Table II. ^{13}C NMR Chemical Shifts for the Heterocyclic Olefins $\overline{X—C^1=C^2—C(C)_n}$ and Their Parent Compounds

X	n	^{13}C shifts (±0.05 ppm)[a] C_1	C_2
O	1	145.64	99.03
O	2	144.00	100.24
O	3	147.86	108.65
C	1	130.22	130.22
C	2	126.67	126.67
C	3	132.12	132.12
S	1	126.11	121.75
S	2	120.26	119.40
		125.90	125.90

[a] Me_4Si at 0.00 is used as internal standard.

as in literature. All other olefins were obtained from commercial sources and distilled under nitrogen over LAH. The internal standards were kept over 5-Å molecular sieves under nitrogen atmosphere and used as such.

Procedure. To an oven-dried, nitrogen-cooled reaction flask fitted with a connecting tube was added 5.0 mmol each of alkenes X and Y and a suitable internal standard (*n*-heptane, 0.5 mL). Several minute aliquots (1 μL) were removed and analyzed by GC to determine the response factors of the two alkenes using a $^1/_8$ in. × 12 ft column of SP-2100 on Chromosorb W protected by a $^1/_8$ in × 12 ft column of THEED on Chromosorb W. 9-BBN in THF (10 mL of 0.5 M) was then added. The reaction mixture was kept at 25 °C. After the reaction was over, samples were removed and analyzed by GC to determine the amounts of residual alkenes. From the initial and final quantities of alkenes, the relative reactivities were calculated by using the Ingold–Shaw expression: relative rate = k_X/k_Y = (ln $[X]_i$ − ln $[X]_f$)/(ln $[Y]_i$ − ln $[Y]_f$) where $[X]_i$ and $[Y]_i$ are the initial concentrations and $[X]_f$ and $[Y]_f$ are the final concentrations of X and Y, respectively.

Relative Reactivities. It is important in relative reactivity studies to choose substrate pairs such that their relative rates do not differ by a factor of more than 10. The olefin pairs studied were 2-methyl-4,5-dihydrofuran/2,3-dihydrofuran, 2,3-dihydrofuran/2-methyl-1-heptene, 2-methyl-1-heptene/1-hexene, 1-hexene/4-methoxy-1-butene, 1-hexene/3,3-dimethyl-1-butene, 3,3-dimethyl-1-butene/cycloheptene, cycloheptene/cyclopentene, cyclopentene/1-methylcyclopentene, cyclopentene/2,5-dihydrofuran, 1-methylcyclopentene/Δ^2-dihydropyran, Δ^2-dihydropyran/2,3,4,5-tetrahydrooxepin, Δ^2-dihydropyran/4-methyl-1-cyclohexene, 4-methyl-1-cyclohexene/cyclohexene, cyclohexene/2,3-dihydrothiophene, and cyclohexene/Δ^2-dihydrothiopyran. The results are summarized in Table I.

Acknowledgment. We thank Dr. J. Chandrasekharan of our Department for helpful suggestions. We gratefully acknowledge support from the United States Army Research Office (Grant DAAG 850062) and the National Institutes of Health (Grant GM 10937-22) in this research.

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Chiral Synthesis via Organoboranes. 4. Synthetic Utility of Boronic Esters of Essentially 100% Optical Purity. Synthesis of Homologated Boronic Acids and Esters of Very High Enantiomeric Purities

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2-Alkyl-1,3,2-dioxaborinanes, $R^*BO_2(CH_2)_3$, of essentially 100% optical purity, prepared by the asymmetric hydroboration of readily available prochiral olefins with subsequent removal of the chiral auxiliary, can be homologated to α-chloroalkyl derivatives, $R^*CHClBO_2(CH_2)_3$, of essentially 100% ee by reaction with $LiCHCl_2$. The intermediates $R^*CHClBO_2(CH_2)_3$ are smoothly reduced with KIPBH to give the corresponding one-carbon-homologated boronic esters $R^*CH_2BO_2(CH_2)_3$ in very high optical purity. The operation can be repeated to produce $R^*CH_2CH_2BO_2(CH_2)_3$ etc. Consequently, it is now possible to synthesize a wide variety of optically active boronic esters, not available by direct asymmetric hydroboration, either (+) or (−), in essentially 100% ee, and to convert these into synthetically valuable compounds.

The transfer of alkyl groups from boron to carbon is one of the most valuable synthetic reactions of organoboranes. It can be achieved under remarkably mild conditions in a number of ways. In particular, the complete replacement of boron in a trialkylborane by a functionalized carbon can be achieved by carbonylation,[2] cyanidation,[3] or reaction with the anion derived from dichloromethyl methyl ether (DCME),[4] i.e., under neutral, acidic, or basic conditions, respectively (eq 1–3).

$$R_3B \xrightarrow[2.\ [O]]{1.\ CO} R_3COH \quad (1)$$

$$R_3B \xrightarrow[2.\ (CF_3CO)_2O]{1.\ CN^-} R_3COH \quad (2)$$

$$R_3B \xrightarrow[2.\ base\ \ 3.\ [O]]{1.\ Cl_2CHOMe} R_3COH \quad (3)$$

(1) (a) Postdoctoral research associate on Grant CHE 79-18881 of the National Science Foundation. (b) Postdoctoral research associate on Grant GM 10937-22 of the National Institutes of Health. (c) Visiting Professor on a grant from the Ministry of Education of the Republic of Korea.

(2) Brown, H. C. *Acc. Chem. Res.* **1969**, *2*, 65.

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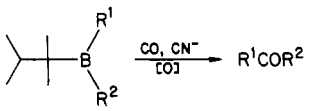
Conversion into ketones by transfer of two groups is also possible, using modifications of the three procedures listed above (eq 4 and 5).[2-4]



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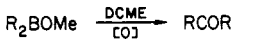
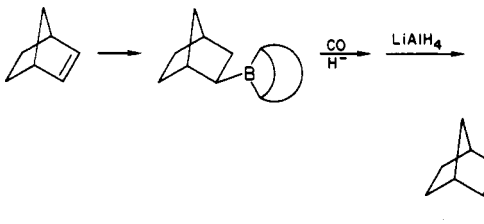


(5)

By contrast, simple procedures for the transfer of a single alkyl group are still lacking. Recently we developed a practical method for extending the alkyl chain via carbonylation of *B*-alkyl-9-borabicyclo[3.3.1]nonane (*B*-alkyl-9–BBN) in the presence of potassium triisopropoxyborohydride (KIPBH), followed by reduction of the intermediate by lithium aluminum hydride (eq 6).[5] Un-

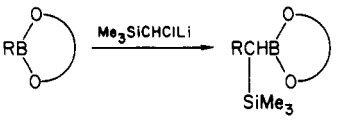


(6)

fortunately, no convenient procedures are currently available to convert the homologated *B*-alkyl-9-BBN derivatives into the desired homologated boronic esters, $RCH_2B(OR')_2$.

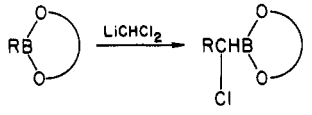
As part of an ongoing program in the synthesis of boronic acids and esters not available via hydroboration,[6] we were interested in a convenient method for the one-carbon homologation of boronic esters. Unfortunately, most of the reagents that homologate trialkylboranes fail to react with boronic esters. For example, $^-CH_2S^+O(CH_3)_2$,[7] $^-CH_2S^+(CH_3)_2$,[8] $^-CH_2N^+(CH_3)_3$,[9] and $^-CH_2SCH_3/CH_3I$[10] practically do not react with boronic esters.

In 1980 Matteson and his co-workers established that [(trimethylsilyl)chloromethyl]lithium successfully homologates boronic esters to α-trimethylsilyl derivatives, $RCHSiMe_3B(OR')_2$,[11] a valuable development since it had been thought that boronic esters were inert to reagents of this kind (eq 7). Soon afterward he utilized (dichloro-



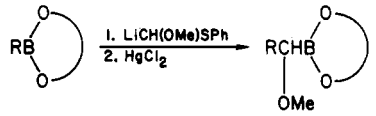
(7)

methyl)lithium in a similar reaction[12] to prepare α-chloro boronic esters, $RCHClB(OR')_2$ (eq 8).



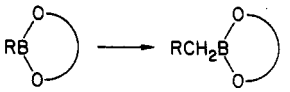
(8)

We then discovered that [methoxy(phenylthio)-methyl]lithium also reacts with boronic esters, providing a valuable route to α-methoxy boronic esters,[13] $RCHOMeB(OR')_2$ (eq 9). We desired a simple synthetic route



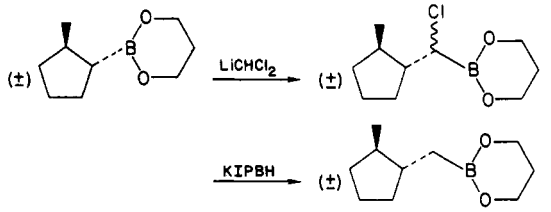
(9)

to the parent one-carbon-homologated boronic ester.



Even though it is possible to convert all of these α-substituted boronic esters, $RCHSiMe_3B(OR')_2$,[14] $RCHOMeB(OR')_2$,[5,15] and $RCHClB(OR')_2$, to the homologated boronic ester, we selected the α-chloro boronic esters as providing the most convenient route for the synthesis of $RCH_2B(OR')_2$.

Indeed, we recently achieved a successful one-carbon homologation of racemic boronic esters by the reaction with (dichloromethyl)lithium, $LiCHCl_2$,[12] followed by reduction of the intermediate $RCHClB(OR')_2$ with KIPBH (eq 10).[16]

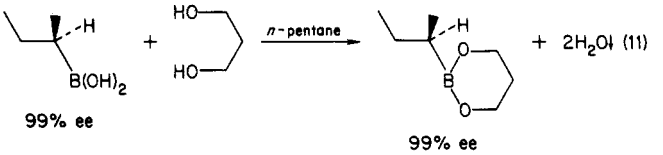


(10)

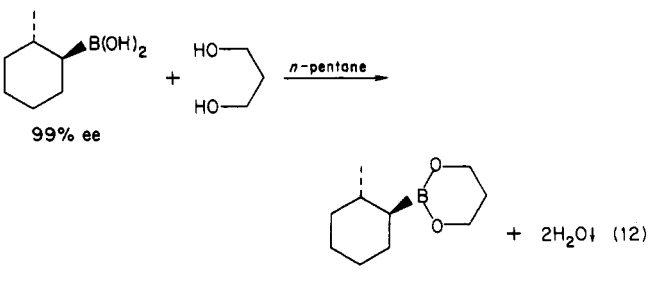
With the ready availability of alkylboronic esters of very high optical purities, we applied the above reaction to these essentially optically pure boronic esters to test the possibility of synthesizing β-chiral boronic esters, not available via asymmetric hydroboration, of comparably high optical purity.

Results and Discussion

The optically active 2-alkyl-1,3,2-dioxaborinanes were prepared by esterification[17] of the corresponding boronic acids with 1,3-propanediol (eq 11 and 12). In this study,



(11)



(12)

we prepared the optically active boronic acids using diisopinocampheylborane, Ipc_2BH (>99% ee),[18] and mono-

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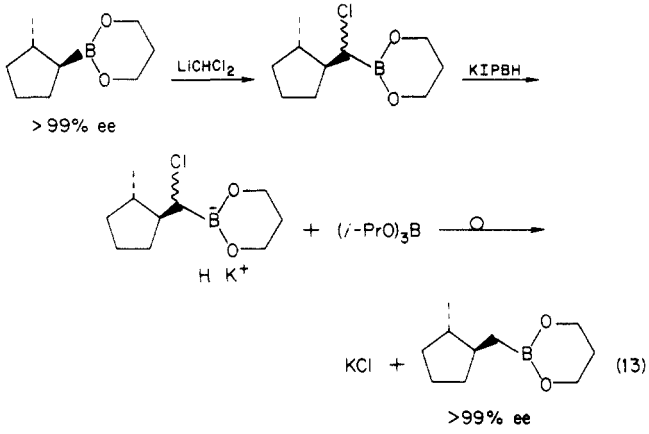
isopinocampheylborane, $IpcBH_2$ (100% ee),[19] prepared from (+)-α-pinene. The optical purity of all these 2-alkyl-1,3,2-dioxaborinanes was determined by measuring the rotations of the alcohols obtained following alkaline hydrogen peroxide oxidation and comparing the values with the maximum reported rotations. The optical purity of these alcohols were also determined by ^{19}F NMR of their MTPA esters[20] and/or by ^{31}P NMR using the Anderson and Shapiro reagent.[21,22]

A slurry of (dichloromethyl)lithium ($LiCHCl_2$) in freshly distilled tetrahydrofuran (THF) was prepared[12] at −100 °C, and the boronic esters were added dropwise maintaining the temperature at −100 °C. After the addition, the reaction mixture became clear and it was allowed to warm to 25 °C. Usually the reaction mixture turned dark at −50 °C due to the decomposition of the small excess (10%) of $LiCHCl_2$. The reaction mixture was stirred at 25 °C for 3 h. The ^{11}B NMR spectrum of the reaction mixture showed cleanly one peak at δ +27–28, due to the formation of α-chloro boronic esters. The intermediate α-chloro boronic esters were reduced in situ by using KIPBH at 25 °C. The reaction was facile and was complete within 1.0 h. The ^{11}B NMR spectrum of the reaction mixture showed the formation of boronic ester (δ +30–32), triisopropoxyborane (δ +18), and the presence of an impurity, potassium tetraisopropoxyborate (δ +1–2), which was originally present in the commercial KIPBH solution.

The reduction of α-chloro boronic esters presumably proceeds through the intermediate formation of the corresponding borohydride (eq 13).



The byproduct triisopropoxyborane is readily removed by washing the diethyl ether (EE) solution of the reaction mixture with water, selectively hydrolyzing $(i\text{-PrO})_3B$, and extracting the boric acid into water. Although the 1,3-propanediol esters were partially hydrolyzed, the resulting boronic acid–ester mixture still remained in the ether phase and could be readily reesterified with 1,3-propanediol prior to distillation. Alternatively, the reaction product could be completely hydrolyzed with MeOH–H_2O (1:1), the resulting β-chiral boronic acids esterified with 1,3-propanediol, and the ester purified by distillation (eq 14).

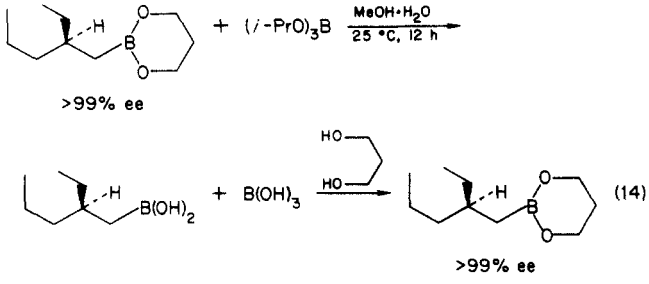
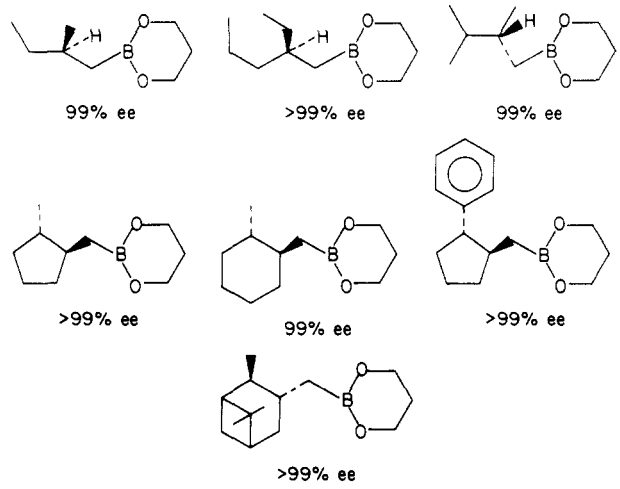
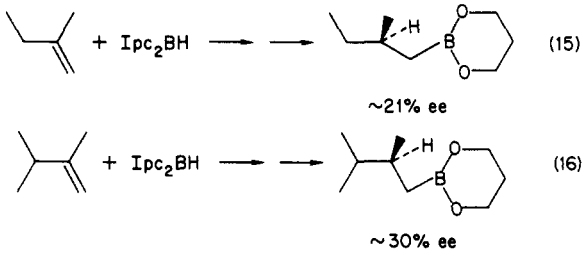


Chart I



With use of the general procedure, the representative β-chiral boronic esters shown in Chart I were prepared in very high optical purities (Table I).

It should be pointed out that Ipc_2BH and $IpcBH_2$ handle three of the four major classes of alkenes in asymmetric hydroboration. Excellent results are realized in the case of unhindered *cis* olefins by using a reagent with large steric requirement, Ipc_2BH.[23] On the other hand, hydroboration of olefins with larger steric requirements, trans and trisubstituted olefins, is more favorable with a reagent of lower steric requirements, $IpcBH_2$.[24,25] Unfortunately, these two reagents do not give high asymmetric induction with alkenes of relatively low steric requirements such as the 2-methyl-1-alkenes. The β-chiral boronic esters such as 2-(2-methylbutyl)-1,3,2-dioxaborinane and 2-(2,3-dimethylbutyl)-1,3,2-dioxaborinane are difficult to prepare in high optical purity by asymmetric hydroboration of the corresponding alkenes[26] (eq 15 and 16).



Utilizing the methodology described here, these β-chiral boronic esters were prepared in very high optical purities (eq 17 and 18).

The sequence described in this paper is also attractive for those cases where stereoisomers are possible. The stereochemistry and optical purity are determined by the asymmetric hydroboration step and the homologation proceeds with retention of configuration. Thus, hydro-

(19) Brown, H. C.; Schwier, J. R.; Singaram, B. *J. Org. Chem.* **1978**, *43*, 4395.
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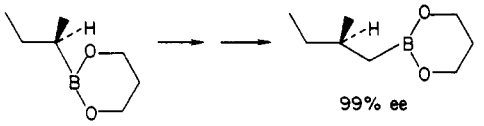
Table I. β-Chiral Boronic Esters of Very High Optical Purity

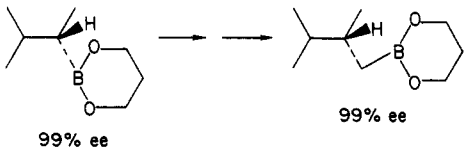
boronic esters $R^*BO_2(CH_2)_3$, R* =	yield, % (isolated)	bp, °C (torr)	$[\alpha]^{23}_D$, deg (c, THF)	% ee[a]	config of $R^*BO_2(CH_2)_3$
2-methyl-1-butyl	75	88–90 (17)	−8.06 ± 0.03 (9)	≥99	*S*
2-ethyl-1-pentyl	80	112–114 (17)	+0.57 ± 0.01 (7)	>99	*R*
2,3-dimethyl-1-butyl	80	100–102 (17)	+10.56 ± 0.02 (10)	≥99	*R*
trans-(2-methylcyclopentyl)methyl	85	45–46 (0.05)	+43.06 ± 0.02 (10)	>99	1*S*,2*S*
trans-(2-methylcyclohexyl)methyl	72	78–80 (0.05)	+33.10 ± 0.05 (10)	≥99	1*S*,2*S*
trans-(2-phenylcyclopentyl)methyl	80	110–112 (0.01)	+35.56 ± 0.02 (6)	>99	1*S*,2*S*
(3-isopinocampheyl)methyl	83	102–104 (0.03)	−32.11 ± 0.02 (5)	>99	1*R*,2*S*,3*R*,5*R*

[a] Optical purity was determined by measuring the rotation of the alcohols obtained on oxidation and comparing the value with maximum reported rotations. See Table II.

boration of 2-methylenemethylcyclopentane yields a mixture predominating in the cis isomer,[5] whereas the

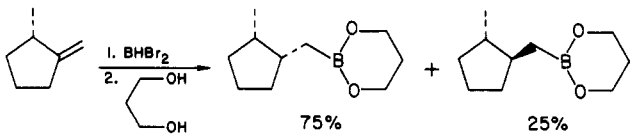


(17)



(18)

procedure described here produces only the pure trans isomer (eq 19 and 20).



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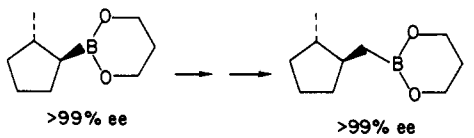
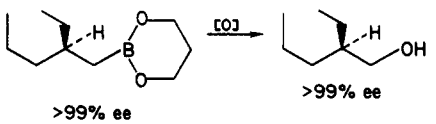


(20)

These β-chiral boronic esters on oxidation afforded the corresponding β-chiral alcohols of very high optical purities (eq 21). The optical purity of these alcohols were de-

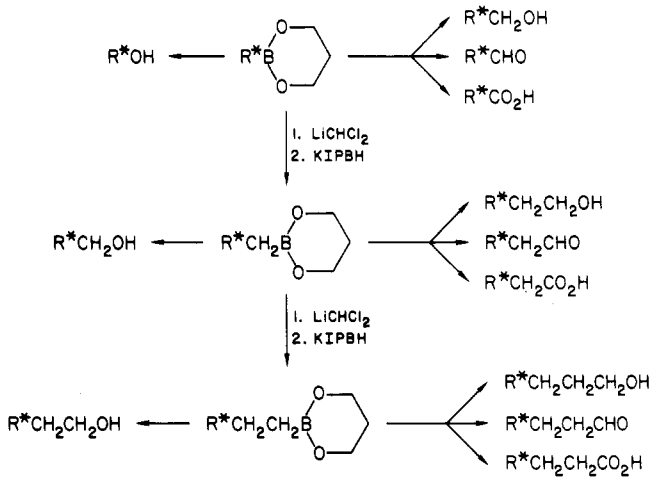


(21)

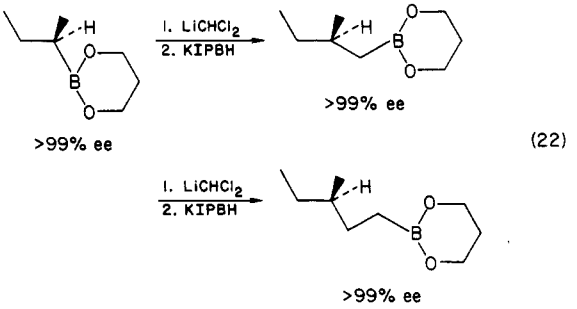
termined by ^{19}F NMR analysis of their MTPA esters and/or by ^{31}P NMR analysis using Anderson and Shapiro reagent.[22] The optical purity and absolute configuration of these β-chiral alcohols were also determined by measuring the rotations and comparing the values with the maximum reported rotations (Table II). From these data, the optical purities of the corresponding β-chiral boronic esters were determined. Additionally, all of the cyclic homologated alcohols were analyzed by capillary GC using 50 M methyl silicone and 20 M Supelcowax columns and were found to be diastereomerically pure. The diastereomeric purity of these alcohols in turn reflect the enantiomeric purity of these alcohols and the corresponding boronate esters.

The homologation procedure can be repeated to produce $R^*CH_2CH_2BO(CH_2)_3$ etc. For example, 2-(2-methylbutyl)-1,3,2-dioxaborinane, the first homologation product, was further homologated to afford the second homologation product 2-(3-methylpentyl)-1,3,2-dioxaborinane (eq 22). The homologated boronic esters upon oxidation provide the corresponding alcohols in very high optical purities (eq 23).

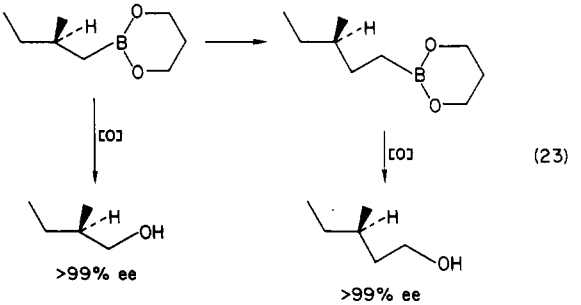
Scheme I



R* is a chiral organic group, both (+) and (−).



(22)



(23)

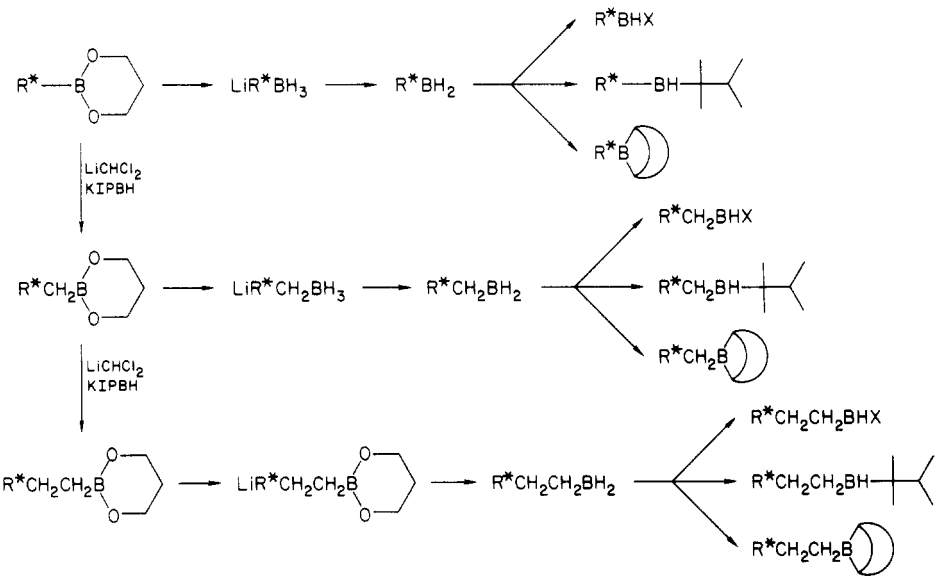
Optically active 2-methyl-1-butanol and 3-methyl-1-pentanol are important chiral building blocks. Recently they were utilized for the synthesis of (*Z*)- and (*E*)-trogodermals, the sex pheromone of the female dermestid beetle (*Trogoderma inclusum*).[27,28] The (*S*)-enantiomer is readily synthesized from the readily available (*S*)-2-methyl-1-butanol (fusel oil) and (*S*)-3-methyl-1-pentanol.

Table II. β-Chiral Alcohols of Very High Optical Purity

R*CH$_2$OH	yield, % (isolated)	bp, °C (torr)	$[\alpha]^{23}_D$, deg	% ee[b]	config of R*CH$_2$OH
2-methyl-1-butanol	90	126–127 (750)	+4.83 ± 0.01 (neat, *l* 1)[a]	≥99[c]	*R*
2-ethyl-1-pentanol	92	78–80 (20)	−3.39 ± 0.01 (neat, *l* 1)	>99[d]	*R*
2,3-dimethyl-1-butanol	90	64–65 (25)	+4.84 ± 0.01 (neat, *l* 1)[a]	≥99[e]	*S*
trans-(2-methylcyclopentyl)methanol	93	110–112 (80)	+54.95 ± 0.01 (*c* 1, MeOH)	>99[f]	1*S*,2*S*
trans-(2-methylcyclohexyl)methanol	95	106–108 (20)	+41.8 ± 0.1 (*c* 1, MeOH)	≥99[g]	1*S*,2*S*
trans-(2-phenylcyclopentyl)methanol	95	92–94 (0.01)	+52.47 ± 0.1 (*c* 1, MeOH)	>99[f]	1*S*,2*S*
(3-isopinocampheyl)methanol	95	*h*	−48.06 ± 0.2 (*c* 1, MeOH)	>99[i]	1*R*,2*R*,3*R*,5*R*

[a] Observed rotation. [b] Based on maximum reported rotations (see footnotes *c*–*g*). [c] Vogler, K.; Chopard-dit-Jean, L. H. *Helv. Chim. Acta* **1960**, *43*, 279; α^{23}_D −4.84° (neat, *l* 1) for (*S*)-2-methyl-1-butanol. [d] Levene, P. A.; Rothen, A.; Meyer, G. M.; Kuna, M. *J. Biol. Chem.* **1936**, *115*, 401. These authors predicted a maximum rotation of $[\alpha]^{25}_{5876}$ +3.34° (neat, *l* 1) for (*S*)-2-ethyl-1-pentanol. [e] Rsuda, K.; Kishida, Y.; Hayatsu, R. *J. Am. Chem. Soc.* **1960**, *82*, 3396; α^{23}_D −4.52° (neat, *l* 1) for (*R*)-2,3-dimethyl-1-butanol. [f] Analyzed by ^{31}P NMR. [g] Analyzed by ^{19}F NMR. [h] Isolated by preparative GC. [i] Blomquist, A. T.; Verdol, J.; Adam, C. L.; Wolinsky, J.; Phillips, D. D. *J. Am. Chem. Soc.* **1957**, *79*, 4976; $[\alpha]_D$ −15.7° (*c* 8.7, EtOH) for a mixture of (3-pinocampheyl)methanol and (3-isopinocampheyl)methanol.

Scheme II



However, the (*R*)-enantiomer is rather difficult to prepare in high optical purity due to the unavailability of (*R*)-2-methyl-1-butanol and (*R*)-3-methyl-1-pentanol. With use of the methodology described herein, one can make both enantiomers of 2-methyl-1-butanol and 3-methyl-1-pentanol readily, in very high optical purities.

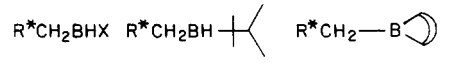
Implications

The present study provides a convenient and simple procedure for the synthesis of various β-chiral boronic esters of essentially 100% ee. The operation can be repeated to give γ-chiral boronic esters, R*CH$_2$CH$_2$BO$_2$(CH$_2$)$_3$ etc. We have recently discovered that [methoxy(phenylthio)methyl]lithium reacts with optically active boronic esters, providing a valuable intermediate that can be readily transformed into optically active aldehydes, primary alcohols, and carboxylic acids. This homologation procedure, when combined with the aldehyde, primary alcohol, and carboxylic acid synthesis, provides a new method for introducing aldehyde, alcohol, and acid functionalities one-, two-, and three-carbon atoms removed from the chiral center (Scheme I).

We have also shown that optically active boronic esters can be readily converted into the corresponding borohydrides by treatment with lithium aluminum hydride.[29] We are now in a position to synthesize LiR*BH$_3$, LiR*CH$_2$BH$_3$, LiR*CH$_2$CH$_2$BH$_3$, etc. From these monoalkylborohydrides we can readily synthesize R*BH$_2$, R*CH$_2$BH$_2$, and R*CH$_2$CH$_2$BH$_2$, the corresponding halo derivatives, thexylborane derivatives, and 9-borabicyclo[3.3.1]nonane derivatives (Scheme II). Consequently, we have a simple entry into essentially all organic derivatives readily synthesized through boron intermediates.

Conclusion

The present study provides a convenient and simple procedure for the synthesis of various β-chiral boronic esters of essentially 100% ee, which are not available by direct asymmetric hydroboration procedure. Both (+)- and (-)-α-pinenes are readily available. Consequently, both enantiomers are readily synthesized. Oxidation of these boronic esters provides the corresponding β-chiral alcohols of high optical purity. The β-chiral boronic esters are much more versatile synthetic intermediates than β-chiral alcohols. For the first time we are in a position to synthesize several β-chiral organoborane intermediates, such as



in essentially 100% optical purity in both (+)- and (−)-isomers. These are valuable reagents, especially promising

(27) (a) Rossi, R.; Carpita, A. *Tetrahedron* **1977**, *33*, 2447. (b) Rossi, R.; Salvadori, P. A.; Carpita, A. *Ibid.* **1979**, *35*, 2039.
(28) (a) Mori, K. *Tetrahedron* **1974**, *30*, 3817. (b) Mori, K.; Suguro, T.; Uchida, M. *Ibid.* **1978**, *34*, 3119. (c) Mori, K.; Kuwahara, S.; Levinson, H. Z.; Levinson, A. R. *Ibid.* **1982**, *38*, 2291.
(29) Brown, H. C.; Singaram, B.; Cole, T. E. *J. Am. Chem. Soc.* **1985**, *107*, 460.

for chiral synthesis proceeding through boron intermediates. We continue to actively explore chiral syntheses via these chiral organoborane intermediates.

Experimental Section

All operations were carried out under a nitrogen atmosphere with oven-dried glassware.[30] The spectra were obtained in an inert atmosphere. The ^{11}B NMR spectra were recorded on a Varian FT-80A spectrometer and the chemical shifts are in δ relative to EE·BF_3 with chemical shifts downfield from EE·BF_3 assigned as positive. The ^1H NMR spectra were scanned on a Varian XL-200 or Nicolet NT-470 spectrometer. ^{13}C NMR spectra were obtained on a Varian FT-80A or a Nicolet NT-470 spectrometer. The chemical shifts are in δ relative to Me_4Si for ^1H and ^{13}C NMR spectra. ^{19}F NMR spectral analysis of the MTPA esters was peformed on a Varian XL-200 spectrometer. ^{31}P NMR spectral analysis was performed on a Varian FT-80A or a Varian XL-200 spectrometer. Gas chromatographic analyses were carried out with a Hewlett-Packard 5750 chromatograph with a TC detector. Optical rotations were measured on a Rudolph Polarimeter Autopol III. Capillary gas chromatographic analyses were carried out with a Hewlett-Packard 5890 chromatograph.

Materials. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl prior to use. Anhydrous diethyl ether (EE) was purchased from Mallinckrodt, Inc., and was used directly. Dichloromethane, purchased from J. T. Baker Chemical Co., was dried over 4-Å molecular sieves. Butyllithium (Alfa) in hexane was estimated to be 2.3 M. Potassium triisopropoxyborohydride (KIPBH, 1.0 M) in THF was purchased from Aldrich Chemical Co.

The boronic esters, used in this study, except isopinocampheylboronic ester, were prepared by procedures described previously[31] starting from (+)-α-pinene.

Preparation of (1′*R*,2′*S*,3′*R*,5′*R*)-(−)-2-(3′-Isopinocampheyl)-1,3,2-dioxaborinane. To a solution of monoisopinocampheylborane of >99% ee[25] (100 mmol) in ethyl ether (150 mL) was added 1,3-propanediol (100 mmol) with stirring at 25 °C. After the complete evolution of hydrogen, the solvent was evaporated (25 °C, 12 torr) and the residue was purified by distillation, 87% yield: bp 85 °C (0.01 torr); ^{11}B NMR δ +30.8 (s); ^1H NMR ($CDCl_3$) δ 0.51–1.33 (m, 12 H), 1.37–2.37 (m, 7 H), 3.97 (t, J = 6 hz, 4 H); $[\alpha]^{23}_D$ − 15.11° ± 0.01 (*c* 6, THF).

Homologation of 2-Alkyl-1,3,2-dioxaborinanes of Very High Optical Purity. General Procedure. A solution of dichloromethane (2 mL) in 30 mL of freshly distilled THF was cooled to −105 to −100 °C in a 1:1 EE–*n*-pentane–liquid nitrogen bath and stirred magnetically during the dropwise addition of 22 mmol of *n*-butyllithium (2.3 M in hexane) from a syringe. The *n*-butyllithium was chilled before contacting the dichloromethane solution by bringing the tip of the syringe needle very close to the surface of the cold solution. After the addition, the reaction mixture was stirred at −100 °C for 15 min. The reaction mixture should remain colorless or pale yellow. Darkening is a sign of decomposition. A solution of 2-alkyl-1,3,2-dioxaborinane (20 mmol) of very high optical purity in 10 mL of THF was then added dropwise, maintaining the temperature below −100 °C. The reaction mixture was allowed to reach 25 °C slowly and stirred at 25 °C for 3 h. The 2-(chloroalkyl)-1,3,2-dioxaborinanes thus obtained were reduced in situ by using KIPBH (20 mmol). The exothermic reaction was controlled by the rate of addition of KIPBH and by water-bath cooling to maintain the temperature below 30 °C. Reaction was complete with 1.0 h, as indicated by the ^{11}B NMR analysis. The solvent was evaporated (25 °C, 12 torr), and the residue was stirred with 40 mL of 1:1 MeOH–H_2O at 25 °C for 12 h to hydrolyze triisopropoxyborane and the product. The reaction mixture was extracted with EE (2 × 20 mL), washed with water (2 × 10 mL), and dried over anhydrous $MgSO_4$. Evaporation (25 °C, 12 torr) of the solvent gave the crude boronic acid which was esterified[17] with 1,3-propanediol and purified by distillation (Table I).

(30) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975.
(31) Brown, H. C.; Imai, T.; Desai, M. C.; Singaram, B. *J. Am. Chem. Soc.*, accepted for publication.

(*S*)-(−)-2-(2-Methylbutyl)-1,3,2-dioxaborinane: prepared from (*R*)-(−)-2-(1-methylpropyl)-1,3,2-dioxaborinane of 99% ee; ^{11}B NMR δ +30.8 (s); ^1H NMR ($CDCl_3$) δ 0.53 (br d, J = 7 Hz, 2 H), 0.80 (t, J = 7 Hz, 3 H), 0.88 (d, J = 7 Hz, 3 H), 1.1–1.7 (m, 3 H), 1.87 (q, J = 6 Hz, 2 H), 3.93 (t, J = 6 Hz, 4 H).

(*R*)-(+)-2-(2-Ethylpentyl)-1,3,2-dioxaborinane: prepared from (*R*)-(+)-2-(1-ethylbutyl)-1,3,2-dioxaborinane of >99% ee; ^{11}B NMR δ +31.0 (s); ^1H NMR ($CDCl_3$) δ 0.6 (d, J = 7 Hz, 2 H), 0.8–1.6 (m, 13 H), 1.9 (q, J = 7 Hz, 2 H), 3.97 (t, J = 7 Hz, 4 H).

(*R*)-(+)-2-(2,3-Dimethylbutyl)-1,3,2-dioxaborinane: prepared from (*S*)-(+)-2-(1,2-dimethylpropyl)-1,3,2-dioxaborinane of 99% ee; ^{11}B NMR δ +30.9 (s); ^1H NMR ($CDCl_3$) δ 0.53 (br d, J = 7 Hz, 2 H), 0.8 (d, J = 7 Hz, 9 H) 1.1–2.0 (m, 2 H), 1.9 (q, J = 6 Hz, 2 H), 3.93 (t, J = 6 Hz, 4 H).

(1′*S*,2′*S*)-(+)-2-[*trans*-(2′-Methylcyclopentyl)methyl]-1,3,2-dioxaborinane: prepared from (1′*S*,2′*S*)-(+)-2-(*trans*-2-methylcyclopentyl)-1,3,2-dioxaborinane of >99% ee; ^{11}B NMR δ +30.5 (s); ^1H NMR ($CDCl_3$) δ 0.35–0.7 (m, 2 H), 0.8–1.1 (m, 3 H), 1.2–2.2 (m, 10 H), 3.97 (t, J = 7 Hz, 4 H).

(1′*S*,2′*S*)-(+)-2-[*trans*-(2′-Methylcyclohexyl)methyl]-1,3,2-dioxaborinane: prepared from (1′*S*,2′S)-(+)-2-(*trans*-2′-methylcyclohexyl)-1,3,2-dioxaborinane of 99% ee. ^{11}B NMR δ +31.0 (s); ^1H NMR ($CDCl_3$) δ 0.53 (m, 2 H), 0.8–2.1 (m, 15 H), 4.0 (t, J = 7 Hz, 4 H).

(1′*S*,2′*S*)-(+)-2-[*trans*-(2′-Phenylcyclopentyl)methyl]-1,3,2-dioxaborinane: prepared from (1′*S*,2′*S*)-(+)-2-(*trans*-2′-phenylcyclopentyl)-1,3,2-dioxaborinane of >99% ee; ^{11}B NMR δ +31.0 (s); ^1H NMR ($CDCl_3$) δ 0.67 (br d, J = 6 Hz, 2 H), 1.1–2.4 (m, 10 H), 3.83 (t, J = 7 Hz, 4 H), 7.2 (s, 5 H).

(1′*R*, 2′*S*, 3′*R*, 5′*R*)-(−)-2-[(3′-Isopinocampheyl)methyl]-1,3,2-dioxaborinane: prepared from (1′*R*, 2′*S*, 3′*R*, 5′*R*)-(−)-(3′-isopinocampheyl)-1,3,2-dioxaborinane of >99% ee; ^{11}B NMR δ +30.7 (s); ^1H NMR ($CDCl_3$) δ 0.58–1.32 (m, 11 H), 1.33–2.75 (m, 10 H), 3.97 (t, J = 6 Hz, 4 H).

Oxidation of these boronic esters with alkaline hydrogen peroxide afforded the corresponding β-chiral alcohols of very high optical purity which were isolated by distillation and further purified by preparative GC. The optical purity of these β-chiral alcohols was determined by measuring their rotations and comparing the values with maximum reported rotations. These alcohols were also analyzed by ^{19}F NMR and/or ^{31}P NMR using chiral derivatizing agents. The results are summarized in Table II. Additionally, all of the cyclic homologated alcohols were analyzed by capillary GC and were found to be diastereomerically pure.

(*R*)-(+)-2-Methyl-1-butanol: ^1H NMR ($CDCl_3$) δ 0.88–1.0 (m, 6 H), 1.15 (m, 1 H), 1.48 (m, 2 H), 3.48 (unresolved quintet, 2 H); ^{13}C NMR ($CDCl_3$) δ 11.4, 16.3, 26.1, 37.6, 67.7.

(*R*)-(−)-2-Ethyl-1-pentanol: ^1H NMR ($CDCl_3$) δ 0.6–1.0 (m, 6 H), 1.1–1.6 (m 7 H), 3.0 (br s, 1 H), 3.3–3.7 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 10.9, 14.3, 20.2, 23.3, 32.8, 41.8, 64.9. Anal. Calcd for $C_7H_{16}O$: C, 72.35; H, 13.88. Found: C, 72.19; H, 14.17.

(*S*)-(+)-2,3-Dimethyl-1-butanol: ^1H NMR ($CDCl_3$) δ 0.84 (d, J = 6 Hz, 3 H), 0.87 (d, J = 6 Hz, 3 H), 0.92 (d, J = 7 Hz, 3 H), 1.4–1.8 (m, 3 H), 3.46 (dd, J = 6 and 10 Hz, 1 H), 3.60 (dd, J = 6 and 10 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 12.5, 17.9, 20.6, 28.9, 41.4, 66.4. Anal. Calcd for $C_6H_{14}O$: C, 70.53; H, 13.81. Found: C, 70.30; H, 14.01.

(1*S*,2*S*)-(+)-*trans*-(2-Methylcyclopentyl)methanol: ^1H NMR ($CDCl_3$) δ 1.01 (d, J = 7 Hz, 3 H), 1.2–1.9 (m, 1 H), 3.48 (dd, J = 5 and 10 Hz, 1 H), 3.63 (dd, J = 5 and 10 Hz); ^{13}C NMR ($CDCl_3$) δ 20.0, 24.0, 29.5, 35.0, 37.0, 49.7, 66.8. Anal. Calcd for $C_7H_{14}O$: C, 73.63; H, 12.36. Found: C, 73.36; H, 12.69.

(1*S*,2*S*)-(+)-*trans*-(2-Methylcyclohexyl)methanol: ^1H NMR ($CDCl_3$) δ 0.92 (d, J = 7 Hz, 3 H), 1.1–1.9 (m, 11 H), 3.53 (dd, J = 5 and 10 Hz, 1 H), 3.69 (dd, J = 5 and 10 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.1, 26.2, 26.4, 29.7, 33.7, 35.7, 46.6, 65.8. Anal. Calcd for $C_8H_{16}O$: C, 74.94; H, 12.58. Found: C, 74.81; H, 12.28.

(1*S*,2*S*)-(+)-*trans*-(2-Phenylcyclopentyl)methanol: ^1H NMR ($CDCl_3$) δ 1.1–2.2 (m, 7 H), 2.65 (m, 1 H), 3.3–3.65 (m, 2 H), 7.2 (s, 5 H); ^{13}C NMR ($CDCl_3$) δ 24.6, 29.5, 35.7, 48.8, 50.2, 65.5, 126.0, 127.4, 128.4, 145.5. Anal. Calcd for $C_{12}H_{16}O$: C, 81.78; H, 9.15. Found: C, 81.44; H, 9.05.

(1*R*,2*R*,3*R*,5*R*)-(−)-(3-Isopinocampheyl)methanol: ^1H NMR ($CDCl_3$) δ 0.65–1.15 (m, 8 H), 1.2–2.53 (m, 10 H), 3.23–3.63 (br s, 2 H); ^{13} NMR ($CDCl_3$) δ 22.1, 22.89, 28.02, 31.25, 33.45, 38.98,

39.05, 39.45, 41.51, 47.90, 69.90. anal. Calcd for $C_{11}H_{20}O$: C, 78.57; H, 11.90. Found: C, 78.63; H, 12.10.

Synthesis of 2-(3-Methylpentyl)-1,3,2-dioxaborinane of Very High Optical Purity. (*S*)-(−)-2-(2-Methylbutyl)-1,3,2-dioxaborinane (10 mmol) of 99% ee, obtained by homologation of (*R*)-(−)-2-(1-methylpropyl)-1,3,2-dioxaborinane, was homologated further by using $LiCHCl_2$ and KIPBH following the general procedure. The crude boronic acid obtained was esterified with 1,3-propanediol and purified by distillation: 1.46 g (86%); bp 106–108 °C (18 torr); ^{11}B NMR δ +31.0 (s); ^1H NMR ($CDCl_3$) δ 0.6–1.7 (m, 11 H), 1.9 (q, J = 6 Hz, 2 H), 3.93 (t, J = 6 Hz, 4 H); $[\alpha]^{23}_D$ −7.73° ± 0.03 (*c* 4, THF).

Oxidation of the boronic ester with alkaline hydrogen peroxide afforded 3-methyl-1-pentanol which was isolated and purified by distillation: 70%; bp 68–70 °C (20 torr); ^1H NMR ($CDCl_3$–D_2O) δ 0.95 (m, 6 H), 1.12–1.82 (m, 5 H), 3.65 (t, J = 6 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 11.0, 18.9, 29.4, 31.0, 39.8, 60.6. Anal. Calcd for $C_6H_{14}O$: C, 70.53; H, 13.81. Found: C, 70.52; H, 13.96.

The alcohol was further purified by preparative GC and dried over 4-Å molecular sieves. The alcohol exhibited α^{23}_D −3.52° ± 0.005 (neat, *l* 0.5), d^{23}_4 0.8227, and $[\alpha]^{23}_D$ −8.53° ± 0.01 (neat), suggesting 99% ee for the boronic ester.[32]

Acknowledgment. We are grateful to the National Science Foundation (Grant CHE 79-18881), the National Institutes of Health (Grant GM 10937-22), and the Ministry of Education, Republic of Korea, for their generous support of this work.

(32) Optical rotations of 3-methyl-1-pentanol of >99% ee: (a) Koppenhoefer, B.; Weber, R.; Schurig, V. *Synthesis* **1982**, 316; $[\alpha]^{20}_D$ +8.24° (neat). (b) Mori, K.; Watanabe, H. *Tetrahedron* **1984**, *40*, 299; $[\alpha]^{20}_D$ −8.5° (neat). (c) Rossi, R.; Carpita, A.; Chini, M. *Ibid.* **1985**, *41*, 627; $[\alpha]^{20}_D$ −8.67° ± 0.02 (neat).

Evidence for an Anionic Sulfene Intermediate in the Alkaline Hydrolysis of Aryl (Methylsulfonyl)methanesulfonate Esters[15]

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Istituto di Chimica Organica dell'Università, CNR Centro di Studio sui Diariloidi e loro Applicazioni, Genova, Italy, and University Chemical Laboratory, Canterbury, England

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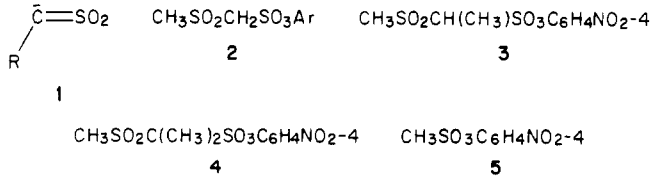
The hydrolysis of aryl (methylsulfonyl)methanesulfonates obeys the kinetic law $k_{obsd} = (k_a + k_b[OH^-])/(1 + [H^+]/K_a)$, where K_a is the ionization constant of the ester. An E1cB mechanism is consistent with the above rate law and the results of studies on Brønsted and Hammett selectivities for variation in the leaving group substituents, entropy of activation data on k_a and k_b, trapping with an amine, oxygen-18 incorporation into the acid products, deuterium exchange from D_2O into the substrates, and the effect on rate constants of substituting one or both hydrogen atoms adjacent to the sulfonate group with methyls. The k_a term involves unimolecular expulsion of the leaving group from the ionized ester to give a sulfene (I). The k_b term is due to further ionization

$CH_3SO_2CH{=}SO_2$ (I) $\qquad$ $CH_3SO_2\bar{C}{=}SO_2$ (II)

of the conjugate base of the ester to give a dianion which expels the leaving group to yield the unprecedented anionic sulfene (II). Deuterium exchange studies indicate that the anion $^-CH_2SO_2CH{=}SO_2$ is not involved kinetically. The variation of effective charge on the leaving oxygen is traced throughout the reaction path.

The reactions of nucleophiles with sulfonate esters and sulfonyl chlorides has been shown in recent years to involve sulfene intermediates provided there is an α hydrogen in the parent acid.[1] Work has progressed to show novel forms of the sulfene mechanism including the S_N2' pathway,[2] the participation of *p*-oxosulfoquinones,[3] and the ketosulfene route.[4]

The present work is aimed at studying systems where a novel anionic sulfene intermediate (**1**) could be formed



1 $\qquad$ 2 $\qquad$ 3 $\qquad$ 4 $\qquad$ 5

from sulfonate esters bearing two α hydrogens. In order to facilitate the formation of the anionic species we looked at the hydrolysis of esters (**2** and **3**) bearing methylsulfonyl activating groups. The hydrolysis of these esters was compared with that for the hydrolysis of esters which should involve regular nucleophilic attack of the hydroxide

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‡ University Chemical Laboratory.

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(2) King, J. F.; Loosmore, S. M. *J. Chem. Soc., Chem. Commun.* **1976**, 1011.

(3) Thea, S.; Guanti, G.; Hopkins, A. R.; Williams, A. *J. Am. Chem. Soc.* **1982**, *104*, 1128.

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