with *m*-chloroperbenzoic acid (1 equiv) in methylene chloride yielded the desired terminal epoxide[7] selectively, and this gave upon reduction with excess diimide ($N_2H_4$ + $H_2O_2$)[9] the epoxy acetate VIII.[7] The conversion of VIII to the imino analog of the $C_{18}$ *Cecropia* JH (IV)[7] was accomplished by the method described above for the synthesis of III from V.

The imino juvenile hormones III and IV *alone* and *in combination* with the $C_{18}$ *Cecropia* JH were assayed on both the silkmoth pupa *Antheraea polyphemus*[10] and the bug *Pyrrhocoris apterus*.[11] In the former assay known amounts of hormone in 0.05 ml of olive oil were injected into the mesothoracic dorsum of a prolongedly chilled *polyphemus* pupa. For the latter assay a known amount of hormone in 1 $\mu$l of acetone was topically applied between the bases of the metathoracic legs of a starved freshly molted fifth instar larva which was then fed and allowed to go through metamorphosis.

As seen in Table I, the imino esters III and IV exhibited *no intrinsic JH activity* up to 0.4 $\mu$g/g live weight of *polyphemus* pupa. However, when injected *in combination* with a dose of $C_{18}$ JH, they increased its activity. With 1 $\mu$g of the $C_{16}$ imino compound the activity of the $C_{18}$ JH was *enhanced tenfold.* This effect occurred only when the pupae began adult development immediately. The $C_{18}$ imino hormone was not as effective but retained its synergistic activity for at least 2 days after injection.

**Table I.** Juvenile Hormone Activity of the Imino Juvenile Hormone Analogs III and IV on Chilled *polyphemus* Pupae

| Compd | No. assayed | Assay score[b] | $\mu$g/g live wt |
|---|---|---|---|
| 50 mg of olive oil | 3 | 0 | 16,000 |
| $C_{18}$ JH | | | |
| 0.01 $\mu$g | 6 | 2 | 0.003 |
| 0.1 $\mu$g | 3 | 5 | 0.03 |
| III | | | |
| 0.1 $\mu$g | 3 | 0 | 0.03 |
| 1.0 $\mu$g | 6 | 0 | 0.4 |
| IV | | | |
| 0.1 $\mu$g | 3 | 0 | 0.03 |
| 1.0 $\mu$g | 3 | 0 | 0.3 |
| 0.01 $\mu$g of $C_{18}$ JH plus III or IV | | | |
| 0.1 $\mu$g of III | 5[a] | 4 | 0.03 |
| 1.0 $\mu$g of III | 6[a] | 5 | 0.3 |
| 0.1 $\mu$g of IV | 5 | 2 | 0.03 |
| 1.0 $\mu$g of IV | 3 | 3 | 0.3 |

[a] Includes only those initiating development within 1 day after injection. [b] Reference 10.

A similar potentiation of activity of the $C_{18}$ JH was seen in the *Pyrrhocoris* assay. In this instance the $C_{16}$ and $C_{18}$ imino JH's had only slightly less intrinsic activity than the $C_{18}$ JH[12] (*i.e.*, about 15 $\mu$g/g live weight gave a type III larval–adult intermediate). But enhancement again was demonstrated by giving the $C_{16}$ or $C_{18}$ imino hormones along with 0.25 $\mu$g/g of $C_{18}$ JH which alone did not interfere with metamorphosis. In such experiments about 2.5 $\mu$g/g of either imino JH produced a type III larval–adult intermediate with the $C_{18}$ imino compound showing slightly more activity than the $C_{16}$ imino compound. Thus, there is about a sevenfold potentiation of the activity.

The striking synergistic effect of the imino JH compounds III and IV in combination with the $C_{18}$ *Cecropia* JH finds explanation in a simple way.[13] The imino compounds would be expected to bind strongly to sites capable of donor hydrogen bonding to the epoxide function of the *Cecropia* JH's I and II. Since a synergistic effect was observed for imino JH–JH mixtures, it would seem likely that these sites are involved in the normal metabolism–deactivation of juvenile hormone. That is, the synergistic effect is the result of a slower rate of deactivation of juvenile hormone in the presence of the imino analogs III or IV. Proton-induced deactivation mechanisms involving the oxide function of JH would be expected to lead to hydrolysis (glycol formation),[14,15] cation–olefin cyclization,[1] or proton elimination to afford an allylic alcohol. Evidence has recently been presented that the $C_{18}$ JH is rapidly deactivated in insects by at least one of these processes in addition to ester hydrolysis.[16]

Detailed studies of the novel synergistic effects described above are in progress and will be reported in due course.

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(9) E. J. Corey and H. Yamamoto, *J. Amer. Chem. Soc.*, **92**, 6636 (1970).
(10) C. M. Williams, *Biol. Bull.*, **121**, 572 (1961).
(11) C. M. Williams and K. Sláma, *ibid.*, **130**, 247 (1966).
(12) The level of activity of the $C_{18}$ *Cecropia* JH in the *Pyrrhocoris* assay is itself low in comparison to, for example, the *polyphemus* pupa.
(13) This argument was first outlined by one of us at the International Conference on Juvenile Hormones held in Basel, Switzerland, Oct 1970.
(14) E. J. Corey, K. Lin, and M. Jautelat, *J. Amer. Chem. Soc.*, **90**, 2724 (1968).
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(16) Report by Dr. John Siddall at the International Conference on Juvenile Hormones, Basel, Switzerland, Oct 1970.

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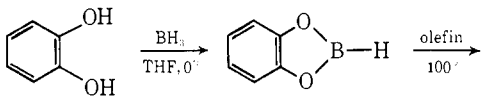
## 1,3,2-Benzodioxaborole, a Convenient Monofunctional Hydroborating Agent. A Simple New Synthesis of Alkaneboronic Esters and Acids from Olefins *via* Hydroboration

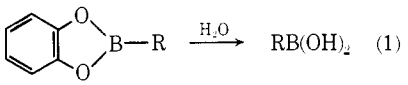
*Sir:*

1,3,2-Benzodioxaborole (**1**), readily available through the rapid reaction of *o*-dihydroxybenzene with borane in tetrahydrofuran (THF), reacts readily at 100° with olefins to produce the corresponding 2-alkyl-1,3,2-benzodioxaboroles (**2**), readily hydrolyzed to the corresponding alkaneboronic acids. The present reaction, therefore, provides a facile and highly convenient transformation of the olefins into the corresponding alkaneboronic acids and esters *via* hydroboration.[1]

(1) H. C. Brown, "Hydroboration," W. A. Benjamin, New York, N. Y., 1962.



1



2

Olefins react readily with borane in THF to form the corresponding organoboranes.[1] Attempts to control the reaction at the monohydroboration stage, so as to provide a convenient synthesis of the monoalkylboranes and the corresponding alkaneboronic acids, have been only partially successful,[2] except for certain highly hindered olefins such as tetramethylethylene.[3] Consequently, we have been exploring possible means of achieving a synthesis which will attach only one alkyl substituent to boron.

A possible solution would appear to be the hydroboration with a disubstituted borane, such as dichloroborane. Unfortunately, this reagent reacts only sluggishly with olefins.[4] A similar disubstituted borane, 4,4,6-trimethyl-1,3,2-dioxaborinane, was examined by Woods and Strong.[5] However, this reagent is also a poor hydroborating agent.[6]

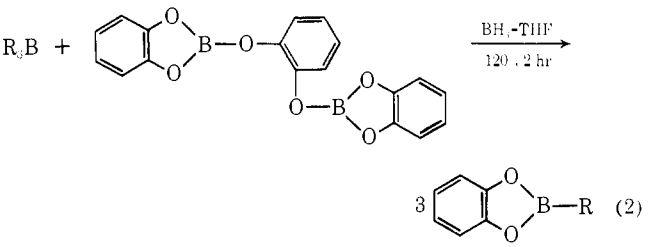
In the course of other work we observed that borane reacts very rapidly, within 5 min at 0°, with *o*-dihydroxybenzene to form 1,3,2-benzodioxaborole.[7] This disubstituted borane is readily distilled and reacts easily with olefins at 100° to give the corresponding 2-alkyl-1,3,2-benzodioxaboroles (**2**) in yields approaching quantitative. The products undergo hydrolysis rapidly to give the corresponding alkaneboronic acids.

The reagent, 1,3,2-benzodioxaborole (**1**), is conveniently prepared by the following procedure. A 2 *M* solution of borane in THF (100 ml, 200 mmol), maintained under nitrogen, was placed in a dry 500-ml flask which was connected to a hood vent through a mercury bubbler. The flask was immersed in an ice bath and a solution of *o*-dihydroxybenzene (22 g, 200 mmol) in THF (50 ml) was added over 30 min with efficient stirring to the borane solution at 0°. After the completion of the addition, the reaction mixture was stirred at 25° for an additional 30 min. Distillation provided 19.2 g (80%) of borole **1**: bp 76–77° (100 mm) [lit.[7] bp 88° (156 mm)]; $n^{20}$D 1.5070; ir (neat) 2680, 1465, 1235, 1130, 740 cm$^{-1}$; mass spectrum (70 eV) *m/e* (rel intensity) 121 (10), 120 (100), 119 (33), 92 (15), 91 (4), 64 (24), 63 (18), 62 (6).

The conversion of norbornene into 2-*exo*-norbornyl-1,3,2-benzodioxaborole is representative of the general hydroboration procedure (method A). A mixture of norbornene (9.4 g, 100 mmol) and borole **1** (13.2 g, 110 mmol) was stirred under nitrogen at 100°. Glpc monitoring of the reaction revealed it to be essentially complete (98% yield) in 4 hr (terminal olefins required 2 hr). Distillation then provided 20.3 g (95%) of isolated product: bp 104° (0.5 mm).

In the case of low boiling olefins a sealed ampoule was required to reach the 100° reaction temperature. In this way highly volatile olefins, such as 1-pentene and cyclopentene, could be readily converted into the corresponding products **2** in 90% yield.

Nevertheless, the inherent hazard and the inconvenience involved in the use of a sealed ampoule for large-scale preparation led us to develop an alternative preparative route to use with such olefins. We have recently reported[8] the facile redistribution of trialkylboranes with trimethylene borate to give the cyclic trimethylene esters of alkaneboronic acids. An analogous redistribution reaction between a trialkylborane and *o*-phenylene borate provided alkylbenzodioxaboroles, **2**, in essentially quantitative yields.



A typical redistribution reaction of a trialkylborane and *o*-phenylene borate[9] follows (method B). 1-Butene (16.8 g, 300 mmol) was converted into tri-*n*-butylborane with borane in THF.[1] The solvent was then distilled off and the residual trialkylborane was stirred with a mixture of *o*-phenylene borate[9] (38 g, 110 mmol) and a catalytic quantity of borane (10 mmol) in THF at 120° for 2 hr. The progress of the reaction was monitored by glpc analysis. At the termination of the reaction, the borane catalyst was quenched with methanol.[10] The distillation provided 45.5 g (258 mmol, 86%) of 2-*n*-butyl-1,3,2-benzodioxaborole: bp 75° (2 mm); $n^{20}$D 1.4955 (lit.[11] bp 65–64° (0.04 mm), $n^{20}$D 1.4897).

The hydrolysis of 2-cyclohexyl-1,3,2-benzodioxaborole to give cyclohexaneboronic acid illustrates the general procedure. The cyclohexylborole (6.06 g, 30 mmol) was stirred rapidly with water (50 ml) at 25° for 1 hr. The white crystalline material formed was filtered and recrystallized from hot water, giving 3.4 g (90%) of cyclohexaneboronic acid, mp 112–114° (lit.[12] mp 116–117°).

The results on the transformation of several of the representative olefins into the corresponding 2-alkyl-1,3,2-benzodioxaboroles[13] by methods A and B are listed in Table I.

(2) H. C. Brown, A. Tsukamoto, and D. B. Bigley, *J. Amer. Chem. Soc.*, **82**, 4703 (1960).
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(4) G. Zweifel, *J. Organometal. Chem.*, **9**, 215 (1967).
(5) W. G. Woods and P. L. Strong, *J. Amer. Chem. Soc.*, **88**, 4667 (1966).
(6) For example, a mixture of cyclohexene, 4,4,6-trimethyl-1,3,2-dioxaborinane, and ethyl ether was heated in a sealed ampoule for 2 days at 110°, followed by 1 day at 210°, to give, after distillation, 57% of the desired product.[5]
(7) This compound has been previously obtained in 42% yield by treating 2-chloro-1,3,2-benzodioxaborole with tributyltin hydride: H. C. Newson and W. G. Woods, *Inorg. Chem.*, 7, 177 (1968).
(8) H. C. Brown and S. K. Gupta, *J. Amer. Chem. Soc.*, **92**, 6983 (1970).
(9) L. H. Thomas, *J. Chem. Soc.*, 820 (1946).
(10) A small quantity (*ca.* 0.5 g) of a white crystalline material, presumably unreacted *o*-phenylene borate, appeared at this stage in some reactions. This may be conveniently filtered off through a sintered-glass funnel prior to the distillation.
(11) J. P. Laurent, *C. R. Acad. Sci.*, **254**, 866 (1962).
(12) H. Hartmann and K. H. Birr, *Z. Anorg. Allg. Chem.*, **299**, 174 (1959).
(13) Satisfactory (within 0.3%) C and H analyses were obtained for all new compounds, which were also examined by nmr and mass spectrometry.

**Table I.** The Synthesis of 2-Alkyl-1,3,2-benzodioxaboroles (**2**) from Olefins *via* Hydroboration

| Alkyl substituent, R, in **2** | Method | Yield,[a] % | Bp, °C (mm) | $n^{20}$D | Mol wt[b] |
|---|---|---|---|---|---|
| 1-Decyl | A | (98)[c] | | | |
| 1-Pentyl | A[d] | 90 | 75 (0.5) | 1.4805 | 190 (58) |
| 2,4,4-Trimethyl-1-pentyl | A | 88 | 78 (0.25) | 1.4890 | 232 (100) |
| Cyclopentyl | A[d] | 90 | 72 (0.2) | 1.5260 | |
| Cyclohexyl | A | 95 | 80 (0.4) | 1.5250 | |
| *exo*-Norbornyl | A | 95 (98) | 104 (0.5) | 1.5405 | |
| 1-Butyl | B | 86 | 65 (0.5) | 1.4925 | 176 (38) |
| 2-Butyl | B | 94 | 48 (0.2) | 1.4975 | 176 (48) |
| Isobutyl | B | 90 | 56 (0.4) | 1.4930 | 176 (33) |
| Cyclopentyl | B | 80 | 72 (0.2) | 1.5260 | 188 (42) |
| Cyclohexyl | B | 88 | 88 (0.5) | 1.5255 | 202 (48) |
| *exo*-Norbornyl | B | 90 | 104 (0.5) | 1.5400 | 214 (100) |

[a] By isolation. The yields by glpc are given in parentheses. [b] By mass spectrometry; based on $^{11}$B. The intensity of the molecular ion ($M^+$) is given in parentheses. [c] Determined by the alkaline hydrogen peroxide oxidation of the product and the estimation of 1-decanol formed by glpc analysis. [d] Experiments were performed in a sealed ampoule at 100° for 2 hr.

The alkaneboronic esters and acids are becoming increasingly important synthetic intermediates.[14] We are currently exploring several other transformations of alkylboroles **2**, providing us with novel applications of alkaneboronic acids and esters in organic synthesis.

(14) D. S. Matteson, *Accounts Chem. Res.*, 3, 186 (1970).

(15) Postdoctorate research associate on a research grant (No. GM-10937) supported by the National Institutes of Health.

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## New Addition Compounds of Dialkylboranes and Aluminum Methoxide. New Practical Syntheses of Dialkylboranes and of Mixed Trialkylboranes Containing Functional Groups

*Sir:*

Aluminum methoxide forms reasonably stable addition compounds with dialkylboranes [$(CH_3O)_3Al\cdot 3R_2BH$]. These addition compounds permit the synthesis of mixed organoboranes containing functional substituents, the synthesis of pyridine–dialkylboranes, and the synthesis of the parent dialkylboranes themselves. Consequently, these new organoborane derivatives should be exceedingly valuable for many applications of the new organoborane chemistry to organic synthesis.

With the exception of certain relatively hindered and cyclic dialkylboranes such as dicyclohexylborane,[1] disiamylborane,[1] diisopinocampheylborane,[1] bisborinane,[2] and 9-borabicyclo[3.3.1]nonane,[3] dialkylboranes have proved to be relatively unstable toward disproportionation.[4] Consequently, they have been difficult to prepare and to utilize for the synthesis of mixed trialkylboranes. One solution to this problem has been the reduction of dialkylborinic esters by lithium aluminum hydride in the presence of olefins[5] (eq 1). The

$$3R_2BOCH_3 + LiAlH_4 + 3olefin \longrightarrow 3R_2BR' + LiAlH(OCH_3)_3 \quad (1)$$

success of this procedure presumably arises from the rapid capture of the dialkylborane intermediate before it can undergo disproportionation.[5]

We were examining the reduction of the methyl esters of dialkylborinic acids with aluminum hydride[6] when we discovered that the precipitate was not the simple aluminum methoxide we had anticipated (eq 2).

$$3R_2BOCH_3 + AlH_3 \longrightarrow 3R_2BH + Al(OCH_3)_3\downarrow \quad (2)$$

Instead, the precipitate contained all of the dialkylborane groups (eq 3). Nevertheless, this complex was

$$3R_2BOCH_3 + AlH_3 \longrightarrow [(CH_3O)_3Al\cdot 3R_2BH]\downarrow \quad (3)$$

an active hydroborating agent, reacting rapidly with an added olefin (eq 4). The purity of the mixed tri-

$$[(CH_3O)_3Al\cdot 3R_2BH] + 3olefin \longrightarrow 3R_2BR' + (CH_3O)_3Al\downarrow \quad (4)$$

alkylboranes thus prepared was determined by glpc analysis of the reaction mixtures, whenever possible, and also by the analysis of the boronates **1** produced *via* the carbonylation[7] reaction.

$$R_2BR' + CO + (CH_2OH)_2 \xrightarrow[3\ hr]{150^\circ} R_2C(R')-B(O-CH_2)(O-CH_2) \quad (5)$$

**1**

The results are summarized in Table I. The high purities of the mixed organoboranes indicate that the formation of the aluminum methoxide addition compounds must stabilize the dialkylboranes against disproportionation. Another major advantage of the

**Table I.** The Hydroboration of Simple and Functionally Substituted Olefins with Dialkylborane Derivatives. Synthesis of Mixed Trialkylboranes and Trialkylcarbinylboronates

| Dialkylmethoxyborane, $R_2BOCH_3$, R | Olefin hydroborated | Trialkylborane, $R_2BR'$ Method | Yield, %[a] | Boronate, **1**, $R_2R'CB(OCH_2)_2$ Yield, %[a] |
|---|---|---|---|---|
| 1-Butyl | 1-Pentene | A | 91 | 85 |
| 1-Butyl | 1-Pentene | B | 90 | |
| 1-Butyl | 11-Acetoxy-1-hendecene | B | 80 | 75[b] |
| Isobutyl | 1-Pentene | A | 95 | 88 |
| Isobutyl | 1-Pentene | B | 90 | |
| Isobutyl | 11-Chloro-1-hendecene | A | 78 | 60[b] |
| 2-Butyl | 1-Pentene | A | 88 | 85 |
| 2-Butyl | 1-Pentene | B | 90 | |
| Cyclopentyl | 11-Dodecene nitrile | A | 82 | 55[b,c] |

[a] By glpc analysis. [b] By isolation. [c] Bp 208–210° (0.3 mm); $n^{20}$D 1.4920; nmr ($CDCl_3$, TMS) δ 4.10 (s, 4), 2.3 (br t, 3), 2.05–1.1 ppm (br, 38).

(1) H. C. Brown and G. J. Klender, *Inorg. Chem.*, 1, 204 (1962).
(2) H. C. Brown and E. Negishi, *J. Organometal. Chem.*, 26, C67 (1971).
(3) E. F. Knights and H. C. Brown, *J. Amer. Chem. Soc.*, 90, 5280 (1968).
(4) G. E. Coates, M. L. H. Green, and K. Wade, "Organometallic Compounds," Vol. I, Methuen, London, 1968, p 232, and references cited there.
(5) H. C. Brown, E. Negishi, and S. K. Gupta, *J. Amer. Chem. Soc.*, 92, 6648 (1970).
(6) N. M. Yoon and H. C. Brown, *ibid.*, 90, 2927 (1968).
(7) H. C. Brown, *Accounts Chem. Res.*, 2, 65 (1969).