air was bubbled through the solution during irradiation. The solvent was evaporated. The orange oil solidified on standing. This was dissolved in 50 mL of a saturated Na_2CO_3 solution and then extracted with ether (3 × 30 mL). The Na_2CO_3 extracts were combined and acidified with concentrated HCl. This was back-extracted three times with 10 mL of ether and the ether extract was washed with water, dried over $MgSO_4$, and evaporated to give **4** (58%), mp 212–224 °C (lit.[12] mp 225–226 °C).

The ether extracts containing neutrals was washed with water, dried, and evaporated. The residue was chromatographed on a short alumina column with benzene/ether to give **5** (25%): mp 215–220 °C (lit.[9] mp 225–226 °C); MS, *m/e* 270 (M^+, 100), 242 (16).

Irradiation of Chrysene-5-carboxylic Acid (4). Preparation of Lactone 5. A solution of 70 mg of **4** and 4 mg of I_2 in 250 mL of benzene was irradiated as described above for 24 h. Evaporation of benzene gave a residue, which was applied on a thin-layer chromatography plate (benzene eluant), giving 35% of lactone **5** identical in all respects with a sample prepared above.

Pentacyclic Ketone 6. A 500-mg sample of chrysene-5-carboxylic acid (**4**) was placed in a Teflon container and cooled to −75 °C. Liquid HF was then added from an inverted gas cylinder with a direct inlet to the reaction vessel. The solution was stirred at −75 °C for 1 h and then placed in an ice bath and stirred overnight while slowly warming to room temperature, and the HF then was allowed to evaporate. The residue was dissolved in THF, adsorbed on silica gel, and evaporated to dryness. The adsorbed compound on silica gel was placed on a short silica gel column and eluted with benzene. A yellow solid **6** was obtained (65% yield), which was recrystallized from 95% ethanol: mp 205–207 °C; IR 1708 (C=O) cm^{-1}; NMR 8.68 (d 1 H), 8.52 (d, 1 H), 8.34 (s, 1 H), 8.22 (d, 1 H), 8.19 (d, 1 H), 8.12 (d, 1 H), 8.07 (d, 1 H), 7.95 (t, 1 H), 7.80–7.87 (m, 2 H); MS, *m/e* 254 (M^+, 100), 226 (20), 224 (30).

4,5-Methanochrysene (2). A solution of 100 mg of pentacyclic ketone **6**, 100 mg of KOH, and 100 mg of hydrazine hydrate in 10 mL of ethanediol was heated and stirred under nitrogen at 175 °C overnight. The suspension was allowed to cool, poured into 30 mL of H_2O, and extracted three times with 25 mL of $CHCl_3$. The $CHCl_3$ extracts were combined, washed with water, and evaporated. The residue was applied on a preparative silica gel (1-mm thickness) thin-layer chromatography plate and eluted with hexane. A white crystalline material (**2**) was obtained (60% yield): mp 174–176 °C (lit.[5] mp 171–173 °C); IR (KBr) 1403, 822, 767, 750 cm^{-1}; NMR 8.65 (d, 1 H), 8.49 (d, 1 H), 8.04 (d, 1 H), 7.98 (d, 1 H), 7.93 (s, 1 H), 7.86 (t, 1 H), 7.5–7.7 (m, 4 H), 4.47 (s, 2 H); MS *m/e* 240 (M^+, 100), 239 (70); UV (EtOH, 95%) max 327, 313, 302, 267, 261, 218 nm.

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Registry No. **2**, 202-98-2; **3**, 71432-05-8; **5**, 71432-00-3; **6**, 86853-91-0; **4**, 68723-48-8.

Asymmetric Reduction of Aliphatic Ketones with the Reagent Prepared from (*S*)-(−)-2-Amino-3-methyl-1,1-diphenylbutan-1-ol and Borane

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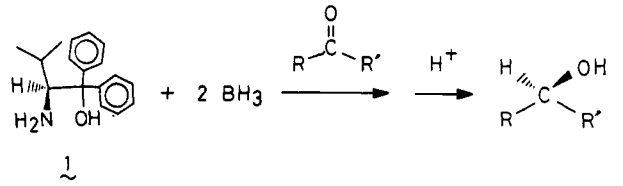
In asymmetric synthesis, both high stereoselectivity and practical usefulness of the reagent have been important subjects. From this point of view, the use of chirally modified metal hydrides for the asymmetric reduction of prochiral ketones has continued to be actively studied. The most widely studied examples are those using lithium aluminum hydride (LAH) modified by optically active alcohols and amines, some of which give substantial stereoselectivities in reductions of α,β-unsaturated ketones such as acylophenone,[1-4] enones,[5,6] and ynones.[7-9] Only limited success, however, has been achieved for aliphatic ketones. For example, the chiral binaphthyl/LAH[4] and chiral diamine/LAH,[3] which are highly effective for aromatic ketones, reduced 2-octanone in only 24% ee and 26% ee, respectively. Besides chirally modified LAH, (bornyloxy)aluminum dichloride,[10] dipinanylborane,[11] and lithium trialkylborohydride (Li(HB-IPC-9-BBN))[12] were examined for the asymmetric reduction of aliphatic ketones to give optical yields below 50% ee. For example, 3,3-dimethyl-2-butanone was tested with these reagents to give the alcohol with 28% ee at most to a low of 3% ee.

Scheme I



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Very recently, lithium trialkylborohydride, NB-Enantride (Aldrich), which is prepared by hydroboration of 6,6-dimethyl-2-[2-(phenylmethoxy)ethyl]bicyclo[3.1.1]-hept-2-ene(nopol benzyl ether) with 9-borabicyclo[3.3.1]-nonane (9-BBN) followed by treatment with *tert*-butyllithium, has been shown to be a very effective chiral reducing agent for the reduction of straight-chain aliphatic ketones.[13] Asymmetric reduction of 2-octanone with NB-Enantride at −78 °C gave (*S*)-2-octanol in 79% ee, which is the highest value so far reported for aliphatic secondary alcohols. However, NB-Enantride was not effective for 3,3-dimethyl-2-butanone, which has a larger steric difference in the alkyl groups on both sides of the carbonyl group.

We have observed that the reagent prepared from (*S*)-(−)-2-amino-3-methyl-1,1-diphenylbutan-1-ol (**1**) and borane can be successfully used in asymmetric reduction of aromatic ketones to give the (*R*)-benzyl alcohols in 94–100% ee.[14] These results encourage us to apply the reagent to asymmetric reduction of aliphatic ketones. We now disclose our finding that the reduction of aliphatic ketones with the reagent prepared from **1** and borane

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Table I. Asymmetric Reduction of Aliphatic Ketones with the Reagent Prepared from 1 and Borane in THF at 30 °C for 2 h[a]

		alcohol produced[b]		
run	ketone	$[\alpha]_D$, deg	optical yield, %	abs config
1	$CH_3(CH_2)_3COCH_3$	−6.73[d]	55	*R*
2	$CH_3(CH_2)_4COCH_3$	−6.36[e]	56	*R*
3	$CH_3(CH_2)_5COCH_3$	−5.86[f]	58	*R*
4	$(CH_3)_2CHCOCH_3$	−3.21[g]	60	*R*
5	$(CH_3)_2CHCH_2COCH_3$	−12.48[h]	61	*R*
6	$(CH_3)_3CCOCH_3$	−5.98[i]	73	*R*
7[c]	$(CH_3)_3CCOCH_3$	−6.32	78	*R*

[a] Conditions: amino alcohol 1, 10 mmol; borane, 20 mmol; ketone, 8 mmol. The ratio of 1, borane, and ketone was 1:2.0:0.8. [b] Based on relative GC peak areas of alcohol and unchanged ketone; all yields were 100%. [c] Reaction was carried out at 0 °C. [d] Maximum value for $[\alpha]_D$ is −11.6° (neat) (see Pickard, R. H.; Kenyon, J. *J. Chem. Soc.* **1911**, *99*, 45). [e] Maximum value for $[\alpha]_D$ is +11.45° (ethanol) (see "Dictionary of Organic Compounds", 5th ed.; Buckingham, J., Ed.; Chapman and Hall: New York, 1982; Vol. 3. [f] Maximum value for $[\alpha]_D$ is +10.1° (*c* 5.575, ethanol) (see Hill, R. K. *J. Am. Chem. Soc.* **1958**, *80*, 1611). [g] Maximum value for $[\alpha]_D$ is +5.34° (neat) (see Pickard, R. H.; Kenyon, J. *J. Chem. Soc.* **1913**, *103*, 1957). [h] Maximum value for $[\alpha]_D$ is −20.5° (neat) (see Levene, P. A.; Rothen, A. *J. Org. Chem.* **1936**, *1*, 76). [i] Maximum value for $[\alpha]_D$ is +8.10° (neat) (see Newman, P.; Lutkin, P.; Mislow, K. *J. Am. Chem. Soc.* **1958**, *80*, 465).

(Scheme I) provides high optical yields of the corresponding chiral aliphatic secondary alcohols at 30 °C (Table I).

Reduction of aliphatic ketones were carried out by using a procedure similar to that in a previous paper on aromatic ketones.[14,15] Complete reduction could be accomplished in 2 h at 30 °C in tetrahydrofuran (THF). Asymmetric inductions obtained with this reagent were above 50% ee in all cases. The chiral auxiliary 1 could be easily separated and recovered without any racemization to recycle. The optical purities were determined by measuring the optical rotation compared with the maximum value reported. All of the produced alcohols have *R* configuration in excess.

Fairly good enantioselectivities were obtained in asymmetric reduction of even straight-chain aliphatic ketones, so the exploited reagent has an ability to discriminate only a small difference of steric size between R and R′ on both sides of the carbonyl group. Unlike NB-Enantride reduction as reported previously, enantioselectivity of the present reagent clearly reflects the order of steric bulkiness of alkyl chain: a longer chain gave a higher selectivity in normal alkyl ketones (runs 1–3), an isoalkyl chain was superior to a normal alkyl chain in selectivity (runs 4, 5), and a tertiary alkyl chain had the most effective steric hindrance (runs 6, 7). Reduction of 3,3-dimethyl-2-butanone yielded (*R*)-(−)-3,3-dimethyl-2-butan-1-ol in 73% ee at 30 °C. It is noteworthy that this system realizes a high enantioselectivity in a mild condition. Lowering of the reaction temperature from 30 to 0 °C resulted in somewhat better enantioselectivity (run 7), again with a quantitative chemical yield. Furthermore, ready accessibility of 1, prepared from a commercially available (*S*)-valine, makes this reagent attractive.

Experimental Section

All reactions were carried out under an atmosphere of nitrogen. Tetrahydrofuran (THF) was heated under reflux over sodium metal and distilled from lithium aluminum hydride in a nitrogen atmosphere. The aliphatic ketones commercially purchased were dried and distilled over calcium hydride. The ketones were confirmed to be pure by GC and NMR. Borane was prepared by the reaction of sodium borohydride with trifluoroborane diethyl ether according to the procedure of Brown.[16] (*S*)-Valine (from Nihon Rika Yakuhin Co.) was used without purification. (*S*)-Valine methyl ester hydrochloride was prepared by the reaction of (*S*)-valine with dimethyl sulfate derived from methanol and thionyl chloride, according to the published procedure,[17] and it was confirmed to be pure by the optical rotation ($[\alpha]^{25}_D$ +23.5° (*c* 2.0, methanol) (lit.[18] $[\alpha]^{21}_D$ +23.5° (*c* 2, methanol)) and the melting point (167–168 °C (lit.[18] mp 167.5–168 °C)). All the materials described were stored under nitrogen prior to use. GC was performed on a Yanaco G180 instrument with a stainless steel analytical column (3 m × 3 m) packed with PEG20M on Diasolid L. The ratio of alcohols and unchanged ketones were determined by their peak areas. NMR spectra were run on a JEOL JNM-PMX-60 spectrometer. Optical rotations were taken on a JASCO DIP-140 digital polarimeter using a 1-cm thermostated microcell. IR spectra were measured with a JASCO A-3 instrument for Nujol mulls.

(*S*)-(−)-2-Amino-3-methyl-1,1-diphenylbutan-1-ol (1). (*S*)-Valine methyl ester hydrochloride (13.4 g, 0.08 mol) was added portionwise in an ice–water bath to a THF solution of phenylmagnesium bromide prepared from bromobenzene (100.5 g, 0.64 mol) and magnesium (17 g, 0.7 mol), and the mixture was stirred at room temperature for 5 h. The additive complex underwent slow decomposition when ice, 2 N HCl, and ammonia were added. When the decomposition was complete, the THF layer was separated, the aqueous layer was extracted four times with ethyl acetate and the organic layer was combined and dried over anhydrous $MgSO_4$. The solvent was evaporated to afford 1 as a pale yellow solid. Recrystallization from ethanol–water (10:1, v/v) gave colorless crystals: mp 94–95 °C; $[\alpha]^{25}_D$ −127.7° (*c* 0.639, $CHCl_3$); 11.5 g, 56%.

General Procedure for Asymmetric Reduction of 3,3-Dimethyl-2-butanone with the Reagent Prepared from Borane and 1 in THF at 30 °C. A solution of borane (20 mmol) in THF (10 mL) was added dropwise to a stirred solution of 1 (10 mmol) in THF (10 mL) at −78 °C during ca. 20 min. The resulting solution was gradually warmed to 30 °C and stirring continued at 30 °C for 10 h, and then a solution of 3,3-dimethyl-2-butanone (8 mmol) in THF (5 mL) was added dropwise during 5 min. The resulting mixture was stirred at 30 °C for 2 h and then decomposed by the addition of 2→ N HCl. After hydrolysis, evaporation of THF deposited the 1·HCl as a white solid, which was washed with ether over a glass filter. Ether layer was separated, dried ($MgSO_4$), and evaporated to give a colorless oil. The crude product was then distilled (bulb-to-bulb) to give 3,3-dimethylbutan-2-ol, which was characterized by IR and NMR spectroscopy and was homogeneous by GC. The optical rotation was $[\alpha]^{25}_D$ −5.98° (neat). The optical yield (73%) was calculated by the observed optical rotation and the known maximum rotation × of 3,3-dimethyl-2-butanol. The hydrochloride salt of 1 was treated with aqueous ammonia, extracted with ethyl acetate, dried ($MgSO_4$), and evaporated to give the crude crystalline 1 which

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was recrystallized from ethanol–water (10:1, v/v), leading to 80% recovery of 1 without racemization.

Registry No. 1, 78603-95-9; $CH_3(CH_2)_3COCH_3$, 591-78-6; $CH_3(CH_2)_4COCH_3$, 110-43-0; $CH_3(CH_2)_5COCH_3$, 111-13-7; $(CH_3)_2CHCOCH_3$, 563-80-4; $(CH_3)_2CHCH_2COCH_3$, 108-10-1; $(CH_3)_3CCOCH_3$, 75-97-8; (*R*)-$CH_3(CH_2)_3CH(OH)CH_3$, 26549-24-6; (*R*)-$CH_3(CH_2)_4CH(OH)CH_3$, 6033-24-5; (*R*)-$CH_3(CH_2)_5CH(OH)CH_3$, 5978-70-1; (*R*)-$(CH_3)_2CHCH(OH)CH_3$, 1572-93-6; (*R*)-$(CH_3)_2CHCH_2CH(OH)CH_3$, 16404-54-9; (*R*)-$(CH_3)_3CCH(OH)CH_3$, 1572-96-9; (*S*)-valine methyl ester hydrochloride, 6306-52-1; bromo benzene, 108-86-1; borane, 13283-31-3.

Chromatographic Resolution of Perchlorotriphenylamine on (+)-Poly(triphenylmethyl methacrylate)

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Perchlorotriphenylamine (1) is the first example of an optically active compound of the type Ar_3Z in which Z is not a chiral center.[2] Optical resolution of 1 has been achieved by liquid chromatography on microcrystalline cellulose triacetate.[2] However, because this method provided only partially resolved enantiomers and resolution by other methods proved fruitless, the optical properties of the pure enantiomers remained unknown. We report here the complete resolution of 1 by high-performance liquid chromatography (HPLC) on optically active (+)-poly(triphenylmethyl methacrylate) (**2**)[3] and the optical rotation and circular dichroism of the pure enantiomers obtained.

Results and Discussion

A typical chromatogram of the resolution of 1 on the (+)-**2** column is shown in Figure 1. The amine was completely resolved and the (+)-isomer was first eluted, followed by the (−)-isomer. The separation factor α[4] was found to be 2.9 under the experimental conditions given in Figure 1. When 6 mg of (±)-1 was injected on the column, the peaks became broader and partial overlap between the enantiomers was observed. In all about 18 mg of (±)-1 was resolved on this column. Recrystallization of the resolved enantiomeric components from hexane afforded the amine of low optical rotation and the impurities eluted from the column as precipitates. The recrystallization was therefore repeated until the precipitated amine and the amine in the mother liquor showed the same optical rotations. The UV spectral pattern of the purified enantiomers is in agreement with that of (±)-1, and the HPLC analysis on the (+)-**2** column showed that these were enantiomerically pure. The specific rotations are

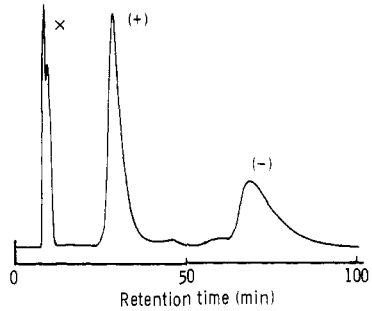

Figure 1. Chromatogram of the resolution of (±)-1 on a (+)-**2** column (30 × 2.2 (i.d.) cm). Flow rate of methanol 12 mL/min, temperature 10 °C, sample 0.6 mg. X: peaks due to CCl_4, which was used to dissolve (±)-1.

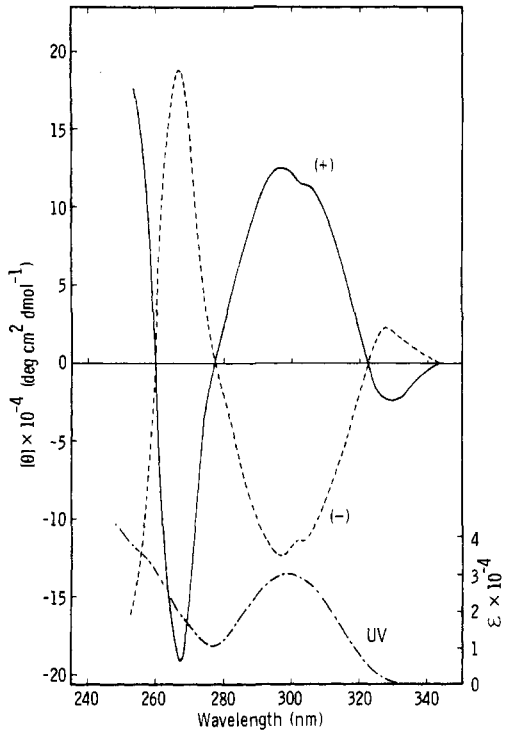

Figure 2. UV and CD spectra of (+)- and (−)-1 in CCl_4.

$[\alpha]^{25}_{435}$ +2385°, $[\alpha]^{25}_{546}$ +1193°, and $[\alpha]^{25}_{589}$ +985° (*c* 0.041, CCl_4) for the first-eluted enantiomer and $[\alpha]^{25}_{435}$ −2344°, $[\alpha]^{25}_{546}$ −1200°, and $[\alpha]^{25}_{589}$ −967° (*c* 0.018, CCl_4) for the second-eluted enantiomer. Accordingly, the optical purities of the partially resolved enantiomers[2] are only ca. 0.4% for (+)-1 and 1% for (−)-1.

The UV and circular dichroism (CD) spectra of the enantiomers of 1 are shown in Figure 2. The enantiomers exhibit the CD pattern of complete mirror images.

Experimental Section

The preparations of (±)-1,[2] (+)-poly(triphenylmethyl methacrylate)[5] and the packing material for HPLC[3] have been reported. The material was packed by the slurry method in a column (30 × 2.2 (i.d.) cm).

The chromatography was accomplished on a JASCO TRI ROTAR II chromatograph equipped with a UV detector. The temperature of the chiral column was controlled at 10 °C and methanol was used as an eluent.

The optical rotation was measured on a JASCO DIP-181 polarimeter at 25 °C. The CD spectrum was obtained with a JASCO J40 CD apparatus at room temperature. The concentrations of

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