Tetrahedron Vol. 49, No. 1, pp. 177-186, 1993
Printed in Great Britain

0040-4020/93 $5 00+.00

β-Boronate Carbonyl Derivatives: Synthesis and Evidence for the Intervention of Boronate "Ate"-Complexes in Enolate Alkylations.

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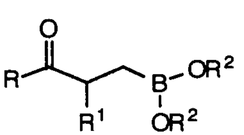
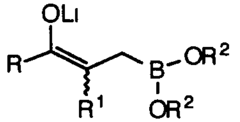
(*Received in UK* 7 *September* 1992)

Abstract: Halomethylboronate derivatives form "ate"-complexes with lithium ester enolates, which are relatively stable at room temperature and can be observed by ^{11}B n.m.r Reaction of an iodomethylboronate derivative with either an ester, ketone or amide enolate provides the corresponding β-boronate carbonyl derivatives in 43-83% yield

The ability to control the geometry of an enolate has a considerable effect upon the degree of stereocontrol that is possible in subsequent alkylation reactions of the enolates[1] As part of a programme aimed at developing new methods for controlling the stereoselectivity of enolate alkylation reactions[2,3], we envisaged that enolisation of β-boronate carbonyl derivatives of type **1** would provide a new method for controlling the geometry of simple enolates, ie. by formation of an intramolecular "ate"-complex **3**[2], *via* (for example) lithium enolate **2**. We therefore required a general route to derivatives **1**, in order to develop the methodology for the possible chelation controlled enolisation of the carbonyl moiety of **1** In this article we report the full details[2] of the preparation of boronates **1**, discuss the evidence for boronate "ate"-complexes in the formation of boronates **1**, report the facile lithiation of boronates **1**, and present evidence for boronate stabilisation of the resulting enolates **2** and **3**



1



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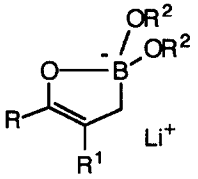
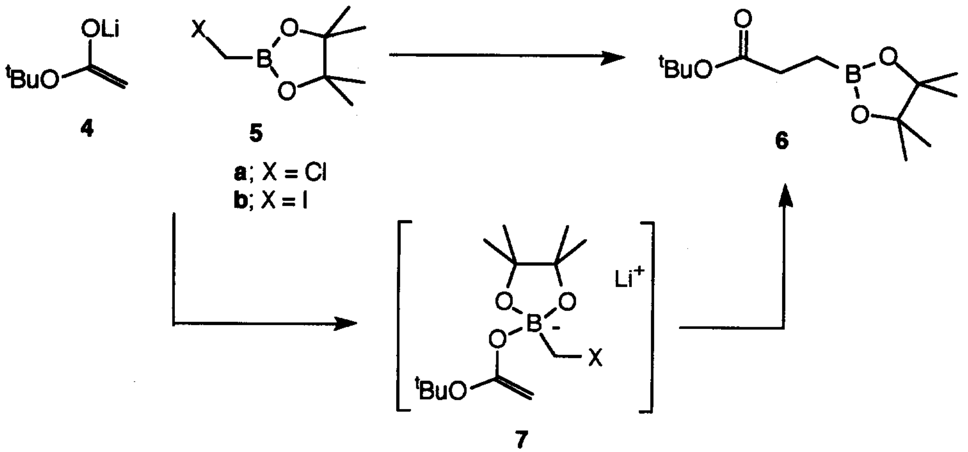


3

Our initial attempts to realise the preparation of a series of derivatives related to **1**, *via* the reaction of an enolate with a chloromethylboronate derivative, provided the required boronates **1** in only poor yields. For example, treatment of lithium *tert*-butyl acetate **4** with chloromethylboronate **5a**[4] in dry tetrahydrofuran at -78 °C followed by warming to room temperature, gave the desired ester **6**[5] in only 30% yield after aqueous work up and distillation

Examination of the ^{11}B n.m r. spectrum of the crude reaction mixture after warming to room temperature and before quenching, clearly showed the existance of a boronate "ate"-complex [δ (25.5 MHz, $CDCl_3$ / THF, ref. ext. BF_3 Et_2O in $CDCl_3$) +5] and the absence of any uncomplexed boronate species [boronate **5a** shows a ^{11}B n.m.r shift of δ +29]. The ^{11}B n.m r. shift of the complex is strongly suggestive of a fully tetrahedral mono-alkyl tri-oxygen substituted borate[6], presumably possessing structure **7a**. Even after 24 hours at room temperature, little collapse of the "ate"-complex had occured by ^{11}B n.m.r. and the addition of various Lewis-acids (including $BF_3.Et_2O$, Ag_2O) did not catalyse the collapse of the "ate"-complex **7a** to boronate **6**[7] (**Scheme 1**).

Scheme 1.



4 **5** **6**

a; X = Cl
b; X = I

7

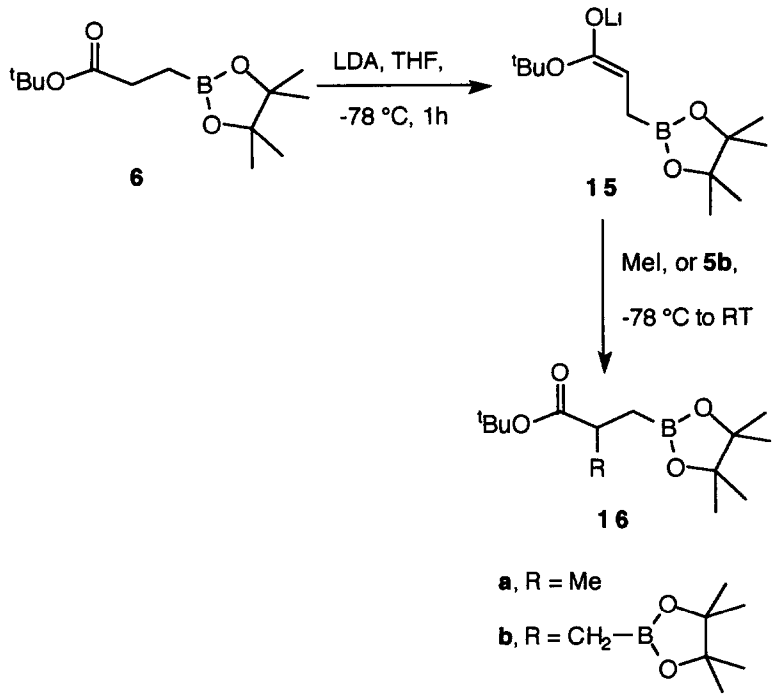
a; X = Cl
b; X = I

In order to circumvent these problems, we prepared the corresponding iodide[8] of boronate **5a** and carried out the reaction of acetate **4** with iodide **5b**. After warming the reaction mixture to room temperature, ^{11}B n.m.r. showed two peaks at δ +5 (major) and +32 (minor). After approximately 2 hours the peak at δ +5 dissappeared and work up of the reaction yielded boronate **6** in quantitative crude yield. Distillation gave pure **6** in 80% yield, which showed a ^{11}B n.m.r. shift of δ +33.

Having demonstrated the utility of iodide **5b** in the alkylation of enolate **4**, we found this approach to β-boronate carbonyl derivatives **1** (OR^2-OR^2 = pinacol ester) to be a generally useful procedure, as shown in **Table 1**. All yields are unoptimised after distillation. The yields in parentheses relate to reactions in which the iodide **5b** was generated *in situ*, by addition of 1.1 molar equivalents of sodium iodide to the "ate"-complex [presumably complex **7a** undergoes halide exchange to give **7b**] after warming to room temperature.

In order to investigate whether the corresponding lithium enolates of carbonyl derivatives **1** could be generated, we treated boronate **6** with lithium diisopropylamide (LDA) at -78 °C for 1h. The resulting enolate **15** was remarkably stable and could be clearly observed by ^{11}B n.m.r. at room temperature. ^{11}B resonance appeared at δ -2, ref. ext $BF_3.Et_2O$) showing clear evidence once again of a trialkoxy monoalkyl "ate"-complex.Subsequent quenching of the enolate **15** with either iodomethane or iodomethylboronate **5b** gave the corresponding alkylated products **16a** and **16b** in 80 and 87 % yield respectively after purification (**Equation 1**) and possessing ^{11}B n.m.r resonances in the usual uncomplexed boronate region (i.e at δ +31 and +33 respectively, ref. ext $BF_3.Et_2O$)

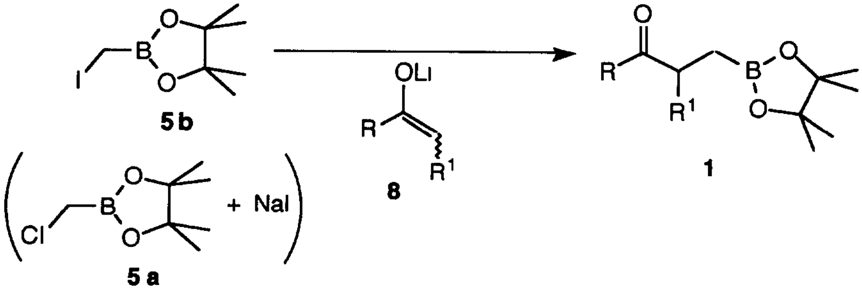
Equation 1.

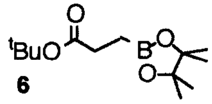
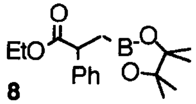
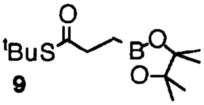
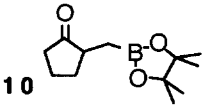
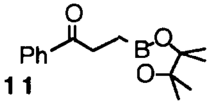
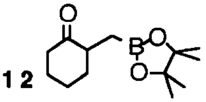
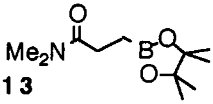
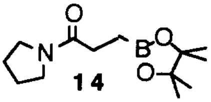


Despite the success of these simple alkylation reactions of the ester **6**, not all our attempts to alkylate enolates derived from the β-boronate compounds were successful For example, deprotonation of the cyclohexanone derivative **12** with LDA over 1 h at -78 °C precedes smoothly to give a lithium enolate as a fine white precipitate However, attempts to alkylate this enolate with iodomethane have been uniformly unsuccessful, even with 10 equivalents of iodomethane at reflux. Upon acidification with dilute hydrochloric acid, the white precipitate dissolved and a quantitative yield of the starting boronate **12** was recovered

This result is consistent with several other β-boronate containing ketone enolates that we have examined, the full details of which will be reported at a later date However, the observation of the low reactivity of enolates derived β-boronate carbonyl compounds serves to reinforce the fact that whatever the enolate geometry, the enolate oxygen is strongly stabilised by chelation with the boronate group (whether intra- or intermolecularly).

Table 1.



Entry	Yield	^{11}B n.m.r.(ref $BF_3.Et_2O$)	Product
1	80	33	 **6**
2	(73)		
3	71	33	 **8**
4	80	33	 **9**
5	83	35	 **10**
6	(43)	34	 **11**
7	53	34	 **12**
8	(54)	31	 **13**
9	41	32	 **14**

In summary, we have developed a general and straightforward procedure for the preparation of β-carbonyl boronate derivatives, provided evidence for the intermediacy of boronate "ate"-complexes in the reaction of lithium enolates with halomethylboronates and demonstrated that ^{11}B n.m r. is a powerful tool for following the fate of the boronate-enolate complex intermediates in these alkylation processes[9].

It is noteworthy that *tert*-butyl ester enolates are not stable at room temperature[10] under normal conditions, however when complexed with boron, as in complex **7a**, lithium *tert*-butyl acetate decomposes slowly over approximately 24 hours This result is consistent with all the other boronates we have examined. Further results[3,11] regarding the use of enolates **2** for stereoselective aldol reaction will be reported in due course.

Experimental

n-Butyllithium was purchased as a solution in hexanes from Aldrich or Janssen Chimica Diisopropylamine was purchased from Aldrich or Janssen Chimica and stored under argon, over KOH pellets Dry tetrahydrofuran was freshly distilled from benzophenone and sodium, under argon, immediately prior to use Dichloromethane was distilled over calcium hydride Light petroleum refers to the fraction boiling in the range 40-60 °C. Bromochloromethane, *tert*-butyl acetate, *tert*-butyl thioacetate and iodomethane were all purchased as 99.8 %+ purity reagents, used directly as purchased and stored under argon Acetophenone, pyrrolidine-N-acetate and N,N-dimethylacetamide were distilled from calcium hydride and stored under argon.

T.l c. was performed on Merck plastic or aluminium sheets coated with silica gel 60 F_{254} (Art. 5735), the chromatograms were initially examined under u.v. light and then developed either with iodine vapour or an ethanolic anisaldehyde (1.0 %) solution containing sulfuric acid (9 %) used as a spray and visualised by heating with a heat gun. Column chromatography was achieved under medium pressure, using Merck Kieselgel H (Type 60)

All anhydrous, low temperature reactions were carried out in glassware which was dried prior to use by storage in a glass oven maintained at 140 °C and cooled under a stream of argon. Evaporations were carried out using a Buchi rotary evaporator or Buchi cold-finger rotary evaporator. Kugelrohr distillations were carried out using a Buchi GKR-51 Kugelrohr apparatus M.p.'s were determined using an Electrothermal melting point apparatus and were uncorrected.

^{1}H spectra were recorded at 200 or 300 MHz on a Bruker AC200 or AC300 n m.r spectrometer. ^{13}C spectra were recorded at 75.5MHz on a Bruker AC300. Both ^{1}H and ^{13}C spectra were recorded using $CDCl_3$ and $CHCl_3$ as internal standards respectively ^{11}B n m r. spectra were recorded at either 25 7 MHz on a Bruker WP80 n m.r. spectrometer or at 64.2 MHz on a Bruker AC200 n m r spectrometer and resonances are quoted upfield of BF_3 Et_2O as external standard I.r spectra were recorded on a Perkin-Elmer 783 equiped with a PE600 data station and u v. spectra were recorded on a Perkin-Elmer λ15 spectrometer Electron impact (e i) (70 e v) and chemical ionisation (c.i) spectra were recorded with a Kratos MS25. Fast atom bombardment (f.a.b.) spectra were recorded on a Kratos MS50, using a *meta*-nitrobenzylalcohol matrix and accurate mass determinations were carried out on a Kratos Concept IS spectrometer Microanalyses were performed using a Carlo-Erba 1106 elemental analyser.

2-Chloromethyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane 5a.

To a mixture of $BrCH_2Cl$ / $B(OMe)_3$ (1.1:1 molar equiv.), ca. 1M in THF at -78 °C, was added n-BuLi (1.1 molar equiv., 2.5 M in hexanes) (dropwise addition). After 30 min., the mixture was quenched with ca. 1.2 molar equiv. TMSCl. The mixture was allowed to warm to room temperature and left overnight. After treating with pinacol dissolved in a minimum of diethyl ether and stirring for 1 hour, the mixture was partitioned between water and ether, dried ($MgSO_4$), evaporated (bath <40 °C) and fractionally distilled under water aspirator vacuum, providing **5a** in 73-85 % yield.

tert-Butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)propionate 6.

To a stirred mixture of diisopropylamine (3.08 ml, 22 mmol) and dry, redistilled tetrahydrofuran (30 ml) at 0 °C under argon, was added n-butyllithium (8.80 ml of a 2.5 M solution in hexanes). After ca. 15 min. the mixture was cooled in a Me_2CO / CO_2 (s) bath and treated with neat *tert*-butyl acetate (2.70 ml, 20 mmol). After 30 min., neat boronate **5a** (3.87 g, 22 mmol) was added followed by solid sodium iodide (3.30 g, 22 mmol). The mixture was allowed to warm to room temperature and stirred overnight. The resulting slurry was partitioned between ethyl acetate and saturated ammonium chloride, dried ($MgSO_4$), evaporated and distilled (Kugelrohr, 90 °C at 0.4 mmHg) to give boronate **6**[5] (3.726 g, 73 %) as a colourless oil.

Ethyl 2-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)propionate 8.

To a stirred mixture of diisopropylamine (1.54 ml, 11 mmol) and dry, redistilled tetrahydrofuran (20 ml) at 0 °C under argon, was added n-butyllithium (4.4 ml of a 2.5 M solution in hexanes). After ca. 15 min. the mixture was cooled in a Me_2CO / CO_2 (s) bath and treated with neat ethyl phenylacetate (1.59 ml, 10 mmol). After 30 min., neat iodomethylboronate **5b** (2.95 g, 11 mmol) was added, the mixture was allowed to warm to room temperature, and stirred overnight. The resulting slurry was partitioned between ethyl acetate and saturated ammonium chloride, dried ($MgSO_4$), evaporated and distilled (Kugelrohr, 180 °C at 0.8 mmHg) to give boronate **8** (2.148 g, 71 %) as a colourless oil: υ_{max} (film) *inter alia* 1735 (C:O) cm^{-1}; λ_{max} (EtOH) 206 (ε 8,173), 252 (ε 156), 258 (ε 195), and 264 (ε 149) nm; δ (^{11}B, $CDCl_3$, 25.7 MHz) + 31; δ (^{13}C, $CDCl_3$) 13.9 ($CH_2.\underline{C}H_3$), 16.0 (br, B.C), 24.4 and 25.4 (2 x $O.C.\underline{Me_2}$), 46.9 ($B.C.\underline{C}$), 60.4 ($O.\underline{C}H_2$), 83.0 (2 x $O.\underline{C}.Me_2$), 126.6, 127.5, 128.2 and 141.0 (Ph), and 174.5 (C:O); δ (^1H, $CDCl_3$, 300 MHz) 1.16 and 1.17 (each 6H, s, 2 x $C.Me_2$), 1.17 (3H, t, J = 7.1Hz, $O.CH_2.\underline{Me}$), 1.27 (1H, dd, J = 15.9 and 7.1Hz, $B.C\underline{H}H$), 1.56 (1H, dd, J = 15.9 and 9.5Hz, $B.CH\underline{H}$), 3.82 (1H, dd, J = 9.5 and 7.1Hz, $B.CH_2.C\underline{H}$), 3.99-4.20(2H, m, $O.C\underline{H_2}.Me$), and 7.18-7.33 (5H, m, Ph); m/z (f.a.b.) 305 (M^+), 231 ($M^+ - C_3H_4O_2$), and 205 (base peak, $M^+ - C_6H_{12}O$); Accurate m.s: $C_{17}H_{26}BO_4$ requires m/z 305.1924, peak at m/z 305.1923.

tert-Butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)thiopropionate 9.

To a stirred mixture of diisopropylamine (3.48 ml, 25 mmol) and dry, redistilled tetrahydrofuran (50 ml) at 0 °C under argon, was added n-butyllithium (10 ml of a 2.5 M solution in hexanes). After ca. 15 min. the mixture was cooled in a Me_2CO / CO_2 (s) bath and treated with neat *tert*-butylthioacetate (3.30 ml, 23.75 mmol). After 30 min., neat iodomethylboronate **5b** (6.62 g, 25 mmol) was added, the mixture was allowed to warm to room temperature, and stirred overnight. The resulting slurry was partitioned between ethyl acetate and saturated ammonium chloride, dried ($MgSO_4$), evaporated and distilled (Kugelrohr, 110 °C at 0.5 mmHg) to give boronate **9** (5.224 g, 80 %) as a colourless oil: υ_{max} (film) *inter alia* 1690 (C:O) cm^{-1}; λ_{max} (EtOH) 232 (ε 4,992), and 279 (ε 593) nm; δ (^{11}B, $CDCl_3$, 25.7 MHz) +33; δ (^{13}C, $CDCl_3$) 8.0 (br, B.C), 25.4 (2 x $O.C.\underline{Me_2}$), 30.5

(S.C $\underline{\mathrm{Me}}_3$), 39.7 (B.C.$\underline{\mathrm{C}}$), 48.1 (S.$\underline{\mathrm{C}}Me_3$), 83.2 (2 x O.$\underline{\mathrm{C}}Me_2$), and 201.6 (C:O); δ (^{1}H, CDCl$_3$, 300 MHz) 1.00 (2H, t, J = 7.5 Hz, B.CH$_2$), 1.23 (12H, s, 2 x C.Me$_2$), 1.44 (9H, s, C.Me$_3$), and 2.60 (3H, t, J = 7.5 Hz, O:C.CH$_2$); m/z (f.a.b.) 273 (M$^+$+H), 183 (base peak, M$^+$-C_4H_9S); Accurate m.s: $C_{13}H_{25}BO_3S$ requires m/z 273.1696, peak at m/z 273.1691.

2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)methylcyclopentanone 10.

To a stirred mixture of diisopropylamine (1.54 ml, 11 mmol) and dry, redistilled tetrahydrofuran (10 ml) at 0 °C under argon, was added n-butyllithium (4.4 ml of a 2.5 M solution in hexanes). After ca. 15 min. the mixture was cooled in a Me_2CO / CO_2 (s) bath and treated with neat cyclopentanone (0.883 ml, 10 mmol). After 30 min., neat iodomethylboronate **5b** (2.95 g, 11 mmol) was added, the mixture was allowed to warm to room temperature, and stirred overnight. The resulting slurry was partitioned between ethyl acetate and saturated ammonium chloride, dried ($MgSO_4$), evaporated and distilled (Kugelrohr, 110 °C 0.3 mmHg) to give boronate **10** (1.854 g, 83 %) as a colourless oil: υ_{max} (film) *inter alia* 1740 (C:O) cm^{-1}; λ_{max} (EtOH) 286 (ε 28) nm; δ (^{11}B, CDCl$_3$, 25.7 MHz) +31; δ (^{13}C, CDCl$_3$) 12.0 (br, C.B), 20.5 and 31.6 (O:C CH$_2$ $\underline{\mathrm{C}}$H$_2$.$\underline{\mathrm{C}}$H$_2$), 24.5 and 24.6 (2 x C.$\underline{\mathrm{Me}}_2$), 37.0 (O.C.$\underline{\mathrm{C}}H_2$), 45.8 (O:C.$\underline{\mathrm{C}}$H), 83.0 (2 x $\underline{\mathrm{C}}$.Me$_2$), and 221.5 (C:O); δ (^{1}H, CDCl$_3$, 300 MHz) 0.84 (1H, dd, J = 15.9 and 6.9Hz, B C$\underline{\mathrm{H}}$H), 1.03 (1H, dd, J = 15.9 and 6.8Hz, B.C$\underline{\mathrm{H}}$H), 1.25 and 1.26 (each 6H, s, 2 x C.Me$_2$), 1.46-1.48 and 1.70-1.86 (each 1H, m), and 1.94-2.35 (5H, m); m/z (f.a.b.) 225 (M$^+$), and 125 (M$^+$-$C_6H_{12}O$); Accurate m.s: $C_{12}H_{21}BO_3$ requires m/z 225.1662, peak at m/z 225.1659.

2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)propiophenone 11.

To a stirred mixture of diisopropylamine (3.08 ml, 22 mmol) and dry, redistilled tetrahydrofuran (30 ml) at 0 °C under argon, was added n-butyllithium (8.80 ml of a 2.5M solution in hexanes). After ca. 15 min. the mixture was cooled in a Me_2CO / CO_2 (s) bath and treated with neat acetophenone (2.33 ml, 20 mmol). After 30 min., neat boronate **5a** (3.87 g, 22 mmol) was added followed by solid sodium iodide (3.30 g, 22 mmol). The mixture was allowed to warm to room temperature and stirred overnight. The resulting slurry was partitioned between ethyl acetate and saturated ammonium chloride, dried ($MgSO_4$), evaporated and distilled (Kugelrohr, 155 °C at 0.5 mmHg) to give boronate **11** (3.952g, 76 %) as a colourless oil: υ_{max} (film) *inter alia* 1690 (C:O) cm^{-1}; λ_{max} (EtOH) 202 (ε 20,514), 241 (ε 12,457), 279 (ε 1,594) nm; δ (^{11}B, CDCl$_3$, 64.2 MHz) +33; δ (^{13}C, CDCl$_3$) 0.6 (br, B.C), 25.4 (2 x C.$\underline{\mathrm{Me}}_2$), 34.3 (O:C.$\underline{\mathrm{C}}H_2$), 83.7 (2 x $\underline{\mathrm{C}}$.Me$_2$), 128, 129.1, 133.4 and 137.6 (Ph), and 201.2 (C.O); δ(^{1}H, CDCl$_3$, 300 MHz) 1.07 (2H, t, J = 7.0Hz, B.CH$_2$), 1.25 (12H, s, 2 x C.Me$_2$), 3.16 (2H, t, J = 7.0Hz, B CH$_2$ C$\underline{\mathrm{H}}_2$), 7.21-7.59, and 7.95-7.98 (3 and 2H, m, respectively, Ph); m/z (+ve c.i.) 278 (M$^+$ + NH$_3$), 261 (base peak, M$^+$ + H), 260 (M$^+$), 161 (M$^+$ - $C_6H_{11}O$), Analysis: $C_{14}H_{28}BO_4$ requires C, 69.3, H, 8.1; B, 4.2 Found C, 69.5; H, 8.2; B, 4.0 %

2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)methylcyclohexanone 12.

To a stirred mixture of diisopropylamine (1.75 ml, 12.5 mmol) and dry, redistilled tetrahydrofuran (20 ml) at 0 °C under argon, was added n-butyllithium (5.0 ml of a 2.5M solution in hexanes). After ca. 15 min. the mixture was cooled in a Me_2CO / CO_2 (s) bath and treated with neat cyclohexanone (1.17 ml, 11.25 mmol) After 30 min., neat iodomethylboronate **5b** (3.31 g, 12.5 mmol) was added, the mixture was allowed to warm to room temperature, and stirred overnight. The resulting slurry was partitioned between ethyl acetate and saturated ammonium chloride, dried ($MgSO_4$), evaporated and distilled (Kugelrohr, 110 °C at 0.25 mmHg) to give boronate **12** (1.42 g, 53 %) as a colourless oil: υ_{max} (film) *inter alia* 1715 (C:O) cm^{-1}; λ_{max} (EtOH) 259 (ε 37) nm; δ (^{11}B, CDCl$_3$, 25.7 MHz) +31, δ (^{13}C, CDCl$_3$) 13 (br, B C), 24.7 and 24.8 (2 x C $\underline{\mathrm{Me}}_2$), 25.4, 27.7 and 36.6

($O{:}C.CH_2.\underline{C}H_2.\underline{C}H_2.\underline{C}H_2$), 41.6 ($O{:}C.\underline{C}H_2$), 47.6 ($O{:}C.\underline{C}H$), 82.9 (2 x $\underline{C}.Me_2$), and 213.0 (C:O); δ (^1H, $CDCl_3$, 300 MHz) 0.67 (1H, dd, *J* = 15.7 and 5.7Hz, $B.C\underline{H}H$), 0.93 (1H, dd, *J* = 15.7 and 8.8Hz, $B.CH\underline{H}$), 1.22 and 1.25 (each 6H, s, 2 x $C.Me_2$), 1.34-1.48 (1H, m), 1.56-1.70 (2H, m), 1.78-1.86 (1H, m), 2.01-2.16 (2H, m), 2.24-2.42 (2H, m), and 2.51-2.62 (1H, m); m/z (e.i.) 245 (M^+-CH_3), 202 (M^+-C_3H_6O), and 105 (base peak, M^+-$C_8H_{16}O_2$); Accurate m.s: $C_{13}H_{23}BO_3$ requires m/z 238.1740, peak at m/z 238.1752.

N,N-Dimethyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)propionamide 13.

To a stirred mixture of diisopropylamine (4.203 ml, 30.2 mmol) and dry, redistilled tetrahydrofuran (45 ml) at 0 °C under argon, was added n-butyllithium (12.08 ml of a 2.5 M solution in hexanes). After ca. 15 min. the mixture was cooled in a Me_2CO / CO_2 (s) bath and treated with neat N,N-dimethylacetamide (2.664 ml, 28.7 mmol). After 30 min., neat boronate **5a** (7.732 g, 30.2 mmol) was added followed by solid sodium iodide (4.531 g, 30.2 mmol). The mixture was allowed to warm to room temperature and stirred overnight. The resulting slurry was partitioned between ethyl acetate and saturated ammonium chloride, dried ($MgSO_4$), evaporated and distilled (Kugelrohr, 140 °C at 0.3 mmHg) to give boronate **13** (3.530 g, 54%) as a colourless oil: υ_{max} (film) *inter alia* 1650 (C:O) cm^{-1}; λ_{max} (EtOH) 204 (ε 6,590) nm; δ (^{11}B, $CDCl_3$, 64.2 MHz) +30; δ (^{13}C, $CDCl_3$) 7.0 (br, B.C), 24.7 (2 x $C.\underline{Me_2}$), 28.1 ($B.C.\underline{C}$), 35.5 and 36.6 ($N.Me_2$), 82.4 (2 x $C.\underline{Me_2}$), and 174.1 (C:O); δ (^1H, $CDCl_3$, 300 MHz) 0.95 (2H, t, *J* = 7.3 Hz, B. CH_2), 1.24 (12H, s, 2 x $C.Me_2$), 2.45 (2H , t , *J* = 7.3Hz, $O{:}C.CH_2$), 2.94 and 2.98 (each 3H, s, $N.Me_2$); m/z (f.a.b.) 228 (base peak, M^+ + H), 212 (M^+ - CH_3), and 168 (M^+ - C_3H_7O); Analysis $C_{11}H_{22}BNO_3$ requires C, 58.2; H, 9.8; N, 6.2; B, 4.7. Found C, 58.4; H, 10.1; N, 6.2; B, 4.5 %.

Pyrrolidine-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)propionamide 14.

To a stirred mixture of diisopropylamine (3.08 ml, 22 mmol) and dry, redistilled tetrahydrofuran (30 ml) at 0 °C under argon, was added n-butyllithium (8.80 ml of a 2.5M solution in hexanes). After ca. 15 min. the mixture was cooled in a Me_2CO / CO_2 (s) bath and treated with neat pyrrolidine-N-acetate (2.26 g, 20 mmol). After 30 min., neat boronate **5a** (5.89 g, 22 mmol) was added. The mixture was allowed to warm to room temperature and stirred overnight. The resulting slurry was partitioned between ethyl acetate and saturated ammonium chloride, dried ($MgSO_4$), evaporated and distilled (Kugelrohr, 95 °C at 0.05 mmHg) to give boronate **14** (2.088 g, 41 %) as a colourless oil which slowly solidifies to a waxy solid on standing: υ_{max} (KBr disc) *inter alia* 1640 br (C:O) cm^{-1}; λ_{max} (EtOH) 204 (ε 6,620) nm; δ (^{11}B, $CDCl_3$, 64.2 MHz) +32; δ (^{13}C, $CDCl_3$) 7.0 (br, B.C), 24.7 (2 x $C.\underline{Me_2}$), 24.3 and 26.0 (2 x $N.C.\underline{C}$), 29.4 ($B.C.\underline{C}$), 45.7 and 46.2 (2 x N.C), 82.6 (2 x $C.Me_2$), and 172.7 (C:O); δ (^1H, $CDCl_3$, 300 MHz) 0.91 (2H, t, *J* = 7.5 Hz, $B.CH_2$), 1.19 (12H, s, 2 x $C.Me_2$), 1.78 and 1.88 (each 2H, quintet, *J* = 6.7 and 6.4 Hz respectively, 2 x $N.CH_2.C\underline{H_2}$), 2.34 (2H , t , *J* = 7.5Hz, $O{:}C.CH_2$), 3.35 and 3.39 (each 2H, t, *J* = 6.8 and 6.9 Hz respectively, 2 x $N.CH_2$); m/z (f.a.b.) 254 (M + H^+), 238 (M^+ - CH_3), 194 (M^+ -C_3H_7O), and 136 (base peak, M^+ - $C_6H_{13}O_2$); Analysis $C_{13}H_{24}BNO_3$ requires C, 61.7; H, 9.6; N, 5.5; B, 4.3. Found C, 61.4; H, 9.8; N, 5.2; B, 4.0 %.

tert-Butyl 2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)propionate 16a.

To a stirred mixture of diisopropylamine (0.72 ml, 5.16 mmol) and n-butyllithium (2.06 ml of a 2.5M solution in hexanes) in tetrahydrofuran (5 ml) at -78 °C under argon was added boronate **6** (1.20 g, 4.69 mmol) in tetrahydrofuran (3 ml). After 45 min., iodomethane (0.64 ml, 10.32 mmol) was added and after 30 min. the reaction mixture was allowed to warm to room temperature. Quenching the reaction mixture after 12 hours with saturated ammonium chloride was followed by extraction with ethyl acetate, drying ($MgSO_4$) and evaporation to give 1.20 g of a crude oil. Purification of the oil by silica gel chromatography (petroleum ether:ethyl acetate, 9:1 as eluant) gave the methylated boronate **16a** as a colourless oil (1.01 g, 80 %): υ_{max} (film) *inter alia* 1730 (C:O) cm^{-1}; λ_{max} (EtOH) 215 (ε 130) nm; δ (^{11}B, $CDCl_3$, 25.7 MHz) + 31; δ (^{13}C, $CDCl_3$) 17.0 (br, B.C), 20.0 (CH.Me), 25.2 (2 x O.C.Me_2), 28.5 (C.Me_3), 36.8 (C.C:O), 79.8 (C.Me_3), 83.4 (2 x O.C.Me_2), and 177.0 (C:O); δ (^{1}H, $CDCl_3$, 300MHz) 0.85 (1H, dd, J = 15.9 and 7.4 Hz, B.CHH), 1.08 (1H, dd, J = 15.9 and 7.4 Hz, B.CHH), 1.14 (3H, d, J = 7.0 Hz, O:C.CH.Me), 1.22 and 1.23 (each 6H, s, 2 x C.Me_2), 1.42 (9H, s, C Me_3), and 2.54 (1H, tq, J =7.4 and 7.0 Hz, O:C.CH); m/z (f.a.b.) 271 (M$^+$), 215 (M$^+$-C_4H_8), and 101 (base peak, $C_6H_{13}O^+$); Accurate m s. $C_{14}H_{28}BO_4$ requires m/z 271.2080, peak at m/z 271.2076.

***tert*-Butyl 2-methyl(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolyl)propionate 16b.**

To a stirred mixture of diisopropylamine (0.72 ml, 5 16 mmol) and n-butyllithium (2.06 ml of a 2.5M solution in hexanes) in tetrahydrofuran (5 ml) at -78 °C under argon was added boronate **6** (1 20 g, 4.69 mmol) in tetrahydrofuran (2 ml). After 45 min., iodomethylboronate **5b** (1.52 g, 5.70 mmol) was added and after 15 min. the reaction mixture was allowed to warm to room temperature. Quenching the reaction mixture after 13 hours with saturated ammonium chloride was followed by extraction with ethyl acetate, drying ($MgSO_4$) and evaporation to give 1 993 g of a crude syrup. Purification of the syrup by Kugelrohr distillation (0.2 mmHg) provided two fractions The first fraction (b.p. 110-115 °C) was boronate **6** (0.087 g, 7 %) and the second fraction (b.p. 150-155 °C) was the methylated boronate **16b**, obtained as a colourless syrup (1.532 g, 83 %): υ_{max} (film) *inter alia* 1730 (C:O) cm^{-1}; λ_{max} (EtOH) 219 (ε 197) nm, δ (^{11}B, $CDCl_3$, 25 7 MHz) + 33; δ (^{13}C, $CDCl_3$) 18.0 (br, 2 x B.C), 25 4 and 25 5 (4 x O.C.Me_2) 28 7 (C.Me_3), 38.2 (C.C:O), 78.1 (C Me_3), 83 6 (4 x O.C Me_2), and 177.3 (C:O), δ (^{1}H, $CDCl_3$, 300 MHz) 0.94 (2H, dd, J = 15.8 and 6.7 Hz, 2 x B.CHH), 1 11 (2H, dd, J = 15.8 and 8 1 Hz, 2 x B CHH), 1.22 and 1.23 (each 12H, s, 4 x C.Me_2), 1 42 (9H, s, C.Me_3), and 2 64 (1H, m, O C.CH); m/z (f.a.b.) 397 (M$^+$ + H), 341 (M$^+$ - C_4H_8), 323 (M$^+$ - $C_4H_{10}O$), and 57 (base peak, $C_4H_9^+$); Accurate m.s. $C_{20}H_{38}B_2O_6$ + H requires m/z 397.2932, peak at m/z 397 2948.

Acknowledgements

The author gratefully acknowledges the Department of Chemistry, U M.I.S.T , for the provision of funding for equipment and consumables; and S E R.C. for an studentship (to R.J.M.). We are grateful to Messers K. Walkling, for i r. and u.v. spectra; C.R. Perkins, for m.s spectra and Dr. R. Perry for elemental analyses

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