# Force field parameters for the boronate function and their carbonyl complexes and application to modelling boronate esters

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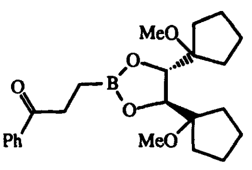
**MM2 force field parameters have been developed for alkyl- and aryl-boronates and for their carbonyl Lewis-acid complexes, from a combination of X-ray crystallographic data, infrared spectroscopy, *ab initio* and semi-empirical calculations. The resulting parameters, when used in conjunction with MacroModel, reproduce the geometry of *ab initio* and MNDO calculated and X-ray crystal structures with high accuracy, and have been used to model chiral boronate esters to explain the origin of stereoselective reduction reactions of boronate complexes 3 and 4.**

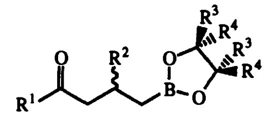
## Introduction

The investigation and understanding of stereochemical arrangements of organic molecules has been greatly assisted in recent years by molecular mechanics calculations.[1] This fact, coupled with considerable interest in boronate mediated reactions in the literature,[2] has prompted us to generate force field parameters for organoboronate esters. This investigation was further prompted by reports from our laboratories[3] and those of Molander *et al.*[4] that the carbonyl groups of compounds **1** and **2** undergo stereoselective reductions, probably as a direct consequence of the interaction of the remote boronate ester with the carbonyl groups, *i.e. via* complexes of type **3** and **4**, respectively.[3b,4]

We therefore decided not only to generate an MM2 force field for use with MacroModel[5] for boronate esters **5**, but also for their carbonyl complexes **6** in order to study the conformational properties of both structures. It was our expectation that this would provide a basis for explaining the sense of asymmetric induction observed for reductions involving ester **1** *versus* ester **2a**. The necessary parameters were derived from X-ray crystallographic data, infrared spectroscopy, *ab initio*[6] and semi-empirical calculations[7] as described by Allinger.[1,8] The parameter set thus derived was then employed to model some simple boronate derivatives to check that the parameters faithfully reproduced the X-ray crystallographic data, *ab initio* and semi-empirical calculations, and the calculations of related boronate systems reported by other workers.[9] Finally, we have used the force field to probe the accessible structures for compounds **1**, **2**, **3** and **4**.

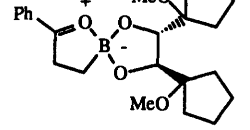


**1**

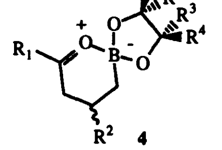


**2**

**a**; $R^1$ = Ph, $R^2$ = $R^4$ = H, $R^3$ = $Pr^i$
**b**; $R^1$ = Cyclohexyl, $R^2$ = $R^4$ = H, $R^3$ = $Pr^i$

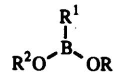


**3**



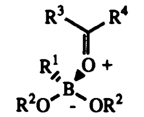
**4**

**a**; $R^1$ = Ph, $R^2$ = $R^4$ = H, $R^3$ = $Pr^i$
**b**; $R^1$ = Cyclohexyl, $R^2$ = $R^4$ = H, $R^3$ = $Pr^i$



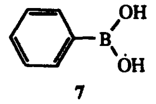
**5**

**a**; $R^1$ = Ph, $R^2$ = Me
**b**; $R^1$ = $Pr^i$, $R^2$ = Me

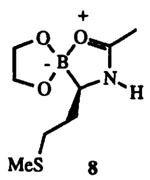


**6**

**a**; $R^1$ = Ph, $R^2$ = Me
**b**; $R^1$ = $Pr^i$, $R^2$ = Me



**7**



**8**

## Discussion

### Force field parameters

**Average bond lengths and bond angles (crystallographic data, *ab initio* and MNDO calculations)**

In order to estimate the average length of the B–C and B–O bonds in alkyl and aryl boron compounds, we required several representative boron containing X-ray structures. Examination of the Cambridge Crystallographic Database[10] using Crystal Structure Search and Retrieval (CSSR),† produced few representative X-ray structures, one of which contained an acyclic boronic acid moiety **7**.[11] Other closely related X-ray crystal structures were also found,[12] such as one which contained a carbonyl chelated boronate, although the carbonyl in question was from an amide carbonyl **8**.[12a] From this data we were able measure bond lengths for the B–O, B–C($sp^2$) and B–C($sp^3$) bonds and bond angles for C–C–B, C–B–O and approximate values for B–O=C (Table 1).

To supplement the X-ray crystal data we carried out *ab initio* and semi-empirical calculations (MNDO)[7] on standard structures **5** and **6**.[13] The resulting values are also shown in Table 1. The calculated values for bond lengths and angles compared well with the limited X-ray crystal data and other calculated values in the literature,[14] and the average values for

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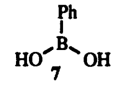
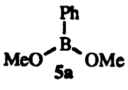
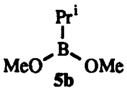
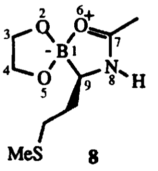
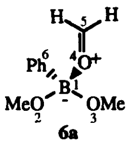
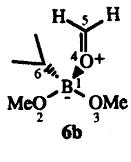
† CSSR was accessed using the EPSRC funded Chemical Database Service at Daresbury.

Table 1 Bond lengths and angles data

| Structure | Data source | Bond lengths/Å | | Bond angles/° | |
|---|---|---|---|---|---|
|  7 | X-Ray[a] | B–C | 1.565 | C–B–O | 121.1 |
| | | B–O | 1.364 | O–B–O | 115.2 |
|  5a | *Ab initio*[b] | B–C | 1.5630 | C–B–O | 117.33 |
| | | B–O | 1.3800 | B–O–C | 132.67 |
| | | O–C | 1.4340 | O–B–O | 125.38 |
| | Semi-empirical[c] | B–C | 1.5673 | C–B–O | 117.70 |
| | | B–O | 1.3657 | B–O–C | 134.45 |
| | | O–C | 1.3892 | O–B–O | 125.60 |
|  5b | *Ab initio*[b] | B–C | 1.9694 | C–B–O | 112.15 |
| | | B–O | 1.5230 | B–O–C | 111.61 |
| | | O–C | 1.5112 | O–B–O | 119.11 |
| | Semi-empirical[c] | B–C | 1.6139 | C–B–O | 118.33 |
| | | B–O | 1.3638 | B–O–C | 135.02 |
| | | O–C | 1.3900 | O–B–O | 125.32 |
|  8 | X-Ray[a] | 1–9 | 1.6130 | 9–1–2(5) | 117.70 |
| | | 1–2(5) | 1.4380 | 9–1–6 | 98.80 |
| | | 1–6 | 1.6410 | 2–1–5 | 106.75 |
| | | 2–3(4–5) | 1.4270 | 2(5)–1–6 | 107.62 |
|  6a | *Ab initio*[b] | 1–2(3) | 1.3852 | 1–4–5 | 132.28 |
| | | 1–4 | 2.5561 | 6–1–2(3) | 100.93 |
| | | 1–6 | 1.5752 | 3–1–2 | 90.00 |
| | | 4–5 | 1.3011 | 6–1–4 | 105.05 |
| | Semi-empirical[c] | 1–2(3) | 1.4309 | 1–4–5 | 133.05 |
| | | 1–4 | 1.6221 | 6–1–2(3) | 114.96 |
| | | 1–6 | 1.6089 | 3–1–2 | 124.29 |
| | | 4–5 | 1.2406 | 6–1–4 | 104.32 |
|  6b | *Ab initio*[b] | 1–2(3) | 1.3852 | 1–4–5 | 132.28 |
| | | 1–4 | 2.5561 | 6–1–2(3) | 100.93 |
| | | 1–6 | 1.5752 | 3–1–2 | 104.28 |
| | | 4–5 | 1.3105 | 6–1–4 | 99.37 |
| | Semi-empirical[c] | 1–2(3) | 1.4006 | 1–4–5 | 134.58 |
| | | 1–4 | 1.8038 | 6–1–2(3) | 105.38 |
| | | 1–6 | 1.6093 | 3–1–2 | 112.78 |
| | | 4–5 | 1.2306 | 6–1–4 | 105.38 |

[a] See ref. 10. [b] See ref. 6. [c] See ref. 7.

the different bond lengths and bond angles, from the measured and calculated data, were entered into the corresponding MacroModel force field sub-structures (*vide infra*).

### Vibrational data (force constant calculations)

The bond stretching parameters were estimated using infrared spectroscopic data[14] and MNDO estimated vibrational frequencies[7,15] where infrared data was not available. Applying eqns. (1) and (2)[16] ($K_s$ = force constant; $v$ =

$$K_s\,(\text{symm}) = 5.3 \times 10^{-7} \times v^2 \times \mu_{\text{symm}} \quad (\text{mdyn Å}^{-1})$$
$$[\text{where}, \mu_{\text{symm}} = 1/(1/M_1 - 1/M_2 + 1/M_3] \quad (1)$$

$$K_s\,(\text{asymm}) = 5.3 \times 10^{-7} \times v^2 \times \mu_{\text{asymm}} \quad (\text{mdyn Å}^{-1})$$
$$[\text{where}, \mu_{\text{asymm}} = 1/(1/M_1 + 1/M_2 + 1/M_3] \quad (2)$$

infrared stretching frequency, cm$^{-1}$; $M_n$ = relative atomic mass for atom $n$ of the triatomic unit) allowed estimation of the force constants for the B–O, B–C(sp$^2$) and B–C(sp$^3$) bonds. Angle bending parameters were similarly calculated from infrared data (where available) using eqn. (3),[16] and the resulting parameters added to the force field. Any bending

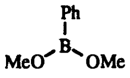
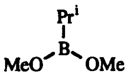
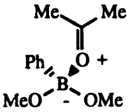
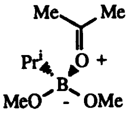
$$K_b = 3.0 \times 10^{-7} \times v^2 \times (M_1 \times M_3/M_1 + M_3) \quad (\text{mdyn rad}^{-2}) \quad (3)$$

parameters for which infrared data were not available were estimated based upon related literature precedent.[17] The observed and calculated vibrational data for the different bonds are listed in Table 2, together with the calculated force constants, which were again entered into the relevant lines in the MacroModel force field sub-structure.

### van der Waals parameters (non-bonded interactions)

The initial selection of the van der Waals parameters was based upon the values already used for boron, carbon and oxygen in the MacroModel version of the MM2 force field. The values chosen are identical for all boron types and proved to reproduce all the structures which have to date been examined with reasonable accuracy. Hence, they have remained unchanged in the final force field (*vide infra*). The van der Waals values are: 1.9800 (0.0340) Å ($\varepsilon$/kcal mol$^{-1}$) for B, 1.7400 (0.0500) for O, 1.9400 (0.0440) for C(sp$^2$) and 1.9400 (0.0440) for C(sp$^3$).[18]

Table 2 Calculated force constants

| Structure | Frequency (corrected[a])/cm$^{-1}$ | | $K_s$/mdyn Å$^{-1}$ ($K_b$/mdyn rad$^{-2}$) | |
|---|---|---|---|---|
|  **5a** | B–C | 1375[b] (1210) | B–C | 4.4145 |
| | B–O | 1337[b] (1177) | B–O | 4.7328 |
| | C–O | 1576[b] (1387) | C–O | 6.9949 |
|  **5b** | B–C | 700[c] | B–C | 1.4470 |
| | B–O | 1659[b] (1459) | B–O | 7.2854 |
| | C–O | 1590[b] (1399) | C–O | 7.1165 |
|  **6a** | B–C | 700[c] | B–C | 1.4470 |
| | B–O | 1659[b] (1459) | B–O | 7.2854 |
| | B–O(=C) | 1337[b] (1176) | B–O(=C) | 4.7328 |
| | C–O | 1590[b] (1399) | C–O | 7.1165 |
|  **6b** | B–C | 700[c] | B–C | 1.4470 |
| | B–O | 1659[b] (1459) | B–O | 7.2854 |
| | C–O | 1590[b] (1399) | C–O | 7.1165 |

[a] See ref. 7(*b*). [b] Semi-empirical calculated, see ref. 7. [c] Observed, see ref. 14.

Table 3 Arylboronate sub-structure for **5a**

```
  C dialkoxyboron (ARYL)
  9 C2-B2(-O3-C3)-O3-C3
-2
  1   1   2                 1.5600      4.4145
  1   2   3                 1.3649      4.7328
  1   2   5                 1.3649      4.7328
  1   3   4                 1.3892      6.9949
  1   5   6                 1.3892      6.9949
  2   1   2   3           117.7000      0.5000
  2   1   2   5           117.7000      0.5000
  2   3   2   5           124.6000      0.5000
  2   2   3   4           135.2000      0.5000
  2   2   5   6           135.2000      0.5000
  2   C2  1   2           121.3000      0.5000
  4   C2  1   2   3         0.0590      6.5300      0.0590
  4   1   2   3   4        13.5120      0.0590      0.5330
  4   1   2   3   Lp        0.0000      0.0000      0.0000
  4   3   2   5   6       -15.6000     -0.6190     -1.4950
  4   3   2   5   Lp        0.0000      0.0000      0.0000
  4   1   2   5   6        13.5120      0.0590      0.1770
  4   C2  1   2   5         0.0590      6.5300      0.0590
  4   1   2   5   Lp        0.0000      0.0000      0.0000
  4   5   2   3   Lp        0.0000      0.0000      0.0000
  4   5   2   3   4       -15.6000     -0.6190     -1.4950
-4
  8  -0.0612  0.2176  -0.3296  0.2529  -0.3300  0.2530
```

### Point energy calculations (torsional parameters)

As already described, semi-empirical calculations were carried out on the general boron containing structures **5** and **6** after choosing particular structures to typify each group of compounds (*i.e.* **5a**, **5b**, **6a** and **6b**). These calculations were extended to include point energy calculations in order to estimate the torsional parameters $V_1$, $V_2$ and $V_3$. Calculation[19] of these torsional parameters was achieved using the truncated Fourier expansion [eqn. (4)].[20] The torsional parameters were

$$E_{\text{Torsion}} = [(V_1/2)(1 + \cos\theta)] + [(V_2/2)(1 - \cos 2\theta)] + [(V_3/2)(1 + \cos 3\theta)] \quad (4)$$

estimated from the difference in the calculated torsional parameters found using MNDO and those from MM2. Energy differences were estimated from MNDO point energies for each of the structures **5a**, **5b**, **6a** and **6b**, and the MM2 point energies for **5a**, **5b**, **6a** and **6b** at 30° intervals of $\theta$, with torsional parameters set to zero in the MM2 force field. The resulting values for $V_1$, $V_2$ and $V_3$ estimated using this method were then added to the MM2 force field.

Table 4 Alkylboronate sub-structure for **5b**

```
  C dialkoxyboron (ALKYL)
  9 C3-B2(-O3-C3)-O3-C3
-2
  1   1   2                 1.5600      1.4470
  1   2   3                 1.3631      7.2854
  1   3   4                 1.3901      7.1165
  1   2   5                 1.3631      7.2854
  1   5   6                 1.3901      7.1165
  2   1   2   3           118.3000      0.5000
  2   1   2   5           118.3000      0.5000
  2   3   2   5           125.3000      0.5000
  2   C3  1   2           113.2000      0.5000
  2   2   3   4           135.1000      0.5000
  2   2   5   6           135.1000      0.5000
  2   H1  1   2           109.4667      0.5000
  4   1   2   3   4         2.1530      6.7950      0.0970
  4   C3  1   2   3         1.1080     -2.0600     -0.2110
  4   H1  1   2   3         0.0570      2.4290     -0.0050
  4   H1  1   2   5         0.0570      2.4290     -0.0050
  4   1   2   3   Lp        0.0000      0.0000      0.0000
  4   3   2   5   6       -14.8140      6.6806     -0.2360
  4   3   2   5   Lp        0.0000      0.0000      0.0000
  4   1   2   5   6         2.1530      6.7950      0.0970
  4   C3  1   2   5         1.1080     -2.0600     -0.2110
  4   1   2   5   Lp        0.0000      0.0000      0.0000
  4   4   3   2   5        -6.3264     -1.8020      0.1350
  4   3   2   5   6        -6.3264     -1.8020      0.1350
  4   5   2   3   Lp        0.0000      0.0000      0.0000
-4
  8  -0.0193  0.1778  -0.3273  0.2502  -0 .3281  0.2504
```

### Lone pair and partial charge parameters

The final approximation made in the new force fields has been to make some allowance for the oxygen lone pairs and partial charges on the boron groups. As an initial approximation of the properties of the dialkoxy boron groups, we have assumed that partial charges alone satisfactorily model these groups without fully parametrising the lone pairs on oxygen. Since the MultiConformer sub-routine of MacroModel, which was used as one of the methods to check the reliability of the force field (*vide infra*), does require lone pairs to be present we have added lines to the force field relating to the lone pairs for the boronates **5** and **6** but reduced their impact on the energy calculations effectively to zero.

The partial charge values for boron, carbon and oxygen added to the force field were all derived from the MNDO calculations (*vide supra*) after suitable scaling.[15] These values were compared and checked against those calculated using *ab initio* calculations as outlined by Still,[21] *i.e.* using the CHelpG (Charges from Electrostatic Potential Grid) procedure[6d] (PoP = CHelpG), fitting to the wavefunction at the MP2/6-31G* level of theory.

### Force field

All the above parameters were added to the MM2 force field of MacroModel, creating three sub-structure force fields for each of the structures described above (Tables 3–5).

### Molecular mechanics calculations

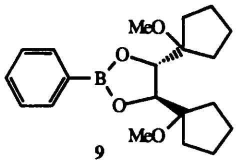
Once the force fields had been formulated, calculations were carried out to check that the parameters would reasonably reproduce the calculated structures **5a**, **5b** and **6b**. In all cases, molecular mechanics calculations on structures **5a**, **5b** and **6b** produced structures which were very similar to those calculated

Table 5 'Ate'- complex sub-structure for boronate-carbonyl complex **6**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| −9 | C3-B3(-O3-C3)(-O3-C3)*O2 = C2 | | | | | | |
| −2 | | | | | | | |
| 1 | 1 | 2 | | | 1.6093 | 1.4470 | |
| 1 | 2 | 3 | | | 1.4000 | 7.2854 | |
| 1 | 3 | 4 | | | 1.3834 | 7.1165 | |
| 1 | 2 | 5 | | | 1.4000 | 7.2854 | |
| 1 | 5 | 6 | | | 1.3834 | 7.1165 | |
| 1 | 2 | 7 | | | 1.8083 | 5.5000 | |
| 1 | 7 | 8 | | | 1.2070 | 10.8000 | |
| 1 | C2 | 8 | | | 1.3510 | 9.6000 | |
| 1 | O3 | Lp | | | 0.6000 | 4.6000 | |
| 1 | O2 | Lp | | | 0.0010 | 6.1000 | |
| 2 | 1 | 2 | 7 | | 98.8452 | 4.7328 | |
| 2 | 1 | 2 | 3 | | 105.3792 | 4.7328 | |
| 2 | 1 | 2 | 5 | | 105.3792 | 0.5000 | |
| 2 | 5 | 2 | 7 | | 98.8450 | 0.5000 | |
| 2 | 3 | 2 | 7 | | 98.8450 | 0.5000 | |
| 2 | 3 | 2 | 5 | | 109.5000 | 0.5000 | |
| 2 | 2 | 5 | 6 | | 133.6762 | 0.5000 | |
| 2 | 2 | 3 | 4 | | 133.6762 | 0.5000 | |
| 2 | 2 | 7 | 8 | | 134.5820 | 0.5000 | |
| 2 | H1 | 1 | 2 | | 108.3851 | 0.5000 | |
| 2 | C3 | 1 | 2 | | 108.3851 | 0.5000 | |
| 2 | C3 | 6 | 5 | | 107.6400 | 0.5000 | |
| 2 | H1 | 6 | 5 | | 113.7214 | 0.5000 | |
| 2 | C3 | 4 | 3 | | 107.6400 | 0.5000 | |
| 2 | H1 | 4 | 3 | | 113.1600 | 0.5000 | |
| 2 | C3 | 8 | 7 | | 122.7214 | 0.5000 | |
| 2 | C3 | 8 | C3 | | 122.7214 | 0.5000 | |
| 2 | H1 | C3 | 8 | | 108.3851 | 0.5000 | |
| 2 | C3 | 8 | C2 | | 115.0000 | 0.4000 | |
| 2 | C2 | 8 | 7 | | 124.5000 | 0.5000 | |
| 2 | C2 | C2 | 8 | | 117.6000 | 0.6000 | |
| 4 | 1 | 2 | 7 | 8 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 1 | 2 | 5 | 6 | 2.1530 | 6.7950 | 0.0970 |
| 4 | 1 | 2 | 3 | 4 | 2.1530 | 6.7950 | 0.0970 |
| 4 | 1 | 2 | 5 | Lp | 0.0000 | 0.0000 | 0.0000 |
| 4 | 1 | 2 | 3 | Lp | 0.0000 | 0.0000 | 0.0000 |
| 4 | 1 | 2 | 7 | Lp | 0.0000 | 0.0000 | 0.0000 |
| 4 | 1 | C3 | C3 | H1 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 1 | C3 | C3 | 8 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 1 | C3 | 8 | 7 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 2 | 3 | 4 | H1 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 2 | 3 | 4 | C3 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 2 | 5 | 6 | H1 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 2 | 5 | 6 | C3 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 2 | 7 | 8 | C3 | 0.8000 | 1.0000 | −1.9000 |
| 4 | 2 | 7 | 8 | C2 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 2 | 7 | 8 | H1 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 2 | 1 | C3 | C3 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 2 | 1 | C3 | H1 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 2 | 1 | C3 | 8 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 3 | 2 | 5 | 6 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 3 | 4 | C3 | H1 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 3 | 2 | 1 | C3 | 1.1080 | −2.0600 | −0.2110 |
| 4 | 3 | 2 | 1 | H1 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 3 | 2 | 1 | C2 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 3 | 2 | 7 | 8 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 3 | 2 | 7 | Lp | 0.0000 | 0.0000 | 0.0000 |
| 4 | 3 | 2 | 5 | Lp | 0.0000 | 0.0000 | 0.0000 |
| 4 | 4 | C3 | C3 | H1 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 4 | 3 | 2 | 7 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 5 | 2 | 3 | 4 | −14.8140 | 6.6806 | −0.2360 |
| 4 | 5 | 2 | 1 | C3 | −14.8140 | 6.6806 | −0.2360 |
| 4 | 5 | 2 | 1 | H1 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 5 | 2 | 1 | C2 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 5 | 2 | 7 | 8 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 5 | 2 | 7 | Lp | 0.0000 | 0.0000 | 0.0000 |
| 4 | 5 | 6 | C3 | C3 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 6 | 5 | 2 | 7 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 6 | C3 | C3 | H1 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 7 | 8 | C2 | C3 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 7 | 8 | C2 | H1 | −0.5500 | 2.5000 | 3.0000 |
| 4 | 7 | 8 | C2 | C2 | 0.9100 | 10.3800 | 0.9100 |
| 4 | 7 | 8 | C3 | C3 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 7 | 8 | C3 | H1 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 8 | C2 | C2 | C2 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 8 | C2 | C2 | H1 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 8 | C3 | C3 | C3 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 8 | C3 | C3 | H1 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 8 | C2 | C2 | C3 | 0.0000 | 0.0000 | 0.0000 |
| 4 | C2 | C2 | 8 | C3 | 0.1500 | 10.3800 | 0.0000 |
| 4 | C3 | 1 | 2 | 7 | 0.0000 | 0.0000 | 0.0000 |
| 4 | H1 | 1 | 2 | 7 | 0.0000 | 0.0000 | 0.0000 |
| 4 | C2 | 1 | 2 | 3 | 0.0000 | 0.0000 | 0.0000 |
| 4 | 7 | 2 | 3 | Lp | 0.0000 | 0.0000 | 0.0000 |
| 4 | | | | | | | |
| 8 | −0.4601 | 1.2310 | −0.7268 | 0.3175 | −0.7542 | 0.3235 | |
| 8 (cont) | −0.4618 | 0.5308 | | | | | |

by *ab initio* calculations (*vide supra*); all bond lengths were virtually identical with only minor differences in some bond angles.

In order to test the force field for the arylboronate **5a** further (as noted above, few crystal structures are currently available which are relevant to force fields for **5b** and **6b**) calculations were carried out on a recently reported crystal structure prepared in these laboratories;[3b] *i.e.* phenylboronate ester **9**.



**9**

Molecular mechanics calculations[22] on ester **9** produced a global energy minimum structure which reproduced the crystal structure with good agreement, as shown in Fig. 1. Most of the differences between the crystal and calculated structures were around the periphery of the structure and may very well be explained by the effects of crystal packing *versus* the gas-phase calculation.[23] Although there were 166 conformations found within 3 kcal mol$^{-1}$‡ of the global energy minimum, the boronate sub-structure remained unchanged in all these calculated structures. The only differences between these higher energy conformations were due to different conformations and orientations of the methoxypentyl rings of **9**.

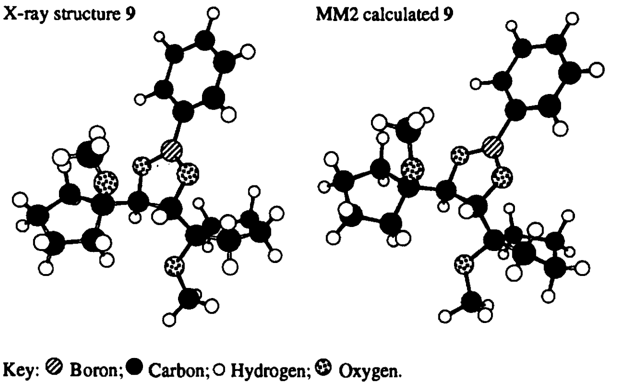


Fig. 1 X-Ray *vs.* MM2 calculated structures of compound **9**

Having examined structure **9**, attention was turned to the structures which were the main reason for initiating this project, *i.e.* the highly stereoselective reduction reactions of **1** and **2**,[3,4] and examination of these reactions to probe the effect of possible mediation by 'ate' -complexes **3** and **4**, respectively, as originally proposed by Molander.[4] For these structures, the

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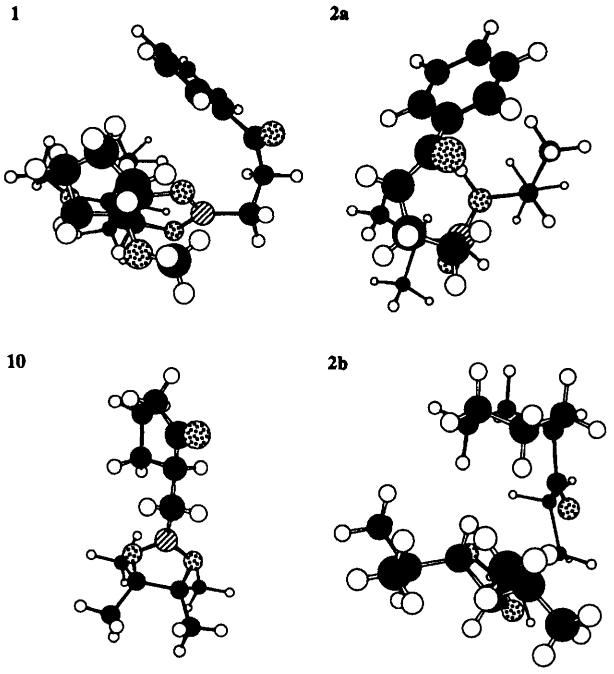
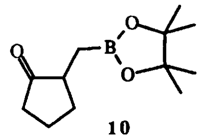
‡ 1 cal = 4.184 J.



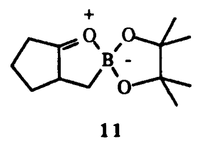
Key: ⊘ Boron; ● Carbon; ○ Hydrogen; ❂ Oxygen.

**Fig. 2** MM2 calculated structures of uncomplexed boronates

main questions which needed to be addressed were as follows: (i) Whether unchelated structures **1** and **2** could adopt low energy conformations which could provide face-selective blocking of the carbonyl groups. (ii) If structures **1** and **2** were incapable of providing face-selective blocking in the unchelated state, could chelated molecules **3** and **4** provide a basis for providing facial blocking of the carbonyl groups during the reduction reaction and therefore what is the origin of the sense of asymmetric induction observed for ester **3**, **4a** and **4b**? (iii) Cyclopentanone boronate **10** gave higher levels of stereocontrol when reduced with borane than might only be explained by simple steric influences of the methyl boronate function alone,[3b] is it possible that was also due to the formation of the chelate **11** in conjunction with steric effects?



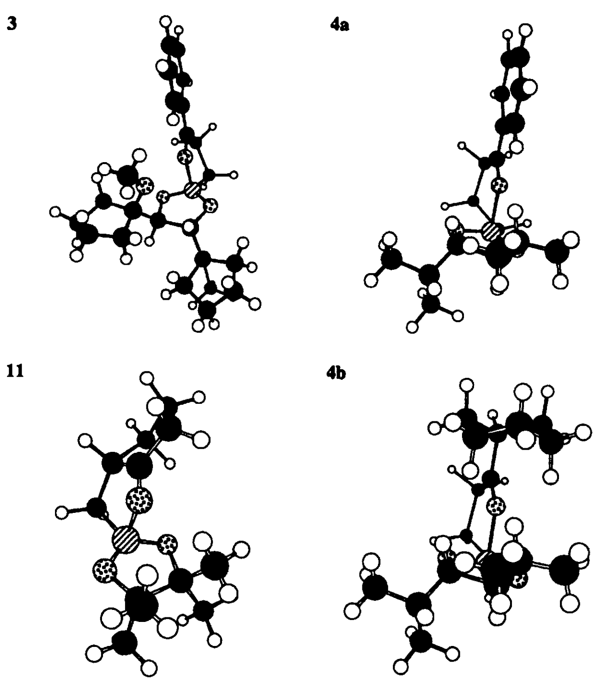
**10**



**11**

Molecular mechanics calculations[22] were therefore initiated on each of the structures **1**, **2a**, **2b**, **3**, **4a**, **4b**, **10** and **11**. The MM2 calculated global energy minimum for each of the unchelated carbonyl compounds are shown in Fig. 2 with the corresponding chelated derivatives in Fig. 3.

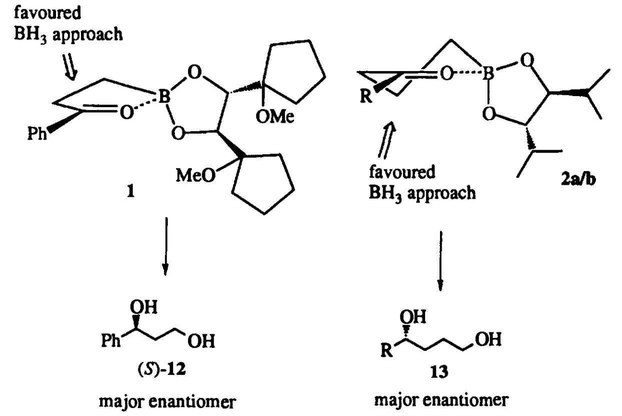
For each of the unchelated structures (Fig. 2), it is clear that there is relatively little selective steric blocking of either face of any of the carbonyl functions of **1**, **2a** and **2b**. This conclusion is reinforced upon examination of higher energy conformations for each of these structures, *i.e.* structures **1**, **2a** and **2b** have a large number of conformations which are accessible within 3 kcal mol$^{-1}$ of the global energy minimum (220 for **1**, 123 for **2a** and 193 for **2b**). The fact that a large number of conformations were found within 3 kcal mol$^{-1}$ of the global energy minima shows that no overall control of a reduction process is likely for these unchelated structures and a mixture of stereoisomers would be obtained upon reduction with borane. For cyclopentanone **10**, however, only 12 conformations were found, all of which were within 2 kcal mol$^{-1}$ of the global energy minimum. All these conformations (including that shown in Fig. 2) have the boronate ester moiety oriented away from the carbonyl group, which suggests little impact is exerted by the boronate upon any reduction process occurring at the carbonyl group.



Key: ⊘ Boron; ● Carbon; ○ Hydrogen; ❂ Oxygen.

**Fig. 3** MM2 calculated structures of carbonyl complexed boronates

In contrast, the complexed boronate structures shown in Fig. 3 show very different results from those in Fig. 2. Firstly, considering complex **3**, the (*S*,*S*)-diol ester shows preferential blocking of the *Si*-face of the phenyl ketone which would result in the (*S*)-alcohol upon reduction and is found experimentally to be the major product. This is also the case for the majority of the 129 conformations found within 3 kcal mol$^{-1}$ of the global energy minimum. However, the (*S*,*S*)-diol esters **4a** and **4b** effectively have the opposite configuration [note the change in priority for determination of (*R*) *versus* (*S*) for the diol esters of **3** and **4**] to **3**, and as can be seen from the global energy minima in Fig. 3, the *Re*-faces of each ketone are blocked to a greater extent than the *Si*-faces, which would result in preferential formation of the (*R*)-alcohols in each case. This is also found experimentally. Examination of higher energy conformations of **4a** and **4b** (8 and 67, respectively, within 3 kcal mol$^{-1}$) reveal a similar trend. These results are summarised by Scheme 1.



**Scheme 1**

Comparing cyclopentanone **11** with derivatives **3** and **4** (Fig. 3), shows that this molecule is much simpler structurally in comparison with boronates **1** and **2**. Only two conformations were found for this molecule, the second was within 2 kcal mol$^{-1}$ of the global energy minimum structure. Examination of the structures calculated for **11** show that there is some difference between the two conformations, but not sufficient to explain the highly face-selective reduction reaction that is observed with borane.[3b] It therefore confirms conclusions reported earlier, that the reduction of **10** is controlled in terms of stereochemistry by the same stereoelectronic effects as 2-methylcyclopentanone, rather than the boronate moiety. However, the boronate may still intervene, presumably merely affecting the rate of reduction.

## Summary

In summary, an MM2 force field has been developed for boronate esters and their carbonyl complexes. This force field was used to provide evidence for the following facts. (i) Unchelated structures **1** and **2** cannot adopt low energy conformations which could provide face-selective blocking of the carbonyl groups. (ii) The asymmetric induction in the reductions of **1** and **2** can be explained by intervention of chelated molecules **3** and **4**, which provide a basis for causing facial blocking of the carbonyl groups. (iii) Reduction of cyclopentanone boronate **10** could involve the intervention of chelate **11**, but this does not significantly affect the stereochemical outcome of the borane mediated reduction.

Although this force field has been used to model boronate systems which have been used to develop new methods for remote asymmetric induction processes,[3,4,24] the force field could be applicable for modelling boronate esters of natural products[25] and, in particular, understanding the recognition of carbohydrates *via* arylboronate complex formation.[26] Moreover, understanding simple boronate–carbonyl complexation has obvious application to Lewis-acid complexation of aldehydes prior to allylation reactions.[2] Further studies in these areas will be reported in due course.

## Acknowledgements

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## Supplementary material

All supplementary material, including the MM2 force fields and all calculated structure files can be accessed and down-loaded from the following web site; http://uchsg11.ch.umist.ac.uk/model/index.htm; or contact *via* e-mail: awhit@dir.mcc.ac.uk.

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calculation of vibrational frequencies to check that these structures were true minima; and (iv) Molecular dynamics simulations on the lowest energy conformer from each search was used to comfirm that no further low energy structures could be found.

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