Crystal Structure Determination. Compound **7a** was recrystallized from *n*-hexane, and the sample used in the structure determination was 0.3 × 0.5 × 0.6 mm. All diffraction measurements were made on a Philips PW 1100 diffractometer using MoKα radiation and a graphite monochromator. The orientation matrix and cell dimensions were determined from 25 accurately centered reflections. Pertinent crystallographic information is summarized in Table IV.

Intensity data were corrected for Lorentz-polarization effects but not for absorption. In all, 1264 unique nonzero reflections were used in the structural analysis. The structure was solved by the direct method ($E \geq 1.2$) with the SHELX crystallographic program system (Sheldrick, 1976). The first E map indicated positions for all the nonhydrogen atoms. The hydrogen atoms were geometrically positioned (assuming a C–H distance of 1.08 Å) and constrained to refine riding on their attached carbon atoms. The final agreement factor R was 0.058, with anisotropic temperature factors assigned to the Br, NO_2, and C=O groups. The weighting scheme was $w = 3.16/[\sigma(F_o)^2 + 0.0007 F_o^2]$.

Figure 1 was made with the PLUTO program (Motherwell, 1976). Selected dihedral angles, interatomic bond lengths, relevant bond angles, and crystallographic data are reported in Tables I–IV, respectively.

Acknowledgment. We gratefully acknowledge Professor Giovanni Valle, Padua University, for the intensity data collection.

Registry No. 1, 4900-63-4; **2a**, 77416-37-6; **2b**, 77416-38-7; **2c**, 77416-39-8; **6a**, 77416-40-1; **6b**, 77416-41-2; **6c**, 77416-42-3; **7a**, 77416-43-4; **7b**, 77416-44-5; **7c**, 77416-45-6; **8a**, 4708-86-5; **8b**, 77416-46-7; **8c**, 77429-55-1; **9a**, 72207-00-2; **9b**, 73323-60-1; **9c**, 73323-61-2.

Supplementary Material Available: Tables of positional coordinates and temperatures factors (2 pages). Ordering information is given on any current masthead page.

Facile Conversion of Alkenes into Alkyl Bromides via Reaction of Organoboranes with Bromine or Bromine Chloride

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Organoboranes react with either bromine or bromine chloride in aqueous media to yield the corresponding alkyl bromides under surprisingly mild conditions. The reaction is ideal for the synthesis of functionally substituted organic bromides. Sodium bromide may be utilized as the bromine source via its in situ conversion to bromine chloride by using mild oxidizing agents.

The use of organoborane technology to synthesize alkyl bromides is well documented and is rather complex.[1-4] In the presence of strong bases such as sodium methoxide, the organoboranes are readily converted to the corresponding alkyl bromides.[5] In the absence of strong bases,

$$R_3B \xrightarrow[NaOCH_3/CH_3OH]{Br_2} RBr$$

a free-radical reaction generally occurs which involves abstraction of an α-hydrogen followed by reaction with bromine. The resultant α-bromo organoborane may either be cleaved by the HBr byproduct (to yield a bromoalkane[6]) or rearrange to form a new organoborane.[7]

We recently developed a new, mild iodination procedure involving the reaction of organoboranes with iodine monochloride.[8] The reaction has proven to be of utility in

$$R_3B \xrightarrow[NaOAc]{ICl} RI$$

the radiopharmaceutical area due to the gentle reaction conditions (a variety of functionality is tolerated) and efficient utilization of the iodine nuclide.[9,10] The reaction presumably occurs via an electrophilic attack on one of the α-carbons in the electron-rich organoborane–acetate complex.[11]

We felt that organoboranes might also react with bormine and bromine chloride under more gentle ionic conditions. We have found this to be the case.

Results and Discussion

The available data suggest that bromine can react with organoboranes in an ionic fashion as well as via a free-radical process. Thus inversion of configuration has been observed when tri-*exo*-norbornylborane reacts with bromine in the presence of base.[12] In addition, the rearrangement of *B*-alkyl-9-borabicyclononanes (when they are subjected to bromine) has been postulated to be ionic in nature.[13] We decided to investigate the reaction of organoboranes with bromine and bromine chloride[14-16] in analogy to our earlier iodination studies.[8] Our results are presented in Table I.

The data indicate that the reaction is most useful for the conversion of terminal olefins into primary bromides and compliments the earlier free-radical bromination reactions which favor secondary alkyl groups.[3,17] The lower yields observed for boranes containing secondary alkyl

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(1) Brown, H. C. "Organic Synthesis Via Boranes"; Wiley-Interscience: Ithaca, NY, 1975.

(2) Pelter, A.; Smith, K. In "Comprehensive Organic Chemistry"; Barton, D., Ollis, W. D., Eds.; Pergamon: Oxford, New York, 1979; Vol. 3, pp 815–817, 832–837.

(3) Lane, C. F. *J. Organomet. Chem.* **1971**, *31*, 421.

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(5) Brown, H. C.; Lane, C. F. *J. Am. Chem. Soc.* **1970**, *92*, 6660.

(6) Lane, C. F.; Brown, H. C. *J. Organomet. Chem.* **1971**, *26*, C51.

(7) Lane, C. F. *Intra-Sci. Chem. Rep.* **1973**, *7*, 133.

(8) Kabalka, G. W.; Gooch, E. E. *J. Org. Chem.* **1980**, *45*, 3578.

(9) Kabalka, G. W.; Gooch, E. E. *J. Labelled Compd. Rad.* **1981**, *18*, 117.

(10) Kabalka, G. W.; Gooch, E. E.; Otto, C. A. *J. Radioanalyt. Chem.*, in press.

(11) Brown, H. C.; Delue, N. R.; Kabalka, G. W.; Hedgecock, H. C. *J. Am. Chem. Soc.* **1976**, *98*, 1291.

(12) Brown, H. C.; Lane, C. F. *Chem. Commun.* **1971**, 522.

(13) Brown, H. C.; Delue, N. R. *Tetrahedron Lett.* **1977**, 3007.

(14) Obenland, C. O. *J. Chem. Educ.* **1964**, *41*, 506.

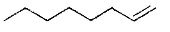
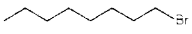
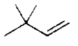
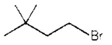
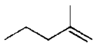
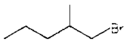
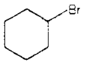
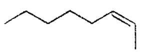
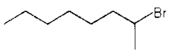
(15) Mills, J. F.; Schneider, J. A. *Ind. Eng. Chem. Prod. Res. Dev.* **1973**, *12*, 160.

(16) We also investigated reagents such as cyanogen bromide and *N*-bromosuccinimide in the presence of water. The yields were modest.

(17) Lane, C. F.; Brown, H. C. *J. Am. Chem. Soc.* **1970**, *92*, 7212.

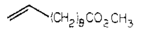
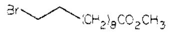
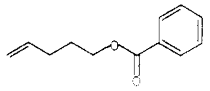
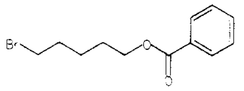
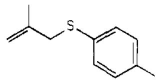
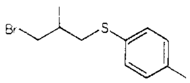
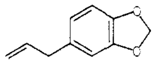
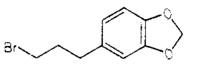
0022-3263/81/1946-3113$01.25/0

Table I. Conversion of Alkenes to Alkyl Bromides[a]

alkene	product	% yield[b] Br$_2$[c]	BrCl[d]	BrCl (in situ)[e]
		69	85	85
		75	75	81
		70	62	92
		72	60	67
		5	5	5

[a] Alkenes were converted to the corresponding organoboranes by reacting them with BH$_3$·THF. [b] Isolated yields; in every case GLC yields are significantly higher. Yields are based on the brominating agent. [c] Equimolar quantities of bromine and organoborane. [d] Slight excess of freshly prepared bromine chloride used. [e] Bromine chloride formed by in situ reaction of sodium bromide with chloramine-T.

Table II. Conversion of Functionally Substituted Alkenes to the Corresponding Organic Bromides[a]

alkene	product	% yield[b] Br$_2$[c]	BrCl[d]
		96	95 (68)[e]
		92	91 (70)[e]
		91	61
		94	94 (78)

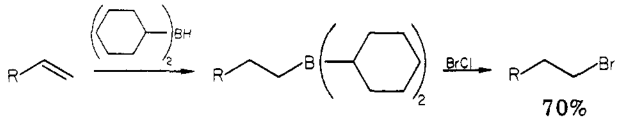
[a] The alkenes were converted to the corresponding organoboranes by reacting them with BH$_3$·THF. [b] Isolated yields. Yields are based on the brominating agent. [c] Equimolar amounts of bromine and organoborane. [d] Bromine chloride formed in situ by reaction of sodium bromide and chloramine-T. [e] The numbers in parentheses refer to isolated yields based on starting alkene in reactions utilizing dicyclohexylborane as the hydroborating agent.

groups is, presumably, due to steric constraints limiting approach of the brominating species to the carbon attached to the boron. Further studies will be required to clarify the situation. We have, however, utilized the preferential reaction of primary alkyl groups to enhance the synthetic utility of the reactions, vide infra.

It is interesting to note that the reaction of trialkylboranes with bromine readily occurs in the presence of water. This observation rules out the formation of an α-bromo organoborane species since they are known to rearrange in the presence of water.[7,18] We postulate that the reaction is occurring via a S$_E$2 mechanism analogous to that observed for iodination reactions.[11]

We applied the new reactions to a series of functionally substituted materials which are models for our radiopharmaceutical studies. We restricted the bromine chloride studies to the in situ preparation of the bromine chloride since it is the most convenient method and is ideally suited for the incorporation of radiobromine. Our results are summarized in Table II.

The new reactions efficiently utilize the bromination agent; the alkyl groups are, however, not completely reacted (only one of the three groups on boron reacts). Traditionally, mixed organoboranes which incorporate "sacrificial" alkyl groups have been employed to maximize the conversion of alkenes to alkyl halides, etc., via organoborane technology. We investigated reagents such as catecholborane,[19,20] 9-borabicyclononane,[6,20] and dicyclohexylborane[10] in these reactions in an effort to increase the efficiency of the conversion of a desired alkene to the alkylbromide. We find that the use of dicyclohexylborane essentially doubles the efficiency of the reaction.



(The maximum yield of alkyl bromide in the trialkylborane case is 33% based on starting olefin.) Representative data appear in Table II.

Experimental Section

Routine NMR spectra were recorded on a Varian Associates T-60 spectrometer. All chemical shifts are reported in parts per million downfield from Me$_4$Si. The mass spectra were obtained with a HP-5982-A GC–mass spectrometer. The gas chromatography work was performed on a Varian Model 1700 instrument with a 6 ft × 0.25 in. 20% SE-30 on Chromosorb W column. Melting points are uncorrected.

Commercially available samples (Aldrich) of 1-octene, cyclohexene, safrole, and methyl 10-undecenoate were distilled prior to use. 5-Benzoxy-1-pentene and 3-(p-tolylthio)-2-methyl-1-propene were prepared according to published procedures.[8]

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[18] It is also of interest to note that an earlier report[3] indicates oxidation occurs if organoboranes are brominated in aqueous systems when hydroxide is present.

[19] Lane, C. F.; Kabalka, G. W. *Tetrahedron* **1976**, *32*, 981.

[20] Alkylboronic acids (from hydrolysis of the corresponding alkylcatecholboranes) were unreactive toward bromine. Alkyl-9-BBN derivatives produced very little of the alkyl bromides; presumably the bicyclooctyl system ring opened as was observed in ref 3.

Bromine Chloride. Bromine chloride solutions (10 mmol) were prepared by adding sodium bromide (1.03 g, 10 mmol) to a solution of 70 mL of water and 35 mL of THF. Chlorine gas (15 mmol, 0.67 mL of condensed Cl_2) was passed through the solution as a gas at room temperature. The solution was used immediately.

Hydroboration: General Procedure. The alkene (15 mmol) was dissolved in 5 mL of THF in a 50-mL, N_2-flushed, round-bottomed flask equipped with a magnetic stirrer, septum inlet, and reflux condenser. The solution was cooled to 0 °C and BH_3–THF (5 mmol, 2.6 mL of a 1.91 M solution) was added via a syringe. The solution was stirred at 0 °C for 1 h.

Hydroboration: Dicyclohexylborane Procedure. Dicyclohexylborane (0.5 M) was prepared according to the published procedure.[21] The alkene (5 mmol) was added to dicyclohexylborane (5 mmol) at 0 °C. The mixture was stirred for 1 h while the temperature rose to 25 °C.

Bromination: Molecular Bromine. The organoborane (5 mmol) in THF was cooled to 0 °C. Water (10 mL) was added and the reaction mixture shielded from light. Bromine (5 mmol) dissolved in THF (10 mL) at 0 °C was added to the organoborane and the mixture stirred for 30 min. Ether (30 mL) was added to extract the product. The ether layer was washed with two 30-mL portions of water and dried over anhydrous $MgSO_4$, and the solvent was removed. The products were isolated by either column chromatography or preparative thick-layer chromatography.

Bromination: Bromine Chloride. The organoborane (5 mmol) in THF was cooled to 0 °C. Water (10 mL) was added and the reaction mixture shielded from light. The bromine chloride solution (~5 mmol) was added at 0 °C and the reaction allowed to proceed for 30 min. The products were isolated as described in the bromine procedure.

Bromination: Bromine Chloride, in Situ. Sodium bromide (5.0 mmol, 0.515 g) in water (10 mL) was added to the organoborane (5.0 mmol) solution. The reaction mixture was cooled to 0 °C and shielded from light. Chloramine-T (2.28 g, 10 mmol) in a mixture of THF (7.5 mL) and H_2O (7.5 mL) was added all at once. An aqueous 10% HCl solution (10 mL) which had been saturated with NaCl was added dropwise to the mixture. The mixture was stirred for 15 min at 0 °C. The mixture was extracted with ether (30 mL) and the products were isolated as described in the bromine procedure. (The yields decrease if reaction times are longer than 15 min.)

1-Bromoalkanes. The respective alkenes, 1-octene, 3,3-dimethyl-1-butene, 2-methyl-1-pentene, were hydroborated as described in the general procedure. Each trialkyl organoborane was brominated according to the three bromination procedures. The products were isolated by column chromatography on silica gel (pentane eluent). The products exhibited physical and spectral characteristics in accord with authentic samples. No effort was made to maximize the yields presented in Table I, but the GLC yields were consistently higher than the isolated yields.

Methyl 11-Bromoundecanoate. (a) Methyl 10-undecenoate (15 mmol, 2.98 g) was hydroborated with BH_3·THF (5 mmol) at 0 °C for 1 h. The brominations were carried out as described in the general procedures. The product was isolated via column chromatography: yield 1.39 g (95%) (96% via Br_2 reaction); mass spectrum, *m/e* 199 (M – Br, calcd *m/e* 278 and 280); IR (neat) 1740 cm^{-1} (C=O); NMR ($CDCl_3$) δ 1.1–1.2 (br s, 16 H, alkane), 2.3 (t, 2 H, CH_2CO_2), 3.4 (t, 2 H, CH_2Br), 3.58 (s, 3 H, OCH_3). (b) A similar reaction was carried out utilizing dicyclohexylborane (5 mmol) and the alkene (5 mmol). The yield of methyl 11-bromoundecanoate was 68%; 1.5 mmol of cyclohexyl bromide was also formed.

1-Benzoxy-5-bromopentane. (a) 5-Benzoxy-1-pentene (15 mmol, 2.85 g) was hydroborated with BH_3·THF (5 mmol) at 0 °C for 1 h. The brominations were carried out as described in the general procedures. The product was isolated via column chromatography: yield 1.23 g (91%) (92% via the Br_2 reaction); mass spectrum, *m/e* 269 and 271 (equal intensity, M – 1, calcd *m/e* 270 and 272); NMR ($CDCl_3$) δ 1.7 (br envelope, 6 H, alkyl), 3.3 (t, 2 H, CH_2–O), 7.3–7.9 (m, 5 H, ArH). (b) A similar reaction was carried out utilizing dicyclohexylborane (5 mmol) and the alkene (5 mmol). The yield of 1-benzoxy-5-bromopentane was 70%; 1.4 mmol of cyclohexyl bromide was also formed.

3-(*p*-Tolylthio)-2-methyl-1-bromopropane. 3-(*p*-Tolylthio)-2-methyl-1-propene (15 mmol, 2.67 g) was hydroborated with BH_3·THF (5 mmol) at 0 °C. The brominations were carried out as described in the general procedure; the product was isolated via chromatography: yield 0.89 g (61%) (90% via Br_2 reactions); mass spectrum, *m/e* 257 and 259 (M – 1, calcd *m/e* 258 and 260); NMR ($CDCl_3$) δ 1.0 (d, 3 H, CH_3), 1.6 (m, 1 H, CH), 2.2 (s, 2 H, $ArCH_3$), 3.4 (m, 2 H, CH_2Br), 3.2 (d, 2 H, SCH_2), 7.0 ($A'_2X'_2$, 4 H, Ar H).

3-[3,4-(Methylenedioxy)phenyl]-1-bromopropane. (a) Safrole (15 mmol, 2.45 g) was hydroborated with BH_3·THF (5 mmol) at 0 °C for 1 h. The brominations were carried out as described in the general procedure. The product was isolated via chromatography: yield 1.20 g (94%) (94% via Br_2 reaction); mass spectrum, *m/e* 242 and 244 (equal intensity, calcd *m/e* 242 and 244); the product contains 12% of the 2-bromo derivative;[22] IR (neat) 1490 (C=C), 1440 (C=C), 1250 (OAr), 1040 (CH_2—O), 940 (ArH), 800 (ArH) cm^{-1}; NMR ($CDCl_3$) δ 2.0 (m, 2 H, CH_2), 2.8 (t, 2 H, $ArCH_2$), 3.4 (t, 2 H, CH_2Br), 5.8 (s, 2 H, OCH_2O), 6.6 (s, 3 H, Ar H). (b) A similar reaction was carried out utilizing dicyclohexylborane (5 mmol) and the alkene (5 mmol). The yield of 3-[3,4-(methylenedioxy)phenyl]-1-bromopropane was 78%; 1.1 mmol of cyclohexyl bromide was also formed.

Acknowledgment. We thank the Department of Energy (DE-AS05-80-EV10363) and the National Institutes of Health (5-R01-GM25817) for support of this research.

Registry No. 1-Octene, 111-66-0; 3,3-dimethyl-1-butene, 558-37-2; 2-methyl-1-pentene, 763-29-1; cyclohexene, 110-83-8; 2-octene, 111-67-1; 1-bromooctane, 111-83-1; 1-bromo-3,3-dimethylbutane, 1647-23-0; cyclohexyl bromide, 108-85-0; 1-bromo-2-methylpentane, 25346-33-2; 2-bromooctane, 557-35-7; methyl 10-undecenoate, 111-81-9; methyl 11-bromoundecanoate, 6287-90-7; 1-(benzoyloxy)-5-bromopentane, 77572-66-8; 5-(benzoyloxy)-1-pentene, 29264-40-2; 3-(*p*-tolylthio)-2-methyl-1-bromopropane, 67207-31-2; 3-(*p*-tolylthio)-2-methylpropene, 77572-67-9; 3-[3,4-(methylenedioxy)phenyl]-1-bromopropane, 28437-31-2; safrole, 94-59-7; Br_2, 7726-95-6; BrCl, 13863-41-7.

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(21) Reference 1, p 28.

(22) The hydroboration of safrole proceeds such that 12% of the alkyl groups are attached to boron at the secondary position. See: Kabalka, G. W.; Hedgecock, H. C. *J. Org. Chem.* **1975**, *40*, 1776.