35.4, 43.4 (CH), 54.8 (CH), 75.4, 204.0; IR (neat) 1789 cm^{-1}; UV (95% EtOH) λ_{max} 297 nm (ϵ 37). Anal. Calcd for $C_9H_{13}ClO$: C, 62.61; H, 7.59. Found: C, 62.45; H, 7.79.

***endo*-2,7,7-Trimethylbicyclo[3.1.1]heptan-6-one (19).**[13] A solution of chloro ketone **12** (37 mg, 0.6 mmol), tri-*n*-butyltin hydride (175 mg, 0.6 mmol), and AIBN (5 mg, 0.03 mmol) in 5 mL of dry THF was heated at reflux for 48 h. The solvent was removed in vacuo and the residue was purified by flash chromatography on silica gel (95:5 hexane–EtOAc) to give 25 mg (84%) of pure **19**: ^1H NMR 0.92 (d, 3, J = 7.0), 1.15 (s, 3), 1.18 (s, 3), 1.10–1.35 (m, 1), 1.53–1.63 (m, 1), 1.72 (ddd, 1, J = 7.0, 7.0, 14.0), 1.96–2.20 (m, 1), 2.25 (d, 1, J = 6.7, H_1), 2.44 (br dd, 1, J = 6.7, 6.7, H_5); IR (neat) 1770 cm^{-1}.

Acknowledgment. We thank the National Institutes of Health for their generous financial support. We thank Bedoukian Research Inc. for gifts of starting materials.

Note Added in Proof: Recent results suggest that the minor cycloadduct obtained from **16** may be the diastereomer of **18** with a β-ethyl group, which could result from epimerization after cyclization, rather than **17**.

Hydroboration. 80. Preparation of (*trans*-2-Phenylcyclopentyl)- and (*trans*-2-Phenylcyclohexyl)boronates of Very High Enantiomeric Purities

Herbert C. Brown,* J. V. N. Vara Prasad,[1] Ashok K. Gupta,[1] and Raman K. Bakshi[1]

Richard B. Wetherill Laboratory, Purdue University, West Lafayette, Indiana 47907

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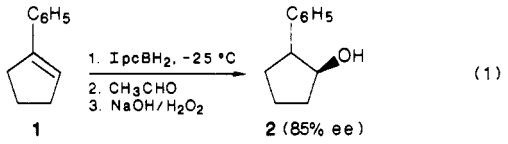
Since the discovery of optically pure monoisopinocampheylborane ($IpcBH_2$),[2] various trans-di- and -trisubstituted olefins of varying structural and steric requirements have been hydroborated to establish the degree of asymmetric induction achievable.[3] The possibility of transferring optically active groups from boron to many other moieties with complete retention of optical activity has led to increased interest in the preparation of borane intermediates of very high enantiomeric purity.[4-6] This study deals with a reexamination of the hydroboration of 1-phenylcyclopentene and 1-phenylcyclohexene and with the preparation of the corresponding boronates of high enantiomeric purity.

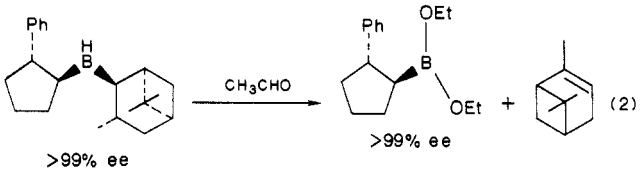
Previously we reported that 1-phenylcyclopentene, upon hydroboration with $IpcBH_2$ (derived from (+)-α-pinene) at −25 °C, followed by oxidation, yields (1*S*,2*R*)-*trans*-2-phenylcyclopentanol.[3] The optical purity of the alcohol, determined by using NMR with chiral shift reagent, was found to be 100%. Recently, a similar experiment gave alcohol of the same rotation. However, capillary GC analysis of the corresponding Mosher (MTPA) ester[7] showed the material to be of only 85% ee (eq 1).



(1)

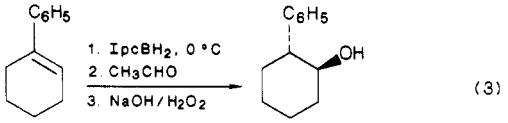
1-Phenylcyclopentene, upon hydroboration with $IpcBH_2$ at −35 °C, followed by treatment with CH_3CHO and alkaline hydrogen peroxide, gave (1*S*,2*R*)-*trans*-2-phenylcyclopentanol in 86% ee. The dialkylborane,[8] isopinocampheyl((1*S*,2*S*)-*trans*-2-phenylcyclopentyl)borane, is a solid and in part crystallizes from the reaction mixture. The crystalline dialkylborane, upon oxidation, yielded (1*S*,2*R*)-*trans*-2-phenylcyclopentanol in 91% ee. The crystalline dialkylborane was dissolved in fresh ethyl ether and the dialkylborane was crystallized at −35 °C. Oxidation of the recrystallized product gave the alcohol in only 95% ee. However, the dialkylborane (91% ee) could be crystallized at 0 °C in ethyl ether to obtain a white crystalline solid, which, upon oxidation, gave (1*S*,2*R*)-*trans*-2-phenylcyclopentanol in >99% ee.

This crystalline dialkylborane (>99% ee), upon treatment with acetaldehyde,[9] yielded the corresponding boronate in >99% ee (eq 2), which could be purified by distillation without loss of activity.



(2)

1-Phenylcyclohexene had also been hydroborated[3] with $IpcBH_2$ [derived from (+)-α-pinene] at 0 °C and the resulting dialkylborane, upon oxidation, yielded (1*S*,2*R*)-*trans*-2-phenylcyclohexanol. The optical purity of the alcohol had been reported to be 88% ee, based on maximum rotation reported earlier.[10] Recently repetition of the experiment gave (1*S*,2*R*)-*trans*-2-phenylcyclohexanol of the same rotation. However, capillary GC analysis of the corresponding Mosher ester showed the material to be ≥97% ee (eq 3). *trans*-2-Phenylcyclohexanol has been shown to be a powerful chiral auxiliary.[11]



(3)

It is evident that capillary GC analysis of the Mosher esters (or other diastereomeric derivatives) provides a far more reliable method for establishing the optical purities than the procedures utilized in the past.

Conclusion

The literature reported values of *trans*-2-phenylcyclopentanol and *trans*-2-phenylcyclohexanol have been corrected. This study makes it possible to obtain *trans*-2-phenylcyclopentyl and *trans*-2-phenylcyclohexylboronates, versatile synthetic intermediates of high optical purities.

Experimental Section

The reaction flasks and other glass equipment were stored in an oven at 150 °C overnight and assembled in a stream of dry

(1) Postdoctoral research associates on Grant GM-10937-23 from the National Institutes of Health. We are indebted to Professor Crhistopher S. Shiner for calling to our attention a discrepancy between the rotation of a sample of optically pure 2-phenylcyclopentanol and the value we had reported.[3]

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(8) Although these dialkylboranes exist in solution as dimers, for convenience, they are referred to as simple dialkylboranes.

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Table I. Hydroboration of 1-Phenylcyclopentene and 1-Phenylcyclohexene with Monoisopinocampheylborane

olefin	product	reactn temp, °C	reactn time, h	yield, %	$[\alpha]^{23}_D$, deg	% ee[a]	abs config
		−25	24	80	+69.65 (*c* 1.565, absolute EtOH)	85	1*S*,2*R*
		−35	36	78	+70.6 (*c* 1.565, absolute EtOH)	86	1*S*,2*R*
		−35	36	65	+83.06[b] (*c* 1.565, absolute EtOH)	>99	1*S*,2*R*
		0	168	69	+56.0 (*c* 0.17, C_6H_6)	>97	1*S*,2*R*
		−25	168			>97	1*S*,2*R*

[a] As determined by capillary GC analysis of the corresponding Mosher ester. [b] After crystallization of dialkylborane, followed by oxidation.

nitrogen gas. Syringes were assembled and fitted with needles while hot and cooled in a stream of dry nitrogen gas. Special techniques used in handling air-sensitive materials are described in detail elsewhere.[9]

Spectra. ^{11}B NMR spectra were recorded on a Varian FT-80A instrument. The chemical shifts are in δ relative to BF_3·OEt_2. ^{1}H NMR and mass spectra were recorded on Perkin-Elmer R-32 and Finnegan GC/mass spectrometers, respectively. Optical rotations were measured on a Rudolph polarimeter Autopol III.

GC Analyses. GC analyses were carried out with a Hewlett-Packard 5750 chromatograph by using 9 ft × 0.125 in. columns packed with 10% Carbowax 20M on Chromosorb W (100–120 mesh). For preparative GC, a 6 ft × 0.5 in. column packed with 20% SE-30 on Chromosorb W (60–80 mesh) was used. All of the MTPA esters of the alcohols were analyzed on a Hewlett-Packard 5890A chromatograph using a 50-ft capillary column packed with methyl silicone. In both cases it was demonstrated that the MTPA esters of the racemic alcohols gave two equal peaks with base line separation.

Materials. Monoisopinocampheylborane ($IpcBH_2$) of 100% ee in ethyl ether was prepared from (+)-α-pinene as described in the literature.[4] Anhydrous ether, available from Mallinckrodt, Inc., was stored over 4-Å molecular sieves under a nitrogen atmosphere. The alkenes used for this study were commercial products of the highest purity available and were used directly.

Hydroboration of 1-Phenylcyclopentene at −25 °C. In a 25-mL flask equipped with a septum inlet, magnetic stirring bar, and connecting tube leading to a mercury bubbler was placed 39.5 mL (0.76 M, 30 mmol) of $IpcBH_2$ in ethyl ether. The reaction flask was cooled to −25 °C, and to it was added 4.45 mL (30 mmol) of 1-phenylcyclopentene and the solution was kept under stirring for 24 h. The dialkylborane thus obtained was treated with 6.7 mL (120 mmol) of acetaldehyde and the reaction mixture was stirred at 25 °C for 6 h. The excess acetaldehyde was pumped off at 15 mm for 1 h. To the boronate thus formed was added 30 mL of THF, followed by 30 mL of 3 N NaOH and 1.5 mL of 30% hydrogen peroxide. The reaction mixture was stirred at 25 °C for 6 h. The aqueous phase was saturated with anhydrous potassium carbonate and extracted with 3 × 10 mL of ether. The ether extract was dried over anhydrous $MgSO_4$ and distilled to give pure alcohol: bp 73–75 °C/0.5 mm, 80% yield. It was further purified by preparative GC to give GC pure material: $[\alpha]^{23}_D$ +69.65° (*c* 1.565, absolute ethanol).

The corresponding Mosher ester was prepared by using the literature procedure.[7] The capillary GC analysis of the material showed it to be of 85% ee.

At −35 °C. The reaction was done as described above at −35 °C for 36 h. The isolated trans alcohol obtained showed $[\alpha]^{23}_D$ +70.6° (*c* 1.565, absolute ethanol). The capillary GC analysis of the corresponding Mosher ester showed it to be 86% ee.

Upgrading the Optical Purity of Isopinocampheyl-((1*S*,2*S*)-*trans*-2-phenylcyclopentyl)borane. In the usual experimental setup was placed 52.6 mL (0.95 M, 50 mmol) of $IpcBH_2$ in ethyl ether, cooled to −35 °C. To it was added dropwise with magnetic stirring 7.2 g (50 mmol) of 1-phenylcyclopentene in 10 mL of ethyl ether cooled to −35 °C. The flask was kept at −35 °C without stirring for 36 h. A white crystalline solid, the dialkylborane, separated. The supernatant layer was removed by use of a double-ended needle and the crystals were washed with cold ethyl ether (3 × 20 mL) at −35 °C. To the crystalline borane thus obtained was added 50 mL of diethyl ether, and the solution was warmed to room temperature for a brief period (5–10 min), whereby a homogeneous solution was obtained. Then it was maintained at 0 °C for 15 h. White crystalline needles separated. The supernatant ether solution was removed with a double-ended needle and the crystalline solid was washed with ice-cold diethyl ether (3 × 10 mL). The solid was then dried under vacuum at 15 mm for 1 h (10.3 g, 70% yield).

Preparation and Isolation of Diethyl (*trans*-2-Phenylcyclopentyl)boronate of >99% ee. The solid dialkylborane (10.3 g, 35 mmol) thus obtained was suspended in 30 mL of ether and treated with 7.84 mL (140 mmol) of acetaldehyde. The reaction mixture was stirred at room temperature for 6 h. ^{11}B NMR examination showed the formation of boronate. The excess acetaldehyde was pumped off and the residue was distilled to give 8 g, 65% yield, of boronate: bp 80–82 °C/0.01 mm, $[\alpha]^{25}_D$ 43.25° (*c* 2.46, absolute ethanol).

The boronate (5 g, 20 mmol) was dissolved in 20 mL of THF and oxidized with 10 mL of 6 N NaOH and 4.8 mL of 30% hydrogen peroxide. The reaction mixture was stirred at 25 °C for 6 h. It was worked up as previously described, which gave (1*S*,2*R*)-*trans*-2-phenylcyclopentanol, exhibiting $[\alpha]^{23}_D$ +83.06° (*c* 1.565, absolute ethanol). Capillary GC analysis of the MTPA ester showed it to be >99% ee.

Preparation of Diethanolamine–(*trans*-2-Phenylcyclopentyl)boronate. Diethyl (*trans*-2-phenylcyclopentyl)boronate (0.67 g, 3 mmol) was taken in 10 mL of ether. To it was added 1 mL of diethanolamine in 2-propanol (3 M) at 0 °C, and the reaction mixture was stirred at room temperature for 1 h. The white crystalline solid thus obtained was filtered and washed with 5 mL of cold ether–pentane (1:1) mixture: 0.73 g, 93% yield, mp 160–161 °C. The mass spectrum showed an M + 1 peak at 260.

Hydroboration of 1-Phenylcyclohexene. In the usual setup was placed 15.38 mL (0.65 M, 10 mmol) of $IpcBH_2$ in tetrahydrofuran and the solution was cooled to 0 °C. To it was added 1.58 g (10 mmol) of 1-phenylcyclohexene. The reaction mixture was maintained with stirring at 0 °C for 7 days. To it was added 0.46 g (22 mmol) of acetaldehyde dropwise, and the reaction mixture was stirred further at room temperature for 4 h. The excess acetaldehyde and solvent were pumped off and the residue was taken up in 25 mL of *n*-pentane. The pentane layer was extracted with 3 × 15 mL of 3 N sodium hydroxide. The alkaline solution was neutralized with 6 N HCl (10 mL) and extracted with 3 × 25 mL of ether.

To the ether layer was added 3.5 mL of 3 N sodium hydroxide and 1.5 mL of 30% hydrogen peroxide. After stirring the reaction mixture for 5 h, it was extracted with ether. The ether extractions were washed with water and dried over anhydrous $MgSO_4$, and the solvent was removed to afford 1.212 g of (1*S*,2*R*)-*trans*-2-phenylcyclohexanol (69% yield). It was further purified by crystallization from *n*-pentane: mp 64–65 °C, $[\alpha]^{23}_D$ +56.0° (*c* 0.17, benzene). Capillary GC analysis of its MTPA ester showed it to be ≥97% ee. The hydroboration reaction is unusually slow, even at 0 °C. Consequently, the reaction was only ~70% complete, even after 7 days. It proved impossible to crystallize the dialkylborane intermediate in the presence of residual $IpcBH_2$ and 1-phenylcyclohexene.

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