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A BROMOMETHANETRIBORONIC ESTER

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Summary

Tetrakis(dimethoxyboryl)methane, $C[B(OMe)_2]_4$, reacts with pinacol to form the corresponding pinacol boronic ester, $C(BO_2C_2Me_4)_4$, which on treatment with alkyllithium yields the corresponding triborylmethide anion, $^-C(BO_2C_2Me_4)_3$, which with bromine gives the bromomethanetriboronic ester, $BrC(BO_2C_2Me_4)_3$. Alkyllithium abstracts a boronic ester group from the bromomethanetriboronic ester to form the carbanion, $^-CBr(BO_2C_2Me_4)_2$, which has been brominated to yield the dibromomethanediboronic ester, $Br_2C(BO_2C_2Me_4)_2$, and has also been treated with triphenyltin chloride to form the tin derivative, $Ph_3SnCBr(BO_2C_2Me_4)_2$. Sodium acetate converts the dibromomethanediboronic ester to the diacetate, $(AcO)_2C(BO_2C_2Me_4)_2$, but the bromomethanetriboronic ester appeared to be inert toward nucleophilic displacement reactions. The bromomethanediboronic ester $BrCH(BO_2C_2Me_4)_2$ has also been made.

Introduction

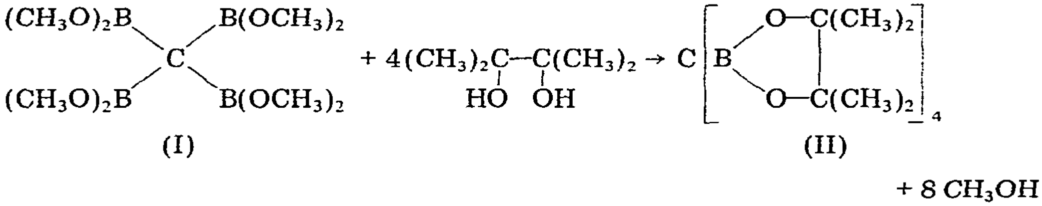
We undertook the synthesis of a halomethanetriboronic ester, $XC[B(OR)_2]_3$, in the hope that it might prove to be a useful synthetic intermediate, and that the adjacent halogen and boronic ester functions might show neighboring group effects. Our goal turned out to be stubbornly elusive, and some of our previous failures have been described [1,2]. For example, conversion of tetrakis(dimethoxyboryl)methane, $C[B(OMe)_2]_4$, (I), to the tris(dimethoxyboryl)methide ion, $^-C[B(OMe)_2]_3$, followed by bromination has consistently yielded only tar and not $BrC[B(OMe)_2]_3$ [1], and this failure was reconfirmed at the beginning of the present work. It was evident that the carbanion was reacting with bromine, and that the problem lay in the instability of the brominated product to the reaction conditions.

Five-membered cyclic boronic esters are more stable than their acyclic analogs in equilibria such as transesterification or hydrolysis, and they are also more easily crystallized. We expected that these properties would help with the isolation of a labile bromo compound. The ethylene glycol ester $C(BO_2C_2H_4)_4$ is too insoluble in organic solvents to be worked with easily [3], and we therefore decided to try the pinacol ester, tetrakis(tetramethylethylenedioxyboryl)methane (II). We had already synthesized an analogous pinacol ester, tris(tetramethylethylenedioxyboryl)methane, $HC(BO_2C_2Me_4)_3$ [1].

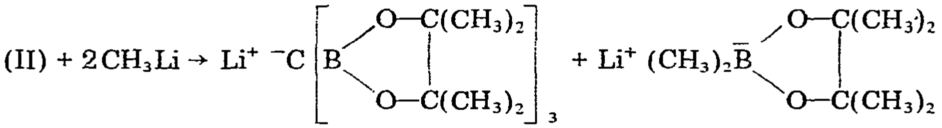
The nomenclature of cyclic boronic esters is discussed briefly in the next paper of this series [4].

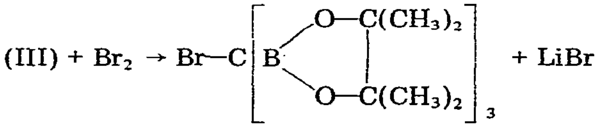
Results and discussion

The transesterification of $C[B(OMe)_2]_4$ (I) with pinacol to form the pinacol methanetetraboronic ester (II) was straightforward. The only problem was separation of the unreacted pinacol from the product, necessary because hydroxylic impurities are incompatible with carbanion formation. Fractional sublimation was effective but tedious, and recrystallization from hexane was found to be more convenient.


(I) (II)

The conversion of the tetraboronic ester (II) to the triborylmethide ion (III) followed by bromination did yield bromotris(tetramethylethylenedioxyboryl)methane (IV) as a crystalline solid which could be sublimed and recrystallized. However, there were number of complications in the synthetic procedure.


(III)


(IV)

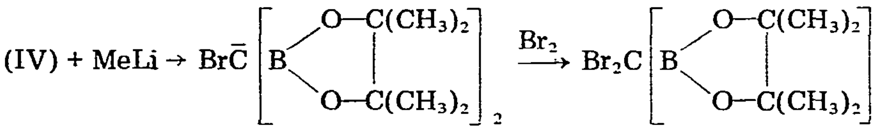
After a few exploratory experiments, the procedure adopted involved precipitation of the lithium salt of the triborylmethide ion (III) at −78°, warming to ensure completion of the reaction, removal of the solvent from the gummy precipitate by filtration under argon with the aid of a filter stick, and treatment of the residue of lithium salt (III) with a large excess of bromine in dichloromethane, preferably at −78°. When the initial precipitation was carried out in tetrahydrofuran or methylcyclohexane with one equivalent of butyllithium as the base, ultimate conversions to the bromo compound (IV) were 5% or less. When the initial solvent was dichloromethane and the base methyllithium, the conversion rose to 17%, the yield to 35% when the recovered methanetetraboronic ester (II) was taken into account. Diethyl ether gave a 27% conversion, 55% yield. The unconverted (II) was only partially removed during the filtration step, and its separation from the product (IV) by fractional crystallization from dichloromethane at —78° was a considerable nuisance.

Since it became apparent that not all of the tetraboronic ester (II) was being converted to the carbanion (III), we tried increasing the amount of methyllithium to two equivalents. The conversion to the bromo compound (IV) rose to 55%, and no unconverted (II) was recovered.

In more recent work, we have found that the lithium salt (III) appears to have some solubility in ether, and the filtration step is not necessary or desirable. Butyllithium gives the same results as methyllithium and is more convenient to use. A slight excess of bromine is sufficient and preferable. By carrying out the bromination in the ether solvent used to precipitate the anion (III), we have obtained yields of 82-90% of the bromo compound (IV). However, the crude material so obtained contains not only some unchanged starting material (II) but also some dibromo compound (V), as if some disproportionation occurs in the basic reaction medium.

We have been writing the triborylmethide anion (III) as a free species, not a complex with boronic ester. Evidence in favor of this formulation has been reported for the analogous tris(trimethylenedioxyboryl)methide ion, $^{-}C(BO_2C_3H_6)_3$ [5]. Also, the apparent stoichiometry from the synthetic results in the present work certainly favors formulation of (III) as a free carbanion, though the evidence is not conclusive by itself.

The preparation of dibromobis(tetramethylethylenedioxyboryl)methane (V) from the monobromo compound (IV) required only a repetition of the bromination sequence.



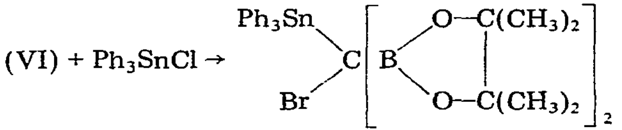
(VI) (V)

Only one equivalent of alkyllithium was used at first in preparing the bromobis(tetramethylethylenedioxyboryl)methide ion (VI). However, the conversion of the monobromo compound (IV) to the dibromo compound (V) is incomplete under these conditions. The presence of residual (IV) was revealed by the NMR spectrum and by low bromine analyses, and its removal by recrystallization was difficult. The mass spectrum leaves no doubt regarding the identity of (V). The use of two equivalents of alkyllithium to prepare (V) decreases the amount of (IV) remaining in the product, which can then be purified by recrystallization.

We had not necessarily expected that reaction of the monobromo compound (IV) with methyllithium would yield the carbanion (VI). If (IV) had shown the reactivity pattern characteristic of other α-haloalkaneboronic esters on alkylation of the boron with Grignard reagents [6], the bromine atom would have been replaced by a methyl group as the result of an intramolecular migration from boron to carbon, which would yield $CH_3C(BO_2C_2Me_4)_3$. The bromo triboronic ester (IV) is sterically hindered, which would tend to retard any sort of intramolecular displacement, and the alternative of forming a boron-stabilized carbanion is readily available.

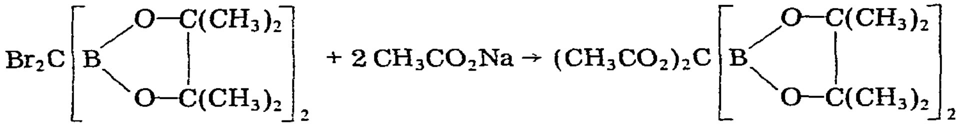
One might also speculate that the bromo anion (VI) could perhaps lose bromide ion to form a diborylcarbene, $C(BO_2C_2Me_4)_2$, but we have not seen any evidence of such behavior. Boronic ester groups are probably not particularly effective for stabilizing carbenes, and a diborylcarbene would probably have a triplet ground state.

The only other reaction we have run with the carbanion (VI) is that with triphenyltin chloride to form the tin derivative (VII).


(VII)

Another subsequently prepared compound of this type, $Ph_3SnCl(BO_2C_3H_6)_2$, has been more fully characterized and reported elsewhere [3]. Both of these tin compounds appear to be stable at 200° and beyond.

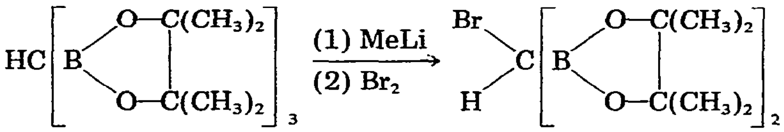
The dibromo compound (V) was found to react with a suspension of sodium acetate in methylene chloride to produce the diacetoxy compound (VIII).


(V) (VIII)

The monobromo compound (IV) failed to react with sodium acetate in 24 hours in refluxing methylene chloride, and also failed to react in tetrahydrofuran, dimethylformamide, and dimethoxyethane. It may be concluded that the dibromo (V) is less hindered sterically than the monobromo compound (IV).

Before we had succeeded in preparing the monobromo compound (IV) in good yields by the route from the methanetetraboronic ester (II), we investigated the possible free radical bromination of tris(tetramethylethylenedioxyboryl)methane, $HC(BO_2C_2Me_4)_3$, with *N*-bromosuccinimide. Mass spectral evidence suggested that a small amount of (IV) was formed after 48 hours reflux in carbon tetrachloride, but there was not enough to isolate. A previous failure to chlorinate $HC(BO_2C_2Me_4)_3$ with tert-butyl hypochlorite has been reported [1].

Reaction of the methanetriboronic ester $HC(BO_2C_2Me_4)_3$ with methyllithium and then bromine yielded the expected bromobis(tetramethylethylenedioxyboryl)methane (IX). It appeared that (IX) was reactive toward sodium acetate, but the oily product was not fully characterized.



(IX)

Experimental

Tetrakis(tetramethylethylenedioxyboryl)methane (II)

A solution of 19.6 g (0.065 mole) of tetrakis(dimethoxyboryl)methane (I) and 30.5 g (0.260 mole) of anhydrous pinacol in 60 ml of tetrahydrofuran was stirred under argon overnight at 25°. The solvent was removed under vacuum and the residue was sublimed at 60°/0.1 mm Hg. This crude product (II) (31 g) still contained pinacol, which was removed by recrystallization from a minimum amount of hot hexane, preferably with slow cooling and seeding of the solution. The yield of pinacol ester (II) was 23.3 g (70%), m.p. 182—183°. NMR (CCl_4): δ 1.15 ppm (with internal TMS). Mass spectrum: maximum *m/e* 520 $[C_{25}H_{48}{}^{11}B_4O_8]^+$; strongest peak *m/e* 504 $[C_{25}H_{45}{}^{10}B{}^{11}B_3O_8]^+$. (Found: C, 57.66; H, 9.16; B, 8.53. $C_{25}H_{48}B_4O_8$ calcd.: C, 57.76; H, 9.27; B, 8.32%.)*

Bromotris(tetramethylethylenedioxyboryl)methane (IV)

A 4.0 g (7.7 mmole) portion of tetrakis(tetramethylethylenedioxyboryl)-methane (II) was placed in a 3-neck flask equipped with a Teflon paddle stirrer, rubber septum-equipped dropping funnel, and argon supply. From a syringe, 80 ml of anhydrous ether was added, and the solution was cooled with a dry ice/acetone bath. 10 ml (16 mmoles) of 1.6 *M* methyllithium in ether (or butyllithium in hexane) was added dropwise to the stirred solution over a period of 15 min. A considerable amount of white solid was precipitated. Stirring was continued 15 min at —78°, and the mixture was warmed briefly to 0° and cooled again. The mixture was stirred at —78° while 1 ml (18.3 mmoles) of bromine in 10 ml of methylene chloride was added dropwise in 30 min. After an additional 1 h of stirring at —78°, the mixture was warmed to 25°, the solvents and excess bromine were removed under vacuum, and the yellow solid residue was transferred under argon to a sublimation apparatus and sublimed at 160°/0.1 mm Hg, yield of (IV) 3.0—3.3 g (82—90%), recrystallized from methylcyclohexane, m.p. 201—202°. NMR (CCl_4): δ 1.22 ppm (with internal TMS). Mass spectrum: *m/e* 472 and 474 $[C_{19}H_{36}{}^{11}B_3O_6{}^{79-81}Br]^+$; 459, with 472 peak strongest in some spectra, 459 in others. (Found: C, 48.40; H, 7.64; B, 7.07; Br, 16.58. $C_{19}H_{36}B_3O_6Br$ calcd.: C, 48.26; H, 7.68; B, 6.88; Br, 16.90%.)

Dibromobis(tetramethylethylenedioxboryl)methane (V)

The procedure followed was similar to that used for the preparation of (IV). A 1.00 g (2.2 mmole) portion of bromotris(tetramethylethylenedioxyboryl)-methane (IV) in 20 ml of ether was stirred at —78° while 2.9 ml (4.6 mmoles) of

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* We thank M.S. Biernbaum for discovering that recrystallization from hexane removes the pinacol impurity much more easily than the tedious fractional sublimation previously used, and we thank P.B. Tripathy, T.H. Paine, and P.K. Mattschei for analytical samples.

bromine in 5 ml of methylene chloride was added dropwise in 30 min. After further stirring and warming to 25°, the solvent was removed under vacuum and the solid was sublimed at 130—160°/0.1 mmHg, yield of (V), 0.58 g (62%), recrystallized twice from methylcyclohexane, m.p. 154°. NMR (CCl_4) : δ 1.28 ppm (with internal TMS). Mass spectrum *m/e* 426 $[C_{13}H_{24}{}^{11}B_2{}^{79}Br^{81}BrO_4]^+$ with isotopic satellites; strongest peak *m/e* 411. (Found: C, 36.86; H, 5.72; B, 5.11; Br, 37.41. $C_{13}H_{24}B_2Br_2O_4$ calcd.: C, 36.67; H, 5.68; B, 5.08; Br, 37.54%.)

Bromo(triphenylstannyl)bis(tetramethylethylenedioxyboryl)methane (VII)

A solution of 1.0 g of bromotris(tetramethylethylenedioxyboryl)methane (IV) in 15 ml of methylene chloride was stirred at —75° under argon and 1.3 ml of 1.6 *M* methyllithium was added dropwise in 30 min. After stirring an additional 30 min, 0.82 g of triphenyltin chloride was added, the mixture was allowed to warm to 25°, and stirring was continued 4 h. The solvent was evaporated under vacuum, the residue was recrystallized from methanol, and the bromo tin compound (VII) was sublimed at 160°/0.1 mmHg, 0.1 g (68%); m.p. 149—151°. NMR (CCl_4) δ 1.02 (s, 24, C—CH_3), 7.3—7.8 ppm (m, 15, C_6H_5). (Found: C, 53.16; H, 5.73; B, 3.02; Br, 10.76. $C_{31}H_{39}B_2BrO_4Sn$ calcd.: C, 53.5; H, 5.61; B, 3.16; Br, 11.5%.)

Diacetoxybis(tetramethylethylenedioxyboryl)methane (VIII)

A solution of 3.0 g of dibromobis(tetramethylethylenedioxyboryl)methane (V) (which was probably an impure sample containing a considerable amout of (IV)) in 50 ml of methylene chloride was stirred with 0.52 g of anhydrous sodium acetate at 25° under argon 4 h. Distillation, recrystallization of the distilled solid from methylcyclohexane, and sublimation at 160°/0.1 mmHg yielded 0.7 g (24%) of the diacetoxy compound (VIII); m.p. 195—196°. NMR (CCl_4) δ 1.19 (s, 24, C—CH_3), 2.12 ppm (s, 6, $COCH_3$). Mass spectrum *m/e* 384, 369, and isotopic satellites; IR (CCl_4) C=O at 1745 cm^{-1}. (Found: C, 52.98; H, 8.01; B, 5.76. $C_{17}H_{30}B_2O_8$ calcd.: C, 53.2; H, 7.8; B, 5.6%.)

Bromobis(tetramethylethylenedioxyboryl)methane (IX)

A solution of 5.0 g of tris(tetramethylethylenedioxyboryl)methane, $HC(BO_2C_2Me_4)_3$ [1], in 50 ml of methylene chloride was stirred under argon at —75° while 7 ml of 1.6 *M* methyllithium in ether was added dropwise in 10 min. The mixture was stirred 30 min at —75°, 5 ml of bromine in 15 ml of methylene chloride was added over a period of 2 min, and the solution was warmed to 25° and stirred 4 h. Concentration and sublimation in a distillation apparatus under vacuum yielded a solid (IX), which was recrystallized from methylcyclohexane and resublimed at 160°/0.1 mmHg, yield 1.0 g (23%); m.p. 153°. NMR (CCl_4) δ (ext. ref.) 0.28 (s, 1, B_2BrCH) and 1.28 ppm (s, 24, C—CH_3). Mass spectrum *m/e* 348 ($C_{13}H_{25}{}^{11}B_2{}^{81}BrO_4$), 333, with usual isotopic satellites. (Found: C, 45.16; H, 7.23; B, 6.31; Br, 19.55. $C_{13}H_{25}B_2BrO_4$ calcd.: C, 45.0; H, 7.23; B, 6.23; Br, 23.0%.)

Acknowledgements

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