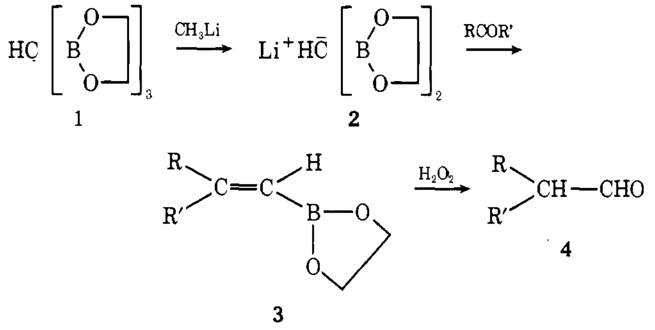
# The Reaction of Aldehydes and Ketones with a Boron-Substituted Carbanion, Bis(ethylenedioxyboryl)methide. A Simple Aldehyde Homologation

*Sir:*

Tris(ethylenedioxyboryl)methane (**1**) with methyllithium yields lithium bis(ethylenedioxyboryl)methide (**2**), which reacts with aldehydes or ketones to give high yields of alkeneboronic esters (**3**). Oxidation with buffered aqueous hydrogen peroxide[1] or alkaline sodium perborate results in a simple and efficient conversion of the carbonyl compound to the homologous aldehyde (**4**). An unexpected and potentially useful additional feature is that the alkeneboronic esters (**3**) derived from aldehydes (R′ = H) are 93-100% trans.



R = alkyl or aryl; R′ = H, alkyl, or aryl

Tris(ethylenedioxyboryl)methane (**1**) was prepared by mixing tetrahydrofuran solutions (1 ml/g) of tris(dimethoxyboryl)methane[2,3] and the theoretical amount of ethylene glycol, concentrating under vacuum, washing the solid residue with ether, and subliming at 150° (0.05 mm): 85%; mp 170-172°.[4] The lithium salt (**2**) was prepared by dropwise addition of 7.2 ml (11.5 mmol) of 1.6 *M* methyllithium in ether to a suspension of 2.60 g (11.5 mmol) of **1** in 20 ml of a 1:1 mixture of anhydrous tetrahydrofuran and dichloromethane stirred at −75° under argon during and for 2.5 hr after the addition. A 10-mmol portion of the aldehyde or ketone was added, the Dry Ice-acetone bath was removed, and stirring was continued 3 hr. The solvents were removed under vacuum at 25° (0.1 mm), leaving a residue of the boronic ester **3** and by-product lithium salt, postulated composition $(LiOBO_2C_2H_4)_x$.

We initially explored the preparation of boronic acids, $RR'C{=}CHB(OH)_2$, which were readily obtained by treating the crude residues of boronic esters (**3**) with dilute phosphoric acid and extracting with ether. Concentration of the ether solution generally yielded a residue of solid boronic acid which appeared fairly pure on NMR examination. Some of the results are included in Table I, and the scope and utility of boronic acid synthesis will be discussed briefly later in this communication.

Aldehydes (**4**) were prepared directly from the crude boronic esters (**3**) by the addition of 15 ml of saturated aqueous sodium bicarbonate at 0°, followed immediately by 3.3 ml of 30% hydrogen peroxide. The ice bath was removed, the solution was stirred 1-1.5 hr, 100 ml of ether was added together with a reference compound for GLC analysis, and the ether phase was separated and dried over 4 Å molecular sieves. The yield of aldehyde was determined by GLC and the retention time was compared with an authentic sample. High yields and only small amounts of unconverted starting material were generally obtained, as summarized in Table I.

Several modifications of this procedure were needed in order to obtain pure aldehydes by simple distillation. It turned out that hydrogen peroxide cleaves purified 2-phenylpropene-1-boronic acid to acetophenone as well as α-phenylpropionaldehyde, yielding up to ~40 mol % of the former in neutral media and 3-4 mol % at pH 14. Somewhat analogous cleavages have been observed by Pasto and coworkers.[5] Recalling Kuivila and Armour's kinetic study in which a term second-order in boronic acid and first-order in $OOH^-$ appeared in the rate law,[6] we tried sodium perborate and found that the amount of carbon-carbon bond cleavage was greatly decreased at any given pH, and fell below 1% at pH 14. (Sodium perborate is a convenient, inexpensive commercial reagent.)

Table I. Homologation of Carbonyl Compounds RCOR′ to Aldehydes RR′CHCHO or Boronic Acids $RR'C{=}CHB(OH)_2$

| | RR′CHCHO | RCOR′ % recovery | | $RR'C{=}CHB(OH)_2$ | |
|---|---|---|---|---|---|
| R–CO–R′ | % yield | | Method | % yield | Mp,[a] °C |
| $CH_3CH_2CH_2$–CO–H | 85 | 0 | GLC | 68 | 79–81[b] |
| $CH_3(CH_2)_4$–CO–H | | | | 81 | 88–90[b] |
| $CH_3(CH_2)_5$–CO–H | 87 | >1 | GLC | | |
| | 83 | 0 | Dist. | | |
| $CH_3(CH_2)_6$–CO–H | 94 | 7 | GLC | 82 | 67–68[b] |
| $CH_2{=}CH(CH_2)_2$–CO–H | 79 | 0 | GLC | | |
| $C_6H_5$–CO–H | 97[c] | 3 | GLC | 87 | 165–166[d] |
| | 77 | 0 | Dist | | |
| $CH_3$–CO–$CH_3$ | 63 | >1[e] | GLC | 65 | 81–82[f] |
| $C_2H_5$–CO–$C_2H_5$ | 74 | 0 | Dist | | |
| Cyclohexanone | 97 | 4 | GLC | 84 | 91–94 dec[b] |
| $(CH_3)_2C{=}CH$–CO–$CH_3$ | 81 | 0.7 | Dist[b] | | |
| $C_6H_5$–CO–$CH_3$ | 80 | 0 | Dist | 80 | 111–118[b,g] |
| $C_2H_5O_2CCH_2CH_2$–CO–$CH_3$ | 65 | 3 | Dist[b] | | |

[a] Recrystallized from ether. [b] Satisfactory elemental analysis.[4] [c] Borate buffer used; $NaHCO_3$ buffer gave 65%. [d] Lit. mp 168–169°.[2] [e] Determined by iodoform test on isolated sample, not separable on GLC column used. [f] Lit. mp 84–86°.[7] [g] Mixture of cis and trans isomers by NMR.

In a typical procedure, the crude boronic ester **3** derived from 23 mmol of **2** and 20 mmol of carbonyl compound was treated with 30 ml of 1 *M* aqueous sodium hydroxide, impurities were extracted with 25 ml of chloroform, and 30 ml of dichloromethane or chloroform was added followed by 3.39 g (22 mmol) of sodium perborate tetrahydrate in several portions while stirring in an ice bath. After stirring 10 min, the layers were separated, extraction with additional solvent was carried out, the extracts were dried over magnesium sulfate, and the aldehyde (**4**) was isolated by simple distillation at reduced pressure and its purity checked by NMR and GLC. Acetophenone, 3-pentanone, and 2-methyl-2-penten-4-one were homologated by this procedure. The α,β-unsaturated ketone gave the unconjugated aldehyde, 2,4-dimethyl-2-penten-5-al: NMR ($CDCl_3$) δ 1.14 (d, 3, $CHCH_3$), 1.68 (s, 3, $=CCH_3$), 1.76 (s, 3, $=CCH_3$), 3.26 (m, 1, $=CHCH(CH_3)CHO$), 4.93 (d, *J* = 9 Hz, of m's, *J* ~ 1 Hz, 1, $=CHCH$), 9.43 (d, *J* = 1.8 Hz, 1, $CHCHO$).[4] Other homologations required variations. Phenylacetaldehyde is degraded rapidly by aqueous base and β-styreneboronic acid is not cleaved to benzaldehyde in significant amounts, and therefore the pH was lowered to 7 with boric acid before adding sodium perborate. 1-Octeneboronic acid has an insoluble lithium salt, and the crude product **3** was treated with aqueous phosphoric acid and the boronic acid extracted into ether before proceeding. Oxidation was carried out at pH 11. Ethyl 4-ketopentanoate led to a boronic acid which was mostly lost in the aqueous base treatment, and this purification had to be omitted. Oxidation at pH 10-11 gave ethyl 4-formylpentanoate sometimes free of 4-ketopentanoate and sometimes not, generally containing some impurity but not enough to interfere with elemental analysis:[4] NMR ($\mathrm{CDCl_3}$) $\delta$ 1.11 and 1.25 (d, 3, $\mathrm{CHC}H_3$ and t, 3, $\mathrm{C}H_3\mathrm{CH_2}$), 1.6–2.2 (m, 3, $\mathrm{C}H\mathrm{C}H_2$), 2.35 (t, 2, $\mathrm{CH_2C}H_2\mathrm{CO}$), 4.10 (q, 2, $\mathrm{CH_3C}H_2\mathrm{O}$), 9.60 (d, $J \sim 1$ Hz, $\mathrm{C}H\mathrm{O}$). Yields are summarized in Table I.

Our yields of aldehydes are consistently better than those reported for two-step homologations using Wittig reagents, $\mathrm{ROCH{=}PPh_3}$; benzaldehyde to phenylacetaldehyde, 55%; 3-pentanone to 2-ethylbutanal 2,4-dinitrophenylhydrazone, 58%; cyclohexanone to cyclohexanecarboxaldehyde 2,4-DNP, 60%.[8] Strong acid hydrolysis of the enol ether intermediate[8] is a limitation. The specificity of $\mathrm{PhSCH{=}PPh_3}$ for aldehyde in the presence of unprotected hydroxyl is unique, but enethiol ether hydrolysis is not very efficient.[9] The classical Darzens glycidic ester route usually gives mediocre yields,[10] a notable exception being the 80% reported for homologation of $\beta$-ionone in the synthesis of vitamin A.[11] Our route suffers from the inconvenience of preparing tris(dimethoxyboryl)methane, but our current procedure is safe and reproducible.[3]

We have previously reported the condensation of various boron-substituted carbanions with aldehydes and ketones, have briefly explored compatibility with other functional groups, and have isolated a triborylmethide salt.[2,3,12–14] The present work is the first to provide yields consistently high enough for general synthetic use and offers several points of novelty in the preparation of alkeneboronic acids. The boronic esters (**3**) from aldehydes and **2** are 93–100% trans, providing an alternative to hydroboration for synthesizing these compounds, which are already known to be useful sources of cis 1-bromoalkenes,[15] trans 1-iodoalkenes,[16] and potentially, by way of B-alkylation and rearrangement with iodine and alkali, of cis alkenes.[17] Crude $\beta$-styreneboronic ester from benzaldehyde showed the NMR $\mathrm{BC}H\mathrm{{=}CH}$ doublet of the trans isomer, $\delta$ 6.0, and none of the cis, reported[18] $\delta$ 5.5. Crude *trans*-1-propeneboronic acid from acetaldehyde, probably the least stereoselective case, showed a $\mathrm{BCH{=}}$ doublet of quartets, $\delta$ 5.56, $J$ = 18 and 1.5 Hz, with 7% cis isomer, $\delta$ 5.50, $J$ = 14 and 1.5 Hz. Other aspects of the structure proof and potential utility of these compounds have recently been outlined elsewhere.[3]

The diborylmethide salt **2** shows the expected selectivity for aldehydes or ketones over unsaturated or carbethoxy functions (Table I). Unexpected selectivity with $p$-nitrobenzaldehyde led to a 34% yield of $p$-nitrostyreneboronic acid, mp 225°, fully characterized as the ethylene glycol ester, mp 175–176°.[4] Potentially more useful selectivity was achieved with 1,3-dichloroacetone, which yielded ~60% of crude 2-(chloromethyl)-3-chloropropene-1-boronic acid, $\mathrm{(ClCH_2)_2C{=}CHB(OH)_2}$, recrystallized from moist chloroform with considerable loss: mp 70–72.5°; NMR ($\mathrm{CDCl_3}$) $\delta$ 4.31 (s, 2, $\mathrm{C}H_2\mathrm{Cl}$), 4.59 (broadened s, 2, $\mathrm{C}H_2\mathrm{Cl}$), 5.76 (broadened s, 2, $\mathrm{{=}C}H$), with a broad $\mathrm{O}H$ band at $\delta$ 4–6.[4] Oxidation with hydrogen peroxide in dilute phosphoric acid, though sluggish and incomplete, netted ~30% overall of $\alpha$-(chloromethyl)acrolein: NMR ($\mathrm{CDCl_3}$) $\delta$ 4.26 (d, $J \sim 1$, 2 Hz, $\mathrm{C}H_2\mathrm{Cl}$), 6.29 (s, 1, $\mathrm{{=}C}H\mathrm{H}$), 6.65 (t, $J \sim 1$, 1 Hz, $\mathrm{{=}CH}H$), 9.63 (s, 1, $\mathrm{C}H\mathrm{O}$).

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## Aluminum Atom–Ethylene Molecular Complex. Matrix Isolation Electron Spin Resonance Study

*Sir:*

Direct addition reaction of aluminum atoms to olefin molecules to produce aluminum-alkyl bonds has been demonstrated by Skell and Wolf.[1] Organoaluminum compounds were produced when aluminum atoms were cocondensed with excess propene. Based upon the product analysis of the (deuterium oxide) hydrolysis of the resultant organoaluminum compounds, they concluded that the primary reaction between aluminum atoms and olefin is an addition of one aluminum atom to the double bond. The structural feature of this primary product was not elaborated. We report, in this communication, the electron spin resonance (ESR) spectra of Al atom-ethylene adduct generated within a rare-gas matrix at near liquid helium temperature. It is concluded that the Al atom-ethylene complex is formed through the dative bonds resulting from the interaction of the $\pi$ orbitals of the olefin and the valence orbitals of the Al atom.

The design of the liquid helium cryostat and an x-band ESR spectrometer assembly that would permit trapping of high temperature vapor phase species in a rare-gas matrix and observation by ESR of the resulting matrix has been described previously.[2] In the present experiment, Al atoms were vaporized from a resistively heated tantalum cell and trapped in a neon matrix together with ethylene molecules introduced through a separate gaseous sample inlet. The composition of the matrix was roughly 1000:10:1 for neon atoms, ethylene molecules, and Al atoms, respectively. The frequency of the spectrometer locked to the sample cavity was 9.420 GHz.

A neon matrix containing Al atoms ($3s^2\ 3p^1$) alone appeared white and showed no ESR spectrum. The absence of ESR signal attributable to Al atoms is ascribed to the extreme broadening caused by the degeneracy of the p orbitals.[3] When Al atoms were trapped together with ethylene, the matrix appeared green, and a strong ESR signal possessing a unique pattern appeared centered about the posi-