

PREPARATION OF HALOMETHANEBORONATES

PETER G.M. WUTS * and PAUL A. THOMPSON

Department of Chemistry, The University of Michigan, Ann Arbor, Michigan 48109 (U.S.A.)

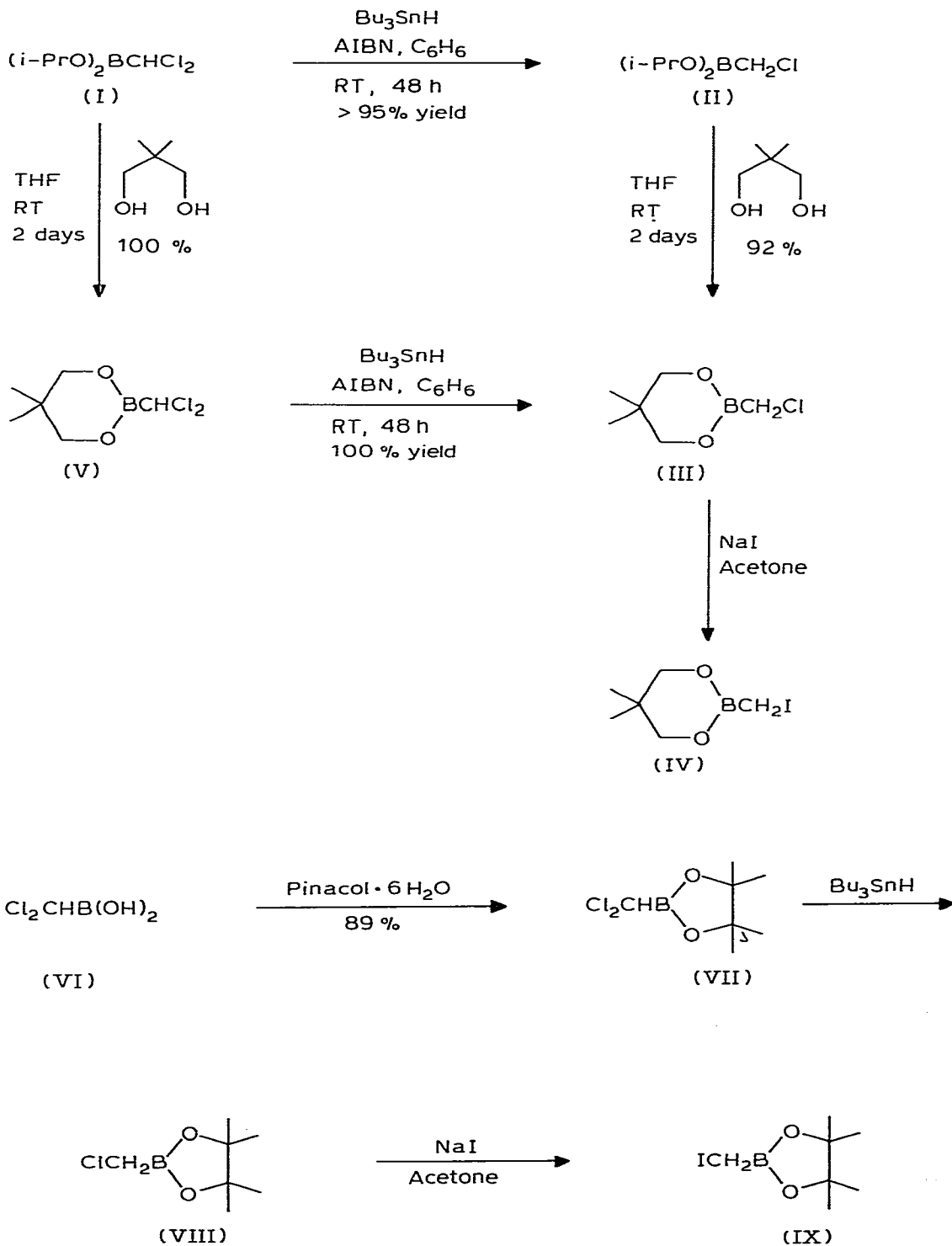
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Summary

A facile preparation of iodomethaneboronic esters is described. The key step utilizes a tin hydride reduction of dichloromethaneboronic esters.

The facility with which α -haloboron compounds undergo substitution with a variety of nucleophiles augurs favorably for their use as potential intermediates in a wide variety of useful synthetic transformations. For example, they have been used to alkylate enamines [1], enolates [2], malonates [1], lithium amides [6], mercaptans [1,2,5], alkyllithiums and Grignard reagents [2,3,4,9]. As an approach to the synthesis of a variety of γ -substituted allylboronates [7], we required a simple and direct source of iodomethaneboronates. Matteson has reported two procedures for iodomethaneboronate preparation but these are encumbered with a number of disadvantages especially when large quantities of material are required [1,8].

We now wish to report a facile and direct synthesis of iodo- and chloromethaneboronates from readily available starting materials. Our approach takes advantage of Rathke's procedure for the preparation of diisopropyl dichloromethaneboronate (I) [9]. Reduction of the dichloride should then provide a useful entry into the chloromethaneboronate esters. Rathke had previously attempted the reduction with sodium hydride in a variety of solvents but found the dichloride inert to sodium hydride. The general ability of tributyltin hydride to selectively reduce geminal dihalides to monohalides [10] led us to believe that the dichloride I should also undergo selective reduction. Indeed, stirring an equimolar amount of tributyltin hydride and dichloride I in benzene with a catalytic amount of AIBN gave after 24 h quantitative conversion to chloromethaneboronate (II). Distillation to remove tributyltin chloride afforded pure monochloride II in quantitative yield. Transesterification with 2,2-dimethylpropane-1,3-diol afforded chloride III in 92% yield. Finkelstein reaction on the chloride provides an 81% yield of iodide (IV). Alternatively, diisopropyl dichloromethaneboronate (I) could first be transesterified to



ester V and then reduced to chloride III. A similar set of transformations was used to prepare the pinacolyl ester IX with equal efficiency except that the pinacolyl ester VII was prepared directly in 89% yield from boronic acid VI. Reduction to the monochloride VIII and iodide substitution gave ester IX. For most purposes, it should not be necessary to carry out the final Finkelstein reaction since the chloride should behave like the iodide except that its reactivity may be somewhat reduced.

In conclusion we have developed a simple and straightforward procedure for the preparation of monohalomethaneboronates on a molar scale. The now ready availability of these reagents should expand the scope of their use in a variety of transformations.

Experimental

Tetrahydrofuran and diethyl ether were distilled from Na and benzophenone under an argon atmosphere. Benzene was distilled from CaH₂ under an argon atmosphere. Acetone was stirred over anhydrous K₂CO₃, anhydrous, and freshly distilled prior to use. Solutions of t-butyllithium (1.9 M in pentane) were obtained from Alfa or Aldrich Chemical Co. All reactions were carried out under an atmosphere of argon in a flamedried apparatus. Proton NMR spectra were taken on a Varian T-60A or Brüker 360 MHz spectrometer using TMS as an internal standard. Carbon-13 NMR were obtained using a JEOL FX-90Q spectrometer, using TMS of CDCl₃ as internal standard. Elemental analyses were performed by Spang Microanalytical Laboratories, Eagle Harbor, Michigan. Infrared spectra were obtained on a Beckman IR 4240 or Perkin-Elmer 727B spectrometer using NaCl windows. Boiling points are uncorrected.

Preparation of diisopropyl chloromethaneboronate (II)

Tri-n-butyltin hydride (3.93 g, 13.5 mmol) was added to diisopropyl dichloromethaneboronate (2.88 g, 13.5 mmol) dissolved in 20 ml of dry benzene. A catalytic amount (20 mg) of 2,2'-azobis-(2-methylpropionitrile) was introduced and the resulting solution stirred for 24 h at room temperature. Fractional distillation gave 2.4 g (quantitative yield) of the α -chloromethaneboronate as a colorless liquid, b.p. 53–56°C/0.8 mmHg, proton NMR (CDCl₃): septet, δ 4.40 (2H); singlet, δ 2.84 (1H); doublet, δ 1.2 (12H). IR (neat): 7.13, 7.25, 7.54, 8.36, 8.52, 8.91, 10.55, 13.58 μ . ¹³C NMR (CDCl₃): 66.30 ppm (d); 24.53 ppm (q), (downfield from TMS). Found: C, 47.20; H, 8.95; Cl, 19.94; C₇H₁₆O₂BCl calcd.: C, 47.11; H, 9.04; Cl, 19.86%.

Preparation of 5,5-dimethyl-2-chloromethyl-2-bora-1,3-dioxacyclohexane (III) from diisopropyl ester (IV)

2,2-Dimethyl-1,3-propanediol (0.44 g, 4.2 mmol) was added to diisopropyl chloromethaneboronate (0.75 g, 4.2 mmol) dissolved in 25 ml of dry THF. The solution was stirred for 3 days at room temperature. Fractional distillation gave 0.63 g (92%) of the chloromethaneboronate as a colorless liquid, b.p. 82–87°C/5 mmHg, identical with the product obtained by the alternative route.

Preparation of 5,5-dimethyl-2-chloromethyl-2-bora-1,3-dioxacyclohexane (III) from ester (V)

Tri-*n*-butyltin hydride (21.64 g, 74.7 mmol) was added to 5,5-dimethyl-2-dichloromethane-2-bora-1,3-dioxacyclohexane (14.64 g, 74.7 mmol) dissolved in 250 ml of dry benzene. A catalytic amount (100 mg) of 2,2'-azobis-(2-methylpropionitrile) was introduced and the resulting solution stirred for 24 h at room temperature. Fractional distillation gave 11.8 g (98%) of the chloromethaneboronate III as a colorless liquid, b.p. 89–90°C/10 mmHg, proton NMR (CDCl₃): singlet, δ 3.62 (4H); singlet, δ 2.85 (2H); singlet, δ 0.97 (6H). ¹³C NMR (CDCl₃): 71.96 ppm (t); 21.26 ppm (q). IR (neat): 6.76, 6.98, 7.27, 7.46, 7.62, 7.91, 8.51, 9.32, 9.91, 12.27 μ . Found: C, 44.51; H, 7.57; Cl, 21.05. C₆H₁₂O₂BCl calcd.: C, 44.37; H, 7.45; Cl, 21.18%.

Preparation of 5,5-dimethyl-2-iodomethyl-2-bora-1,3-dioxacyclohexane (IV)

Sodium iodide (16.2 g, 108.2 mmol) was added to 5,5-dimethyl-2-chloromethyl-2-bora-1,3-dioxacyclohexane (11.7 g, 72.1 mmol) dissolved in 150 ml of dry acetone. The mixture was refluxed for 48 h. All volatile materials were distilled (Kugelrohr) to remove insoluble salts. Fractional distillation of the resulting yellow mixture gave 14.9 g (81%) of the iodomethaneboronate IV as a colorless liquid, b.p. 40–43°C/0.2 mmHg, which was stored over Cu wire. Proton NMR (CDCl₃): singlet, δ 3.61 (4H); singlet, δ 2.08 (2H); singlet, δ 0.99 (6H). ¹³C NMR (CDCl₃): 71.92 ppm (t); 21.43 ppm (q). IR (neat): 6.78, 7.01, 7.13, 7.61, 7.80, 7.94, 9.00, 9.93, 12.28 μ . Found: C, 28.44; H, 4.68; I, 49.90. C₆H₁₂O₂BI calcd.: C, 28.39; H, 4.76; I, 49.99%.

Preparation of 5,5-dimethyl-2-dichloromethyl-2-bora-1,3-dioxacyclohexane (V)

2,2-Dimethyl-1,3-propanediol (41.08 g, 0.395 mol) was added to diisopropyl dichloromethaneboronate (84 g, 0.395 mol) dissolved in 500 ml of dry tetrahydrofuran. Stirring for 3 days at room temperature followed by fractional distillation gave 74.6 g (96%) of the 2,2-dimethyl-1,3-propanediol ester as a colorless liquid, b.p. 89–91°C/5 mmHg, proton NMR (CDCl₃): singlet, δ 5.19 (1H); singlet, δ 3.71 (4H); singlet, δ 1.02 (6H). IR (neat): 6.62, 6.71, 6.92, 7.22, 7.43, 7.60, 7.84, 8.61, 9.27, 9.84, 13.62 μ . Found: C, 36.72; H, 5.71; Cl, 35.95. C₆H₁₁O₂BCl₂ calcd.: C, 36.60; H, 5.63; Cl, 36.02%.

Preparation of 4,4,5,5-tetramethyl-2-dichloromethyl-2-bora-1,3-cyclopentane (VII) from dichloromethane

By use of 63.7 g (0.75 mol) of dichloromethane, 437.5 ml (0.7 mol) of *n*-butyllithium (1.6 M in hexane), and 78.7 g (0.75 mol) of trimethylborate, the dichloromethaneboronic acid was prepared by Rathke's method. The crude material obtained following workup and solvent removal (in vacuo) was taken up in 1500 ml of benzene along with 170 g (0.75 mol) of pinacol · 6H₂O. The biphasic mixture was then heated to reflux under an argon atmosphere, utilizing a Dean-Spark trap to remove water as an azeotrope. After 72 h at reflux, the homogeneous yellow solution was cooled to room temperature and then fractionally distilled (all under inert atmosphere) to yield 140.6 g (89%) of the desired dichloromethaneboronate, b.p. 103°C/20 mmHg. NMR (CDCl₃): singlet, δ 5.36 (1H); singlet, δ 1.36 (12H). IR (neat): 3.36, 3.41, 6.77, 6.82, 7.11,

7.25, 7.33, 7.38, 7.87, 8.25, 8.58, 8.79, 9.01, 10.32, 11.13, 11.82, 13.55, 15.47 μ . Found: C, 39.93; H, 6.24; Cl, 33.67. $C_7H_{13}O_2BCl_2$ calcd.: C, 39.87; H, 6.21; Cl, 33.62%.

Preparation of 4,4,5,5-tetramethyl-2-chloromethyl-2-bora-1,3-dioxacyclopentane (VIII)

The procedure for the preparation of ester III from ester V was followed. Distillation gave the monochloride in 90% yield, b.p. 81°C/14 mmHg. NMR: singlet: δ 2.77 (2H); singlet, δ 1.22 (12H). IR (neat): 3.35, 3.41, 6.78, 7.04, 7.16, 7.21, 7.26, 7.35, 7.80, 8.19, 8.37, 8.50, 8.70, 8.97, 10.25, 11.17, 11.65, 13.60, 14.75 μ . Found: C, 47.44; H, 7.89; Cl, 19.96. $C_7H_{14}O_2BCl$ calcd.: C, 47.65; H, 8.00; Cl, 20.09%.

Preparation of 4,4,5,5-tetramethyl-2-iodomethyl-2-bora-1,3-dioxacyclopentane (IX) from ester (VIII)

The procedure for the preparation of iodide IV was followed. Distillation gave iodide IX in quantitative yield, by 71°C/15 mmHg. NMR: singlet, δ 2.12 (2H); singlet, δ 1.23 (12H). IR (neat): 3.38, 3.40, 3.46, 6.75, 7.01, 7.12, 7.28, 7.59, 7.76, 7.94, 8.25, 9.05, 9.38, 9.92, 10.25, 12.30 μ . Found: C, 31.47; H, 5.32; I, 47.25. $C_7H_4O_2BI$ calcd.: C, 31.3837; H, 5.2674; I, 47.3694%.

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