

## PRELIMINARY NOTES

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### Dibutyl iodomethaneboronate

We have been searching for a practical route to a halomethaneboronic ester. Previously, frustratingly small yields of chloromethaneboronic ester were obtained from di-*t*-butyl methaneboronate and *t*-butyl hypochlorite<sup>1</sup>.

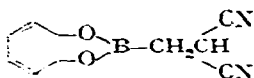
We have now obtained useful quantities of dibutyl iodomethaneboronate,  $(C_4H_9O)_2BCH_2I$ , by starting from boron tribromide and iodomethylmercuric iodide,  $ICH_2HgI$ . Although displacement of mercury(II) by boron halides is well-known in the aromatic and vinyl series<sup>2</sup>, this appears to be the first extension to a saturated system. Dibutyl iodomethaneboronate yields substituted methaneboronic esters when the iodide is displaced by a variety of nucleophiles, including amines and malononitrile anion. Previous attempts to alkylate nitrogen or carbon with  $\alpha$ -haloalkaneboronic esters have failed<sup>3-5</sup>, although chloromethyldimethylborane alkylates azide ion<sup>6</sup>. Thus, dibutyl iodomethaneboronate opens new possibilities in our search for an effective compound for the <sup>10</sup>B neutron capture therapy of brain tumors<sup>3,3,7</sup> and our studies of neighboring group effects of boron<sup>3-5</sup>.

Iodomethylmercuric iodide<sup>8</sup> was recrystallized from methylene iodide, collected by suction filtration, and used without further drying. The methylene iodide content was about 15-20%, and its presence appeared to accelerate the reaction. The iodomethylmercuric iodide (100 g), sodium iodide (53 g), and boron tribromide (250 ml) were stirred\* vigorously at room temperature (22°) under argon for 24 h. All liquid volatile up to ~130° (0.5 mm) was distilled under vacuum into a receiver cooled with dry ice and methylene chloride (chosen for safety with boron tribromide). Most of the boron tribromide, suitable for recycling, was recovered by fractionation at atmospheric pressure, with care not to overheat the residue of halomethylboron dibromides. These were distilled under vacuum, diluted with toluene, and esterified with butanol at -70°. Dibutyl bromomethaneboronate (Br-CH<sub>2</sub>-B peak in the NMR at  $\tau$  7.6) constituted a variable proportion of the products. It boiled too close to the by-product, butyl borate, to be isolable and was converted to the iodo compound by sodium iodide in butanol-acetone. Fractionation in a spinning-band column yielded 22-26 g (35-40%) of dibutyl iodomethaneboronate, b.p. 60° (0.1 mm), I-CH<sub>2</sub>-B singlet in the NMR at  $\tau$  7.95. (Found: C, 36.58; H, 6.76; B, 3.71; I, 42.86. C<sub>9</sub>H<sub>20</sub>BIO<sub>2</sub> calcd.: C, 36.30; H, 6.72; B, 3.63; I, 42.61%.)

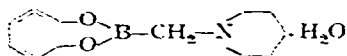
The alkylation of malononitrile was accomplished by the addition of 0.79 g of potassium *t*-butoxide in 15 ml of *t*-butyl alcohol over a period of 30 min to 0.5 g of malononitrile and 2.10 g of dibutyl iodomethaneboronate in 15 ml of *t*-butyl alcohol. Addition of 2 ml of *n*-butyl alcohol followed by distillation yielded 1.56 g (94%) of dibutyl 2,2-dicyanoethaneboronate, b.p. 105-115° (0.05 mm), not yet fully characterized. Treatment with an equimolar amount of catechol followed by sublimation and

\* The Trubore glass stirrer shaft was lubricated with equal parts of Kel-F 90 chlorofluorocarbon grease and perchlorobutadiene, mixed hot.

recrystallization from toluene-methylcyclohexane yielded catechyl 2,2-dicyanoethaneboronate, m.p. 119–122°, weak  $C\equiv N$  band in the infrared at  $4.42\ \mu$ ,  $CH_2$  doublet in the NMR at  $\tau\ 7.82$ , CH triplet at  $\tau\ 5.89$ , splitting 7.5 cps (in  $CDCl_3$ ). (Found: C, 60.51; H, 3.61; B, 5.26; N, 14.36.  $C_{10}H_7BN_2O_2$  calcd.: C, 60.63; H, 3.56; B, 5.46; N, 14.20%.)



Addition of 3 g of dibutyl iodomethaneboronate to 10 ml of piperidine in 20 ml of butanol followed by filtration of the piperidine hydriodide and concentration of the filtrate yielded amorphous piperidinomethaneboronic acid. The catechol ester crystallized from acetonitrile-water as the monohydrate, m.p.  $> 250^\circ$ ,  $N-CH_2-B$  singlet in the NMR at  $\tau\ 8.0$  (in  $CD_3SOCD_3$ ). (Found: C, 61.36; H, 7.53; N, 5.76; B, 4.48.  $C_{12}H_{15}BNO_3$  calcd.: C, 61.05; H, 7.72; N, 5.96; B, 4.60%.) Work on other aminomethaneboronic acids is in progress.



Hydroxymethaneboronic acid,  $HOCH_2B(OH)_2$ , was obtained by treatment of dibutyl iodomethaneboronate with water and anion exchange resin in the bicarbonate form. The dimeric cyclic ester<sup>5</sup>,  $[-B(OH)CH_2O-]_2$ , crystallized from acetone-water, m.p. 147–148°,  $O-CH_2-B$  peak in the NMR at  $\tau\ 6.4$  (in  $D_2O$ ). (Found: C, 20.86; H, 5.29; B, 18.93.  $C_2H_6B_2O_4$  calcd.: C, 20.87; H, 5.23; B, 18.70.) Other substituted methaneboronic acids having known higher homologs<sup>5</sup> will be reported later.

We have also prepared methanediboronic acid,  $(HO)_2BCH_2B(OH)_2$ . Stirring 30 g of methylenebis(mercuric iodide)<sup>8</sup> with 15 ml of boron tribromide for 20 h yielded 8.9 g of methylenediboron tetrabromide,  $CH_2(BBr_2)_2$ , b.p.  $44^\circ/0.7\ mm$ . Treatment with ethanol at  $-70^\circ$ , then water, yielded methanediboronic acid, recrystallized from acetone-water, m.p. 155–155.5°. (Found: C, 11.15; H, 5.87; B, 20.41.  $CH_6B_2O_4$  calcd.: C, 11.59; H, 5.83; B, 20.87.)

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