Appendix I

A.1 Boron, Borazine & Diazaborines

As a main group element *i.e.* no partially filled orbitals for *l* 'orbital angular momentum quantum number' ≥ 2.0, boron is commercially extracted from *borax* ($Na_2[B_4O_5(OH)_4]\cdot 8H_2O$), and *kernite* ($Na_2[B_4O_5(OH)_4]\cdot 2H_2O$), which are naturally abundant in Mojave Desert, California.[*] A combination of high ionisation energy and charge to radius ratio, renders B^{3+} completely non-existent in any chemical compounds, as even the most spherical bases such as F^- will become distorted, resulting in a breakdown of true ionic bonding, and hence propensity towards covalency; as such, all boron containing compounds are covalent in character. In addition, in the absence of Lewis bases, all boron compounds are inherently '*trivalent*' by virtue of low excitation energies (Fig. AI).[*]

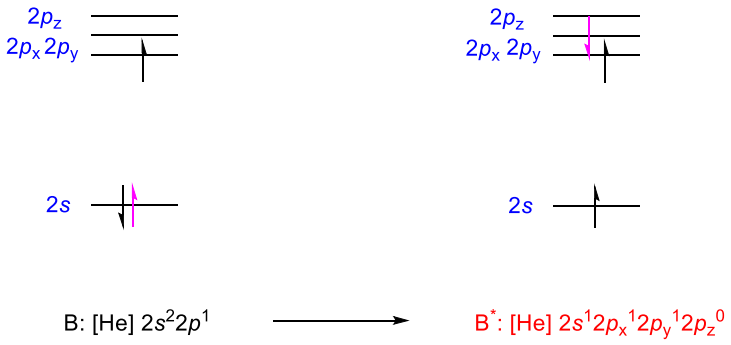


Figure AI Electron configuration of boron in the gas phase.

Thus, all BX_3 compounds are '*trigonal planar*' and exhibit a X–B–X bond angle of ~ 120° *e.g.* BCl_3, BBr_3 *etc.* This leaves trivalent boron compounds with vacant $2p_z$ orbitals (Fig. AI), so as to act as Lewis acids and form acid-base adducts with Lewis bases *e.g.* amines, compensating for the '*electron deficiency*' of boron, and generating '*electron-precise*' structures which are therefore stable; *nota bene*: B–N is *isoelectronic* with C–C.

To this end, borazine which is both '*isoelectronic* and *isostructural'* with benzene can be obtained from the action of ammonium chloride on sodium borohydride. Similar but different to benzene, borazine is also a colourless liquid at ambient temperatures with an aromatic odour which bears the closest peripheral resemblance to benzene, as well as other physical properties, in particular, density which is identical for both *i.e.* 0.81 g cm^{-3}. Whilst theoretical calculations[†] have shown that the nitrogen lone pairs in borazine may be delocalised in a similar fashion to that of benzene (Fig. AII), the chemical reactivity of borazine is in a stark contrast to that of benzene; in point of fact, borazine decomposes on storage, but benzene is fairly stable. Likewise, borazine is susceptible to attack by both nucleophiles and electrophiles on its boron and nitrogen constituents, respectively.

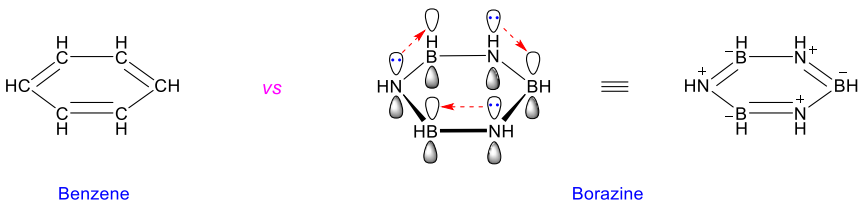


Figure AII Borazine features a Kekule type structure similar to benzene.

Imidazo-fused diazaborines which serve as intermediary structures somewhat along the two extremes *i.e.* benzene and borazine, had been of particular interest to Dewar[‡] and Snyder[§] more than 60 years ago. On his first account of these aromatic boronic acids, Dewar reported his obtained oxazaborine as a '*trivalent*' boron species, and the thus obtained diazaborine **3**[‡] in a manner that has been reported by us herein *cf.* Experimental p. S6.

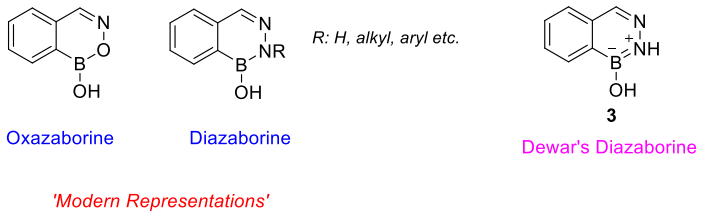


Figure AIII Trivalent and quadrivalent diazaborines.

Inasmuch as diazaborines and oxazaborines are typically drawn as '*trivalent*' boron species today, as opposed to that in the old literature (Fig. AIII), a brief discussion of such an indolence and ignorance merits a revision. For though, bonding in boron species has never been straightforward to such an extent that the orthodox 'ethane' like diborane *i.e.* $H_3B–BH_3$,[**] which conferred to the paradigmatic rules of molecular structure, in particular, hybridisation and electronegativity was later evolved to a more realistic '*3-centre 2-electron*' bonding, which augments reality so as to mock the type of structural arrangements that have been observed for diborane B_2H_6 by means of X-ray diffraction.[††] Such augmented realities led to the 1976 Nobel Prize in Chemistry for William N. Lipscomb.[‡‡] Longuet-Higgins who was an undergraduate at Balliol College, in Oxford, also came to the same conclusion as Schlesinger[††] about bonding in diborane.[§§] This is intriguing in virtue of the fact that Dewar was also completing either his BA or MA at Balliol College in Oxford when Longuet-Higgins was an undergraduate in the late '30s,[***] as such whether these two scholars who revolutionised our understanding of bonding in boron compounds influenced one another or even copied each other, remains a mystery, but what cannot be undermined in the face of the significance of these two Oxford alumni's contributions to knowledge, is the role of Oxford in advancing chemical sciences, in particular, boron chemistry as evidenced by the work of their successors here as elsewhere.[†††]

As illustrated above (Fig. AIII), Dewar initially envisaged oxazaborines as trivalent boron species, as it goes a long way against the grain of electronegativity and structural chemistry to have the more electronegative oxygen as an '*oxonium ion*', and the more electropositive boron as a '*boronate anion*' sitting comfortably next to one another; however, Dewar was a controversial figure, and never afraid of expressing his views.[***] This coupled with his '*π-complex theory*',[‡‡‡] which later developed into Dewar-Chatt-Duncanson model,[§§§] gave him the confidence to draw even oxazaborines as well as diazaborines as formally charged and '*quadrivalent*' boron species (Fig. AIV).[****]

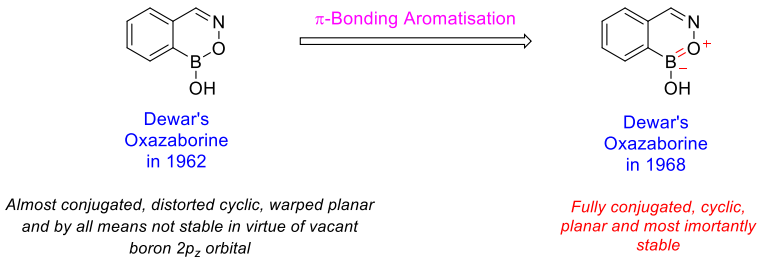


Figure AIV It took Dewar several years to propose the correct structure of oxazaborines.

Support for the above assertion is provided by the fact that, as Dewar himself reiterated, these true heteroaromatic boronic acids, in particular, diazaborine **3** (Fig. AIII):

> *"[…] may be recovered after boiling for 2.0 hours in 15% potassium hydroxide or 12 N hydrochloric acid. Aliphatic hydrazones or aromatic boronic acids would be destroyed by this treatment. [Diazaborine **3**] is not deborylated by bromine in refluxing acetic acid. To our knowledge this is the first example of a borazaro compound containing more than two heteroatoms that withstands such treatment."*[‡]

In the light of what has been said above, what makes borazine with an '*aromatic odour*' and a density identical to that of benzene, not to forge the kind of '*aromatic inertness*' towards chemical reactivity that has been observed for both benzene and diazaborines, is something that cannot be fully explained by our current embryonic models of chemical bonding, as the conceptual '*orbital hybridisation*' is flawed, and looks upon molecules as though they are inanimate; however, molecules are animate, and it is this '*electronics*' of the molecules which makes us also animate, and gone astray by hybridisation and X-ray diffraction techniques, as though the atomic nuclei are just dead skeletons which all pretty much look similar. Thus, if we are to have a full understanding of chemical bonding, in particular, peculiar bonding in boron species and beyond, we must come out of the '*hybridisation prison cell*', and start visualising molecules the way in which they are, and not how we would like to perceive them with hybridisation models *e.g. sp*, sp^2, sp^3 *etc.* To this end, the explanation that I can offer for the intense chemical reactivity of borazine, in spite of its aromatic odour and some physical similarities with benzene, is that whilst borazine is cyclic and almost planar (Fig. AII), it is not '*fully conjugated*' such that the electrons flow erratically, contrary to that of say, diazaborines or benzene (Fig. AV).

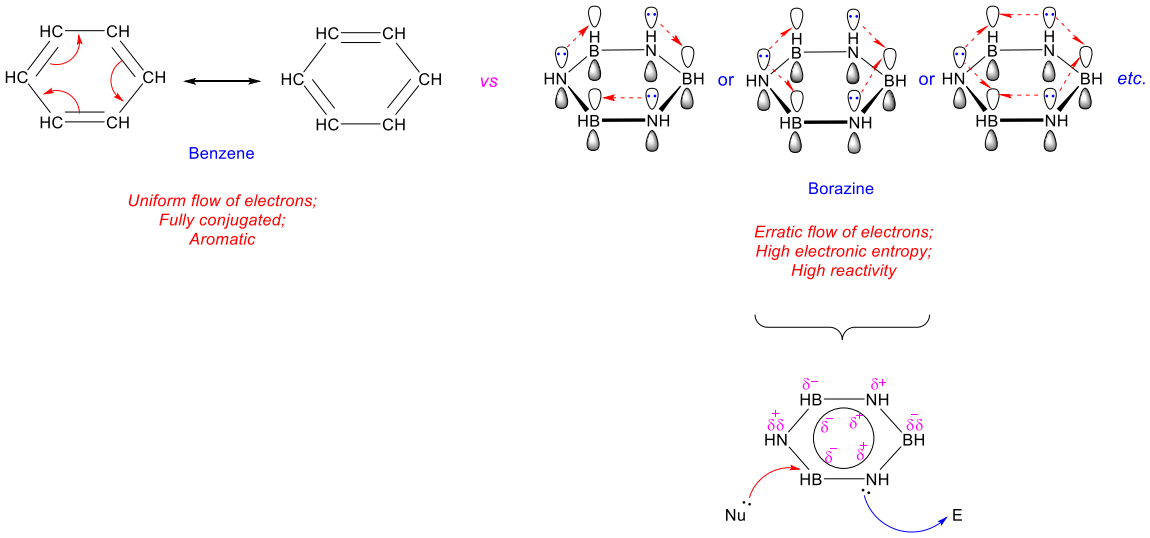


Figure AV It is not '*electronegativity*' that renders borazine highly reactive relative to benzene; '*electronic entropy*' is very likely to be responsible for such peculiar phenomena, as the nitrogen in borazine is just as electronegative as that found in '*kinetically inert*' diazaborines and oxazaborines.

It is this '*electronic imbalance*' – no matter how symmetrical borazine may be delineated by X-ray diffractors – that provides the entropic driving force for chemical reactivity so as to make the overall Gibbs free energy of the system negative *i.e.* $\Delta G < 0$, and hence spontaneous reactivity, which is yet again another application of entropy.

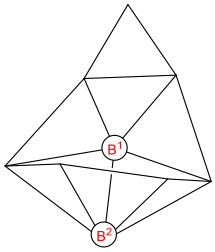
A.2 Boron NMR

Unlike ^{1}H and ^{13}C with a '*nuclear spin*' $I = ½$, both naturally occurring isotopes of boron *i.e.* ^{10}B ($I = 3$) and ^{11}B ($I = 5/2$) are NMR active; however, the latter is more versatile than the erstwhile for NMR investigations by virtue of the fact that ^{10}B has a natural abundance of only 19.6%, whereas ^{11}B exhibits a natural abundance of 80.4%,[††††] as such ^{10}B comes with a much lower receptivity *i.e.* receiver gain (RG), and quadrupole moment almost thrice as much as that for ^{11}B, which broadens ^{10}B NMR signals. Moreover, the Larmor frequency of ^{10}B is almost three times lower than that for ^{11}B, resulting in a much lower signal resolution and coupling constants *i.e.* J (in Hz) in ^{10}B NMR spectra.[‡‡‡‡] Despite these drawbacks ^{10}B NMR can be particularly useful in niche mechanistic studies such as rearrangements.[§§§§]

NMR spectroscopy much to contemporary efforts has proved exceptionally advantageous in elucidating structures of boron compounds, and their behaviour in solutions.[*****,†††††] The extrapolation of NMR activities of other common NMR active nuclei such as ^{1}H, ^{13}C, ^{15}N, ^{31}P *etc.*, to ^{11}B NMR suggests that the following factors should determine chemical shifts (δ) in ^{11}B NMR spectra:

- Electron density
- Coordination number
- Hybridisation
- Ring current

However, the above is found not to be true for many ^{11}B NMR spectra. For example, the signals from B^1 and B^2 in the ^{11}B NMR spectrum of *n*-B_9H_{15} are ~ 64.7 ppm apart, such that B^2 resonates at the highest field and B^1 at the lowest field in the aforementioned ^{11}B NMR spectrum,[‡‡‡‡‡] in spite of both B^1 and B^2 in *n*-B_9H_{15} exhibiting identical connectivity, hybridisation and even immediate bonding environment (Fig. AVI).



n-B_9H_{15}

Capped Archimedean Antiprism

Figure AVI Despite having identical coordination and chemical environment the signals from B^1 & B^2 are the furthest apart from each other in B^{11} NMR spectrum of *n*-B_9H_{15}. Both B^1 & B^2 are connected to five other boron atoms and one proton in the capped Archimedean antiprism *n*-B_9H_{15}; *nota bene*: for simplicity protons are omitted from the borane cluster.

On the other hand, in a stark contrast to other NMR active nuclei, electron density does not appear to preponderate over other factors in determining the position of chemical shifts in ^{11}B NMR spectra, as the boron atoms of higher electron density in $B_7H_7^{2-}$ are less shielded than their counterparts of lower electron density in the same cluster.[§§§§§]

To this end, there are no hard and fast rules as yet to fully predict or explain some of the anomalies that have been observed for ^{11}B NMR spectra, and each and every single boron compound can give rise to distinctive and unexpected ^{11}B NMR spectra, which have been observed for the novel boronate esters herein, and forms the basis of the discussions below.

A.3 Structural Assignments of Diazaborines & Boronate Esters

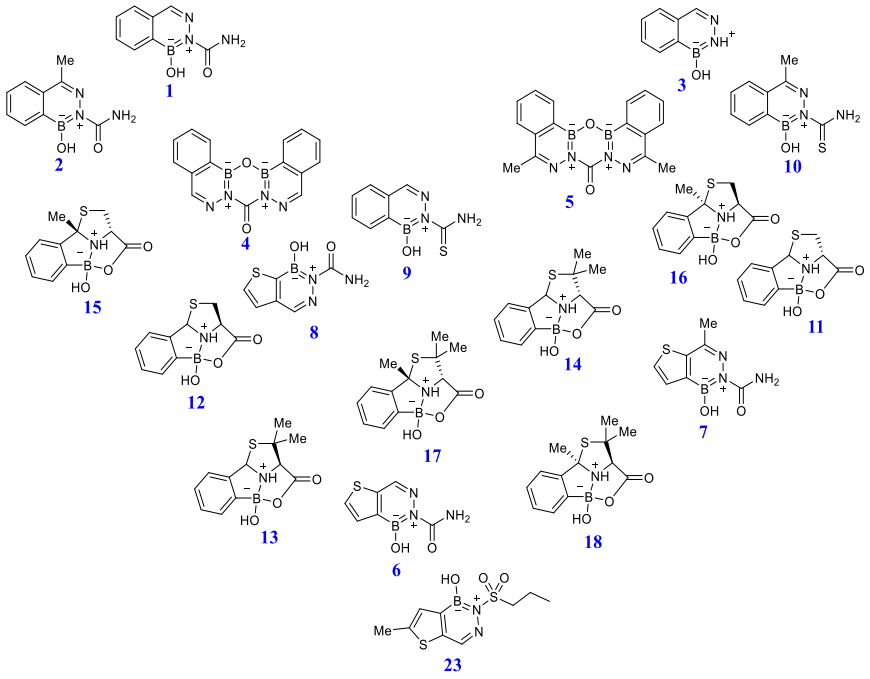


Figure AVII Benzodiazaborines, diazaborines & boronate esters.

Whilst almost all the diazaborines (Fig. AVII) as well as boronate ester **12**[******] described in this work have, one way or another, been reported in the literature, and we were not the first to investigate them, we were, by all means, the first to delineate a '*tetracyclic caged*' structure for novel boronate esters **11** & **13**–**18**, and report full chemical characterisation *i.e.* mp, optical rotation, IR, NMR (^{1}H, ^{13}C & ^{11}B), LC-MS and HRMS of the aforementioned benzodiazaborines, diazaborines and novel boronate esters *cf.* Experimental p. S4–S21 & S24–S26 for which to the best of our knowledge there are no known precedents.

Given that the proposed '*tetracyclic caged*' structure for boronate ester **12** has been observed *in crystallo* (Fig. AVIII) by us (unpublished data), and in solution by Gao and coworkers,[******] it is conceivable that based on the observed spectroscopic and X-ray crystallographic data, the boronate esters **11** & **13**–**18** should also follow suit.

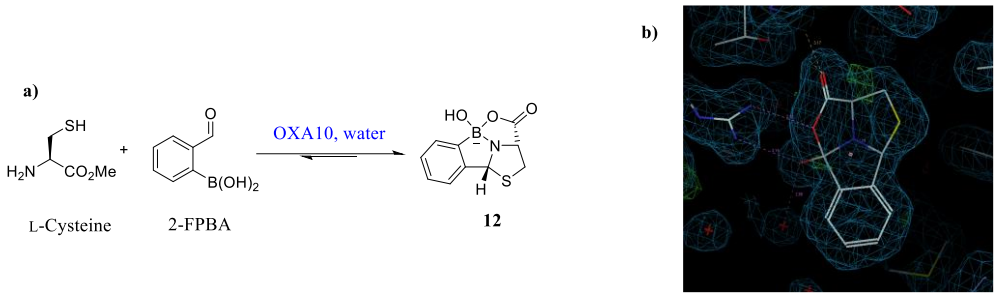


Figure AVIII a) DCC of L-cysteine methyl ester with 2-FPBA on the surface of OXA-10; b) X-ray crystal structure of the boronate ester 12 on OXA-10 (courtesy of Dr Jürgen Brem).

Inasmuch as, both the diazaborines and boronate esters herein presumably, almost certainly feature '*quadrivalent*' boron species (Section A.1), a comparison of chemical shifts (*vide infra)* in ^{11}B NMR spectra of the thus obtained diazaborines and boronate esters (Fig. AVII) not only provides structural insight into these novel scaffolds, but also paves the way for a better understanding of bonding in such boron species, and salient factors in their ^{11}B NMR resonance frequencies.

Reference has already been made to the unpredictability and irregularity of trends in ^{11}B NMR resonance frequencies (Section A.2); however, typically, though it need not of necessity, the vacant $2p_z$ orbital of boron plays a crucial role in the position of chemical shifts in ^{11}B NMR spectra. Strictly speaking, trivalent boron species resonate at much lower fields than their quadrivalent counterparts. For instance, trimethyl borane as a true trivalent boron species resonates at the lowest field, whereas trimethyl borate as a somewhat quadrivalent boron species with considerable π-bonding character resonates at much higher fields in ^{11}B NMR.

The belief that the determinant factor in the position of chemical shifts in ^{11}B NMR spectra is the π-donating ability of substituents on boron, implies that diethylamino substituents on boron should bring about upfield shifts for the ^{11}B signals in their NMR spectra, relative to that from –OMe by virtue of the fact that $–NEt_2$ is mesmerically more π-donating than –OMe. However, this effect appears to be reversed in aliphatic boron species, as such $B(NEt_2)_3$ resonates at a much lower field in ^{11}B NMR than that observed for $B(OMe)_3$.[††††††]

The chemical shift δ_R^C (in ppm) between a compound C and reference R is given by the following equation:

$$\text{Eq. I} \qquad \delta_R^C = 10^6 (H_C - H_R) / H_R \approx 10^6(\sigma_C - \sigma_R)$$

Where H_C and H_R are the resonance frequencies of the applied magnetic field for compounds C and R, respectively, and σ_C and σ_R are the resulting shielding tensors. Ramsey[‡‡‡‡‡‡,§§§§§§] has devised an expression for calculating the NMR shielding tensor σ, as such for most solution NMR applications the shielding tensor σ can be replaced by a scalar quantity σ to give the following equation:

$$\text{Eq. II} \qquad \sigma = \frac{e^2}{2mc^2} \langle 0 | \sum_j (x_j^2 + y_j^2)/r_j^3 | 0) \rangle$$

Neglecting the deferential overlaps of the above expression can lead to the following simplified expression for the chemical shift δ_i of the nucleus of atom *i*:[****]

$$\text{Eq. III} \qquad \delta_i = Aq_i + \sum_{j \neq i} Bq_j / r_{ij}^3$$

Where q_i is the π-electron density of atom *i*, r_{ij} is the internuclear distance between atom *i* and *j*, and *A* and *B* are constants. To this end, another salient factor other than the π-donating capabilities of the substituents attached to boron in ^{11}B NMR, would be the '*electronic cloud*' of the substituents attached to boron *i.e.* the availability of lone pairs above and below of the plane of the π-bond.[****] As exemplified by the last equation above (Eq. III), atoms *j* with lone pairs orthogonal to the plane of the covalent bond would have a significant impact on the chemical shift by virtue of a large q_j and small r_{ij} (Table A.1).

Table A.1 ^{1}H, ^{13}C, ^{11}B and IR Data for 2-FPBA, Diazaborines & Boronate Esters

Entry	^{11}B[§]	C*HO*/*γ*-C*H*/*δ*-C*H*[¥]	*C*HO/*γ*-C/*δ*-C[¶]	IR: C=O[†]
2-FPBA	29.9	10.05	197.0	
1	29.8	8.08	142.7	1673s
2	29.8		146.9	1687s
3	27.7	7.96	140.4	
4	16.2[‡]	8.35[‡]	175.5[‡]	1682s
5	28.3			1683s
6	28.6	8.20	140.0	1698s
7	28.4		142.4	1699s
8	28.8	8.15	145.0	1700s
9	29.9	8.13	144.0	
10	30.0		147.6	
11[*]	11.4	6.16	65.6	1730s
13[*]	11.3	6.25	71.2	1713s
15[*]	11.1		66.8	1715s
17[*]	11.5		76.2	1723s

[*]; Boronate esters **11**, **13**, **15** and **17** are enantiomers of **12**, **14**, **16** and **18**, respectively, with identical spectroscopic data. [§]; 193 MHz, acetonitrile-d_3. [¥]; 600 MHz, acetonitrile-d_3. [¶]; 151 MHz, acetonitrile-d_3. [‡]; benzodiazaborine **4** is much less soluble in acetonitrile-d_3, its NMR spectra were recorded in methanol-d_4 instead. [†]; ν_{max}/cm^{-1} (ATR), s stands for sharp.

Analysis of the ^{1}H, ^{13}C and ^{11}B NMR data above (Table A.1), on looking more closely, reveals that whilst the boron in 2-FPBA has a much greater trivalent character, less shielded and non-aromatic relative to that of quadrivalent diazaborines which should be more shielded, they all absorb at about the same field in their ^{11}B NMR; on the flipside, the proton of the formyl group in 2-FPBA, resonates at a much lower field than that from *γ*-C*H* of the benzofused-imadazo ring in their ^{1}H NMR by virtue of greater shielding that the *γ*-C*H* moieties of benzofused-imadazo rings experience, which is in a stark contrast to that observed for ^{11}B NMR. The same is also true for ^{13}C NMR data, the *γ*-*C*H and *γ*-*C*Me of the imidazo rings are significantly upshifted compared to the non-ring carbon of the formyl group in 2-FPBA (Table A.1).

Intriguingly, the solvation effects of methanol-d_4 on benzodiazaborine **4** (*vide infra*) relative to that of acetonitrile-d_3 for its closely related benzodiazaborine **5** has clearly been echoed by both the upshifted and downshifted signals from boron and *γ*-*C*H of benzodiazaborine **4** in its ^{11}B and ^{13}C NMR spectra, respectively.

The ^{11}B chemical shifts from the boronate esters, in comparison with those from the diazaborines, exhibit a whopping three-fold upfield shift in their spectra, in spite of the fact that both species are quadrivalent, and potentially negatively charged.

Whilst the aromaticity of diazaborines can play a crucial role in the observed data, as illustrated above (Eq. III) the electronic cloud of heteroatoms with available lone pairs adjacent to the boron centre in question can account for the aforementioned large upfield shift of almost 20 ppm in their ^{11}B NMR spectra (Fig. AIX).

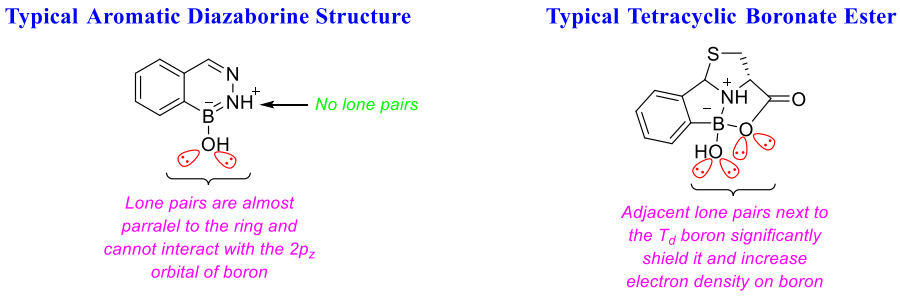


Figure AIX The accessible electronic cloud of the oxygens on boron can account for the upfield shift in ^{11}B NMR of the '*tetracyclic caged*' boronate esters.

In view of the above, it is conceivable that the boronate esters are tetracyclic and '*ring-closed*', as if they were '*ring-open*' and tricyclic, the thus C_{3h} boron species, would be less shielded, and would absorb at about the expected field in ^{11}B NMR, just like that of 2-FPBA with similar chemical environment and shielding effects (Fig. AX).

Figure AX Both ^{11}B centres *i.e.* D_{3h} in 2-FPBA, and that *i.e.* C_{3h} in the '*ring-open*' boronate esters should resonate with similar frequencies in ^{11}B NMR by virtue of similar bonding and shielding effects; however, the boron signal is upshifted in ^{11}B NMR spectra of '*ring-closed*' boronate esters (Table A.1).

The effects of electronic cloud of adjacent substituents on boron (Fig. AIX) is further evident from the upshifted signal of the boron in benzodiazaborine **4** in its ^{11}B NMR spectrum in methanol-d_4 *i.e.* δ_B 16.2 (Fig. AXI), relative to that obtained in acetonitrile-d_3 for benzodiazaborine **5** *i.e.* δ_B 28.3 (Table A.1).

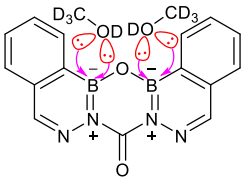


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Figure AXI No matter what the hybridisation of boron is, the solvation effect of methanol-d_4 is sufficient to significantly shield the boron centres in benzodiazaborine 4.

Further support for the assertion that the aforementioned boronate esters (Fig. AVII) are '*ring-closed*' and tetracyclic is provided by the upfield shift of their *δ-C*H and *δ-C*Me signals in ^{13}C NMR, relative to that observed for the *C*=O of their precursors *i.e.* 2-FPBA and 2-APBA, which suggests that the D_{3h} carbon of the formyl or acyl moieties, is now a T_d centre, bonded to four substituents, and fully saturated. This arrangement brings the carboxyl moiety in the '*ring-open*' structure in close proximity to the boronic acid so as to further cyclise, close the ring and form a '*tetracyclic caged*' structure. This is in agreement with the observed IR frequencies *i.e.* ~ 1730–1710 cm^{-1} expected for esters (Table A.1), as the parent carboxyl moieties should resonate at lower frequencies *i.e.* ~ 1600–1550 cm^{-1}.

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