Organoboranes for Synthesis. 16. A Convenient Synthesis of Enantiomerically Pure Isopinocampheylamine, a Chiral Derivatizing Agent for Gas Chromatographic Analysis of Optically Active Carboxylic Acids

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Received July 6, 1995[⊗]

Both isomers of enantiomerically pure isopinocampheylamine (**1**) have been synthesized from the corresponding *B*-chlorodiisopinocampheylborane by treatment with either methylmagnesium bromide or trimethylaluminum to form *B*-methyldiisopinocampheylborane, followed by treatment of the intermediate with hydroxylamine-*O*-sulfonic acid. Application of **1** as a derivatizing agent for the gas chromatographic analysis of optically active carboxylic acids has been demonstrated.

Introduction

The Thalidomide tragedy[2] and the new regulations of the U.S. Food and Drug Administration[3] stimulated the development of asymmetric synthetic methodologies. Enantiomerically pure primary amines have also received their share of attention in asymmetric synthesis.[4] Traditionally enantiopure primary amines have been used for the resolution of racemic carboxylic acids.[5] However, recently they have been utilized as chiral auxiliaries for the synthesis of optically active molecules. For example, Sugasawa and Toyoda carried out asymmetric aldol condensations via chiral vinylaminodichloroboranes.[6] Kitamoto and co-workers achieved the synthesis of optically active 2-alkylcycloalkanones via chiral lithio enamines.[7] Bertz and co-workers lithiated chiral amines to prepare chiral amidocuprates for use in the synthesis of alkyl cycloalkanones.[8] Yamaguchi and co-workers achieved an asymmetric addition of thiols to diene polymers in the presence of optically active amines as catalysts.[9] Fiorini and Giongo used chiral aminophosphine−rhodium complexes to catalyze the asymmetric hydrogenation of olefins.[10]

Our success in asymmetric syntheses via chiral organoboranes based on the superchiral auxiliary α-pinene encouraged several groups to utilize pinane-based structures as chiral auxiliaries for asymmetric synthesis.[11] On this basis we believed that isopinocampheylamine (**1**) might also find valuable applications for asymmetric organic synthesis. However, since its original synthesis some three decades ago,[12] no such applications have been described. The lack of interest in **1** could be due to the relatively poor yields and inefficient aminating process utilized in the original synthesis.

The laboratory synthesis of optically pure amines often involved kinetic resolution[13] or synthesis from readily available optically active precursors.[14] Recently, we had made a systematic study of the conversion of organoboranes to primary amines which identified chloramine and hydroxylamine-*O*-sulfonic acid (HSA) as reagents of choice for achieving such aminations (eqs 1 and 2).[15] However, the yields in the reaction were relatively low and the migratory aptitudes of the alkyl groups posed problems.

$$R_3B + 2\ NH_2Cl \xrightarrow{NaOH} 2\ RNH_2 + RB(OH)_2 \qquad (1)$$

$$R_3B + 2\ NH_2OSO_3H \rightarrow R{-}B\begin{matrix}NHR\\NHR\end{matrix} + 2\ H_2SO_4 \xrightarrow{H_2O} R{-}B\begin{matrix}OH\\OH\end{matrix} + 2\ RNH_2 \qquad (2)$$

We then studied the possibilities for a more effective utilization of the alkyl groups attached to boron and discovered that while monoalkylboronic acid derivatives are essentially inert to HSA, dialkylborinates react readily with the aminating agent.[16] This methodology became more useful by choosing a nonmigrating blocking group, such as a methyl group, to transfer the alkyl group preferentially from boron to nitrogen to provide the desired amine (eq 3).[16]

[⊗] Abstract published in *Advance ACS Abstracts,* December 15, 1995.

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(2) Thalidomide is a tragic example of one optical isomer being a safe drug, whereas the other is a potent mutagen. Phocomelia, a teratogenic effect characterized by the absence of arms and legs, is ascribed exclusively to the *S*-isomer. Blaschke, G.; Kraft, H. P.; Fickentscher, K.; Koehler, F. *Arzneim.-Forsch.* **1979**, *29*, 1640.

(3) Stinson, S. C. *Chem. Eng. News* **1992**, *70*(39), 46.

(4) The wide use of a chiral amine, for example α-methylbenzylamine, is evident from the large number of references in the literature. A CAS ONLINE (American Chemical Society) search for (*S*)-α-methylbenzylamine (Registry No. 2627-86-3) showed ∼1500 references and (*R*)-α-methylbenzylamine (Registry No. 3886-69-9) showed ∼1300 references.

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(6) Sugasawa, T.; Toyoda, T. *Tetrahedron Lett.* **1979**, 1423.

(7) Kitamoto, M.; Hiroi, K.; Terashima, S.; Yamada, S. *Chem. Pharm. Bull.* **1974**, *22*, 459.

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(10) Fiorini, M.; Giongo, G. M. *J. Mol. Catal.* **1979**, *5*, 303.

(11) Brown, H. C.; Ramachandran, P. V. *J. Organomet. Chem.* **1995**, *500*, 1.

(12) (a) Brown, H. C.; Heydkamp, W. R.; Breuer, E.; Murphy, W. S. *J. Am. Chem. Soc.* **1964**, *86*, 3365. (b) Rathke, M. W.; Inoue, N.; Varma, K. R.; Brown, H. C. *Ibid.* **1966**, *88*, 2870.

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(14) (a) Santaniello, E.; Casati, R.; Milani, F. *J. Chem. Soc., Perkin Trans. 1* **1985**, 919.

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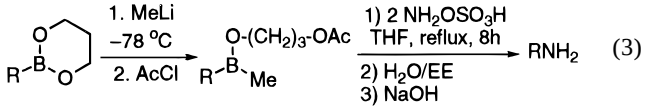
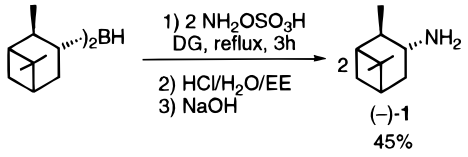


(3)

Asymmetric organoboranes are converted to the corresponding primary amines with complete retention of configuration.[16] As part of our program on chiral syntheses via organoboranes, we undertook to improve the synthesis to obtain **1** in high yield. The modifications that achieved isolated yields of 96% and the application of **1** as a chiral derivatizing agent for the gas chromatographic analysis of optically active acids are described below.

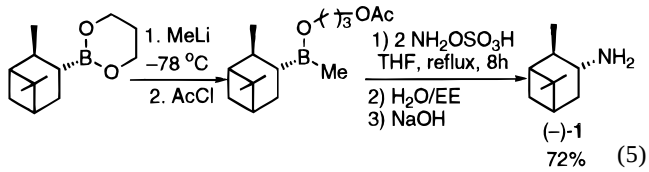
Results and Discussion

Our original synthesis of **1** involved the treatment of diisopinocampheylborane and HSA in refluxing diglyme (eq 4). The yield is 45% on the basis of the two isopinocampheyl groups in Ipc_2BH.



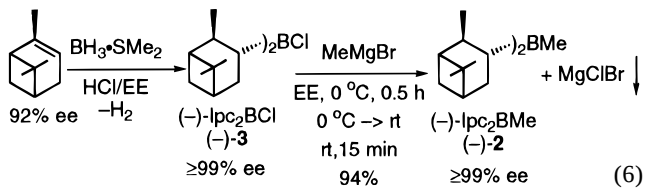
(4)

Our improved synthesis produced a 72% yield of **1** starting with monoisopinocampheylborane ($IpcBH_2$) (eq 5). Considering that the synthesis of $IpcBH_2$ begins with 2 equiv of α-pinene, the yield based on the α-pinene utilized was not yet satisfactory.



(5)

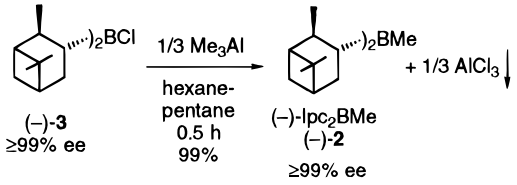
***B*-Methyldiisopinocampheylborane.** On the basis of our previous experience,[15] we designed an improved synthesis of **1** from *B*-methyldiisopinocampheylborane (**2**), which in turn can be readily prepared from commercially available *B*-chlorodiisopinocampheylborane (Ipc_2BCl; Aldrich, DIP-Chloride, **3**) of ≥99% ee.[17] Treatment of **3** with methylmagnesium bromide provides **2** in 94% yield (eq 6).



(6)

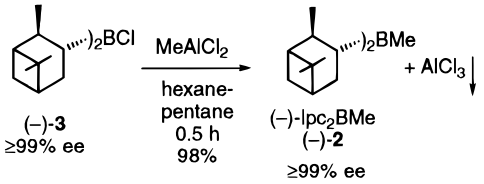
An essentially quantitative yield of **2** is achieved by using trimethylaluminum for the transfer of the methyl group to the boron atom of **3**. The reaction of **3** with 0.33 equiv of a solution of the aluminum reagent in hexane provides a 99% yield of **2** (eq 7), which can be used without further purification for the preparation of **1**.

(17) Brown, H. C.; Chandrasekharan, J.; Ramachandran, P. V. *J. Am. Chem. Soc.* **1988**, *110*, 1539. DIP-Chloride is a trademark of the Aldrich Chemical Co.



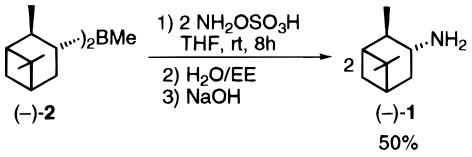
(7)

A molar equivalent of methylaluminum dichloride or dimethylaluminum chloride can also be used for transfer of the methyl group with equal efficiency (eq 8). The diisopinocampheylmethylborane was decanted from the inorganic salts and used without further purification for the preparation of **1**.



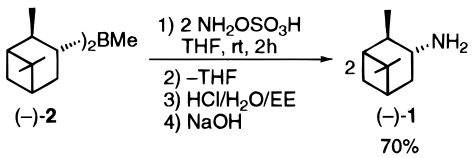
(8)

Isopinocampheylamine. Having achieved the synthesis of **2** in essentially quantitative yield, we reinvestigated the procedure for the preparation of **1** via the amination reaction using HSA. Using the reported procedure,[16] the amination was performed in tetrahydrofuran (THF) at room temperature (rt) using 2 equiv of HSA (eq 9). After the reaction was over (~8 h), ethyl ether (EE) and water were added to the mixture, and the aqueous layer was separated. Treatment with alkali and workup furnished (−)-**1** in around 50% isolated yield (on the basis of 2 Ipc groups).



(9)

As a first modification, THF was removed before the addition of EE−H_2O. This procedure improves the yield of **1** to 67%. However, a considerable amount of pot residue remained after distillation. The ^{11}B NMR spectrum of this residue dissolved in $CDCl_3$ shows two peaks, a singlet at δ 31 probably corresponding to $MeB(OH)_2$ and another singlet at δ 0.1 presumably due to a borazene type of derivative formed by the reaction of $MeB(OH)_2$ and **1**. Attempts to avoid the formation of the borazene by treatment of the reaction mixture with aqueous 6 N HCl during the workup did not improve the yield. Thus, in our second modification, we substituted THF with EE and treated the mixture with 6 N HCl, followed by the usual workup. Distillation provided (−)-**1** in 70% isolated yield with a large amount of the same viscous pot residue (eq 10).



(10)

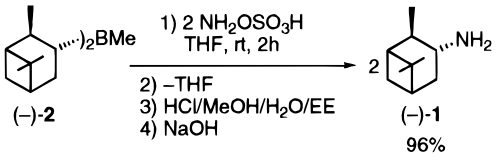
However, utilization of a mixture of methanol and 12 N HCl improves the yield considerably. Treatment of the above residue with such methanolic HCl, followed by extraction with EE, gave a solution whose ^{11}B NMR

Table 1. Column Temperatures and Retention Times for the Separation of Isopinocampheylamides Using Different Capillary Columns

	Supelcowax[a]			SPB-5[b]			methylsilicone[c]		
	temp,	t_R (min)		temp,	t_R (min)		temp,	t_R (min)	
acid	°C	t_1	t_2	°C	t_1	t_2	°C	t_1	t_2
(±)-α-methoxyphenylacetic acid	165	80.96	85.88	180	67.32	69.45	180	67.60	69.61
(±)-2-phenylbutyric acid	165	66.63	69.49	180	93.84	95.20	180	62.13	62.99
(±)-mandelic acid	170	295.80	304.70		no separation				
(±)-tetrahydro-2-furoic acid	135	65.08	66.20	130	168.15	171.18			
(±)-*N*-trifluoroacetylproline	130	230.00	237.84	140	175.86	180.07			
(±)-methoxy(trifluoromethyl)phenylacetic acid	165	40.22	41.39	180	52.42	53.48			

[a] Column inlet pressure, 6 psi; linear flow rate, 20 cm/min; split ratio, 100:1. [b] Column inlet pressure, 26 psi; linear flow rate, 20 cm/min; split ratio, 100:1. [c] Column inlet pressure, 14 psi; linear flow rate, 20 cm/min; split ratio, 100:1.

spectrum reveals only a sharp singlet at δ 32, probably due to $MeB(OMe)_2$. The aqueous layer, upon saponification followed by fractional distillation furnishes an additional 17% yield of (−)-**1**, without any pot residue. Thus, a total yield of 87% is realized. Application of this modification—the addition of MeOH−HCl−H_2O to the reaction mixture after the removal of THF—early in the workup improves the isolated yield of (−)-**1** to 96% (eq 11).



(11)

As with the majority of transfer reactions of organoboranes which proceed with complete stereochemical integrity, this amination reaction provides **1** without loss of optical activity. Gas chromatographic analysis of its methoxy(trifluoromethyl)phenylacetamide (MTPA amide) on a 15 m Supelcowax column reveals an ee of ≥99%.

Following the same sequence of reactions, (+)-**1** is prepared from (+)-DIP-Chloride derived from (−)-α-pinene.

Chiral Derivatization of Optically Active Carboxylic Acids. Having achieved an excellent synthesis of **1**, we tested the utility of this pinane-based chiral amine as a derivatizing agent for the separation of racemic carboxylic acids on a gas chromatograph using a capillary column. (±)-α-Methoxyphenylacetic acid, (±)-2-phenylbutyric acid, (±)-mandelic acid, (±)-tetrahydro-2-furoic acid, (±)-methoxy(trifluoromethyl)phenylacetic acid, and (±)-*N*-(trifluoroacetyl)proline were chosen as representative examples for this study. Capillary columns of different polarities, such as Supelcowax,[18a] SPB-5,[18a] or methylsilicone[18b] were used for the analysis to show the generality of this procedure. The acids were activated with 1,1'-carbonyldiimidazole (CDI)[19] and treated with **1** in THF to provide the corresponding amides (eq 12). Analyses of the THF solution of the diastereomeric amides using the above columns showed a 1:1 correspondence with excellent resolution. All of the six amides tested were separated on the Supelcowax column whereas the non-polar SPB-5 column separated only five amides. The details of the gas chromatographic analyses are presented in Table 1. Figure 1 shows the chromatogram of *N*-isopinocampheyl-α-methoxyphenylacetamide using a methylsilicone column.

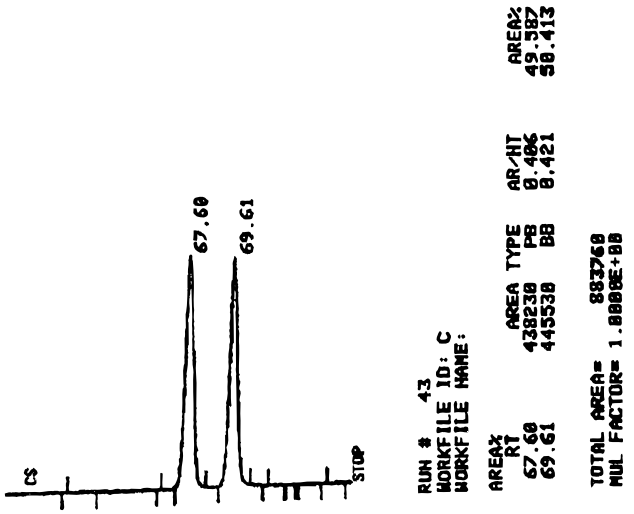
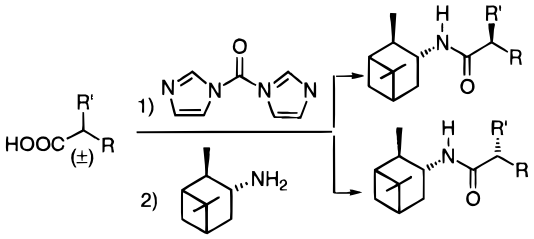


Figure 1. Gas chromatogram of diastereomeric *N*-(1*R*,2*S*,3*R*,5*R*)-(−)-3-isopinocampheyl-α-methoxyphenylacetamides on a methylsilicone (50 m) column at 180 °C.



(12)

Conclusions

In conclusion, we have developed a modified synthesis of *B*-methyldiisopinocampheylborane and an improved workup procedure for obtaining isopinocampheylamine in essentially quantitative yield. Application of **1** for the preparation of diastereomeric pairs of amides of racemic carboxylic acids for determining their enantiomeric purity using capillary gas chromatography has been demonstrated. Our earlier studies of the hydroboration of a number of terpenes, such as 2-[20a] and 3-carene,[20b] sabinene,[20c] thujene,[20c] α- and β-cedrene,[20d] thujopsene,[20e] and limonene,[20f] suggest that there should not be any significant difficulty in extending this development to the syntheses of other terpene-based chiral amines. The

(18) Suplecowax and SPB-5 are trademarks of Supelco. (b) The methylsilicone column was purchased from Hewlett-Packard.

(19) Paul, R.; Anderson, G. W. *J. Org. Chem.* **1962**, *27*, 2094.

(20) (a) Acharya, S. P.; Brown, H. C. *J. Am. Chem. Soc.* **1967**, *89*, 1925. (b) Brown, H. C.; Suzuki, A. *J. Am. Chem. Soc.* **1967**, *89*, 1933. (c) Acharya, S. P.; Brown, H. C.; Suzuki, A.; Nozawa, S.; Itoh, M. *J. Org. Chem.* **1969**, *34*, 3015. (d) Acharya, S. P.; Brown, H. C. *J. Org. Chem.* **1970**, *35*, 196. (e) Acharya, S. P.; Brown, H. C. *J. Org. Chem.* **1970**, *35*, 3874. (f) Brown, H. C.; Pfaffenberger, C. D. *Tetrahedron* **1975**, *31*, 625.

syntheses of several of these chiral amines are in progress.

Experimental Section

General Methods. Techniques for handling air-sensitive compounds have been previously described.[21] Analyses of the *N*-isopinocampheylamides were performed on a Hewlett-Packard 5890A gas chromatograph (GC) using a Supelcowax (15 m), a SPB-5 (30 m), or a methylsilicone capillary column (50 m), at appropriate temperatures.

Materials. Anhydrous ethyl ether purchased from Mallinckrodt, Inc., was used as received. THF was distilled from sodium benzophenone ketyl. (+)- and (−)-DIP-Chloride, methylmagnesium bromide, trimethylaluminum, methylaluminum dichloride, hydroxylamine-*O*-sulfonic acid, 1,1′-carbonyldiimidazole (CDI), and all of the carboxylic acids were obtained from Aldrich Chemical Co.

Preparation of *B*-Methyldiisopinocampheylborane (2). (a) Using Methylmagnesium Bromide. Methylmagnesium bromide (24.2 mmol, 8.07 mL of 3 M solution in EE) was added, dropwise, to a stirred solution of Ipc_2BCl (7.76 g, 24.20 mmol) in EE (40 mL) maintained at 0 °C in a 250 mL round-bottom flask. The reaction mixture was stirred at 0 °C for 0.5 h, warmed to rt, and stirred for an additional 15 min. A white precipitate of MgClBr separated, and the ^{11}B NMR spectrum of an aliquot of the supernatant showed a singlet at δ 81 corresponding to a trialkylborane. Anhydrous *n*-pentane (10 mL) was added to the reaction mixture to ensure the complete precipitation of MgClBr. The organic portion was transferred to another flask by means of a cannula. The precipitate was washed with *n*-pentane (2 × 10 mL), and the combined organic portion was washed with saturated ammonium chloride solution (20 mL) and dried over $MgSO_4$. Removal of the volatiles furnished 6.89 g of air-sensitive and pyrophoric **2** as a thick syrup.

(b) Using Trimethylaluminum. Trimethylaluminum (9.8 mL of 2 M solution in hexane, 19.54 mmol) was added, dropwise, to a stirred solution of Ipc_2BCl (18.80 g, 58.63 mmol) in *n*-pentane (51 mL) at 0 °C. The reaction is mildly exothermic, and the temperature was controlled by the slow addition of Me_3Al. Upon addition of Me_3Al, the colorless reaction mixture became pale yellow and a brown viscous mass (presumably $AlCl_3$) precipitated out of the hexane−pentane mixture. The reaction mixture was warmed to rt and allowed to stir for 0.5 h. The ^{11}B NMR spectrum of an aliquot of the supernatant showed the total disappearance of Ipc_2BCl (δ 74) and the formation of Ipc_2BMe (δ 81). The hexane−pentane mixture was separated by means of a cannula, washed with saturated NH_4Cl solution (20 mL) under nitrogen, and dried over $MgSO_4$. Upon washing with NH_4Cl solution, the pale yellow solution became colorless. Removal of the volatiles furnished 17.39 g (57.96 mmol, 98%) of **2**.

(c) Using Methylaluminum Dichloride. The preparation of **2** was carried out by using a similar procedure as described above, substituting methylaluminum dichloride for trimethylaluminum. Methylaluminum dichloride (8.2 mL of 1 M solution in hexane, 8.2 mmol) was added, dropwise, to a stirred solution of Ipc_2BCl (2.625 g, 8.18 mmol) in *n*-pentane (8 mL) at 0 °C. The reaction was mildly exothermic, and the temperature was controlled by the slow addition of $MeAlCl_2$ solution. Upon addition of $MeAlCl_2$, the reaction mixture changed from colorless to pale yellow and a brown viscous mass precipitated out ($AlCl_3$). The organic portion was separated, washed with saturated NH_4Cl solution under nitrogen, dried over $MgSO_4$, and concentrated to obtain 2.42 g (8.07 mmol, 98%) of **2**. ^{11}B NMR ($CDCl_3$) = δ 81.

Preparation of (1*R*,2*S*,3*R*,5*R*)-(−)-Isopinocampheylamine. Procedure a. Hydroxylamine-*O*-sulfonic acid (2.37 g, 21 mmol) was slowly added at rt, using a solid addition tube, to a solution of the above Ipc_2BMe (3.0 g, 10 mmol) in THF (10 mL). The reaction was mildly exothermic, and the temperature was controlled by the slow addition of HSA. The mixture was stirred at rt until the initial slurry became a clear solution (2 h). The ^{11}B NMR spectrum of an aliquot showed a singlet at δ 10 which shifted to a sharp singlet at δ 31 upon methanolysis, indicating completion of the reaction. Solvent THF was pumped off under aspirator. (*It is important to pump off THF.*) The white viscous mass was suspended in EE (10 mL) followed by the addition of water (10 mL). The acidic aqueous layer was separated, cooled to 0 °C, and layered with EE (20 mL). It was then made strongly alkaline by the addition of solid sodium hydroxide (40 mmol) with stirring. The organic phase was separated, and the aqueous layer was extracted with EE (10 mL). The combined organic phase was dried over Na_2SO_4, concentrated, and distilled at 94−96 °C/16 mmHg to obtain 2.06 g (13.4 mmol, 67% on the basis of the migration of two Ipc groups during amination reaction) of (−)-**1** whose structure was ascertained by ^1H NMR.

A substantial amount of pot residue remained after distillation.

Procedure b: Modified Amination Reaction Using 6 N HCl−EE. Under nitrogen, hydroxylamine-*O*-sulfonic acid (5.75 g, 50.82 mmol) was added using a solid addition tube to a solution of **2** (7.26 g, 24.20 mmol) in THF (25 mL). The reaction was exothermic, and the temperature of the reaction mixture was controlled by slow addition of HSA. The reaction mixture was allowed to stir at rt for 2 h during which period the initial slurry became a clear solution. The completion of the reaction was confirmed by ^{11}B NMR spectroscopy, and the solvent was removed under aspirator. The viscous residue was treated with 6 N HCl (9 mL), and 25 mL of EE was added. The acidic aqueous layer was separated, cooled to 0 °C, and layered with EE (30 mL). It was then made strongly alkaline by adding solid NaOH with stirring. The organic phase was separated, and the aqueous layer was extracted with EE (3 × 25 mL). The combined organic phase was dried over Na_2SO_4, concentrated, and distilled to provide 5.18 g (33.88 mmol, 70%) of (−)-**1**, bp 94−96 °C/16 mm.

The ^{11}B NMR spectrum of the residue dissolved in $CDCl_3$ showed two major peaks at δ −0.1 and 31. This residue was treated with MeOH (2 mL), concd HCl (3 mL), and water (2 mL) and stirred at rt for 0.5 h. The organics were extracted with EE (10 mL). The ^{11}B NMR spectrum of the organic portion showed a singlet at δ 31 attributed to the presence of a $RB(OMe)_2$ species. The acidic aqueous layer was separated, layered with EE (10 mL), and cooled to 0 °C. This was made strongly alkaline by adding solid NaOH. The organic portion was separated, and the aqueous layer was extracted with EE (2 × 10 mL). The combined organic portion was dried over $MgSO_4$, concentrated, and distilled *in vacuo* to furnish 1.3 g of (−)-**1** (8.02 mmol, 16.6%), bp 94−96 °C/16 mmHg. There was no pot residue remaining after distillation. The total yield of (−)-**1** is 6.48 g (41.90 mmol, 86.6%).

Procedure c: Recommended Modified Procedure Using Methanolic HCl. Hydroxylamine-*O*-sulfonic acid (13.77 g, 121.8 mmol, 2.1 equiv) was added slowly using a solid addition tube to 17.39 g (57.96 mmol) of **2** dissolved in freshly distilled THF (58 mL). The temperature of the reaction was controlled by the slow addition of HSA. The reaction mixture was stirred at rt until the initial slurry became a clear solution (2 h). The completion of the reaction was ascertained by ^{11}B NMR spectroscopy, and the solvent was pumped off *in vacuo* (20 mm). The residual viscous mass was treated with methanol (5 mL), concd HCl (13 mL), and water (10 mL), and to this mixture was added 60 mL of EE. The reaction mixture was allowed to stir at 25 °C for 0.5 h. The ^{11}B NMR spectrum of the organic portion showed a sharp singlet at δ 32 [Me-$B(OMe)_2$]. The acidic aqueous layer was separated, cooled to 0 °C, and layered with EE (40 mL). It was then made strongly alkaline by adding solid NaOH with stirring. The EE layer was separated, and the aqueous layer was extracted with EE (3 × 40 mL), combined, dried over Na_2SO_4, concentrated, and distilled to furnish 17.05 g (111.3 mmol, 96%) of (−)-**1**, bp 91−92 °C/16 mmHg: $[\alpha]^{23}_D$ of (−)-**1**·HCl = −23.68° (*c* 4, MeOH), mp >250 °C.

(21) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Syntheses via Boranes*; Wiley-Interscience: New York, 1975; Chapter 9.

The MTPA amide of this amine was prepared and analyzed on a Supelcowax glass capillary column (15 m) using a gas chromatograph (180 °C, isothermal) which showed an ee of ≥99%.

Preparation of (1*S*,2*R*,3*S*,5*S*)-(+)-Isopinocampheylamine [(+)-1]. Using procedure c, 6.55 g (96%) of (+)-**1** was prepared from 6.68 g (22.28 mmol) of (+)-Ipc_2BMe that was obtained from 7.24 g (22.63 mmol) of (+)-DIP-Chloride and 7.54 mmol of trimethylaluminum, bp 94−96 °C/16 mmHg: $[\alpha]^{23}_D$ of (+)-**1**·HCl = +23.64° (*c* 4, MeOH), mp >250 °C.

Preparation of Racemic *N*-(1*R*,2*S*,3*R*,5*R*)-Isopinocampheylamides. General Procedure. The racemic carboxylic acid (0.1 mmol) was added to a vial containing 0.016 g (0.1 mmol) of CDI in 3 mL of dry THF. To this solution was added 0.015 g (0.1 mmol) of (−)-**1**, and the solution was stirred for 1 h. (In those cases where the acid is a solid, the acid (0.1 mmol) and CDI (0.1 mmol) were weighed into a vial and dissolved in 3 mL of THF, followed by the addition of (−)-**1**.) Then 1 μL of the THF solution of the resulting diastereomeric amides was injected directly into a gas chromatograph fitted with an appropriate capillary column maintained isothermally at the required temperature. The diastereomeric amides revealed a 1:1 correspondence with the corresponding retention times. The details of the GC analyses are presented in Table 1.

Acknowledgment. Financial support from the United States Army Research Office (DAAH-94-G-0313) is gratefully acknowledged.

JO9512158