overnight) leaving 0.3 g of a colorless oil. Dissolution in 5% NaOH solution was followed by heating to 65 °C for 3 h. The solution was cooled to 0 °C and neutralized with 5% HCl using a pH meter (pH = 6.6). The water layer was evaporated under pressure (3 mmHg) at ambient temperature, and the resulting yellow powder was recrystallized from ethanol/water to give 0.07 g of (*S*)-4-aminohex-5-enoic acid, **2** (0.75 mmol, 44%): mp 190–205 °C (lit.[12] mp 208 °C); $[\alpha]^{25}_D = -13.5°$ (*c* 0.02 g/mL, H_2O at pH 6.6) [lit.[19] $[\alpha]^{22}_D = +12.3 \pm 0.3$, *c* = 0.200, H_2O at pH 6.6].

An Alternative Preparation of (*S*)-4-Aminohex-5-enoic Acid (2). Ten milliliters of 10% aqueous HCl solution was added to 0.252 g (1.53 mmol) of 5-ethenyl-*N*-(1-butenyl-2-pyrrolidinone (8) and heated to 90 °C in a steam bath for 5 h. The clear solution was cooled to room temperature, and the solvents were evaporated under reduced pressure to give a yellow oil. The oil was dissolved in 50 mL of water, treated with about 5 g of activated charcoal, and filtered. Evaporation of the water under reduced pressure gave 0.160 g (1.24 mmol, 81%) of an oil that gave all spectral characteristics of pure (*S*)-4-aminohex-5-enoic acid, **2**. Recrystallization from aqueous acetone provided 0.124 g (0.96 mmol, 63%) of **2**: mp 207–209 °C (lit.[12] mp 208 °C); ^1H NMR (D_2O) δ 2.03 (2 H, m), 21.6 (2 H, m), 2.57 (2 H, dist t), 4.97 (2 H, bd s), 5.53 (1 H, m), 5.86 (1 H, m), and 9.60 ppm (1 H, bd s); ^{13}C NMR (D_2O) δ 29.7 (t), 32.4 (t), 58.1 (d), 124.5 (t), 134.9 (d), and 179.4 ppm (s); IR (neat, film) 3100–2800 (s), 1730 (s), 1680 (s), 1410 (m), 1070 (m), and 950 cm^{-1} (m); $[\alpha]^{25}_D = +12.2°$, *c* = 0.095, H_2O at pH 6.4–6.8 [lit.[19] $[\alpha]^{23}_D = +12.3 \pm 0.3°$, *c* = 0.200, H_2O at pH 6.6].

Organoboranes for Synthesis. 14. Convenient Procedures for the Direct Oxidation of Organoboranes from Terminal Alkenes to Carboxylic Acids[1]

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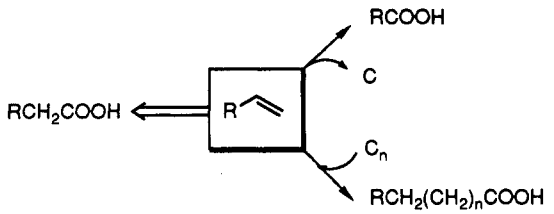
For the first time, a highly efficient and direct oxidation of a variety of organoborane intermediates into carboxylic acids has been demonstrated, without an increase or decrease of carbon atoms. Synthetically useful procedures have been developed for the ready conversion of representative terminal alkenes into carboxylic acids via oxidation of the organoboranes obtained by hydroboration of the terminal alkenes. The oxidation works well with a variety of organoboranes derived from reagents such as dibromoborane–methyl sulfide ($HBBr_2 \cdot SMe_2$), monobromoborane–methyl sulfide ($H_2BBr \cdot SMe_2$), monochloroborane–methyl sulfide ($H_2BCl \cdot SMe_2$), borane–methyl sulfide ($H_3B \cdot SMe_2$), thexylborane (H_2BThx), and dicyclohexylborane ($HBChx_2$). The oxidation is achieved in a convenient manner with pyridinium dichromate (PDC), sodium dichromate in aqueous sulfuric acid ($Na_2Cr_2O_7$–H_2SO_4) and chromium trioxide in 90% aqueous acetic acid (CrO_3–HOAc–H_2O). These oxidations afford carboxylic acids in very good yields with complete retention of the structure of the organic group attached to boron.

Carboxylic acids and their derivatives are valuable for organic synthesis as well as biological studies.[3] Many procedures are available for the synthesis of carboxylic acids from olefinic precursors involving oxidative cleavage of the carbon–carbon double bond and a loss of carbon atoms.[4] Similarly, the preparation of higher homologous carboxylic acids from terminal olefins is also well-known.[5] However, highly efficient and practically useful procedures are not available for the synthesis of carboxylic acids from olefinic precursors without skeletal cleavage or side reactions.[6-8]

Scheme I



The importance of organoboranes as versatile intermediates in organic synthesis is well established.[9] In the past, organoboranes have been shown to undergo oxidation to

(1) For a preliminary account of this work, see: Racherla, U. S.; Khanna, V. V.; Brown, H. C. *Tetrahedron Lett.* **1992**, *33*, 1037. Oxidation of primary alcohols to carboxylic acids without concurrent formation of carboxylic esters with chromium trioxide in 90% aqueous acetic acid was reported earlier. See ref 8a.

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(3) Rieu, J. P.; Boucherle, A.; Cousse, H.; Mouzin, G. *Tetrahedron* **1986**, *42*, 4095.

(4) Larock, R. C. *Comprehensive Organic Transformations*; VCH Publishers: New York, 1989; pp 596, 828–829.

(5) (a) Hara, S.; Kishimura, K.; Suzuki, A.; Dhillon, R. S. *J. Org. Chem.* **1990**, *55*, 6356. (b) Brown, H. C.; Imai, T.; Desai, M. C.; Singaram, B. *J. Am. Chem. Soc.* **1985**, *107*, 4980. (c) See also ref 4, pp 849–850.

(6) Wiberg, K. B. *Oxidations in Organic Chemistry*; Academic Press: New York, 1965; Part A, pp 69–184.

(7) (a) Lee, D. G. In *Oxidation*; Augustine, R. L., Ed.; Dekker: New York, 1969; Vol I. (b) Lee, D. G. *The Oxidation of Organic Compounds by Permanganate Ion and Hexavalent Chromium*; Open Court: La Salle, IL, 1980. (c) See: Haines, A. H. *Methods of Oxidation of Organic Compounds*; Academic Press: New York, 1988, pp 148–165 and 391–401. (d) Periasamy, M.; Narayana, C.; Anitha, N. *Ind. J. Chem.* **1986**, *25B*, 844.

(8) A number of excellent methods are available for the synthesis of carboxylic acids from primary alcohols. See: (a) Pattison, F. L. M.; Stothers, J. B.; Woolford, R. G. *J. Am. Chem. Soc.* **1956**, *78*, 2255. (b) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399. (c) Firouzabadi, H.; Tamani, B.; Goudarzian, N.; Lakouraj, M. M. *Synth. Commun.* **1991**, *21*, 2077.

(9) Pelter, A.; Smith, K.; Brown, H. C. *Borane Reagents*; Academic Press: New York, 1988; pp 1–27.

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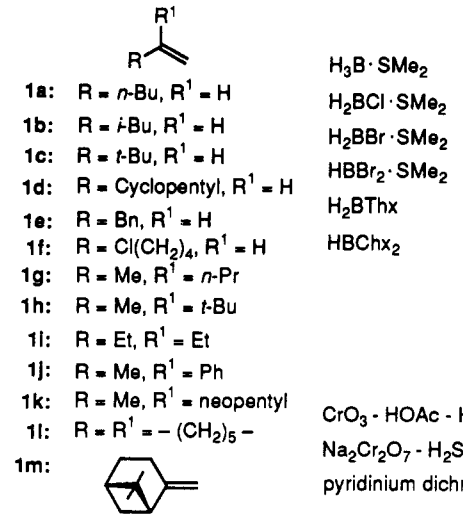
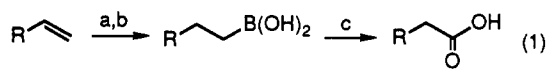


Figure 1. The terminal alkenes, hydroborating agents, and the oxidizing agents employed for the synthesis of carboxylic acids.

alcohols, aldehydes, and ketones.[10] Recently, in a preliminary communication, we reported that alkylboronic acids, readily obtained by the hydroboration of a variety of terminal olefins with dibromoborane–methyl sulfide, followed by hydrolysis, undergo a facile oxidation with chromium trioxide in 90% aqueous acetic acid to provide carboxylic acids in 80–97% isolated yields (eq 1).[1]



(1)

(a) $HBBr_2·SMe_2$, 40 °C, CH_2Cl_2, 2 h; (b) H_2O, 25 °C, 0.5 h; (c) CrO_3, AcOH/H_2O, 25 °C, 12 h

In continuation of the study, we decided to explore the full scope of this reaction with a representative set of terminal alkenes, a variety of hydroborating agents and a select set of oxidizing agents (Figure 1), with the aim of establishing synthetically useful procedures for the direct conversion of terminal alkenes into carboxylic acids without loss of carbon atoms.

Results and Discussion

(a) The Choice of Oxidant. In order to establish the ideal oxidant, we explored the oxidation of *n*-hexylboronic acid to *n*-hexanoic acid with three different oxidants:

(1) pyridinium dichromate (PDC) in dimethylformamide (DMF);

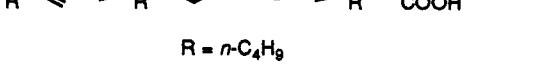
(2) $Na_2Cr_2O_7$ in aqueous sulfuric acid;

(3) CrO_3 in 90% aqueous acetic acid.

We found that the conversion of the simple primary carbon–boron bond into carboxylic acid can be achieved by all of the above oxidants (Table I).

n-Hexylboronic acid undergoes oxidation with PDC in DMF and affords *n*-hexanoic acid in 75% isolated yield.[11] This oxidant will be valuable when the substrate possesses acid-sensitive functionalities. It must be mentioned that in the oxidation with PDC, *n*-hexyl hexanoate (5–10%) is also obtained.[11] However, this does not cause any serious problems as the pure carboxylic acid is isolated by the bicarbonate workup developed. The oxidation of *n*-hexylboronic acid to *n*-hexanoic acid can also be achieved in 80% isolated yield by $Na_2Cr_2O_7$ in aqueous sulfuric acid. However, even in this method, 3–5% ester is obtained.[12] On the contrary, the oxidation with CrO_3 in 90% aqueous acetic acid proceeds in a very clean fashion at 25 °C and provides *n*-hexanoic acid in 87% yield.

Table I. Oxidation of *n*-Hexylboronic Acid with Various Oxidants[a]



R = n-C_4H_9

entry	oxidant	reaction conditions	% yield of carboxylic acid[b]
1	PDC[c] in DMF	25 °C, 24 h	75[f]
2	$Na_2Cr_2O_7$[d] in aqueous H_2SO_4	50 °C, 2 h	80[g]
3	CrO_3[e] in 90% aqueous HOAc	25 °C, 12 h	87

[a] *n*-Hexylboronic acid was prepared from 10 mmol of 1-hexene according to ref 16. [b] Isolated yields based on 1-hexene. [c] 5.25 equiv/equiv of *n*-hexylboronic acid. [d] 1.5 equiv/equiv of *n*-hexylboronic acid. [e] 6 equiv/equiv of *n*-hexylboronic acid. [f] 5–10% ester is also obtained. See ref 11. [g] 3–5% ester is also obtained. See ref 12.

Table II. Oxidation of *n*-Hexylboronic Acid with Various Amounts of CrO_3 in 90% Aqueous Acetic Acid at 25 °C[a]

		% excess of CrO_3 if e^- change is		% yield of *n*-hexanoic acid[b]	
entry	mmol of CrO_3	$2e^-$	$3e^-$	2 h	12 h
1	20	deficient[c]	0	50	62
2	30	0	50	90	94
3	40	33	100	93	96
4	60	100	200	97	

[a] A solution of 10 mmol of *n*-hexylboronic acid (prepared according to ref 16) in 30 mL of dichloromethane was used in each case. [b] Isolated yield based on *n*-hexylboronic acid. [c] Amount of CrO_3 is deficient by 33%.

CrO_3 is a polymer practically insoluble in glacial acetic acid but highly soluble in acetic acid containing 10% (by weight) of water. The oxidation of *n*-hexylboronic acid with CrO_3 is rapid under this homogeneous condition, but is also possible in glacial acetic acid (heterogeneous condition) at slower reaction rates.[13] The stoichiometry of this oxidation was studied experimentally by carrying out the oxidation of *n*-hexylboronic acid with various amounts of CrO_3 (Table II). On the basis of this study, the stoichiometry of this oxidation was established to be as follows (eq 2):[14]

$$n\text{-}C_5H_{11}CH_2B(OH)_2 + 3CrO_3 + 12HOAc \rightarrow n\text{-}C_5H_{11}COOH + B(OH)_3 + 3Cr(OAc)_4 + 6H_2O \quad (2)$$

It can be seen from Table II that 3 equiv of CrO_3 are required for the complete oxidation of *n*-hexylboronic acid (a 6 e^- change). The oxidation takes place in three stages (eq 3) involving a transfer of only 2 e^- from chromium in each stage ($Cr^{VI} \rightarrow Cr^{IV}$).[15]

(10) Cainelli, G.; Cardillo, G. *Chromium Oxidations in Organic Chemistry*; Springer–Verlag: New York, 1984; Chapter 6, pp 229–237.

(11) We have also examined the PDC oxidation of symmetrical trialkylboranes (R_3B) derived from 2-methyl-1-pentene, 3,3-dimethyl-1-butene, 1-octene, and 1-decene. The isolated yields of the carboxylic acids in these cases are 63%, 62%, 75%, and 78%, respectively. In these cases also 3–12% esters are obtained as side products.

(12) $Na_2Cr_2O_7$ oxidation of *n*-Hex_2BCl and *n*-Hex_2BOH afforded 1-hexanoic acid in 78 and 84% isolated yields. Even in these cases the formation of esters (3–7%) was observed.

(13) In glacial acetic acid (heterogeneous condition), the oxidation of *n*-hexylboronic acid takes place at higher temperature (50 °C, 12 h) and provides *n*-hexanoic acid in 92% yield.

(14) Although the stoichiometry of oxidation was found to be 3 equiv of CrO_3/equiv of boronic acid, best results were obtained when 6 equiv of CrO_3 were employed.

Table III. Comparison of Oxidations of Various Organoborane Intermediates into Carboxylic Acids with CrO_3 in 90% Aqueous Acetic Acid[a]

entry	alkene	hydroborating agent	organoborane intermediate	carboxylic acid (% yield)[b]
1	1a	$HBBr_2{\cdot}SMe_2$	n-$C_6H_{13}B(OH)_2$[c]	2a (87)
2		$HBBr_2{\cdot}SMe_2$[d]	n-$C_6H_{13}B(OH)_2$	2a (92)
3		$H_2BBr{\cdot}SMe_2$	$(n$-$C_6H_{13})_2BOH$[c]	2a (86)
4		$H_2BCl{\cdot}SMe_2$	$(n$-$C_6H_{13})_2BCl$[e]	2a (91)
5		$H_3B{\cdot}SMe_2$	$(n$-$C_6H_{13})_3B$[f]	2a (80)
6		H_2BThx	$(n$-$C_6H_{13})_2BThx$	2a (87)
7		$HBChx_2$	n-$C_6H_{13}BChx_2$	2a (82)
8	1d	$HBBr_2{\cdot}SMe_2$	$C_7H_{11}B(OH)_2$[c]	2d (87)
9		$HBBr_2{\cdot}SMe_2$[d]	$C_7H_{11}B(OH)_2$	2d (91)
10		$H_2BBr{\cdot}SMe_2$	$(C_6H_{11})_2BOH$[c]	2d (85)
11		$H_2BCl{\cdot}SMe_2$	$(C_7H_{11})_2BCl$[e]	2d (90)
12		$H_3B{\cdot}SMe_2$	$(C_7H_{11})_3B$[f]	2d (81)
13		H_2BThx	$(C_7H_{11})_2BThx$	2d (88)
14		$HBChx_2$	$C_7H_{11}BChx_2$	2d (83)
15	1g	$HBBr_2{\cdot}SMe_2$	$C_6H_{13}B(OH)_2$[c]	2g (82)
16		$HBBr_2{\cdot}SMe_2$[d]	$C_6H_{13}B(OH)_2$	2g (86)
17		$H_2BBr{\cdot}SMe_2$	$(C_6H_{13})_2BOH$[c]	2g (79)
18		$H_2BCl{\cdot}SMe_2$	$(C_6H_{13})_2BCl$[e]	2g (81)
19		$H_3B{\cdot}SMe_2$	$(C_6H_{13})_3B$[f]	2g (87)
20		H_2BThx	$(C_6H_{13})_2BThx$	2g (86)
21		$HBChx_2$	$C_6H_{13}BChx_2$	2g (77)

[a] All oxidations were performed in dichloromethane for 12 h. [b] Isolated yields. [c] Direct oxidation of alkyldibromoboranes and dialkylbromoboranes yield significant amounts of alkyl bromides as side products. [d] In the presence of 10 mol % BBr_3. [e] Direct oxidation is not harmed by HCl that is liberated. [f] Protonolysis is not competitive with oxidation.

These studies established the most efficient oxidant as CrO_3 in 90% aqueous acetic acid.

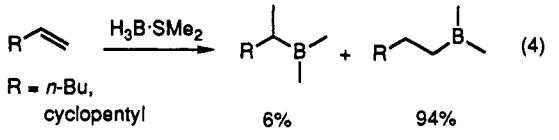
$$RCH_2B(OH)_2 \xrightarrow{CrO_3} RCH_2OH \xrightarrow{CrO_3} RCHO \xrightarrow{CrO_3} RCOOH \quad (3)$$

(b) The Scope and Generality of CrO_3 Oxidation. Next, we decided to examine CrO_3 oxidation of a variety of organoborane intermediates other than the boronic acid that was the basis of the original study.

$(RCH_2)_2BOH$ $(RCH_2)_3B$ $(RCH_2)_2BCl$ $(RCH_2)_2BThx$ RCH_2BChx_2

The organoboranes employed for the study were prepared from a select set of alkenes and representative hydroborating agents. The alkenes selected were 1-hexene (**1a**), vinylcyclopentane (**1d**), and 2-methyl-1-pentene (**1g**). The hydroborating agents were $HBBr_2{\cdot}SMe_2$ (with/without BBr_3), $H_2BBr{\cdot}SMe_2$, $H_2BCl{\cdot}SMe_2$, $H_3B{\cdot}SMe_2$, thexylborane (H_2BThx), and dicyclohexylborane ($HBChx_2$). *This study revealed that a variety of organoborane intermediates (such as shown above) undergo oxidation with chromium trioxide in 90% aqueous acetic acid, and afford carboxylic acids in excellent isolated yields (Table III).*

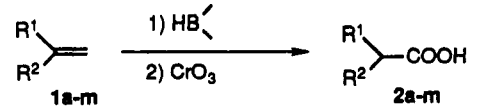
In our preliminary communication, we synthesized $RB(OH)_2$ via hydroboration of olefins with $HBBr_2{\cdot}SMe_2$ (40 °C, CH_2Cl_2 2 h) followed by hydrolysis (according to our previously published procedure)[16] and achieved the synthesis of carboxylic acids in 82–87% overall yields (Table III, entries 1, 8, and 15).[1] In the present study, we improved the synthesis of $RB(OH)_2$ by conducting hydroborations with $HBBr_2{\cdot}SMe_2$ under a different set of reaction conditions (10 mol % BBr_3, 25 °C, 15 min).[17] This procedure provides the synthesis of carboxylic acids in 86–92% overall yields (entries 2, 9, and 16). In a similar manner, we found that the R_2BOH derivatives, obtained via hydroboration of the olefins with $H_2BBr{\cdot}SMe_2$ followed by hydrolysis, also undergo a facile oxidation and afford carboxylic acids in 79–86% yields (entries 3, 10, and 17). It must be pointed out that both $RBBr_2{\cdot}SMe_2$ and $R_2BBr{\cdot}SMe_2$, undergo direct oxidation with chromium trioxide but afford carboxylic acids in poor yields. In these oxidations, alkyl bromides are obtained as side products in significant amounts (20–40%). On the contrary, R_2BCl derivatives undergo direct oxidation with CrO_3 and afford carboxylic acids in excellent yields (81–91%, entries 4, 11, and 18). Oxidation of the symmetrical trialkylborane (R_3B), obtained via hydroboration of 2-methyl-1-pentene with $H_3B{\cdot}SMe_2$ is exceptionally efficient (87% yield, entry 19). On the other hand, oxidations of the trialkylboranes derived from 1-hexene and vinylcyclopentane are relatively less efficient (80–81% yields) because of regioselectivity problems (entries 5 and 12; eq 4):[18]



(4)

It was observed that trialkylboranes (R_2BThx) derived from H_2BThx undergo oxidation with CrO_3 in an efficient

Table IV. CrO_3 Oxidation of Organoboranes Derived from Representative Alkenes and Preferred Hydroborating Agents[a]



entry	alkene	R^1	R^2	hydroborating agent	carboxylic acid (% yield)[b,e]
1	1a	n-C_4H_9	H	$H_2BCl{\cdot}SMe_2$	2a (91)
2	1b	i-Bu	H	$H_2BCl{\cdot}SMe_2$	2b (87)
3	1c	t-Bu	H	$H_2BCl{\cdot}SMe_2$	2c (83)
4	1d	cyclopentyl	H	$H_2BCl{\cdot}SMe_2$	2d (90)
5	1e	$PhCH_2$	H	$H_2BCl{\cdot}SMe_2$	2e (80)[c]
6	1f	$Cl(CH_2)_4$	H	$H_2BCl{\cdot}SMe_2$	2f (87)
7	1g	n-C_3H_7	Me	$H_3B{\cdot}SMe_2$	2g (87)
8	1h	t-Bu	Me	$H_3B{\cdot}SMe_2$	2h (86)
9	1i	Et	Et	$H_3B{\cdot}SMe_2$	2i (84)
10	1j	Ph	Me	$H_3B{\cdot}SMe_2$	2j (63)[d]
11	1k	t-$BuCH_2$	Me	$H_3B{\cdot}SMe_2$	2k (84)
12	1l	$-(CH_2)_5-$		$H_3B{\cdot}SMe_2$	2l (82)
13	1m	β-pinene		$H_3B{\cdot}SMe_2$	2m (50)[e]

[a] All oxidations were performed in dichloromethane for 12 h. [b] Isolated yields. [c] Oxidation was performed for only 4 h. Longer reaction period (12 h) slightly decreased the yield (76%). [d] Hydroboration with $HBBr_2{\cdot}SMe_2$ in the presence of 10 mol % BBr_3, followed by oxidation gave 70% yield. [e] *cis*-Myrtanic acid was obtained.

(15) (a) Wiberg, K. B.; Lepse, P. A. *J. Am. Chem. Soc.* **1961**, *86*, 2612. (b) Makhija, R. C.; Stairs, R. A. *Can. J. Chem.* **1968**, *46*, 1255. (c) *Ibid* **1969**, *47*, 2293.

(16) Brown, H. C.; Bhat, N. G.; Somayaji, V. *Organometallics* **1983**, *2*, 1311.

(17) Hydroboration of terminal alkenes with $HBBr_2{\cdot}SMe_2$ in the presence of 10 mol % BBr_3 in CH_2Cl_2 is complete in ≤15 min at 25 °C. Hydrolysis of the resulting alkyldibromoborane–methyl sulfide adducts ($RBBr_2{\cdot}SMe_2$) leads to the formation of $RB(OH)_2$ along with $B(OH)_3$ and HBr. In the case of low molecular weight alkylboronic acids, extraction of the hydrolysis mixture with CH_2Cl_2 results in an incomplete recovery of the alkylboronic acids. This is because $RB(OH)_2$ are not highly soluble in CH_2Cl_2 while they are partially soluble in water. Since $RB(OH)_2$ are highly soluble in Et_2O, the hydrolysis mixture was first extracted with CH_2Cl_2–Et_2O (3:1). The extract was then washed with small amount of water (2 × 5 mL) to selectively get rid of $B(OH)_3$ and HBr with minimal loss of alkylboronic acids. Thus, this method provides a rapid synthesis of pure alkylboronic acids in essentially quantitative yields.

(18) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1960**, *82*, 4708.

manner and afford the carboxylic acids in 86–88% yields (entries 6, 13, and 20). The oxidation of trialkylboranes ($RBChx_2$) derived from $HBChx_2$ is also satisfactory (77–82%), entries 7, 14, and 21).

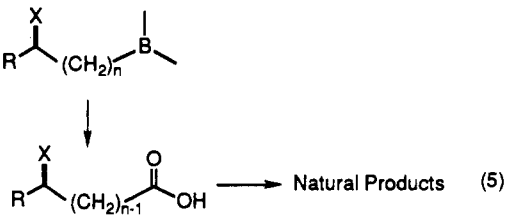
From this study, the relative advantages of the various hydroborating agents examined became clear. *For terminal unsubstituted alkenes, $HBBr_2{\cdot}SMe_2$ or $H_2BCl{\cdot}SMe_2$ works very well. However, as R_2BCl derivatives can be directly utilized for carboxylic acid synthesis (without hydrolysis of the initial hydroboration intermediate), the use of $H_2BCl{\cdot}SMe_2$ is relatively more convenient. For 2-alkyl-substituted alkenes, $H_3B{\cdot}SMe_2$ works best as there are no regiochemistry problems. Moreover, the fact that R_3B derivatives can be directly used for carboxylic acid synthesis makes the utilization of $H_3B{\cdot}SMe_2$ very attractive.* It is our belief that H_2BThx and $HBChx_2$ will be especially useful in carboxylic acid synthesis involving functionalized alkenes.

Finally, we investigated the CrO_3 oxidation of organoboranes derived from representative alkenes **1a–m** with $H_2BCl{\cdot}SMe_2$ and $H_3B{\cdot}SMe_2$. Table IV summarizes these results.

Thus, oxidation of the dialkylchloroborane intermediates ($R_2BCl{\cdot}SMe_2$), obtained from the hydroboration of terminal alkenes **1a–f** with $H_2BCl{\cdot}SMe_2$, provides carboxylic acids in 80–91% yields (entries 1–6). Except in the cases of **1j** and **1m**, oxidation of the trialkylboranes (R_3B) derived from a number of 2-substituted alkenes and $H_3B{\cdot}SMe_2$ affords carboxylic acids in 82–87% yields (entries 7–9, 11, and 12). The CrO_3 oxidation of the symmetrical trialkylborane derived from **1j** gives a poor yield of 2-phenylpropionic acid (63%) along with acetophenone (35%).[19,20]

Conclusion

Highly convenient and preparatively useful procedures have been developed for the conversion of $RB(OH)_2$, R_2BOH, R_2BCl, R_3B, R_2BThx, and $RBChx_2$ derivatives (containing primary alkyl groups) into carboxylic acids in excellent yields. The oxidation can be accomplished using PDC in DMF, $Na_2Cr_2O_7$ in aqueous sulfuric acid, and CrO_3 in 90% aqueous acetic acid. The oxidations of organoboranes with PDC and $Na_2Cr_2O_7$ afford 70–80% yields of carboxylic acids whereas CrO_3 in 90% aqueous acetic acid achieves the oxidation of a variety of organoboranes in a very clean manner and affords carboxylic acids in 80–92% yields. Oxidation of organoboranes using CrO_3 in 90% aqueous acetic acid presents significant advantages over the method reported earlier by Periasamy et al.[7d] for the direct oxidation of organoboranes to carboxylic acids. The earlier method did not demonstrate the intermediacy of a specific organoborane and suffers from moderate yields (50–75%) and the requirement for strongly acidic reaction conditions (concd H_2SO_4), limiting its synthetic utility. The present method, on the other hand, demonstrates the conversion of a number of well-defined organoborane intermediates into carboxylic acids in excellent yields under much milder reaction conditions. It is now possible to choose an appropriate hydroborating agent related to the structure of the terminal olefin to convert it into carboxylic acid in high yield. We believe that this method will find important synthetic applications (eq 5):



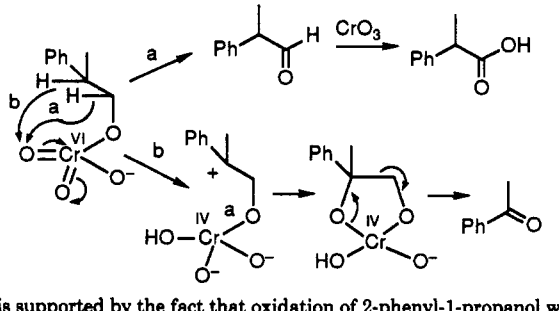
Experimental Section

All reaction flasks and equipment were dried at 150 °C for several hours prior to use and assembled hot under a stream of nitrogen. Special techniques for handling air-sensitive materials are described elsewhere.[21] Melting and boiling points reported are uncorrected. All carboxylic acids reported in this paper are known in the literature and have been fully characterized by ^1H and ^{13}C NMR and mass spectra. All ^1H NMR spectra were recorded on a Gemini-300 BB NMR spectrometer while all ^{13}C NMR spectra were recorded on a Gemini-200 BB spectrometer. Alkenes were purchased from Aldrich and dried over molecular sieves prior to use. CrO_3 (Mallinkrodt, AR grade) and PDC (Aldrich) were used directly. Dichloromethane (spectral grade, Baker analyzed) was stored over molecular sieves and used directly in all experiments. $HBBr_2{\cdot}SMe_2$, $H_2BBr{\cdot}SMe_2$, $H_2BCl{\cdot}SMe_2$, $H_3B{\cdot}SMe_2$, and BBr_3 were purchased from Aldrich and used directly.

Oxidation of Organoboranes with PDC in DMF. The following procedure described for the oxidation of *n*-hexylboronic acid is representative.[11] To a stirred solution of $HBBr_2{\cdot}SMe_2$ in CH_2Cl_2 (11.0 mL, 1.0 M, 11.0 mmol) was added 1-hexene (0.84 g, 10.0 mmol) dropwise at 25 °C. Following completion of the addition, the reaction mixture was refluxed (40 °C) for 2 h, cooled to 0 °C and hydrolyzed with water (20 mL). The aqueous mixture was stirred at 25 °C for 30 min and diluted with CH_2Cl_2 (10 mL), and the organic layer was separated. The aqueous phase was further extracted with CH_2Cl_2 (2 × 20 mL), and the CH_2Cl_2 extracts were combined and dried over anhydrous Na_2SO_4.[22] Next, the solvent was removed under vacuum to obtain *n*-hexylboronic acid as an amorphous white solid. It was dissolved in DMF (10.0 mL) and added dropwise to a stirred solution of pyridinium dichromate (19.75 g, 52.5 mmol) in DMF (40.0 mL) and stirred at 25 °C for 16 h. The reaction mixture was then poured into water (500 mL), stirred for 2 h, and extracted with ether (3 × 40 mL). The combined ether layer was extracted with a saturated solution of $NaHCO_3$ (3 × 25 mL), and the extract was acidified with concd HCl. The aqueous mixture was extracted with ether (2 × 25) and dried over anhydrous $MgSO_4$, and the

(19) This type of C–C bond cleavage has been reported in the oxidation of longifolol with CrO_3 in aqueous acid conditions. See: Lhomme, J.; Ourisson, G. *Tetrahedron* **1968**, *24*, 3167.

(20) It appears that acetophenone is formed by C–C bond cleavage side reaction during the oxidation of the intermediate 2-phenyl-1-propanol by Cr(VI) and may be rationalized as follows:



This is supported by the fact that oxidation of 2-phenyl-1-propanol with 4 equiv of CrO_3 in 90% aqueous acetic acid under identical reaction conditions gave the same ratio of 2-phenylpropionic acid and acetophenone. The hydroboration of 1,1-diphenylethylene with $H_3B{\cdot}SMe_2$, followed by oxidation with CrO_3 in 90% aqueous acetic acid, gave only 33% of diphenylacetic acid and 65% of benzophenone, in further support of this kind of phenomenon. See ref 10.

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

(22) Anhydrous alkylboronic acids readily lose water and form boroxines which are highly air-sensitive. However, they are quite stable as wet solids or in solutions containing 2–3% water.

solvent was removed under vacuum to obtain 0.87 g (75%) of pure *n*-hexanoic acid.

Oxidation of Organoboranes with $Na_2Cr_2O_7$ in Aqueous H_2SO_4. The following procedure is representative.[12] A solution of *n*-hexylboronic acid, prepared as described above from 1-hexene (0.84 g, 10.0 mmol) and $HBBR_2{\cdot}SMe_2$ (11.0 mL, 1.0 M, 11.0 mmol) in CH_2Cl_2, was added dropwise to a stirred mixture of $Na_2Cr_2O_7{\cdot}2H_2O$ (4.47 g, 15.0 mmol), concd H_2SO_4 (6.06 g, 60.0 mmol), and water (20.0 mL) at 0 °C. The mixture was then refluxed at 40 °C for 2 h and extracted with ether (2 × 30 mL). By using the bicarbonate workup described above, 0.93 g (80%) of pure *n*-hexanoic acid was isolated.

Oxidation of Organoboranes with CrO_3 in 90% Aqueous Acetic Acid. (a) Synthesis of Carboxylic Acids Utilizing $HBBr_2{\cdot}SMe_2$. The procedure described below for the synthesis of *n*-hexanoic acid is representative.

A solution of *n*-hexylboronic acid, prepared as described above from 1-hexene (0.84 g, 10.0 mmol) and $HBBr_2{\cdot}SMe_2$ (11.0 mL, 1.0 M, 11.0 mmol) in CH_2Cl_2, was added dropwise to a stirred mixture of CrO_3 (5.99 g, 60.0 mmol) in acetic acid (36.0 mL) and water (4.0 mL). The reaction mixture was stirred at 25 °C for 12 h, and subsequently water (50 mL) and CH_2Cl_2 (25 mL) were added to it. The organic layer was separated, the aqueous layer was further extracted with CH_2Cl_2 (2 × 20 mL), and the extracts were combined. The extracts were washed with brine (2 × 25 mL) and extracted with a saturated solution of $NaHCO_3$ (3 × 25 mL) to dissolve the acid. The bicarbonate layer was acidified with concd HCl and extracted with CH_2Cl_2 (2 × 25 mL). Finally the organic layer was dried over anhyd $MgSO_4$, and 1.00 g (87%) of pure *n*-hexanoic acid was isolated after removal of the solvent.

(b) Synthesis of Carboxylic Acids Utilizing $BHBr_2{\cdot}SMe_2$ in the Presence of 10 mol % BBr_3. The procedure described below for *n*-hexanoic acid is representative.

To a stirred solution of $HBBr_2{\cdot}SMe_2$ (11.0 mL, 1.0 M, 11.0 mmol) in CH_2Cl_2 were added 1-hexene (0.84 g, 10.0 mmol) followed by BBr_3 (1.0 mL, 1.0 M, 1.0 mmol, 10 mol %) in CH_2Cl_2 in a dropwise manner at 25 °C. The reaction mixture was stirred for 15 min and hydrolyzed with water (15 mL) at 0 °C. It was stirred at 25 °C for 30 min, and ether (30 mL) was added.[17] The aqueous layer (lower layer) was discarded, and the organic layer was washed with water (2 × 5 mL) to remove HBr and boric acid. Next, the solvents were pumped off to obtain an essentially quantitative yield of *n*-hexylboronic acid.[22] It was then dissolved in warm CH_2Cl_2 (30 mL) and added dropwise to a mixture of CrO_3 (5.99 g, 60.0 mmol) in acetic acid (36.0 mL) and water (4.0 mL) and stirred at 25 °C for 12 h. The reaction mixture was worked up as described in procedure a to obtain 1.07 g (92%) of pure hexanoic acid.

(c) Synthesis of Carboxylic Acids Utilizing $H_2BBr{\cdot}SMe_2$. The procedure described below for *n*-hexanoic acid is representative.

To a solution of $H_2BBr{\cdot}SMe_2$ (11.0 mL, 1.0 M, 11.0 mmol) in CH_2Cl_2 was added 1-hexene (1.68 g, 20.0 mmol) in a dropwise manner, and the mixture was stirred at 25 °C for 2 h. Next, water (30 mL) was added, the solution was stirred at 25 °C for 30 min, and the mixture was transferred into a nitrogen-purged, septum-capped separating funnel. The aqueous layer (upper layer) was discarded using a cannula. The organic layer was added dropwise to a mixture of CrO_3 (11.98 g, 120.0 mmol) in acetic acid (72.0 mL) and water (8.0 mL) and stirred at 25 °C for 12 h. Utilizing the workup described in procedure a, 1.99 g (86%) of pure hexanoic acid was obtained.

(d) Synthesis of Carboxylic Acids Utilizing $H_2BCl{\cdot}SMe_2$. The procedure described below for cyclopentylacetic acid is representative.

To a solution of $H_2BCl{\cdot}SMe_2$ (1.21 g, 11.0 mmol) in CH_2Cl_2 (20.0 mL) was added vinylcyclopentane (1.92 g, 20.0 mmol) while the reaction mixture was stirred at 25 °C. Following completion of the addition, the reaction mixture was stirred at 25 °C for 2 h. It was then cooled to 0 °C and slowly added to a mixture of CrO_3 (11.98 g, 120.0 mmol) in acetic acid (72.0 mL) and water (8.0 mL). Stirring was continued at 25 °C for 12 h, and the reaction mixture was worked up as described in procedure a to obtain 2.33 g (91%) of pure cyclopentylacetic acid.

(e) Synthesis of Carboxylic Acids Utilizing $H_3B{\cdot}SMe_2$. The procedure described below for 2-methylpentanoic acid is representative.

To a solution of $BH_3{\cdot}SMe_2$ (1.1 mL, 10.0 M, 11.0 mmol) in CH_2Cl_2 (30.0 mL) was slowly added 2-methyl-1-pentene (2.52 g, 30.0 mmol) with stirring at 25 °C. After 2 h, the reaction mixture was slowly added to a solution of CrO_3 (17.97 g, 180.0 mmol) in acetic acid (108.0 mL) and water (12.0 mL) maintained at about 5 °C during the addition. After the completion of oxidation (25 °C, 12 h), the reaction mixture was worked up as described in procedure a to obtain 3.02 g (87%) of pure 2-methylpentanoic acid.

(f) Synthesis of Carboxylic Acids Utilizing Thexylborane. The procedure described below for 2-methylpentanoic acid is representative.

The preparation of thexylborane reagent was carried out under neat conditions.[23] 2,3-Dimethyl-2-butene (0.97 g, 11.55 mmol) was slowly added to neat $H_3B{\cdot}SMe_2$ (1.1 mL, 10.0 M, 11.0 mmol) at −10 °C while the mixture was stirred. After the addition was complete, the reaction mixture was stirred at 0 °C for 2 h to obtain a quantitative yield of thexylborane (H_2BThx).

A solution of 2-methyl-1-pentene (1.68 g, 20.0 mmol) in CH_2Cl_2 (20.0 mL), chilled to 0 °C, was added dropwise to the neat H_2BThx, and the hydroboration was allowed to go to completion in 2 h at 0 °C. The trialkylborane was then added to a mixture of CrO_3 (15.97 g, 160.0 mmol) in acetic acid (96.0 mL) and water (10.7 mL) maintained at about 5 °C during the addition. The reaction mixture was stirred at 25 °C for 12 h. The reaction mixture was worked up as described in procedure a to obtain a 1.99 g (86%) yield of 2-methylpentanoic acid.

(g) Synthesis of Carboxylic Acids Utilizing Dicyclohexylborane. The procedure described below for cyclopentylacetic acid is representative.

Dicyclohexylborane ($HBChx_2$) was obtained by hydroboration of cyclohexene (2.23 g, 22.0 mmol) with $H_3B{\cdot}SMe_2$ (1.1 mL, 10.0 M, 11.0 mmol) in CH_2Cl_2 (10.0 mL) for 3 h at 0 °C.[23] Vinylcyclopentane (0.96 g, 10.0 mmol) was then hydroborated with Chx_2BH (2 h at 25 °C) and added dropwise to a mixture of CrO_3 (11.98 g, 120.0 mmol) in acetic acid (72.0 mL) and water (8.0 mL) maintained at about 5 °C during the addition. After 12 h at 25 °C, the reaction mixture was worked up as described in procedure a to obtain 1.06 g (83%) of pure cyclopentylacetic acid.

Acknowledgment. The financial support of the National Institutes of Health (GM 10937) is gratefully acknowledged.

(23) Brown, H. C.; Mandal, A. K.; Kulkarni, S. U. *J. Org. Chem.* **1977**, *42*, 1392.