Reductive Alkylation and Reduction of Tertiary, Secondary, and Benzylic Alcohols with Trimethyl-, Triethyl-, and Triisopropylboron/Trifluoromethanesulfonic (Triflic) Acid[1]

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Tertiary, secondary, and benzylic alcohols were reductively alkylated and reduced with trimethyl-, triethyl-, and triisopropylboron/trifluoromethanesulfonic (triflic) acid. A postulated mechanism for the reactions is discussed.

Introduction

Trialkylborons generally do not react, as do Grignard reagents or organolithiums, with allyl halides or carbonyl compounds. They show, however, a strong tendency to undergo reaction with nucleophiles to form the corresponding organoboron "ate" complexes.[2] The use of organoborons as highly versatile reagents for organic synthesis has been amply demonstrated.[2] The application of organoborates in various chemical transformations is also rapidly growing.[3]

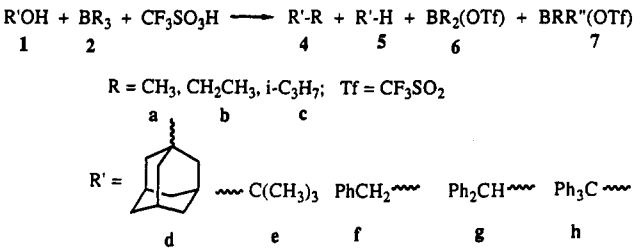
Reactions of organoborates with carbonyl compounds are considered to be similar to those of Grignard reagents. Various organoborates have been found to react smoothly with acyl halides to form the corresponding ketones.[4,5] The reactions are not complicated by the concomitant formation of tertiary alcohols, which are usually obtained in the reaction of acyl halides with alkylmagnesium halides or alkyllithiums. In the reaction of "mixed" tetraalkylborates containing different alkyl groups, primary alkyl groups are transferred almost exclusively, regardless of statistical factors.[3] If, however, other more nucleophilic groups are present (such as aryl, benzyl, and methylsulfinylmethyl), they react preferentially over primary (or secondary) alkyl groups.

Organoborates usually do not react with alkyl halides and sulfonates. The only reaction of synthetic interest is that of arylborates with certain allylic halides to give the corresponding cross-coupled products.[6] Protonation of organoborates such as alkylborates, arylborates, and benzylborates giving the corresponding hydrocarbons[7,8] involves intermolecular alkyl (aryl, benzyl) transfer.

The limited scope of intermolecular alkyl transfer in the reactions of organoborates with electrophiles is mainly attributed to their strong tendency to undergo hydride transfer resulting in formation of boron ylides that subsequently undergo intramolecular alkyl transfer to the corresponding trialkylborons.[9] Tetraalkylborates were also found to be suitable hydride sources to reduce a variety of organic compounds.[10]

Alkali tetrahydroborates and diborane are effective reducing agents under acidic conditions, affecting also various chemical transformations. We reported previously that sodium borohydride/triflic acid and borane/triflic acid systems[11] are efficient ionic hydrogenating agents reducing various functionalities into hydrocarbons. In extension of our previous studies, we report now the use of trialkylborons with trifluoromethanesulfonic acid (triflic acid) as an effective reducing system for a variety of alcohols to the corresponding alkanes, as well as their conversion into alkylated alkanes.

Scheme I



Results and Discussion

When alcohols are reacted with trialkylborons upon addition of trifluoromethanesulfonic (triflic) acid, they are reduced to the corresponding alkanes and are reductively alkylated (Scheme I).

In a typical example, to a well-stirred solution of equimolar trimethylboron **7a** and 1-adamantyl alcohol (**1d**) in freshly distilled 1,1,2-trichlorotrifluoroethane (Freon-113) solution at −30 °C was slowly added 1 equiv of trifluoromethanesulfonic acid. The reaction mixture was then allowed to warm to ambient temperature while stirring was continued for several hours. Usual workup and extraction gave adamantane (**5d**) along with 1-methyladamantane (**4ad**). 2-Methyl-2-propyl (*tert*-butyl), benzyl, diphenylmethyl, and triphenylmethyl alcohol reacted under similar reaction conditions with trimethylboron/triflic acid as well as with triethylboron/triflic acid to give the corresponding alkylated alkanes and cycloalkanes, respectively (Table I).

Protolytic ionization of the alcohols first gives the corresponding carbocations and trimethyltriflatoborate **3**, a boron "ate" complex. Subsequent hydride abstraction via carbon–hydrogen bond insertion gives the reduced hydrocarbons. Alkyl abstraction via boron–carbon bond insertion results in the methylated products. At the same time, the borate anion forms a boron ylide **8**,[9,13] which leads by intramolecular 1,2-alkyl migration to trivalent methy-

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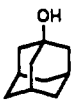
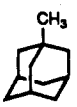
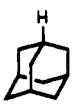
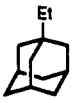
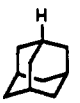
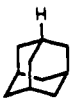
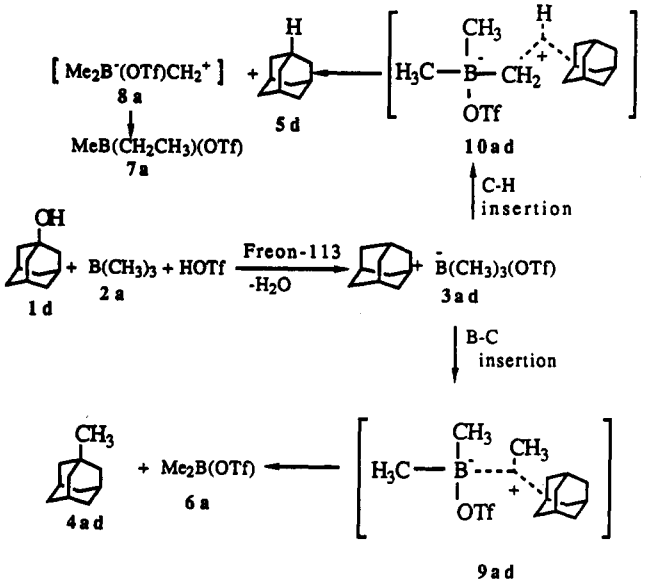
Table I. Reduction and Reductive Alkylation of Alcohols with Trialkylboron/Triflic Acid

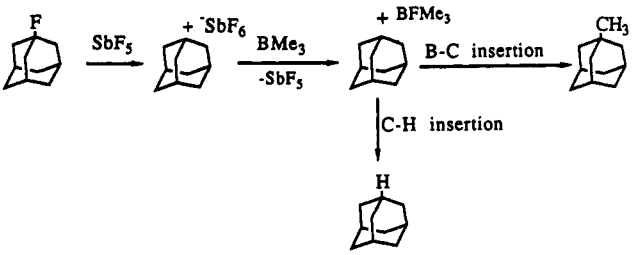
	BMe_3/HOTf (% yield)		BEt_3/HOTf (% yield)		$B(i\text{-}Pr)_3$/HOTf (% yield)	
alcohol R'OH (1)	R'CH_3 (4)	R'H (5)	R'Et (4)	R'H (5)	R'-*i*-Pr (4)	R'-H (5)
						
1d	**4ad**	**5d**	**4bd**	**5d**	**4cd**	**5d**
	(52.6)	(47.4)	(9.2)	(90.8)	(0.1)[a]	(99.9)
$(H_3C)_3COH$	$(CH_3)_4C$	$(CH_3)_3CH$	$(CH_3)_3CCH_2CH_3$	$(CH_3)_3CH$	$(CH_3)_3CCH(CH_3)_2$	$(CH_3)_3CH$
1e	**4ae**	**5e**	**4be**	**5e**	**4ce**	**5e**
	(49.3)	(50.7)	(7.5)	(92.5)	(0.1)[a]	(99.9)
$PhCH_2OH$	$PhCH_2Me$	$PhCH_3$	$PhCH_2Et$	$PhCH_3$	$PhCH_2Pr\text{-}i$	$PhCH_3$
1f	**4af**	**5f**	**4bf**	**5f**	**4ce**	**5f**
	(56.8)	(43.2)	(11.4)	(88.6)	(0.1)[a]	(99.9)
Ph_2CHOH	Ph_2CHMe	Ph_2CH_2	Ph_2CHEt	Ph_2CH_2	$Ph_2CHPr\text{-}i$	Ph_2CH_2
1g	**4ag**	**5g**	**4bg**	**5g**	**4cg**	**5g**
	(52.6)	(47.4)	(9.4)	(90.6)	(0.0)	(100.0)
Ph_3COH	Ph_3CMe	Ph_3CH	Ph_3CEt	$Ph_3C\text{-}H$	$Ph_3C\text{-}Pr\text{-}i$	$Ph_3C\text{-}H$
1h	**4ah**	**5h**	**4bh**	**5h**	**4ch**	**5h**
	(44.1)	(55.9)	(4.1)	(95.9)	(0.0)	(100.0)

[a] Based on GC–MS spectroscopic analysis and comparison with authentic samples.

Scheme II



Scheme III



lethylboron triflate **7** or forms dimethyl triflate **6**. The proposed mechanism for the reaction of 1-adamantanol (**1d**) with trimethylboron (**2a**) in the presence of trifluoromethanesulfonic acid (triflic acid) is depicted in Scheme II.

The electrophilic insertion[14] into carbon–carbon or carbon–hydrogen bonds is dependent on the relative stability of the involved carbocations.[15,16] In general, tertiary C–H and carbon–carbon bonds react preferentially over secondary or primary C–H bonds. However, steric factors can also affect the reactivities. Furthermore, the overall number of involved carbon–carbon and carbon–hydrogen bonds also must be considered in determining relative reactivities.

The trend of insertion into the boron–carbon and carbon–hydrogen bonds in the trialkylboron/triflic acid system is similar to that previously observed in electrophilic reactions of alkanes. The 1-adamantyl cation formed via protolytic ionization of 1-adamantanol (**1d**) inserts either into the carbon–hydrogen or boron–carbon bonds of the trimethylboron triflate "ate" complex **3ad** to afford adamantane (**5d**) and 1-methyladamantane (**4ad**), respectively. The electrophilic insertion involves two-electron-three-center bond formation, **9ad** and **10ad**, which determines competing carbon–hydrogen and boron–carbon bond insertions. The corresponding reduced or alkylated products, obtained via competing insertion reactions into the carbon–hydrogen and boron–carbon bonds, are obtained in about equal amounts (Table I).

2-Methyl-2-propyl (*tert*-butyl), triphenylmethyl, diphenylmethyl, and benzyl alcohols react similarly to 1-adamantyl alcohol, showing the scope of the reaction. The stability of the intermediately formed carbocations is essential for the reactions to take place.

In reactions using triethyl- and triisopropylboron, respectively, as shown in Table I, the yield of reductive alkylation significantly decreases because of the increasing difficulty of boron–carbon bond insertion as compared with carbon–hydrogen bond insertion (i.e., involving secondary and tertiary C–H bonds; Scheme III).

Further justification for the suggested mechanism also comes from the study of Kennedy et al.,[17] who fould that neoalkanes are formed from the reaction of *tert*-alkyl chlorides with methylaluminum dichloride.

$$R_3CCl + CH_3AlCl_2 \rightleftharpoons [R_3C^+AlCl_3CH_3^-] \rightarrow R_3CCH_3 + AlCl_3$$

Boron ylides have been known for their tendency for intramolecular boron to carbon alkyl group migration.[18] Methyl migration of intermediate boron ylides **8a** gener-

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Table II. ^{11}B NMR Chemical shifts (δ) of Dialkylboron Triflates Formed in the Reaction of 1-Adamantanol with Trialkylborons and Triflic Acid

trialkylboron (BR_3)	dialkylboron triflate	intensity ratio	ratio of adamantane to alkyladamantane 5d:4ad
BMe_3 86[19]	7a:6a = 61.4:62.3	1:1	47:53
BEt_3 85[20]	7b:6b = 62.0:63.1	10:1	91:9
B-*i*-Pr_3 86[21]	7c = 63.8		

ated via intermolecular hydride abstraction of **3ad**, giving methyl ethylboron triflate (**7a**), was also observed in present work. A ^{11}B NMR spectroscopic study (64 MHz; BF_3/ether as external standard) of the reaction of 1-adamantanol with trimethylboron/triflic acid gave two slightly differing trivalent peaks of nearly identical intensity, consistent with the isolated ratio of adamantane (**5d**) and 1-methyladamantane (**4ad**). Apparently, the two boron chemical shifts are due to the two corresponding boron triflates, **6ad** and **7d** (Table II). Similar ^{11}B NMR spectroscopic studies were carried out for the reaction of the 1-adamantanol with triethylboron/triflic acid and triisopropylboron/triflic acid systems. The assignment of the observed ^{11}B NMR signals of trivalent boron triflates is based on the ratio of the isolated carbon–hydrogen and boron–carbon bond insertion products (i.e., adamantane and alkyladamantanes). Attempted isolation of dialkylboron triflates has not been successful.

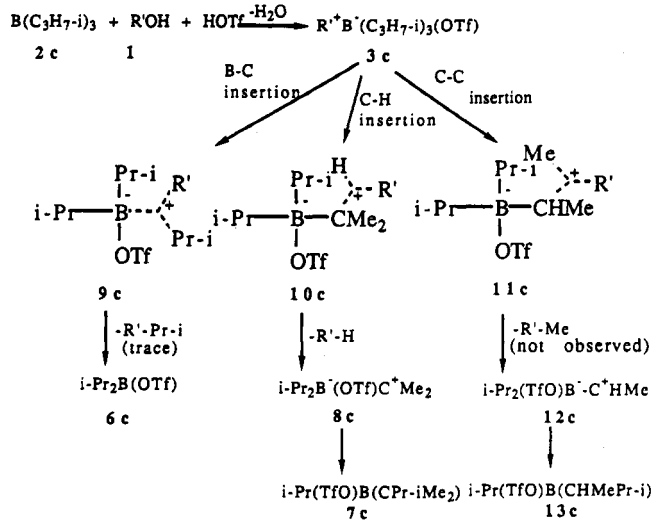
Similar results were obtained in the reaction of alcohols with lithium tetraalkylborates (methyl, ethyl, and isopropyl) in the presence of 2 equiv of triflic acid. The first equivalent of triflic acid is needed to convert the tetraalkylborates into the corresponding trialkylborons. These can be indeed observed in the equimolar reaction by ^{11}B NMR spectroscopy (δ 86.5, 85.9, and 86.2 represent trimethylboron, triethylboron, and triisopropylboron, respectively). The in situ generated trialkylborons, when reacted with excess triflic acid, form the same boron "ate" complexes as previously discussed and react accordingly.

$$Li^+B(CH_3)_4^- + CF_3SO_3H \rightarrow CF_3SO_3Li + CH_4 +$$
$$B(CH_3)_3 \xrightarrow{CF_3SO_3H} CF_3SO_3H_2^+B(CH_3)_3O_3SCF_3^-$$

When the alkyl groups in trialkylborons are changed from methyl to ethyl to isopropyl, intermolecular hydride transfer becomes more predominant (via carbon–hydrogen bond insertion) (Table I). For example, in reactions with triethylboron/triflic acid, alkylation (i.e., boron–carbon bond insertion) becomes minor (5–10%) compared to the trimethyl boron/triflic acid system and reduction (i.e., carbon–hydrogen bond insertion) predominates. In case of the triisopropylboron/triflic acid system, the alkylation products are found only in traces (ca. <0.1%) and reduction is nearly exclusive.

In a control experiment, we also reacted 1-adamantyl hexafluoroantimonate (prepared from 1-fluoroadamantane and antimony pentafluoride in 1,1,2-trichlorotrifluoroethane solution) with trimethyl boron. It gave results similar to those of the previously studied reaction of 1-adamantanol (**1d**) with trimethylboron/triflic acid. This is in accord with carbocation formation as the initial step

Scheme IV



of the reaction of alcohols with trialkyl boron/triflic acid, followed by electrophilic insertion into the C–H or B–C bonds to give adamantane and 1-methyladamantane, respectively (Scheme IV).

Experimental Section

All chemicals not otherwise mentioned were commercially available and used as such. Trimethylboron,[19] triisopropylboron,[21] lithium tetramethylborate,[22] lithium tetraethylborate,[7] and lithium tetraisopropylborate[7] were prepared according to literature procedures. Gas chromatographic analyses were carried out with use of a silica-quartz capillary column coated with DB-5. Mass spectroscopic analyses were performed on a GC–MS Spectrometer. NMR spectra were recorded on a 200-MHz superconducting NMR spectrometer. All alkylation and reduction products reported in this study are known, and authentic samples available in this laboratory were used for comparison.

Typical Procedure. Reaction of 1-Adamantanol with Trimethylboron/Triflic Acid. To a well-stirred solution of 1-adamantanol (1.52 g; 10.0 mmol) and trimethylboron (0.56 g; 10.0 mmol) in freshly distilled 1,1,2-trichlorotrifluoroethane (from P_2O_5; 20 mL) under nitrogen atmosphere at −30 °C ($MgCl_2$/ice bath) was added 1.50 g (10.0 mmol) of freshly distilled trifluoromethanesulfonic acid (triflic acid) during a period of 5 min. After the addition had been completed, the reaction mixture was stirred at −30 °C for another 30 min. After the cold bath was removed, the reaction mixture was further stirred at ambient temperature for another 5–6 h. The reaction mixture was then quenched with 20% aqueous sodium bicarbonate solution (50 mL). Extraction with methylene chloride (50 mL × 3) was followed by combining the organic layers, drying over anhydrous magnesium sulfate, filtration, and evaporation in vacuo giving the product hydrocarbons. Products were separated by column chromatography on silica gel (hexane as eluent). 1-Methyladamantane (**4ad**; 0.79 g; 5.26 mmol; 52.6% yield from 1-adamantanol) and adamantane (**5d**; 0.64 g; 4.74 mol; 47.4% yield from 1-adamantanol) were obtained in pure form. Physical and spectroscopic data of **4ad** and **5d** were consistent with those reported in the literature.

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