluminum compounds was achieved by molecular distillation at 10^{-5} mmHg since the usual distillative procedure at 0.05 mmHg causes the formation of dialkylaluminum monohydride and olefin. The trialkylalanes were characterized through quantitative determination of the aluminum[8] and through cryoscopic molecular weight determinations.

Scheme I



Scheme II



The minimum optical purity of the organometallic compounds was evaluated by their stereospecific conversion into optically active organic products. So (*S*)B2,3DMB and (*R*)-Al2,3DMB were related to (*R*)-1-bromo-2,3-dimethylbutane[9] by reaction with bromine and sodium methoxide in methanol solution[10] and with bromine in diethyl ether at 0 °C,[11] respectively (Scheme II). Based on the maximum rotatory power of the alkyl bromide,[9b-d,12] both (*S*)B2,3DMB and (*R*)-Al2,3DMB were assigned the same optical purity as that of the starting alkyl chloride (Scheme I). Accordingly, a sample of (*R*)Al2,3,3TMB yielded (*R*)-1-bromo-2,3,3-trimethylbutane (Scheme III). In order to determine the minimum optical purity of this product, a sample of (*R*)-1-bromo-2,3,3-trimethylbutane, $[\alpha]^{25}_D$ −31.83° [from (*R*)-2,3,3-trimethyl-1-butanol, $[\alpha]^{25}_D$ −26.22° (ethanol)[13]], was converted into (*S*)-3,4,4-trimethylpentanoic acid, $[\alpha]^{25}_D$ −13.58° (ethanol), optical purity 65.9%,[2] through the corresponding Grignard reagent and successive treatment with carbon dioxide. Un-

Scheme III

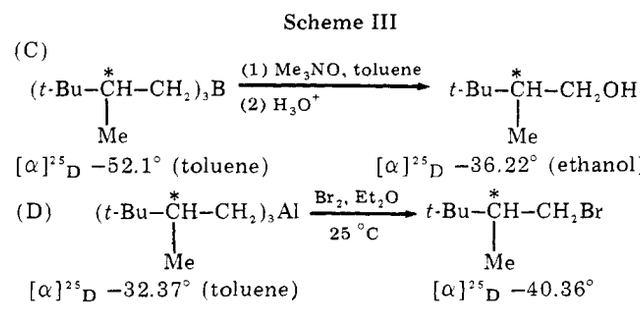


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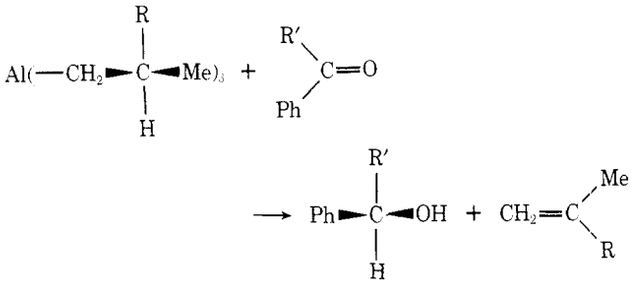
Table I. Asymmetric Reduction of Phenyl Alkyl Ketones by Optically Active Organoaluminum Compounds



R	R′	Temp, °C	Asymmetric reduction, %	$\Delta\Delta G^{\ddagger}$,[a] cal/mol
Et[b]	Et	0	13.2	−144
	i-Pr	0	44.3	−515
	t-Bu	0	29.9	−335
i-Pr	Et	0	22.2	−245
	i-Pr	0	56.1	−688
	t-Bu	0	25.8	−286
t-Bu	Et	0	23.0	−254
		68.7	32.2	−453
	i-Pr	0	19.9	−219
		36	57.4	−802
		68.7	53.1	−803
		98.4	44.4	−703
	t-Bu	0	[12.8][c]	+139
		36	0.0	
		68.7	13.7	−187

[a] Calculated from $\Delta\Delta G^{\ddagger} = -RT \ln (k_R/k_S) = -RT \ln([R]/[S]) = -RT \ln [(1 + a)/(1 - a)]$, where a = asymmetric reduction. [b] See ref 5. [c] Brackets indicate opposite configuration.

fortunately the bromination of (*S*)B2,3,3TMB, according to the above procedure,[10] gives rise, in low yield, to the corresponding alkyl bromide together with considerable amounts of byproducts. Therefore, (*S*)B2,3,3TMB was converted into (*R*)-2,3,3-trimethyl-1-butanol[13] by reaction with trimethylamine oxide in boiling toluene[14] (Scheme III). Also in these cases the optical purity of the products of conversion of the organometallic compounds was the same as that of the starting alkyl chloride. The overall results therefore confirm the stereospecificity of the schemes of sequences adopted, and in particular, that of the alkyl exchange reaction.[7]

Asymmetric Reduction of Alkyl Phenyl Ketones. The asymmetric reductions have been carried out in hydrocarbon solvents, following previously published procedures;[3-5] the results are summarized in Table I. Analogous to what has been observed for the reduction of ketones by tris[(*S*)-2-methylbutyl]aluminum [(*S*)Al2MB],[3] (*R*)Al2,3DMB and (*R*)-Al2,3,3TMB react with alkyl phenyl ketones to give essentially the corresponding carbinol. The reactions are very fast in the case of Al2,3DMB, the reduction being practically complete within 30 min, but the reduction rate drops using Al2,3,3TMB, and the reaction requires more than 1 h at 0 °C. In all the cases investigated, the recovered carbinols were optically active and had the absolute *R* configuration, with the exception of the reduction product from phenyl *tert*-butyl ketone by (*R*)-Al2,3,3TMB at 0 °C (Table I).

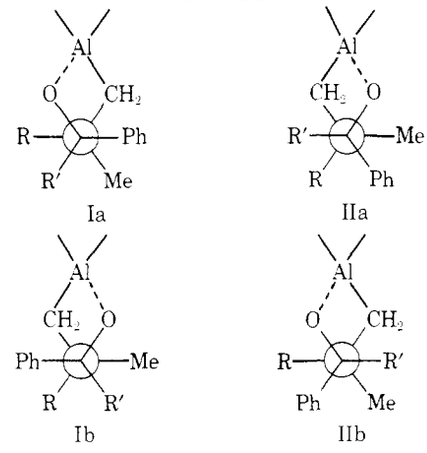
By comparing these results with those previously reported,[3,5] we can observe that the stereoselectivity of reduction depends upon the structure of the alkyl phenyl ketone employed and on that of the alkyl substituent on the chiral carbon atom in the position β to the aluminum atom. In particular, at 0 °C, on increasing the bulkiness of the *R* alkyl group of the aluminum compound in the order Et < *i*-Pr < *t*-Bu, the extent of asymmetric reduction of ethyl phenyl ketone increases while that of *tert*-butyl phenyl ketone decreases. Regarding the reduction of isopropyl phenyl ketone at 0 °C, the highest value of stereoselectivity is encountered when the reducing agent is (*R*)Al2,3DMB (Table I). The trend of asymmetric reduction of phenyl alkyl ketones by (*R*)-Al2,3DMB is, however, similar to that observed in the reduction of the same series of ketones by (*S*)Al2MB,[3] while the stereoselectivity of the reduction at 0 °C by (*R*)Al2,3,3TMB decreases in the order of Et > *i*-Pr > *t*-Bu. Contrary to what has been observed for the reduction of alkyl phenyl ketones by (*S*)Al2MB,[5] in the case of (*R*)Al2,3,3TMB an increase of reaction temperature generally results in an increase of stereoselectivity of the reduction. It is noteworthy that the reduction of *tert*-butyl phenyl ketone by (*R*)Al2,3,3TMB at 69 °C occurs with a reversal of the stereochemistry at 0 °C (Table I).

On the basis of our previous considerations,[3-5] the reduction of ketones by chiral organoaluminum compounds is assumed to proceed via diastereomeric cyclic transition states, not essentially planar but able to minimize their mutual steric and electronic interactions by assuming more of a chair-like conformation.[15] Thus, we can now consider four transition-state conformations, viewed as Newman-type projections along the C - - - H - - - C axis (Scheme IV). Under the assumption that electronic interactions play the main role in stabilizing the transition states, the conformations IIa and IIb must have the highest energies. Therefore the extent of stereoselectivity should depend on the balance between the conformations Ia and Ib in relation to the different ability of the groups to minimize their steric compression. Since the conformation Ia is more favored than Ib for steric requirements, the carbinol from asymmetric induction must have the absolute *R* configuration. According to this picture, when R or R′ increase in bulk, a buttressing effect will operate in both the conformations to separate R and R′. So the conformation Ib is further destabilized, as the phenyl and R groups are pushed together. Consequently, the extent of stereoselectivity might rise with increasing bulk of the alkyl groups both in the reagent and in the substrate.

However, this stereochemical approach does not fit all the results obtained. In fact, when a *tert*-butyl group is present either in the reagent or in the substrate, the stereoselectivity of the reduction drops, and when the *tert*-butyl phenyl ketone is reduced at 0 °C by (*R*)Al2,3,3TMB, the carbinol recovered has the absolute configuration opposite to the predicted one (Table I).

In this respect a helpful suggestion is to consider that as the alkyl groups both in the organoaluminum compound and in the ketone increase in bulk, the conformational mobility of the phenyl group decreases, its size changing formally.[3,5] On this basis the anomalous results (Table I), and in particular those relating to the reduction by (*R*)Al2,3,3TMB, may be due

Scheme IV



to a combined effect of noncoplanarity and consequent change in steric and electronic interactions of the phenyl group. If the electronic interactions cannot contribute any more to stabilize the transition-state conformations, it is evident that conformation IIb, leading to (*S*)-carbinol, may become the most stable one for steric reasons, and its contribution to the stereoselectivity of the reduction will become more important the more conformationally rigid the transition state becomes. In this manner we can rationalize both the decrease in stereoselectivity observed in the reduction of *tert*-butyl phenyl ketone as well as the formation of the wrong enantiomer when the same ketone is reduced by (*R*)Al2,3,3TMB at 0 °C.

An increase of the reaction temperature will tend to reduce the conformational rigidity of the groups and thus permit the electronic interactions to again stabilize the conformation Ia, leading to the (*R*)-carbinol. So one can predict that increasing the reaction temperature will result in an increase of the extent of asymmetric reduction. Indeed the results obtained at different temperatures (Table I) are consistent with this last hypothesis,[16] confirming the stereochemical approach previously proposed.[3-5] In this context, it is interesting to note that the reduction of *tert*-butyl phenyl ketone by (*R*)-Al2,3,3TMB at 69 °C leads to the formation of the predicted *R* enantiomer.

However, it is noteworthy that the free-energy differences, $\Delta\Delta G^{\ddagger}$, involved are generally relatively small, indicating subtle differences of the group interactions in the transition states, so that even minor changes in the experimental conditions may result in different stereochemical courses. Therefore, it appears that only a more accurate knowledge of other variables, e.g., reaction rate, solvent effect, etc., will clarify the actual nature of the transition-state models for asymmetric hydride transfer.

Experimental Section

Boiling points are uncorrected. GLC analyses (200 × 0.29 cm column packed with 8% Carbowax + 2% KOH on 80–100 mesh Chromosorb W) were performed on a Perkin–Elmer F 30A instrument with flame ionization detectors and nitrogen as a carrier gas, while preparative GLC was carried out on a Perkin-Elmer F 21 chromatograph. Optical rotations were measured with a Perkin-Elmer 142 photopolarimeter and refer to pure liquids unless otherwise stated.

The solvents and commercial reagents were distilled and dried by conventional methods before use. The ketones employed were obtained by purification of commercial products; *tert*-butyl phenyl ketone was prepared according to the procedure already mentioned.[3] (*R*)-1-Chloro-2,3-dimethyl- and (*R*)-1-chloro-2,3,3-trimethylbutane were synthesized from the corresponding optically active 1-butanols by treatment with thionyl chloride in pyridine.[2] All the organoaluminum compounds were stored under nitrogen in sealed glass vials in weighed amounts, and all the reactions were carried out in a dry purified nitrogen atmosphere.

Tris[(*S*)-2,3-dimethylbutyl]boron [(*S*)B2,3DMB]. Freshly distilled boron trifluoride etherate (40.8 g, 0.290 mol) was added dropwise at room temperature to an ethereal solution of the Grignard reagent from (*R*)-1-chloro-2,3-dimethylbutane (104 g, 0.86 mol), $[\alpha]^{25}_{D}$ −7.17°. The reaction mixture was refluxed (4 h), cautiously hydrolyzed with dilute sulfuric acid, and extracted with ether. The solvent was evaporated under reduced pressure, and the crude product was twice distilled (53.6 g, 73% yield): bp 65.5 °C (0.1 mmHg); $[\alpha]^{25}_{D}$ −34.20° (*c* 2.99, toluene).

Anal.[6] Calcd for $C_{18}H_{39}B$: B, 4.05. Found: B, 4.19.

Tris[(*S*)-2,3,3-trimethylbutyl]boron [(*S*)B2,3,3TMB]. By the same general procedure, (*R*)-1-chloro-2,3,3-trimethylbutane, $[\alpha]^{25}_{D}$ −41.62°, was converted (73% yield) into (*S*)B2,3,3TMB: bp 80 °C (0.005 mmHg); $[\alpha]^{25}_{D}$ −48.7° (*c* 9.32, toluene).[17]

Anal.[6] Calcd for $C_{21}H_{45}B$: B, 3.50. Found: B, 3.52.

Tris[(*R*)-2,3-dimethylbutyl]aluminum [(*R*)Al2,3DMB]. To (*S*)B2,3DMB (53.6 g, 0.201 mol), $[\alpha]^{25}_{D}$ −34.20° (toluene), was added triethylaluminum (22.9 g, 0.201 mol) at room temperature. After 2 h, all of the volatile products were removed from the mixture by prolonged evacuation (48 h, 0.5 mmHg) with stirring at 25 °C and the residue was transferred under nitrogen into a molecular distillation apparatus. Pure (*R*)Al2,3DMB was recovered at 4 × 10^{-5} mmHg (oil bath temperature, 70°C; 66% yield), $[\alpha]^{25}_{D}$ −25.28° (*c* 4.03, toluene).

Anal.[8] Calcd for $C_{18}H_{39}Al$: Al, 9.50; mol wt, 282.4. Found: Al, 9.52; mol wt (cryoscopic determination in benzene), 282.

Tris[(*R*)-2,3,3-trimethylbutyl]aluminum [(*R*)Al2,3,3TMB]. By an analogous procedure, (*S*)B2,3,3TMB, $[\alpha]^{25}_{D}$ −48.7° (toluene), yielded (75%) (*R*)Al2,3,3TMB, $[\alpha]^{25}_{D}$ −32.37° (*c* 5.94, toluene), after molecular distillation (5 × 10^{-5} mmHg; oil bath temperature, 75 °C).

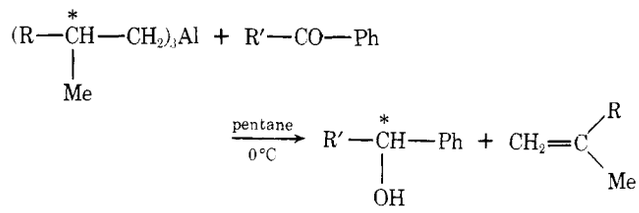
Anal.[8] Calcd for $C_{21}H_{45}Al$: Al, 8.31; mol wt, 324.5. Found: Al, 8.33; mol wt (cryoscopic determination in benzene), 327.

(*R*)-1-Bromo-2,3-dimethylbutane. A. From (*S*)B2,3DMB. An ice-cooled solution of (*S*)B2,3DMB (5.97 g, 22.4 mmol), $[\alpha]^{25}_{D}$ −34.20° (toluene), in 30 mL of dry THF was treated with bromine (14.3 g, 89.6 mmol), followed by a dropwise addition of a 4.16-M solution (32 mL) of sodium methoxide in anhydrous methanol at such a rate that the temperature of the reaction mixture never rose above 5 °C. The mixture was allowed to warm to room temperature and was worked up as previously described.[10] Distillation gave (*R*)-1-bromo-2,3-dimethylbutane (pure by GLC analysis) (7.7 g, 69.6% yield): bp 97 °C (165 mmHg); n^{25}_{D} 1.4486; $[\alpha]^{25}_{D}$ −8.50° (lit.[9b] bp 140 °C; d^{25}_{4} 1.187).

B. From (*R*)Al2,3DMB. Bromine (6.14 g, 38.4 mmol) was added dropwise at −25 °C to a solution of (*R*)Al2,3DMB (3.62 g, 12.8 mmol), $[\alpha]^{25}_{D}$ −25.28° (toluene), in ether (40 mL). The reaction mixture was kept at 25 °C (1 h), hydrolyzed with dilute sulfuric acid, and extracted with ether. Careful distillation gave pure (*R*)-1-bromo-2,3-dimethylbutane (3.6 g, 57% yield): n^{25}_{D} 1.4486; $[\alpha]^{25}_{D}$ −8.47°.

(*R*)-1-Bromo-2,3,3-trimethylbutane. A. From (*R*)-2,3,3-Trimethyl-1-butanol. A sample of (*R*)-2,3,3-trimethyl-1-butanol (30 g, 0.26 mol), $[\alpha]^{25}_{D}$ −26.22° (*c* 2.41, ethanol),[13] in pyridine (7.3 mL) was treated at 0 °C with phosphorus tribromide (28 g, 0.10 mol), and the reaction mixture was kept at 0 °C for 3 h. The crude bromide was distilled at reduced pressure (20 mmHg), diluted with hexane, and treated with concentrated sulfuric acid. The organic layer was washed with water and dried (Na_2SO_4). Distillation gave (*R*)-1-bromo-

Table II. Experimental Reduction Data



Run	R	R′	Carbinol: Conversion,[a] %	Carbinol: $[\alpha]^{25}_{D}$ (*c*, ether),[b] deg
1[c]	*i*-Pr	Et	87	+4.56 (neat)
2[c]			89	+8.36 (6.64)
3[c]		*i*-Pr	96	+19.52 (8.29)
4[c]			89	+19.24 (4.77)
5[c]		*t*-Bu	98	+6.67 (8.79)
6[c]			99	+6.87 (7.10)
7[d]	*t*-Bu	Et	63	+5.26 (neat)
8[d]			75	+5.46 (neat)
9[e]		*i*-Pr	90	+5.85 (6.90)
10[d]			70	+7.98 (9.06)
11[d]		*t*-Bu	99	−3.74 (7.91)
12[d]			95	−3.76 (8.05)
13[f,g]		*i*-Pr	97	+22.41 (8.08)
14[d,g]		*t*-Bu	99	+0.94 (8.74)
15[d,g]			99	−1.21 (8.52)
16[f,h]		Et	92	+7.59 (neat)
17[f,h]		*i*-Pr	96	+20.35 (10.27)
18[d,h]		*t*-Bu	95	+4.10 (8.22)
19[d,h]			95	+4.06 (7.85)
20[f,i]		*i*-Pr	93	+17.36 (9.45)

[a] Based on GLC analyses of the crude products. [b] See ref 2. [c] (*R*)Al2,3DMB, $[\alpha]^{25}_{D}$ −25.28° (toluene). [d] (*R*)Al2,3,3TMB, $[\alpha]^{25}_{D}$ −32.37° (toluene). [e] (*R*)Al2,3,3TMB, $[\alpha]^{25}_{D}$ −24.48° (toluene). [f] (*R*)Al2,3,3TMB, $[\alpha]^{25}_{D}$ −32.66° (toluene). [g] In pentane at 36 °C. [h] In hexane at 68.7 °c. [i] In heptane at 98.4 °C.

2,3,3-trimethylbutane (46% yield), which was further purified by preparative GLC (20% Carbowax 20M, 100 °C): bp 82 °C (60 mmHg); n^{25}_D 1.4545; d^{25}_4 1.1545; $[\alpha]^{25}_D$ −31.83°.

In order to determine its optical purity, (*R*)-1-bromo-2,3,3-trimethylbutane (8.7 g, 48.3 mmol) was converted into the corresponding Grignard reagent, which was then carboxylated to yield 42% of (*S*)-3,4,4-trimethylpentanoic acid: bp 126 °C (18 mmHg); n^{25}_D 1.4312; $[\alpha]^{25}_D$ −13.58° (*c* 3.84, ethanol).[2]

B. From (*R*)Al2,3,3TMB. An ethereal solution of (*R*)Al2,3,3TMB (2.0 g, 61.6 mmol), $[\alpha]^{25}_D$ −32.37° (toluene), was treated at room temperature with bromine (3.28 g, 20.5 mmol), and the reaction mixture was worked up as described above. After preparative GLC (20% Carbowax 20M, 100 °C), a sample of (*R*)-1-bromo-2,3,3-trimethylbutane, n^{25}_D 1.4545, $[\alpha]^{25}_D$ −40.36°, was recovered.

(*R*)-2,3,3-Trimethyl-1-butanol from (*S*)B2,3,3TMB. A solution of (*S*)B2,3,3TMB (3.5 g, 11.3 mmol), $[\alpha]^{25}_D$ −52.1° (*c* 6.08, toluene), in toluene (40 mL) was dropped into a boiling suspension of trimethylamine oxide (2.6 g, 34.4 mmol) in toluene (13 mL), and the reaction mixture was refluxed for 1 h. After removal of the solvent, the residue was treated with dilute sulfuric acid and extracted with ether. Distillation gave (*R*)-2,3,3-trimethyl-1-butanol (1.9 g, 50% yield), which was purified by preparative GLC (20% Carbowax 20M, 100 °C), $[\alpha]^{25}_D$ −36.22° (*c* 3.54, ethanol).[13]

Asymmetric Reductions of Alkyl Phenyl Ketones. A. By (*R*)Al2,3DMB in Pentane at 0 °C (runs 1–6). The following procedure (run 3, Table II) is representative of all the experiments. Isopropyl phenyl ketone (1.57 g, 10.6 mmol) in anhydrous pentane (10 mL) was added rapidly at 0 °C to a pentane solution (20 mL) of (*R*)-Al2,3DMB (3.15 g, 11.2 mmol), $[\alpha]^{25}_D$ −25.28° (toluene), in a flame-dried two-neck 100-mL flask fitted with a reflux condenser, a dropping funnel, and a magnetic stirrer. A yellow–orange coloration developed immediately and faded slowly. After 2 h the resulting mixture was cautiously hydrolyzed with dilute sulfuric acid and the organic products were extracted with purified ether. GLC analysis of the ether layer showed the presence of unreacted ketone (4%). Preparative GLC purification (8% Carbowax 20M + 2% KOH, 160 °C) afforded isopropyl phenyl carbinol: bp 104 °C (18 mmHg); n^{25}_D 1.5114; $[\alpha]^{25}_D$ +19.52° (*c* 8.29, ether).

B. By (*R*)Al2,3,3TMB in Pentane at 0 °C (runs 7–12). In a typical run, to an ice-cooled solution of (*R*)Al2,3,3TMB (2.83 g, 8.7 mmol), $[\alpha]^{25}_D$ −32.37° (toluene), in pentane (20 mL) was added rapidly *tert*-butyl phenyl ketone (1.34 g, 8.3 mmol) in pentane (10 mL). After 2 h at 0 °C the resulting mixture was allowed to warm to room temperature (10 min) and then hydrolyzed and worked up as above. By preparative GLC, *tert*-butylphenylcarbinol, bp 115 °C (21 mmHg), $[\alpha]^{25}_D$ −3.74° (*c* 7.91, ether), was recovered.

C. By (*R*)Al2,3,3TMB in Pentane at 36 °C (runs 13–15). In a representative run, a solution of *tert*-butyl phenyl ketone (1.91 g, 11.8 mmol) in pentane (10 mL) was placed in an addition funnel and (*R*)Al2,3,3TMB (4.04 g, 12.5 mmol), $[\alpha]^{25}_D$ −32.37° (toluene), was placed in a second addition funnel. The ketone and trialkylaluminum were added simultaneously to boiling pentane (20 mL) at a rate such that reflux was always maintained. After 1 h, the reaction mixture was hydrolyzed and worked up as previously described. By preparative GLC, *tert*-butylphenylcarbinol, $[\alpha]^{25}_D$ −1.21° (*c* 8.52, ether), was obtained.

Runs 16–19 and 20 (Table II) were carried out using the same procedure at 68.7 and 98.4 °C in boiling hexane and heptane, respectively.

Registry No.—(*S*)Al2MB, 4023-25-0; (*R*)Al2,3DMB, 65337-63-5; (*R*)Al2,3,3TMB, 65337-64-6; 1-phenyl-1-propanone, 93-55-0; 2-methyl-1-phenyl-1-propanone, 611-70-1; 2,2-dimethyl-1-phenyl-1-propanone, 938-16-9; (*R*)-α-ethylbenzenemethanol, 1565-74-8; (*R*)-α-(1-methylethyl)benzenemethanol, 14898-86-3; (*R*)-α(1,1-dimethylethyl)benzenemethanol, 23439-91-0; (*S*)-α(1,1-dimethylethyl)benzenemethanol, 24867-90-1; (*S*)B2,3DMB, 65337-61-3; boron trifluoride etherate, 353-42-4; (*R*)-1-chloro-2,3-dimethylbutane, 20205-13-4; (*S*)B2,3,3TMB, 65337-62-4; (*R*)-1-chloro-2,3,3-trimethylbutane, 16726-89-9; triethylaluminum, 97-93-8; (*R*)-1-bromo-2,3-dimethylbutane, 15019-28-0; (*R*)-1-bromo-2,3,3-trimethylbutane, 64001-89-4; (*S*)-3,4,4-trimethylpentanoic acid, 64043-89-6; (*R*)-2,3,3-trimethyl-1-butanol, 13332-16-6.

References and Notes

(1) Part of this research has been presented at the 3rd IUPAC Conference on Physical Organic Chemistry, La Grande Motte, France, September 1976, Abstracts, p 21.
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(11) The stereospecificity of the procedure[10] was previously checked by converting a sample of tris[(*R*)-2-methylbutyl]boron, optical purity 96%,[6] into (*S*)-1-bromo-2-methylbutane (90% yield), optical purity 96%: P. Salvadori, L. Lardicci, and M. Stagi, *Gazz. Chim. Ital.*, **98**, 1400 (1968). Analogously, tris[(*S*)-2-methylbutyl]aluminum, optical purity 95.8%,[3] by bromination at 0 °C yielded (*R*)-1-bromo-2-methylbutane (64%), optical purity 95.6%.
(12) The maximum rotatory power reported, $[\alpha]^{25}_D$ 18.5°,[9a] is to be considered erroneous; in fact, a sample of the bromide, $[\alpha]^{25}_D$ −7.00°, through carboxylation of the corresponding Grignard reagent yielded (*R*)-3,4-dimethylpentanoic acid, $[\alpha]^{25}_D$ −7.38°, optical purity 59.8%: L. Lardicci, R. Rossi, S. Pucci, M. Aglietto, C. Botteghi, and P. Pino, *Chim. Ind. (Milan)*, **50**, 227 (1968). This result is in a good agreement with those of the sequences reported by other authors.[9b–d]
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(16) The decrease of stereoselectivity of the reduction of isopropyl phenyl ketone by (*R*)Al2,3,3TMB from 36 to 98 °C is not easily rationalized. In our opinion, taking into account that the reduction process is not reversible and not time dependent,[3,5] this trend might be due to the competitive thermal racemization of the organoaluminum compound in the reaction mixture, even if we can not exclude the eventual racemization of the aluminum alkoxide formed: G. Giacomelli, L. Lardicci, and R. Santi, *J. Org. Chem.*, **39**, 2736 (1974).
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