Hydroboration. 90. Synthesis of 2-Isobutyl- and 2-Isopropylapopinenes. Rates and Stoichiometry of the Hydroboration of 2-Organylapopinenes with Borane–Methyl Sulfide and Borane–Tetrahydrofuran

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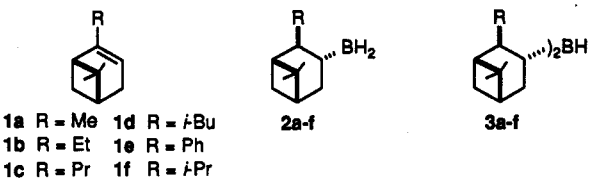
Two higher analogues of α-pinene, 2-isobutyl- and 2-isopropylapopinenes, promising chiral auxiliaries for asymmetric hydroboration, were readily synthesized from α-pinene in good chemical yield. A quantitative study was made of the rates and stoichiometry of the hydroboration of a number of representative 2-organylapopinenes (2-R-apopinenes) with representative boranes, such as BH_3·SMe_2 (BMS) and BH_3·THF, in order to develop a convenient procedure for the synthesis of mono- and bis(2-organylapoisopinocampheyl)boranes [2-R-apoisopinylborane ($RapBH_2$) and bis(2-R-apoisopinyl)borane (Rap_2BH), respectively], under investigation as possible improved asymmetric hydroborating reagents. It was evident that the sterically bulkier 2-R-apopinenes such as 2-phenyl- and 2-isopropylapopinenes reacted with boranes at room temperature to form essentially $RapBH_2$ in ≥95% yield, while a yield of ≥90% was realized in the case of 2-isobutylapopinene. However, α-pinene, and 2-ethyl- and 2-*n*-propylapopinenes smoothly reacted with boranes to form a mixture of $RapBH_2$ and Rap_2BH. Under the reaction conditions employed, 2-ethyl-, 2-*n*-propyl-, 2-isobutyl-, 2-phenyl-, and 2-isopropylapopinenes failed to produce clean Rap_2BH. The rate of hydroboration decreased significantly with increase in bulk of the organyl group at the 2-position of the apopinene.

In recent years asymmetric synthesis has become a major focus of interest for many researchers.[2] Current activities in organic chemistry in developing asymmetric reactions have initiated searches for improved, easily accessible chiral auxiliaries and reagents. In the past decade we have been exploring asymmetric synthesis *via* chiral organoboranes derived from terpenes.[3] A number of chiral organoborane reagents based on such 2-R-apopinenes have proven to be successful for hydroboration of prochiral olefins,[4] reduction of prochiral ketones,[5] asymmetric allyl- and crotylboration,[6] asymmetric ring opening of *meso*-epoxides,[7] and asymmetric homologation.[8]

The hydroboration of α-pinene, depending on the reaction conditions, has led to the synthesis of the useful chiral monoalkylborane, $IpcBH_2$ (**2a**),[9] and the dialkylborane, Ipc_2BH (**3a**).[9] The former reagent of lower steric demand has been shown to hydroborate hindered prochiral *trans*- and trisubstituted alkenes to give optical inductions ranging from 53 to ≥99% ee, with the higher values obtained with aryl-substituted olefins.[4e] The latter reagent, Ipc_2BH of higher steric demand, is preferred for the hydroboration of the less-crowded *cis*-alkenes, providing the product alcohols in optical purities of up to ≥99% ee.[4c] These results indicate that the effectiveness of these two complimentary reagents depends on the nature of the substrate alkene. Introduction of ethyl and *n*-propyl groups at the 2-position of apopinene provided new pinene-based chiral auxiliaries, 2-ethylapopinene (**1b**) and 2-*n*-propylapopinene (**1c**), respectively. A sterically bulkier 2-ethylapoisopinylborane ($EapBH_2$) derived from **1b** was employed for the hydroboration of a series of prochiral alkenes. It provided improved enantiomeric purities of the alcohol produced than those derived from $IpcBH_2$.[4f] Some other examples of the borane reagents incorporating these ethyl and *n*-propyl analogues of α-pinene, *viz.* Eapine–borane (**4a**), Prapine–borane (**4b**), and Eapine–borohydride (**5**), respectively, have provided significant enhancements in the optical purity of the product alcohols produced by the asymmetric reduction of prochiral ketones.[10ab] An analogue of α-pinene, nopol benzyl ether,



1a R = Me **1d** R = *i*-Bu
1b R = Et **1e** R = Ph
1c R = Pr **1f** R = *i*-Pr

2a-f **3a-f**

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(2) Crosby, J. *Tetrahedron* **1991**, *47*, 4789.

(3) Brown, H. C.; Ramachandran, P. V. *Pure Appl. Chem.* **1991**, *63*, 307.

(4) (a) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 486. (b) Brown, H. C.; Yoon, N. M. *J. Am. Chem. Soc.* **1977**, *99*, 5514. (c) Brown, H. C.; Jadhav, P. K.; Mandal, A. K. *Tetrahedron* **1981**, *37*, 3547. (d) Brown, H. C.; Desai, M. C.; Jadhav, P. K. *J. Org. Chem.* **1982**, *47*, 5065. (e) Brown, H. C.; Jadhav, P. K.; Mandal, A. K. *J. Org. Chem.* **1982**, *47*, 5074. (f) Brown, H. C.; Randad, R. S.; Bhat, K. S.; Zaidlewicz, M.; Weissman, S. A.; Jadhav, P. K.; Perumal, P. T. *J. Org. Chem.* **1988**, *53*, 5513.

(5) Brown, H. C.; Ramachandran, P. V. *Acc. Chem. Res.* **1992**, *25*, 16.

(6) (a) Brown, H. C.; Jadhav, P. K. *J. Am. Chem. Soc.* **1983**, *105*, 2092. (b) Brown, H. C.; Jadhav, P. K.; Perumal, P. T. *Tetrahedron Lett.* **1984**, *25*, 5111. (c) Brown, H. C.; Jadhav, P. K. *Tetrahedron Lett.* **1984**, *25*, 1215. (d) Jadhav, P. K.; Bhat, K. S.; Perumal, P. T.; Brown, H. C. *J. Org. Chem.* **1986**, *51*, 432. (e) Brown, H. C.; Bhat, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 5919.

(7) Joshi, N. N.; Srebnik, M.; Brown, H. C. *J. Am. Chem. Soc.* **1988**, *110*, 6246.

(8) (a) Matteson, D. S.; Majumdar, D. *J. Am. Chem. Soc.* **1980**, *102*, 7588. (b) Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, *2*, 1529. (c) Matteson, D. S.; Sadhu, K. M.; Peterson, M. L. *J. Am. Chem. Soc.* **1986**, *108*, 810. (d) Brown, H. C.; Singh, S. M.; Rangaishenvi, M. V. *J. Org. Chem.* **1986**, *51*, 3150. (e) Brown, H. C.; Rangaishenvi, M. V. *J. Organomet. Chem.* **1988**, *358*, 15. (f) Matteson, D. S. *Pure Appl. Chem.* **1991**, *63*, 339.

(9) This molecule actually exists in solution as a dimer. However, it is convenient to represent in the monomeric form.

(10) (a) Brown, H. C.; Ramachandran, P. V.; Weissman, S. A.; Swaminathan, S. *J. Org. Chem.* **1990**, *55*, 6328. (b) Ramachandran, P. V.; Brown, H. C.; Swaminathan, S. *Tetrahedron Asymm.* **1990**, *1*, 433.

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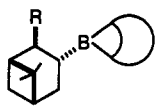
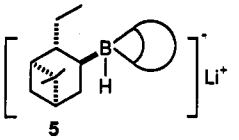
has been successfully utilized to make NB-enantrane (**4c**), an efficient chiral reducing reagent for the reduction of α,β-acetylenic ketones.[11]



4a R = Et
4b R = Pr
4c R = $(CH_2)_2OBz$



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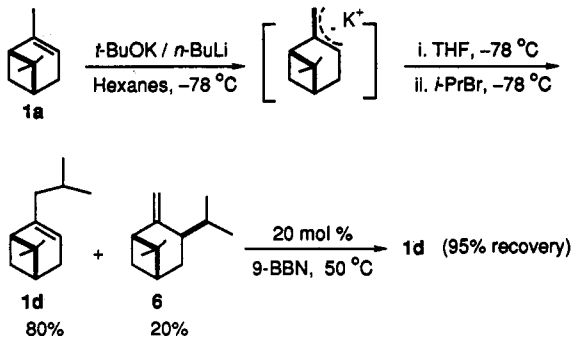
These results prompted a study where the steric requirements of the reagent were increased systematically in order to observe the effect of optimizing the fit between the substrate and the reagent. In this study we have modified the apopinene moiety by introducing in the 2-position even bulkier groups, isobutyl and isopropyl. The synthesis of 2-*n*-propylapopinene (**1c**) and 2-phenylapopinene (**1e**) have been reported by us earlier.[10a,12] In this paper we wish to report the synthesis of higher analogues of α-pinene *viz.* 2-isobutylapopinene (**1d**) and 2-isopropylapopinene (**1f**) and the quantitative study of the rates and stoichiometry of the hydroboration at room temperature of the currently available 2-R-apopinenes derivatives (**1a–f**) with the commonly used borane reagents, BMS and BH_3·THF, in THF in representative molar ratios. It is known that hydroboration of simple unhindered olefins with BMS or BH_3 in THF proceeds rapidly past the monoalkylborane stage (RBH_2), through the dialkylborane stage (R_2BH), to the trialkylborane stage (R_3B).[13] However, the hydroboration of moderately hindered olefins, such as 2-methyl-2-butene, proceeded to the dialkylborane stage (disiamylborane, Sia_2BH).[14] The more-hindered olefin, tetramethylethylene, undergoes hydroboration exclusively to the monoalkylborane stage, producing $ThxBH_2$.[15] In this context, it appeared desirable to explore in more detail the hydroboration characteristics of chiral trisubstituted 2-R-apopinenes **1b–f** with the boranes in the hope of arriving at conditions which would permit the convenient synthesis of sterically bulkier mono- or bis(2-R-apoisopinyl)boranes, $RapBH_2$ or Rap_2BH (**2** or **3**).

Results and Discussion

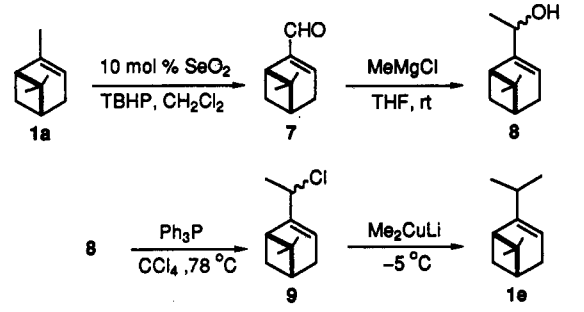
Schemes 1 and 2 outline the synthesis of 2-isobutyl- (**1d**) and 2-isopropylapopinenes (**1f**) starting from the easily accessible monoterpene, (+)-α-pinene [$[\alpha]^{22}_D$ +47.1° (neat), 91% ee].

Preparation of (+)-2-Isobutylapopinene (1d). The best method to synthesize **1d** is to subject α-pinene (**1a**) to the Schlosser metalation, followed by treatment with isopropyl bromide. Thus the metalation[4f] of **1a** with 1.25 equiv *t*-BuOK/*n*-BuLi at −78 °C provided the potassium salt of **1a**. Treatment of this salt with an excess of isopropyl bromide gave **1d** as the major product. The GC analysis

Scheme 1



Scheme 2



revealed two products, the desired terpene and a close-boiling isomeric product in a 80:20 ratio. The minor product, a close-boiling regioisomer, was separated by preparative GC and characterized as a β-pinene derivative **6**, the result of alkylation at the 3-position of α-pinene. Taking advantage of the fact that terminal double bonds, such as is present in the impurity **6**, are known to hydroborate more rapidly with bulky dialkylboranes than do internal, trisubstituted double bonds,[16] as in the desired 2-isobutylapopinene (**1d**), we readily separated the two components by treatment of the mixture with 20 mol % of 9-BBN at 50 °C under neat reaction condition. At the end of the reaction period, the ^{11}B-NMR spectrum of the reaction mixture indicated the quantitative consumption of the 9-BBN. Short-path distillation provided chemically pure **1d** [$[\alpha^{20}]_D$ +13.67° (neat)] (Scheme 1).

Preparation of (+)-2-Isopropylapopinene (1f). Treatment of α-pinene (**1a**) with a stoichiometric amount of selenium dioxide gives (+)-myrtenal (**7**) in 33% yield.[17] Both selenium dioxide and the byproducts of the stoichiometric allylic oxidation are extremely toxic and difficult to remove from the reaction mixture. Therefore, we adopted the Sharpless modification,[18] which uses a catalytic amount of selenium dioxide in combination with 2–4 equiv of *tert*-butyl hydroperoxide (TBHP) as a cooxidant. Treatment of α-pinene in methylene chloride at 24 °C for 60 h provided myrtenal (**7**) [$[\alpha]^{22}_D$ +15.05° (neat)] in 69% yield without any trace of unreacted **1a** or the allylic alcohol, myrtenol. Application of H_2O_2 as a cooxidant instead of TBHP produced a complicated mixture of products, probably resulting from the peracid behavior of the peroxide to give epoxides and diols as noted in the literature for other substrates.[17] The Grignard

(11) Midland, M. M.; Kazubski, A. *J. Org. Chem.* **1982**, *47*, 2495.
(12) Brown, H. C.; Weissman, S. A.; Perumal, P. T.; Dhokte, U. P. *J. Org. Chem.* **1990**, *55*, 1217.
(13) (a) Brown, H. C. *Boranes in Organic Chemistry*; Cornell University Press: New York, 1972. (b) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Synthesis Via Boranes*; Wiley-Interscience: New York, 1975. (b) Brown, H. C. *Hydroboration*: W. A. Benjamin: New York, 1962. (d) Brown, H. C.; Tsukamoto, A.; Bigley, B. B. *J. Am. Chem. Soc.* **1960**, *82*, 4703
(14) (a) Brown, H. C.; Moerikofer, A. W. *J. Am. Chem. Soc.* **1962**, *84*, 1478.
(15) Brown, H. C.; Klender, G. J. *Inorg. Chem.* **1962**, *1*, 204.
(16) Brown, H. C.; Liotta, R.; Scouten, C. G. *J. Am. Chem. Soc.* **1976**, *98*, 5297.
(17) (a) Ipatieff, V. N.; Czajkowski, G. J.; Pines, H. *J. Am. Chem. Soc.* **1951**, *73*, 4098. (b) Bochwic, B.; Markowicz, S. *Roczniki Chemii Ann. Soc. Chim. Polonorum* **1970**, *44*, 1595.
(18) Umbreit, M. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 5526.

Table 1. Reaction of 2-R-Apopinenes 1a–f with BMS and BH_3·THF in THF at 24 °C (molar ratio 1:1)

	BMS[a]			BH_3·THF[a]		
		% yield[b]			% yield[b]	
entry[a]	h	$RapBH_2$	Rap_2BH	time, h	$RapBH_2$	Rap_2BH
1a	1	82	18	0.08	72	28
1b	4	86	14	0.08	75	25
1c	8	89	11	0.25	78	22
1d	24	90	10	1.00	89	11
1e	24	95	5	2.00	95	5
1f	24	95	5	4.00	95	5

[a] Molar concentration 0.50 M each in 2-R-apopinene and borane, and ≥99 and ≥97% reaction was complete for the 2-R-apopinenes 1a–d and 1e,f, respectively. [b] Approximate percentage of organylboranes was determined by ^{11}B NMR of an aliquot after methanolysis.

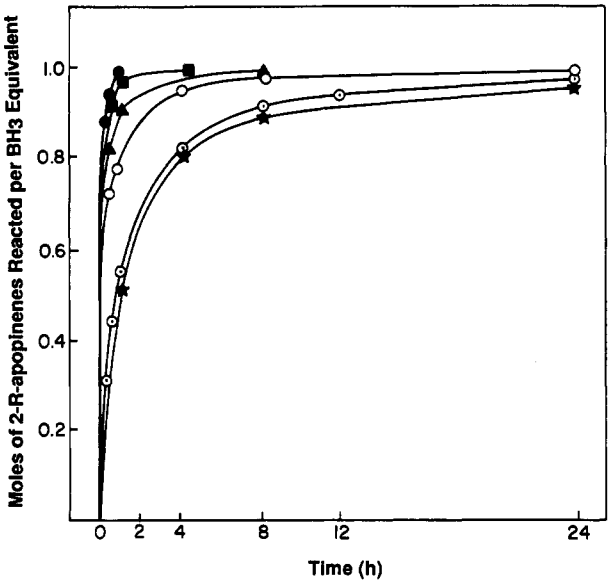


Figure 1. Rate study of the hydroboration of 2-R-apopinenes (0.50 M) with BMS (0.50 M) in THF at 24 °C. Molar ratio 1:1. ●, 1a; ■, 1b; ▲, 1c; ○, 1d; ⊙, 1e; ★, 1f.

reaction of **7** with methylmagnesium chloride in THF provided 2-(1-hydroxyethyl)apopinene (**8**) (92% yield) as a 60:40 diasteriomeric mixture, as indicated by ^1H NMR. This mixture of alcohols was treated with triphenylphosphine[19] in refluxing CCl_4 to provide 2-(1-chloroethyl)-apopinene (**9**) (81% yield) in a 60:40 diasteriomeric mixture. A nucleophilic substitution of **9** with lithium dimethylcuprate,[20] prepared *in situ* from methyllithium and cuprous iodide, gave (+)-isopropylapopinene (**1f**) [$[\alpha]^{25}_D$ +27.84° (neat)] in 83% yield (Scheme 2).

Rates and Stoichiometry of the Hydroboration of 2-R-Apopinenes 1a–f with Boranes (BMS and BH_3·THF) in THF at 24 °C. 2-R-Apopinenes 1a–f were subjected to hydroboration in THF at 24 °C with the boranes in 1:1, 2:1 and 3:1 molar ratios (eq 1).

$$\text{1a-f} + BH_3 \xrightarrow[24\ ^\circ C]{THF} \text{2a-f} \rightleftharpoons \text{3a-f} \qquad (1)$$

The reaction rate was followed by three methods: (i) the ^1H NMR spectrum (olefinic proton) was examined for residual 2-R-apopinene at appropriate intervals of time,

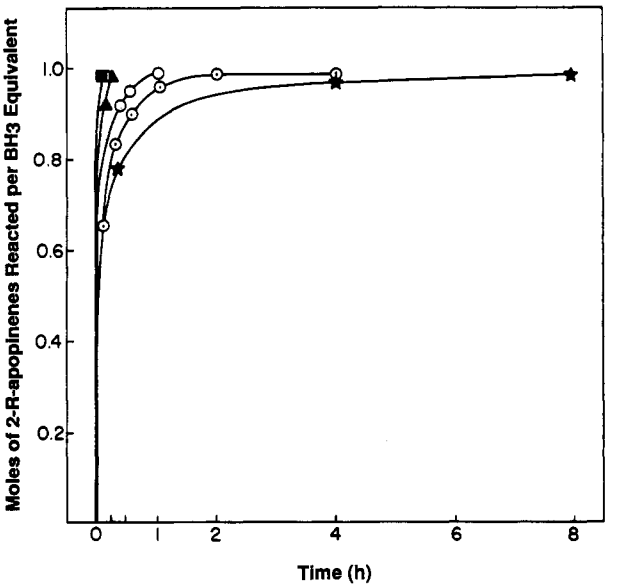


Figure 2. Rate study of the hydroboration of 2-R-apopinenes (0.50 M) with BH_3·THF (0.50 M) in THF at 24 °C. Molar ratio 1:1. ●, 1a; ■, 1b; ▲, 1c; ○, 1d; ⊙, 1e; ★, 1f.

using benzene as an internal standard;[21] (ii) aliquots of the solution were removed at appropriate periods of time and analyzed for residual hydride;[13b] (iii) hydrolyzed aliquots were oxidized with alkaline hydrogen peroxide and analyzed by GC analysis for 2-R-apopinene and/or the silyl ether of the alcohol, produced by hydroboration–oxidation, using a suitable internal standard (eq 2).

$$\text{1a-f} + \text{2a-f} + \text{3a-f} \xrightarrow[H_2O_2]{^-OH} \text{1a-f} + \underset{\text{10a-f}}{\text{R, OH}} \qquad (2)$$

All these analytical procedures gave concurring results. The results are summarized in Tables 1–3 and depicted graphically in Figures 1–6.

Hydroboration of (+)-α-Pinene (1a) with Boranes: Molar Ratio 1:1. The hydroboration of **1a** with BMS in THF is over in 1 h at 24 °C, and the ^{11}B NMR, after methanolysis, shows a mixture of boronate and borinate indicating the formation in the reaction mixture of $RapBH_2$ (**2a**) and Rap_2BH (**3a**) in ~82 and 18% yields, respectively. The reaction in THF of **1a** with BH_3·THF, a more reactive borane complex than BMS, is much faster, almost over in 5 min providing 72% **2a** and 28% **3a**. The Rap_2BH (**3a**) is formed in a larger amount in comparison with the reaction with BMS. This is owing to the fact that BH_3 is more loosely complexed with THF than SMe_2 (DMS), so that the first product of hydroboration, $RapBH_2$ (**2a**), therefore, more readily reacts with a second molecule of 2-R-apopinene to give **3a**. However, in the case of BMS, **2a**, which is probably complexed with the liberated DMS, the second hydroboration is slower, resulting in the formation of a lesser amount of **3a** and a larger amount of **2a**.

(19) Appel, R. *Angew Chem. Int. Ed. Engl.* **1975**, *14*, 801.
(20) Johnson, C. R.; Dutra, G. A. *J. Am. Chem. Soc.* **1973**, *95*, 7777.
(21) (a) Brown, H. C.; Dhar, R. K.; Ganesan, K.; Singaram, B. *J. Org. Chem.* **1992**, *57*, 499. (b) Brown, H. C.; Dhar, R. K.; Ganesan, K.; Singaram, B. *J. Org. Chem.* **1992**, *57*, 2716. (c) Brown, H. C.; Ganesan, K.; Dhar, R. K. *J. Org. Chem.* **1992**, *57*, 3767. (d) Brown, H. C.; Ganesan, K. *Tetetrahedron Lett.* **1992**, *33*, 3421. (e) Brown, H. C.; Ganesan, K.; Dhar, R. K. *J. Org. Chem.* **1993**, *58*, 147.

Table 2. Reaction of 2-R-Apopinenes 1a–f (1.00 M) with BMS (0.50 M) and BH_3·THF (0.50 M) in THF at 24 °C

	BMS[a,b]				BH_3·THF[a,b]			
		residual	relative % of[c]			residual	relative % of[c]	
entry[a]	mole/BH_3	1a–f (%)	$RapBH_2$	Rap_2BH	mole/BH_3	1a–f (%)	$RapBH_2$	Rap_2BH
1a	1.86	7	7	93	1.90	5	5	95
1b	1.84	8	9	91	1.89	6	6	94
1c	1.80	10	11	89	1.85	8	8	92
1d	1.68	18	22	78	1.77	11	13	87
1e	1.44	27	37	63	1.57	22	27	73
1f	1.27	37	58	42	1.45	28	38	62

[a] 2:1 Molar ratio of 2-R-apopinene to borane. [b] Analysis of reaction mixture at 48 h. [c] A sample calculation for 1c is given in the Experimental Section.

Table 3. Reaction of 2-R-Apopinenes 1a–f (1.0 M) with BMS (0.33 M) and BH_3·THF (0.33 M) in THF at 24 °C

	BMS[a,b]				BH_3·THF[a,b]			
		residual	relative % of[c]			residual	relative % of[c]	
entry[a]	mole/BH_3	1a–f (%)	$RapBH_2$	Rap_2BH	mole/BH_3	1a–f (%)	$RapBH_2$	Rap_2BH
1a	1.98	34	≤2	98	1.98	34	≤1	99
1b	1.93	36	4	96	1.94	35	3	97
1c	1.87	38	7	93	1.93	37	4	96
1d	1.80	40	11	89	1.87	38	7	93
1e	1.70	43	18	82	1.79	41	12	88
1f	1.40	53	43	57	1.63	46	23	77

[a] 3:1 Molar ratio of 2-R-apopinene to borane. [b] Analysis of reaction mixture at 48 h. [c] A sample calculation for 1c is given in the Experimental Section.

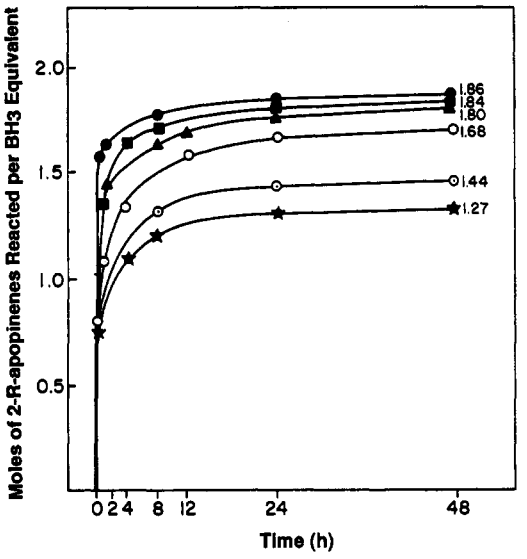


Figure 3. Rate study of the hydroboration of 2-R-apopinenes (1.00 M) with BMS (0.50 M) in THF at 24 °C. Molar ratio 2:1. ●, 1a; ■, 1b; ▲, 1c; ○, 1d; ⊙, 1e; ★, 1f.

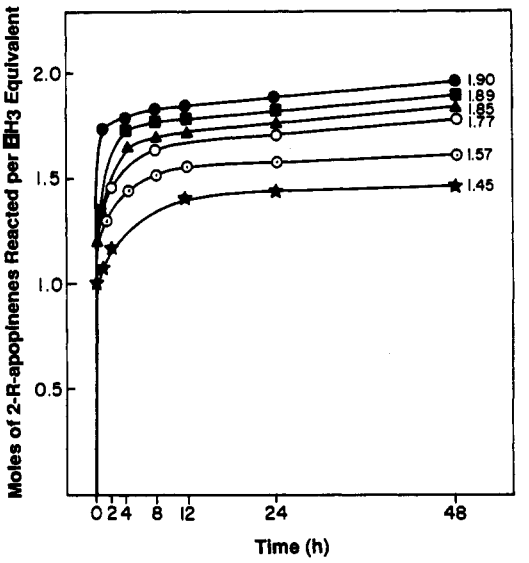


Figure 4. Rate study of the hydroboration of 2-R-apopinenes (1.00 M) with BH_3·THF (0.50 M) in THF at 24 °C. Molar ratio 2:1. ●, 1a; ■,1b; ▲, 1c; ○, 1d; ⊙, 1e; ★, 1f.

Molar Ratio 2:1. The reaction of **1a** (1.00 M) with BMS (0.50 M) in THF proceeds rapidly past the $RapBH_2$ (**2a**) stage in less than 15 min and then continues slowly to the Rap_2BH (**3a**) stage. After 48 h, uptake of **1a** was 1.86 equiv (93% reaction) per borane equiv, at which point the reaction mixture contains relatively 7% **2a** and 93% **3a**, respectively. The reaction of **1a** (1.00 M) with BH_3 in THF (0.50 M), under similar reaction conditions, is relatively fast, with 95% of utilization of **1a** after 48 h, corresponding to the uptake of 1.90 equiv of 2-R-apopinene (**1a**) per equiv of borane. The approximate ratio of **2a** and **3a** are 5 and 95%, respectively.

Molar Ratio 3:1. The rate of the reaction of **1a** (1.00 M) with either BMS (0.33 M) or BH_3 (0.33 M) in THF is faster, as expected, the reaction being ~99% complete in 24 h with BMS or in 12 h with BH_3·THF. The approximate ratio of Rap_2BH (**3a**) in these reactions is 98 and 99%, respectively.

Hydroboration of Ethylapopinene (1b) with Boranes: Molar Ratio 1:1. The hydroboration of **1b** (0.50 M) with BMS (0.50M) proceeds very fast. A quantitative consumption of olefin is observed after 4 h. ^{11}B NMR of the reaction mixture, after methanolysis, shows a mixture of boronate and borinate, indicating the formation of $RapBH_2$ (**2b**) in ~86% and Rap_2BH (**3b**) in ~14% yield. However, in the case of hydroboration with BH_3·THF, the reaction is much faster, almost over in 5 min, providing **2b** in ~75% and **3b** in ~25% yields.

Molar Ratio 2:1. The hydroboration of **1b** (1.00 M) with BMS (0.50 M) in THF proceeds rapidly to the $RapBH_2$ (**2b**) stage in less than 15 min, and then it proceeds slowly to the Rap_2BH (**3b**) stage. After 48 h, the uptake of 2-R-apopinene is 1.84 equiv (92% reaction) per borane equiv, which corresponds to 9% **2b** and 91% **3b**. However, the reaction of **1b** with BH_3·THF under similar reaction

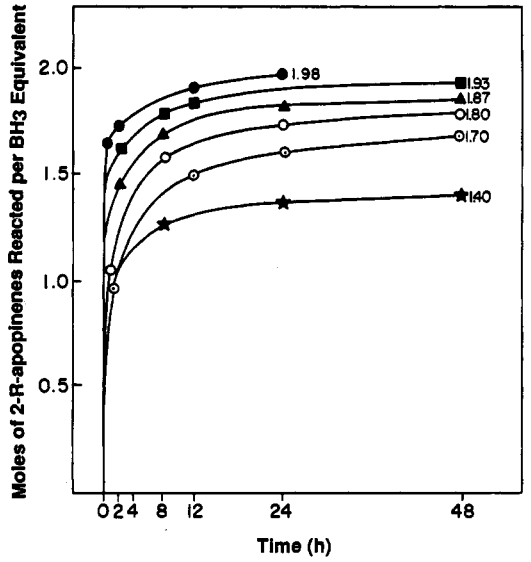


Figure 5. Rate study of the hydroboration of 2-R-apopinenes (1.00 M) with BMS (0.33 M) in THF at 24 °C. Molar ratio 3:1. ●, 1a; ■, 1b; ▲, 1c; ○, 1d; ⊙, 1e; ★, 1f.

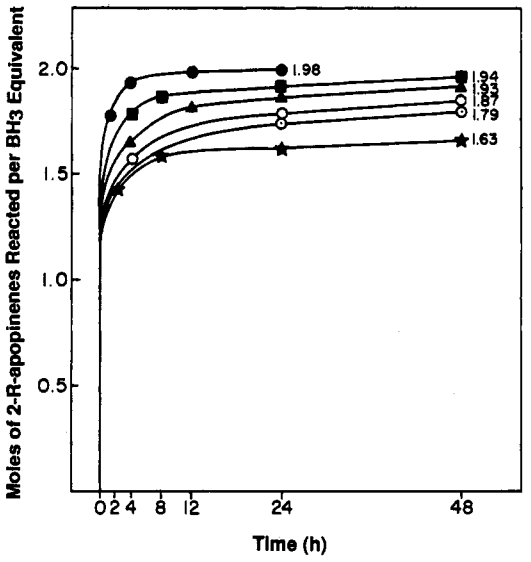


Figure 6. Rate study of the hydroboration of 2-R-apopinenes (1.00 M) with BH_3·THF (0.33 M) in THF at 24 °C. Molar ratio 3:1. ●, 1a; ■, 1b; ▲, 1c; ○, 1d; ⊙, 1e; ★, 1f.

conditions as described above, is faster, with 96% of utilization of **1b** observed after 48 h, corresponding to the uptake of 1.89 equiv of 2-R-apopinene per equiv of borane. The relative approximate formations of **2b** and **3b** are 6 and 94%, respectively. It is apparent from the results observed that the formation of bis(2-R-apoisopinyl)borane (**3b**) is more than the 2-R-apoisopinylborane (**2b**) formed, when BH_3·THF is used.

Molar Ratio 3:1. In the reaction of 2-R-apopinene (**1b**) (1.00 M) with BMS (0.33 M) or BH_3·THF (0.33 M) at 24 °C, 1.93 and 1.94 equiv of **1b** react, respectively, corresponding to almost 93% completion of the reaction after 48 h, and the relative formation of Rap_2BH (**2b**) in 96 and 97% yields, respectively. The rate of the reaction is slower in comparison with the rate observed for **1a**.

Hydroboration of 2-*n*-Propylapopinene (1c) with Boranes: Molar Ratio 1:1. The rate of the hydroboration of **1c** with BMS, 0.50 M each, resembles closely that of **1b**, 99% of the reaction being complete after 8 h at 24 °C. The reaction mixture, after methanolysis, showed the formation of ~89% **2c** and ~11% **3c** as determined by ^{11}B NMR. In the case of hydroboration with BH_3·THF, the former is formed in ~78% and the latter in ~22%, and the hydroboration is over in 15 min at 24 °C.

Molar Ratio 2:1. 2-R-apopinene (**1c**) in THF is added to a solution of BMS in the same solvent at 24 °C, giving a solution which is 1.00 M in the 2-R-apopinene and 0.50 M in borane. The reaction proceeds toward the Rap_2BH (**3c**) stage in less than 2 h, but proceeds at a slower rate to completion of the Rap_2BH stage, in comparison with **1b**. After 48 h, 1.80 equiv of **1c** reacts per borane equiv, indicating a mixture of 11 and 89% of **2c** and **3c**, respectively. Under similar reaction conditions, hydroboration with BH_3·THF shows the uptake of 1.85 equiv of **1c** per equiv of borane, corresponding to 8% of **2c** and 92% of **3c**.

Molar Ratio 3:1. After 48 h, reaction in THF at 24 °C of **1c** (1.00 M) with BMS (0.33 M) or BH_3·THF (0.33 M) furnishes **3c** in 93 and 96% yield, respectively; the reaction represents total consumption of 1.87 and 1.93 equiv of **1c**, respectively, per equiv of the borane. The rate of the reaction is slower than that observed for 2-R-apopinenes (**1a,b**).

Hydroboration of 2-Isobutylapopinene (1d) with Boranes: Molar Ratio 1:1. Compared with the 2-R-apopinenes studied (**1a–c**), **1d** (0.50 M) shows an even slower rate of hydroboration with BMS (0.50 M), requiring 24 h for 100% reaction, providing ≥90% of **2d** and ≤10% of **3d**. Interestingly, almost the same percentage formation of a mixture of mono- and bis(2-R-apoisopinyl)boranes were realized when **1d** (0.50 M) was subjected to the reaction under the same condition with BH_3·THF (0.50 M), but the reaction was complete in 1 h.

Molar Ratio 2:1. 2-R-Apopinene (**1d**) (1.00 M), a sterically bulkier olefin than the aforementioned 2-R-apopinenes **1a–c**, exhibits a slower rate of the reaction with BMS (0.50 M). After 48 h, 1.68 equiv (84% reaction) of **1d** reacted per equiv of borane resulting in a mixture consisting relatively of 22% **2d** and 78% **3d**, respectively. The reaction of **1d** with BH_3·THF, under similar reaction conditions, proceeds relatively faster, 89% of the reaction being complete after 48 h, corresponding to the 1.77 equiv of **1d** reacted per equiv of borane providing 13% **2d** and 87% **3d**.

Molar Ratio 3:1. The reaction of 3 equiv of 2-R-apopinene **1d** with equiv of BMS or BH_3·THF shows the relative formation of **3d** in 89 and 93% yield, respectively, after 48 h.

Hydroboration of 2-Phenylapopinene (1e) with Boranes: Molar Ratio 1:1. The hydroboration with stoichiometric quantities of **1e** (0.50 M) with BMS (0.50 M) requires 24 h to complete 97% of the reaction, corresponding to essentially pure $PapBH_2$ (**2e**). Minor amounts, ≤5% of **3e**, may be present. Similar results are realized when **1e** is hydroborated with BH_3·THF (0.50 M in each) with considerable shorter reaction time, ~2 h, required.

Molar Ratio 2:1. The reaction of **1e** at 24 °C under standard reaction conditions (1.00 M in **1e** and 0.50 M in BMS) proceeds rapidly to the $RapBH_2$ (**2e**) stage, but relatively slowly beyond. After 48 h, consumption of **1e** was only 1.44 equiv (72% reaction) per borane equiv, corresponding to the formation of 37% **2e** and 63% **3e**. Obviously, the presence of the additional 2-phenylapop-

inene (1e) results in an increased formation of 3e, as expected; the amount of 3e formed under these conditions is less for the more-hindered 1e, than for the less-hindered derivatives studied, 2-R-apopinene (R = Me, Et, Pr, and *i*-Bu). The reaction with BH_3·THF (0.50 M) proceeds readily to the 2e stage in 5 min, but at a much slower rate beyond, with uptake of 1.57 equiv (79% reaction) of 1e per borane equiv; 27% 2e and 73% of Rap_2BH (3e) are formed. This is representative of the changes observed for the previous cases in utilizing BH_3·THF as compared to BMS.

Molar Ratio 3:1. The reaction of hindered 2-R-apopinene (1e) (1.00 M) with BMS (0.33 M) produced 18% 2e and 82% 3e, while the reaction with BH_3·THF (0.33 M) provides 12% of the former and 88% of the latter, after 48 h. Consequently, the pattern of behavior is consistent.

Hydroboration of 2-Isopropylapopinene (1f) with Boranes: Molar Ratio 1:1. The hydroboration of 1f resembles closely to the corresponding reaction of 2-phenylapopinene (1e). At 24 °C, hydroboration of 1f with BMS (0.50 M in each) requires 24 h for the reaction to be 97% complete, giving the same percentage mixture of mono- and bis(2-R-apoisopinyl)boranes as that formed for 1e. Similar results are realized when BH_3·THF is used, with the only difference being the faster rate of the reaction, complete in 4 h.

Molar Ratio 2:1. Unlike 1e, the sterically bulkier isopropylapopinene (1f) under similar experimental conditions (1.00 M in 1f, 0.50 M in BMS) shows a much slower rate. Only 1.27 equiv (64% reaction) of 1f reacted per equiv of borane after 48 h, providing more of 2-isopropylapoisopinylborane (58%, 2f) than the corresponding bis(2-isopropylapoisopinyl)borane (42%, 3f), while only 1.45 equiv (73% reaction) of 1f is used up per equiv of borane in the hydroboration with BH_3·THF (0.50 M), resulting in the relative formation of 38% 2f and 62% 3f.

Molar Ratio 3:1. The reaction of 1f (1.00 M) with BMS (0.33 M) or BH_3·THF (0.33 M) shows consumption of 1.40 and 1.63 equiv per equiv of boranes corresponding to the relative formation of Rap_2BH (3f) in 57 and 77% yields, respectively.

Consideration of the Steric Requirements of the Groups R in 1a–f. In our early work with molecular addition compounds we frequently observed that the steric requirements of the R groups in RNH_2 and in 2-R-pyridine increased from Me < Et < *i*-Pr < *t*-Bu.[13a,22] The term steric requirements does not refer to the size of the groups, but its steric influence on a neighboring reaction center.[13a,22] Consequently, we had no hesitation in predicting that the steric effect of R in the 2-R-apopinenes 1a–f studied would increase from R = Me < Et < Pr < *i*-Bu < *i*-Pr.

But the phenyl group was never included in these early studies of steric strains. The group is much larger, but it is not possible to predict whether the steric effect of R groups on the double bond undergoing hydroboration in 1a–f will be larger or smaller for Ph as compared to 2-*i*-Pr. However, the hydroboration results clearly reveal that the effective steric influence of the R groups in 2-R-apopinenes 1a–f increases in the order, Me < Et < Pr < *i*-Bu < Ph < *i*-Pr. Accordingly, we are adopting this order as representing the increasing steric requirements by these six groups for the hydroboration of these six 2-R-apopinenes 1a–f.

(22) Brown, H. C. *J. Chem. Soc.* **1956**, 1248.

Conclusions

The hitherto unknown 2-isobutyl- (1d) and 2-isopropylapopinene (1f) have been synthesized from α-pinene by relatively simple procedures. This made available a group of six 2-R-apopinenes (R = Me, Et, Pr, *i*-Bu, Ph, and *i*-Pr) for study of the effects of the steric requirements of the R groups on the rate and stoichiometry of the hydroboration to form the corresponding mono- and bis-(2-R-apopisopinyl)boranes.

This comparative study of the hydroboration of these six closely related 2-R-apopinenes derivatives has revealed a number of simple relationships between the steric requirements of the groups R (Me, Et, Pr, *i*-Bu, Ph, and *i*-Pr) and the hydroboration results realized. These may be summarized as follows.

1. In each case hydroboration with BMS or BH_3·THF proceeds more rapidly with the latter than with the former.
2. With increasing steric requirements of R there is an increasing tendency for the reaction to stop short of the Rap_2BH stage, tending to proceed cleanly to $RapBH_2$ in the cases where R = Ph (1e) and *i*-Pr (1f).
3. Both BMS and BH_3·THF in the molecular ratio of 1:1 for the borane and R-2-apopinene give essentially pure $RapBH_2$ for R = Ph (1e) and *i*-Pr (1f).
4. With excess 2-R-apopinenes, the reaction proceeds toward the Rap_2BH stage, with the amount of these derivatives decreasing with increasing steric requirements of R.
5. Hydroboration with BH_3·THF proceeds further toward the Rap_2BH stage than occurs with BMS under the same conditions.

The present study is proving very valuable in developing practical procedures for the synthesis of chiral hindered 2-R-apoisopinocampheylboranes and other derivatives of considerable promise for the rapidly developing area of asymmetric synthesis *via* chiral organoboranes.

Experimental Section

All glassware was dried at 140 °C overnight, assembled hot, and cooled to room temperature in a stream of nitrogen.[13b] All reactions involving air- or moisture-sensitive compounds were performed under static pressure of nitrogen.[13b] All reported boiling points are uncorrected. ^{11}B NMR were obtained at 96 MHz and are referenced relative to BF_3·EE. The rate of reaction was followed by ^1H NMR spectra, which were recorded at 300 MHz while ^1H and ^{13}C NMR spectra for all new compounds were recorded at 200 and 50 MHz, respectively, in $CDCl_3$ solution with tetramethylsilane (TMS) as an internal standard. Chemical shifts in the ^1H and ^{13}C NMR spectra are reported as parts per million (ppm) downfield from TMS. Mass spectra were recorded at an ionizing voltage of 70 eV. GC analyses for chemical purity and rate data were performed on either 10% SP-2100 (6 ft × 1/8 in.) on Supelcoport (80–10 mesh) or 10% Carbowax (6 ft × 1/8 in.) on Chromosorb W (80–100 mesh). All materials for which optical rotation information is provided were purified by preparative GC on a 6 ft × 0.5 in. column packed with 20% SE-30 on Chromosorb W (60–80 mesh). Optical rotations were measured on a digital polarimeter in a 1-dm cell.

Materials. Fresh tetrahydrofuran (THF) distilled from sodium benzophenone ketyl was used. BMS, BH_3·THF, (+)-α-pinene, methyllithium, *n*-butyllithium, 9-BBN, copper(I) iodide, anhydrous *tert*-butyl hydroperoxide (TBHP), isopropyl bromide, methylmagnesium chloride, potassium *tert*-butoxide, and selenium dioxide were used without any further purification. Dichloromethane (CH_2Cl_2), and carbon tetrachloride (CCl_4) were

distilled from phosphorus pentoxide prior to use. Straight-chain hydrocarbons (used as internal standards for GC analyses) and benzene were obtained in 99+% purity and used directly.

Preparation of (+)-2-Isobutylapopinene by Metalation and Alkylation (*i*-PrBr) of (+)-α-Pinene of 91% ee. In a 1-L flask equipped with a magnetic stirring bar, septum inlet, and adaptor for nitrogen was placed *t*-BuOK (50 g, 446 mmol) and it was cooled to −78 °C. To it were added hexane (150 mL) and (+)-α-pinene (56.8 mL, 357 mmol, 91% ee), followed by *n*-BuLi (2.5 M, 178 mL, 446 mmol). The reaction mixture was allowed to warm up to room temperature and stirring was continued for 60 h. The resulting potassium salt was dissolved in THF (200 mL) at −78 °C. 2-Bromopropane (41.9 mL, 446 mmol) was added to this solution over a period of 45 min. Stirring was continued at −78 °C for 1 h and the mixture was warmed up to room temperature and stirred for an additional 12 h. It was then poured into 500 mL of ice-cold water. The organic layer was separated, and the aqueous layer was extracted with pentane (2 × 100 mL). The organics were washed with water and brine, dried, and evaporated. Distillation of the residue gave an oil (53.5 g, 84% yield), consisting mainly of (+)-2-isobutylapopinene (**1d**), along with ~20% of a close-boiling compound identified as a β-pinene derivative **6**, by ^{1}H and ^{13}C NMR. The resulting oil was stirred over 9-BBN (7.32 g, 20 mol %) at 50 °C for 12 h. Distillation (53–54 °C, 0.9 mmHg) afforded **1d** (40.7 g, 95% recovery) of 97% GC purity. A small portion of the sample was further purified by preparative GC to obtain the 100% pure sample: α^{20}_D +13.67° (neat); ^{1}H NMR δ 5.15 (m, 1H), 2.29–2.40 (m, 1H), 2.22 (br, 2H), 1.97–2.13 (m, 2H), 1.79–1.85 (m, 2H), 1.55–1.75 (m, 1H), 1.27 (s, 3H), 1.15 (br d, 1H), 0.89 (d, 3H), 0.85 (s, 3H), 0.84 (d, 3H); ^{13}C NMR δ 148.17 (C_2), 117.46 (C_3), 47.18 (C_1), 46.13 (C_5), 41.11 (C_{10}), 38.12 (C_6), 32.00 (C_7), 31.57 (C_4), 26.64 (C_8), 26.11 or 23.08 or 22.88 (C_{11} or C_{12} or C_{13}), 21.40 (C_9); MS (70 ev) *m/z* (relative intensity) 178 (M^+, 10), 57 (M^+ − 121, 100). Anal. Calcd for $C_{13}H_{22}$: C, 87.56; H, 12.44. Found: C, 87.20; H, 12.79.

^{1}H NMR of **6**: δ 4.70 (br d, 2H), 2.50–2.65 (m, 1H), 2.41 (t, *J* = 6.0 Hz, 1H), 2.20–2.35 (m, 1H), 1.90–2.25 (m, 2H), 1.75–1.90 (m, 1H), 1.55–1.65 (m, 1H), 1.25 (s, 3H), 1.15 (br d, 1H), 0.95 (d, 3H), 0.85 (d, 3H), 0.81 (s, 3H); ^{13}C NMR of **6** δ 155.36 (C_2), 107.75 (C_{10}), 53.14 (C_1), 41.25 (C_5), 40.54 (C_6), 40.20 (C_3), 28.57 (C_7), 26.41 (C_8), 26.16 (C_4), 32.87 or 22.04 or 17.57 (C_{11} or C_{12} or C_{13}); MS (70 eV) *m/z* (relative intensity) 178 (M^+, 2), 135 (M^+ − 43, 64), 33 (M^+ − 153, 100).

(1*S*)-(+)-Myrtenal (7). To a suspension of SeO_2 (12.4g, 0.11 mol, 10 mol %) in CH_2Cl_2 (500 mL) cooled to 0 °C was added TBHP (3 M, 690 mL, 2.07 mol) followed by a slow addition of (+)-α-pinene (152.4 g, 1.12 mol, 91% ee). The reaction mixture was warmed up to room temperature and allowed to stir for 72 h, during which time the solution turned to orange color with the selenium-based precipitate deposited along the side of the flask. Dimethyl sulfide (147 mL) was added to the reaction mixture and the solution was stirred at room temperature for 3 h. The volatiles of the reaction mixture were removed in *vacuo*, and the residual oil was dissolved in ether (400 mL) and treated with aqueous 1 N NaOH solution (2 × 50 mL). The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in *vacuo*. Distillation of the crude oil furnished 116 g (69%) of **7**: bp 52–54 °C (0.45 mmHg); $[\alpha]^{22}_D$ +15.05° (neat). ^{1}H and ^{13}C NMR spectral data agree with the reported data.[23]

2-(1-Hydroxyethyl)apopinene (8). To a solution of (+)-myrtenal (103 g, 686 mmol) in freshly distilled THF (200 mL) at 0 °C was added slowly a solution of methylmagnesium chloride (3 M, 286 mL, 858 mmol) in THF over 1-h period. The solution was allowed to warm up to room temperature and stirred for 12 h. The reaction mixture was poured into a cold solution of saturated ammonium chloride. The aqueous layer was extracted with pentane. The organic layers were combined, washed with brine, and dried over Na_2SO_4, and the solvent was removed. The crude product, a viscous oil, was distilled (bp 60–62 °C, 0.40 mmHg) to give a 60:40 diasteriomeric mixture (by ^{1}H NMR) of alcohols **8** (105 g, 92%); ^{1}H NMR δ 5.41 (m, 1H), 4.20 (m, 1H), 2.33–2.50 (m, 1H), 2.22–2.33 (m, 3H), 1.58 (br, 1H), 1.31 (s, 3H), 1.10–1.25 (m, 4H), 0.85 (s, 1.8H), 0.81 (s, 1.2H); ^{13}C NMR δ 152.09/152.04 (C_2), 116.95/115.99 (C_3), 70.77/70.24 (C_{10}), 42.58 or 41.80/41.19 (C_5/C_1), 31.92/31.88/31.13 (C_7/C_4), 21.48/21.40 and 21.11/21.01 (C_{11} and C_9), 37.94/37.85 (C_6), 26.32 (C_8); MS (70 eV) *m/z* (relative intensity) 166 (M^+, 4), 107 (M^+ − 59, 52), 79 (M^+ − 87, 65), 45 (M^+ − 121, 100).

2-(1-Chloroethyl)apopinene (9). To a refluxing solution of alcohols **8** (89.0 g, 535 mmol) in carbon tetrachloride (700 mL) was added slowly triphenylphosphine (196.6 g, 749.6 mmol) over a 1-h period. The reaction mixture was further refluxed for additional 5 h, and the solvent was removed. To the residual solid was added pentane (200 mL) and the solution was filtered. The solid was washed with pentane (200 mL) and the organic layer was removed. The combined organic layers were dried over Na_2SO_4, and the solvent was removed. Distillation (58–60 °C, 0.50 mmHg) of the oil provided 80.3 g (81%) of **9**: ^{1}H NMR δ 5.51 (br, 1H), 4.48–4.61 (m, 1H), 2.30–2.55 (m, 2H), 2.21–2.31 (m, 2H), 2.02–2.19 (m, 1H), 1.55 (br, 1.8 H or 1.2H), 1.51 (br, 1.8H or 1.2H), 1.30 (s, 3H), 1.18 (br, 0.6H or 0.4H), 1.11 (br, 0.6H or 0.4H), 0.82 (s, 1.2H), 0.79 (s, 1.8H); Anal. Calcd for $C_{11}H_{17}Cl$: C, 71.53; H, 9.28; Cl, 19.19. Found: C, 71.39; H, 9.51; Cl, 19.06; MS (70 eV) *m/z* (relative intensity) 184/186 (M^+, 12), 149 (M^+ − 35, 72), 105 (M^+ − 79, 100).

(+)-2-Isopropylapopinene (1f). To a suspension of cuprous iodide (94.9 g, 498 mmol) at 0 °C in ether (250 mL) was added methyllithium (711 mL, 996 mmol) dropwise over 1.5-h period. The suspension turned bright yellow (methylcopper)[20] and then as more methyllithium was added, turned into a light tan solution. The chloro compound **9** (80 g, 433.1 mmol) in EE (100 mL) was slowly added at −5 °C to the above lithium dimethylcuprate solution over 1 h and the mixture was allowed to stir for 12 h at ambient temperature. The reaction mixture was poured into a cold saturated solution of ammonium chloride and stirred for 30 min and then filtered. The organic layer was treated with brine and dried over Na_2SO_4. The solvent was removed and distillation (70–72 °C, 12 mmHg) of the residual oil from $LiAlH_4$ provided **1f** (58.3 g, 82%) of ≥98% GC purity: α^{25}_D +27.84° (neat), $[\alpha]^{25}_D$ +35.31° (*c* 1.00, MeOH); ^{1}H NMR δ 5.15 (m, 1H), 2.30–2.41 (m, 1H), 2.20 (br, 2H), 2.02–2.27 (m, 3H), 1.28 (s, 3H), 1.11 (br d, 1H), 0.95 (d, 3H), 0.91 (d, 3H), 0.80 (s, 3H); ^{13}C NMR δ 154.53 (C_2), 113.61 (C_3), 44.33 (C_1), 41.32 (C_5), 37.98 (C_6), 34.33 (C_{10}), 32.02 (C_7), 31.41 (C_4), 26.58 (C_8), 21.56 (C_9), 20.84, 20.48 (C_{11} or C_{12}); MS (70 eV) *m/z* (relative intensity) 164 (M^+, 20), 121 (M^+ − 43, 64), 93 (M^+ − 71, 60), 79 (M^+ − 85, 100). Anal. Calcd for $C_{12}H_{20}$: C, 87.73; H, 12.27. Found: C, 87.43; H, 12.51.

Rate and Stoichiometry for the Reaction of 2-R-Apopinenes 1a–f with 10 M BMS and 1.0 M BH_3·THF in THF at 24 °C. The reactions were carried out in THF in three different molar concentrations, namely 1 equiv of borane and 1, 2, and 3 equiv of 2-R-apopinene, respectively. In all of these experiments 6–12 mmol of 2-R-apopinenes were used for the reaction with boranes. The concentration of 2-R-apopinenes with boranes was maintained at 0.50 M each, 0.50 M to 1.00 M, and 0.33 M to 1.00 M, respectively. The progress of the reaction was monitored at appropriate time intervals by either or all of the following techniques: (i) measuring the hydrogen liberated by hydrolysis[18b] of 0.50 mL of an aliquot; (ii) ^{1}H NMR analysis [~0.1 mL of sample was diluted with $CDCl_3$ (0.60–0.70 mL)] of the olefinic proton (5.1–5.2 ppm for **1a–d,f** and 5.7–5.8 ppm for **1e**) of the residual 2-R-apopinene in comparison with the 1.0 M solution of benzene in THF as an internal standard; and (iii) GC analysis of either residual 2-R-apopinene or silyl ether (silylation was done with bis(trimethylsilyl)acetamide using catalytic amount of pyridine in THF) of the product alcohol **10** resulting from the hydroboration, using a suitable internal standard whose response factor had been calculated. In the experiments involving 2-R-apopinenes (**1a,b**) was used dodecane, while for the 2-R-apopinenes (**1c–f**) was used *n*-tridecane as an internal standard. In the reaction of 2-R-apopinene to borane in 2:1 and 3:1 ratio, respectively, an aliquot of the reaction was methanolyzed after 48 h and analyzed by ^{11}B NMR which showed the absence of a peak at δ +18 due to $B(OMe)_3$ which was indicative of the total consumption of the BH_3 species.

The reaction of 10 M BMS (3.50 mmol, 0.50M) with 2-*n*-propylapopinene (**1c**) (7.00 mmol, 1.00 M) is described as representative. To a oven-dried, 25-mL round-bottom flask

(23) (a) Laihia, K.; Kolehmainen, E.; Malkavaara, P.; Korvola, P.; Mänttäri, P.; Kauppinen, R. *Magn. Reson. Chem.* **1992**, *30*, 754. (b) Coxon, J. M.; Hydes, G. J.; Steel, P. J. *J. Chem. Soc. Perkin Trans. 2* **1984**, 1351.

Table 4. Reaction of 2-*n*-Propylapopinene with BMS in THF at 24 °C (molar ratio 1:2)[a]

time, h	residual olefin 1c, mmol	alcohol formed (10c), mmol	residual hydride, mmol	moles/BH_3
0.25	3.90	3.10	–	0.89
0.50	2.93	3.83	6.67	1.16
1	1.91	5.09	–	1.45
2	1.59	5.41	5.15	1.55
8	1.18	5.82	4.70	1.66
12	1.04	5.96	4.53	1.70
24	0.96	6.04	4.45	1.73
48	0.67	6.30	4.21	1.80

[a] BMS (0.50 M, 3.50 mmol) and 2-*n*-propylapopinene (1.00 M, 7.00 mmol).

Table 5. Reaction of 2-R-Apopinenes 1a–f (1.00 M) with BMS (0.50 M)[a] in THF at 24 °C

entry	2-R-apopinene 1a–f, mmol	BMS, mmol	residual 1a–f, mmol	alcohol 10a–f, mmol	residual hydride, mmol	mole/BH_3
1a	12.48	6.24	0.87	11.61	7.09	1.86
1b	11.74	5.87	0.98	10.77	6.83	1.84
1c	7.00	3.50	0.67	6.30	4.21	1.80
1d	9.42	4.71	1.69	7.91	6.22	1.68
1e	9.12	4.56	2.45	6.57	7.05	1.44
1f	7.80	3.90	2.85	4.94	6.72	1.27

[a] 2:1 Molar ratio of 2-R-apopinene to BH_3. Analysis of reaction mixture at 48 h.

equipped with a septum inlet and magnetic stirring bar was charged 1c (1.15 g, 7.00 mmol), THF (3.54 mL), *n*-tridecane (0.60 mL, 2.50 mmol), benzene (1.07 M in THF, 1.20 mL, 1.28 mmol), and BMS (0.35 mL, 3.5 mmol) successively. An aliquot of the solution was analyzed following the aforementioned analytical procedures. The results are summarized in Table 4.

At 48 h, ^{1}H NMR analysis showed that 0.67 mmol of residual 1c, therefore 6.30 mmol of 1c, reacted relative to the benzene internal standard while GC analysis showed 0.71 mmol of the residual 1c and 6.29 mmol of the corresponding alcohol, a product of hydroboration.

From these data the amounts of $PrapBH_2$ (2c) and $Prap_2BH$ (3c) are calculated. The amount of $PrapBH_2$ is assigned equal to the unreacted 2-*n*-propylapopinene, 0.67 mmol, and the amount of $Prap_2BH$ is calculated to be 2.82 mmol: 1/2[6.30 mmol (alcohol) – 0.67 mmol ($PrapBH_2$)]. Therefore, the percentage of unreacted 1c is calculated to be 10% [(0.67/7.00) × 100], and the relative percentages of $PrapBH_2$ and $Prap_2BH$ are calculated to be 11% [(0.67/6.30) × 100] and 89% [(5.63/6.30) × 100], respectively. The material balance of the B–H bond is calculated as follows: hydride in the solution (4.21 mmol) + alcohol formed (6.30 mmol) = 10.51 mmol. The expected value is 10.50 mmol (3 × 3.5 mmol of BH_3). The analysis of the reaction mixture after 48 h for the reaction of 2-R-apopinenes 1a–f (1.00 M) with BMS (0.50 M) is shown in Table 5. From these data the relative percentages for $RapBH_2$ (2a–f) and Rap_2BH (3a–f) are calculated and included in Table 2. The data for the reaction of 2-R-apopinenes 1a–f (1.00 M) with BH_3·THF (0.50 M) is provided as supplementary material in Table 6. Similarly, the data for the reaction of 2-R-apopinenes (1a–f) (1.00 M) with BMS (0.33 M) and BH_3·THF (0.33 M), respectively, is provided as supplementary material in Tables 7 and 8.

A representative calculation for the reaction of 1c (8.70 mmol, 1.00 M) with BMS (2.90 mmol, 0.33 M) follows. From the ^{1}H NMR analysis, 3.30 mmol of residual 1c is present. Therefore, 1c reacted is calculated as 5.40 mmol (8.70–3.30 mmol), corresponding to the amount of alcohol 10c formed. If 100% of $Prap_2BH$ had formed, the amount of 1c reacted would have been 2 × 2.90 mmol of BH_3, i.e. 5.80 mmol. From these data the amount of $PrapBH_2$ is calculated as 0.40 mmol [2 × 2.90 mmol (BH_3) – 5.40 mmol (alcohol 10c)] and the $Prap_2BH$ is 2.50 mmol: 1/2[5.40 mmol (alcohol) – 0.40 mmol ($PrapBH_2$)]. Therefore, the percentage of unreacted 1c is calculated to be 38% [(3.30/8.70) × 100], and the relative percentages of $PrapBH_2$ and $Prap_2BH$ are calculated to be 7% [(0.40/5.40) × 100] and 93% [(5.00/5.40) × 100], respectively. The material balance of the B–H bond is calculated as before: hydride in the solution (3.22 mmol) + alcohol formed (5.40 mmol) = 8.62 mmol. The expected value was 8.70 mmol (3 × 2.90 mmol BH_3). All other experiments were performed using these techniques and calculations. The results are summarized in Tables 2 and 3, and are graphically depicted in Figures 1–6.

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Supplementary Material Available: Contains ^{1}H NMR spectra for 1d, 1f, 6, 8, and 9, ^{13}C NMR spectra for all compounds except 9, plus Tables 6–8 summarizing the calculations for the hydroboration results (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.