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C═O and C═S bond activation by an annulated 1,4,2-diazaborole†

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The reaction of an ambiphilic 1,4,2-diazaborole with C═O and C═S bonds results in formal (3 + 2) cycloaddition and has allowed the synthesis of a family of 1,3,2-oxazaborole and 1,3,2-thiazaborole derivatives. Computational calculations have indicated a dipolar mechanism where the π bond is concertedly activated *via* the Lewis acidic boron centre and the nucleophilic C5 position of the 1,4,2-diazaborole. In the case of methylisothiocyanate, preference for C═S over C═N addition is observed, and has been rationalized according to mechanistic calculations. A spirocyclic bis(1,3,2-thiazaborole) has been observed from the double activation of CS_2.

Introduction

The activation of π-bonds by ambiphilic metal centres according to the Dewar-Chatt-Duncanson model[1–3] is a cornerstone of transition metal catalysis, facilitating the hydroelementation,[4–11] metathesis,[12–19] and catenation[20–26] of unsaturated bonds. This interaction involves the donation of electrons from a π bond of an unsaturated substrate to a vacant metal orbital and simultaneous backdonation from the metal to a vacant substrate π* orbital. This has the net effect of lengthening and weakening the bond and lowering its thermodynamic barrier to reactivity. An essential component of this activation is the ambiphilicity of the metal centre, serving as both a Lewis acid and base in this interaction.

This concept was extended to bimolecular main group systems through the advent of frustrated Lewis pairs,[27–30] where non-interacting Lewis acid/base pairs have been shown to activate challenging substrates such as hydrogen,[31–34] C–H bonds,[35–38] as well as a wealth of π-bonded species in the absence of transition metals.[39–44] More recently, ambiphilic boron heterocycles have been shown to activate a large variety of unsaturated species such as alkenes, alkynes, carbonyls, and arenes[45–52] and their applications in catalytic CO_2 hydroboration and *N*-formylation have recently been reported.[53]

Despite the multitude of reports involving diboron systems, aromatic B_1-heterocycles have received considerably less attention as platforms for bond activation.[54–57] Aromatic 1,4,2-diazaboroles were first prepared by Kinjo and co-workers,[58] and were shown to be boron nucleophiles, participating in a B-centred electrophilic fluorination reaction with Selectfluor. Our research group recently reported a novel tricyclic 1,4,2-diazaborole featuring a dearomatized annulated pyridyl group.[59] This species displays markedly increased reactivity with respect to monocyclic analogues, and its reaction with various borane Lewis acids resulted in the formation of ring-expanded 1,4,2,5-diazadiborinine derivatives *via* a 1,3-dipolar addition. These observations made us question whether this reactivity could be extended to heterocycle formation *via* the activation of polar unsaturated bonds. Herein, we report the activation of C═O and C═S bonds by an annulated 1,4,2-diazaborole to form 1,3,2-oxazaborole and 1,3,2-thiazaborole derivatives. Notably, while other borole derivatives have been previously observed to react with C═O/S bonds *via* 1,2-insertion to form ring-expanded products,[51,60,61] we here report the first examples of (3 + 2) cycloaddition reactions with these unsaturated species (Scheme 1).

Results and discussion

In an initial experiment, a solution of the annulated 1,4,2-diazaborole **1** in benzene was placed under an atmosphere of CO_2 and was heated at 80 °C overnight, resulting in a colour change from deep red to pale brown. Removal of the solvent, followed by washing of the residue with n-hexane yielded a colourless solid. An ^{11}B NMR spectrum of this material revealed a single resonance at 7.0 ppm. ^1H NMR indicated a C_1 symmetric molecule and the presence of 2-pyridyl and mesitylimi-

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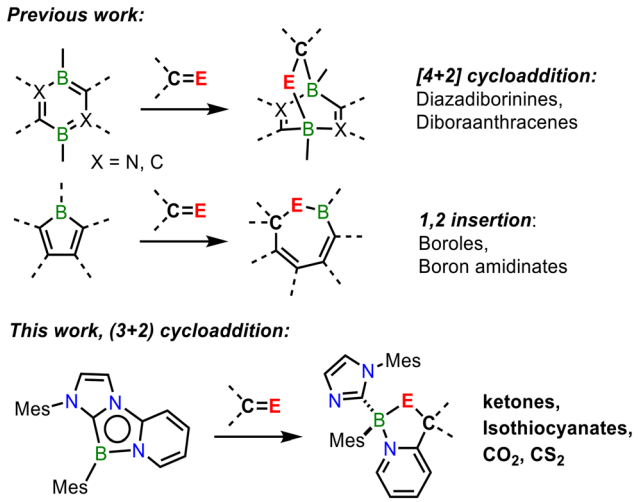
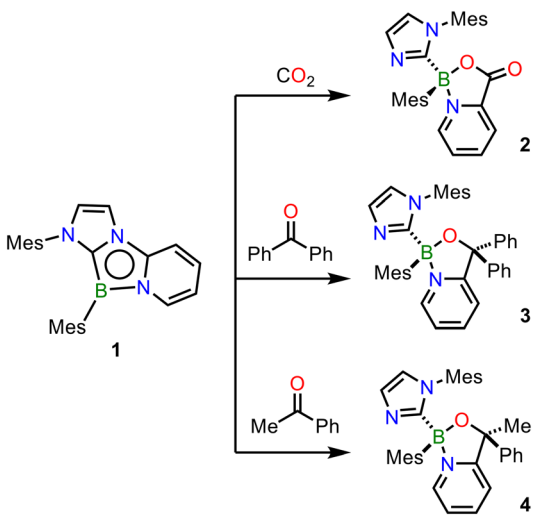


Scheme 1 C═O and C═S bond activation by boron heterocycles.

dazol-2-yl moieties. The appearance of a new peak at 163.4 ppm in the $^{13}C\{^1H\}$ NMR suggested the incorporation of the CO_2 moiety *via* esterification. A single crystal X-ray diffraction study revealed the product **2** as a 1,3,2-oxazaborole derivative (Scheme 2, Fig. 1).

To shed light on the mechanism of this transformation, the reaction of **1** with CO_2 was investigated using DFT methods (M062X-D3/Def2SVP). The first transition state is a rate-limiting (3 + 2) cycloaddition of the C═O bond across the B2–C5 positions of the 1,4,2-diazaborole **1**. This transition state is asynchronous yet concerted, where the C–C bond is formed slightly before the B–O bond (Fig. S26 in the ESI†). This intermediate subsequently undergoes loss of the imidazole moiety *via* C–N bond cleavage, concomitant with re-aromatization of pyridine ring to form the 1,3,2-oxazaborole derivative **2**.

To explore the scope of this novel bond activation, the reaction of **1** with ketones was next attempted. Treatment of a



Scheme 2 Reactions of **1** with C═O bonded species.

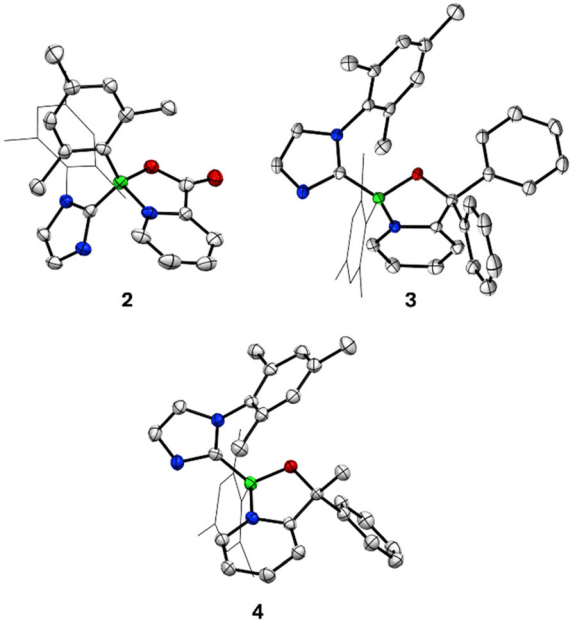


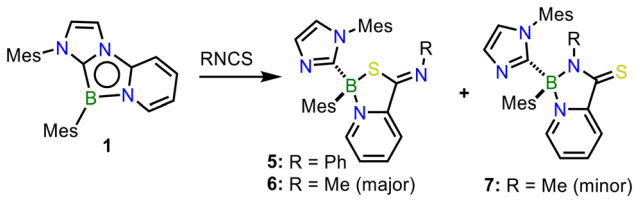
Fig. 1 Molecular structures of compounds **2**, **3** and **4**. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity. Mesityl groups are drawn as wireframe for clarity where appropriate. Selected bond lengths (Å): (**2**) B–N: 1.620(4), B–O: 1.521(4), B–C_{Imidaz}: 1.605(4). (**3**) B–N: 1.627(2), B–O: 1.484(3), B–C_{Imidaz}: 1.617(3). (**4**) B–N: 1.605(6), B–O: 1.483(6), B–C_{Imidaz}: 1.615(6). (grey = carbon, blue = nitrogen, red = oxygen, green = boron).

benzene solution of **1** with benzophenone at 75 °C cleanly resulted in the formation of a new product after 24 h. Similar to **2**, ^1H NMR indicated a C_1 symmetric product bearing both mesitylimidazol-2-yl and 2-pyridyl moieties. ^{11}B NMR revealed a single resonance at 9.2 ppm. A single crystal X-ray diffraction study indicated the product **3** is similarly derived from cycloaddition of the C═O bond across the C–N–B linkage of **1** (Scheme 2, Fig. 1). A reaction with acetophenone (60 °C for 24 h) also afforded the analogous compound **4**, and its structure was confirmed crystallographically (Scheme 2, Fig. 1). Notably, only one diastereomer of compound **4** was observed. Somewhat surprisingly, the reaction of **1** with these bulky ketones were observably faster than with CO_2, suggesting that these latter reactions are facilitated by the relative electrophilicity of the ketone carbonyl centres. Accordingly, no reactivity was observed of **1** with esters, amides, isocyanates, or carbodiimides under more forcing conditions. This observation is also in line with the calculated reaction barriers for these transformations (21.6 kcal mol^{-1} for **2**, 17.4 kcal mol^{-1} for **4**) (M062X-D3/Def2SVP). In all cases, these compounds are generated as racemic mixtures.

This reactivity was next extended to C═S bonded species in the form of isothiocyanates. The presence of both C═N and C═S bonds in the same molecule was particularly intriguing due to the possibility of regioisomerism in the reaction products. An equimolar reaction of **1** and phenylisothiocyanate at room temperature over the course of 1 hour cleanly afforded a new product **5** with an ^{11}B NMR resonance at 3.7 ppm. A

single crystal X-ray diffraction study revealed **5** to be the 1,3,2-thiazaborole derivative (Scheme 3, Fig. 2) derived from selective (3 + 2) cycloaddition of the C=S bond. Interestingly, preferential C=N bond activation of isothiocyanates had been previously observed with boroles by Martin and co-workers.[61] In these systems, it is proposed that adduct formation between the Lewis acidic B centre and the nucleophilic N atom precedes 1,2 insertion, resulting in the selective C=N incorporation in the ring expanded products. Conversely, it has been calculated in the formation of **5** that C–C bond formation occurs first *via* nucleophilic attack of the C5 position of **1** on the isothiocyanate carbon (Fig. S26†). The bulkier N–Ph moiety likely results in steric preference for subsequent B–S bond formation and the exclusive formation of a 1,3,2-thiazaborole in this case.

We next examined the reactivity of a sterically unencumbered isothiocyanate. A reaction of **1** with MeNCS under analogous conditions produced a mixture of two products clearly identifiable by ^{1}H NMR in an approximate ratio of 9 : 1. An ^{11}B NMR spectrum revealed a peak at 3.1 ppm corresponding to the major product and an additional minor resonance at 1.4 ppm. When single crystals were grown directly from the reaction mixture, a three-component co-crystal was obtained. The first component was free MeNCS; the second component was the C=S activated 1,3,2-thiazaborole isomer **6** (Scheme 3, Fig. 2). The final component was substitutionally disordered, the minor contributor of which (39%) is also compound **6**. The major contributor (61%) of this component is the C=N activated 1,3,2-diazaborole isomer **7** (Scheme 3, Fig. 2), indicating that C=N activation is competitive with C=S activation in this case. As these compounds co-crystallize, attempts to purify **7** from the reaction mixture were unfortunately unsuccessful. However, compound **6** could be isolated through repeated recrystallization and was fully characterized.



Scheme 3 Reactions of **1** with isothiocyanates.

The formation of C=N *versus* C=S activated products in the reaction of **1** with MeNCS was evaluated computationally (Fig. 3). The formation of compound **6** follows a similar mechanistic pathway as **2**, **4**, and **5** involving a concerted (3 + 2) cycloaddition of the C=S bond with an energy barrier of 20.6 kcal mol^{-1} (Fig. 3). However, the formation of **7** was determined to follow a stepwise mechanism involving distinct C–C (**TS 1**) and C–N (**TS 1′**) bond formation steps. Despite the greater thermodynamic stability of **7**, the barrier to formation of **6** (20.6 kcal mol^{-1}) is lower than that of **7** (23.9 kcal mol^{-1}), which is in good agreement with the observed reaction selectivity.

Given the propensity of **1** to activate C=S bonds, its reactivity with CS_2 was next evaluated. This more strongly electrophilic compound resulted in an instantaneous reaction at ambient temperature to form a new product **8**, which crystallized directly from the reaction mixture (Scheme 4). An ^{11}B NMR spectrum revealed a new resonance at 5.7 ppm. A single crystal X-ray diffraction study revealed **8** to be a spiro compound bearing two fused 1,3,2-thiazaborole rings that share a

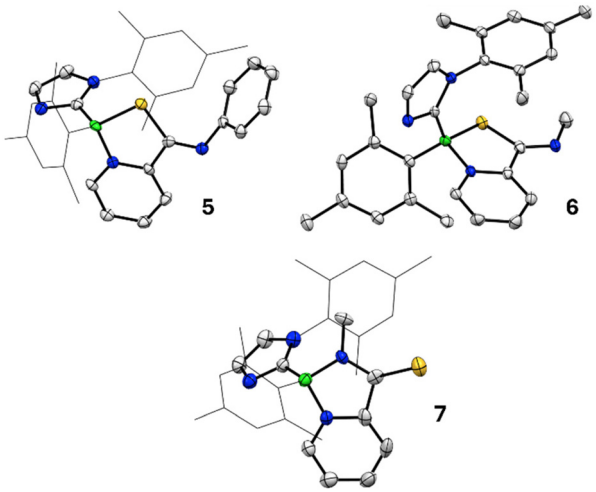


Fig. 2 Molecular structures of **5**, **6** and **7**. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity. Mesityl groups are drawn as wireframe for clarity where appropriate. Selected bond lengths (Å): (**5**) B–N: 1.605(4), B–S: 1.963(4), B–C_{Imidaz}: 1.608(4). (**6**) B–N: 1.616(6), B–S: 1.959(5), B–C_{Imidaz}: 1.615(6). (**7**) B–N: 1.613(6), B–N_{MeNCS}: 1.507(13), B–C_{Imidaz}: 1.610(6). (grey = carbon, blue = nitrogen, yellow = sulfur, green = boron).

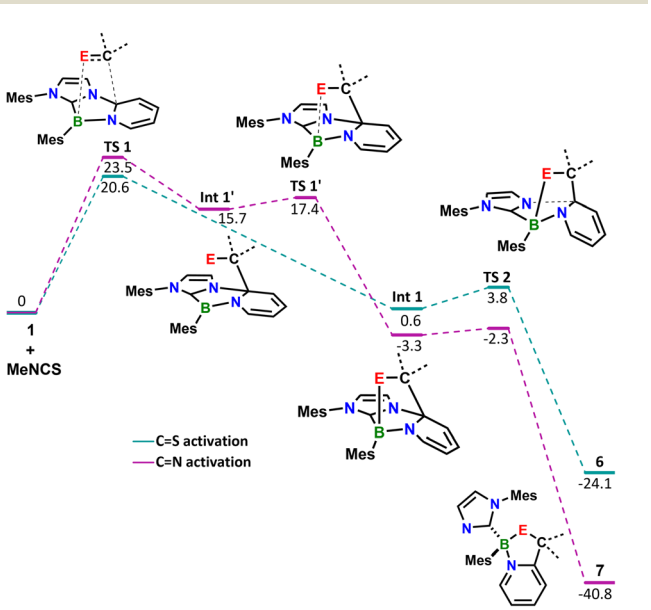
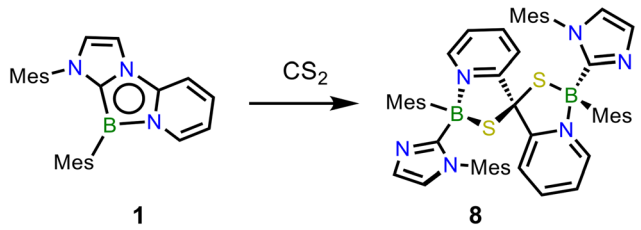


Fig. 3 Computed reaction pathways for the formation of **6** and **7** from **1** and MeNCS (M062X-D3/Def2SVP). Values are given in kcal/mol.



Scheme 4 Reaction of **1** with CS_2.

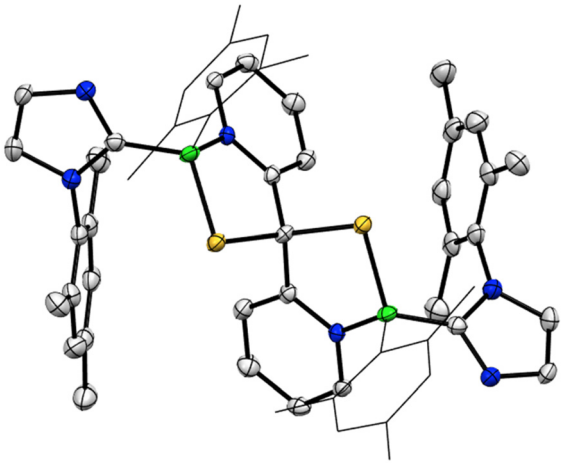


Fig. 4 Molecular structure of **8**. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity. Mesityl groups are drawn as wireframe for clarity where appropriate. Selected bond lengths (Å): B–N: 1.611(6), B–S: 1.962(5), B–C_{Imidaz}: 1.625(6), C–S: 1.841(3). (grey = carbon, blue = nitrogen, yellow = sulfur, green = boron).

common carbon centre (Fig. 4). This reaction is highly selective toward the double addition product **8** – a deficiency of CS_2 in this reaction results in the formation of a mixture of **8** and unreacted **1**. Mechanistically, it was found the formation of **8** also proceeds similarly *via* a double (3 + 2) cycloaddition of both C=S moieties across two equivalents of **1** (Fig. S26†).

Conclusion

In summary, we have determined the reactivity of an annulated 1,4,2-diazaborole **1** with various C=O and C=S bonded species to form rare examples of 1,3,2-oxazaboroles and 1,3,2-thiazaboroles *via* (3 + 2) cycloaddition. These transformations constitute a unique reaction pathway in the activation of π bonds by boron heterocycles, and display unusual regioselectivity in the preferential activation of C=S bonds of isothiocyanates.

Data availability

The data supporting this article have been included as part of the ESI.† Crystallographic data for **2**, **3**, **4**, **5**, **6**, [**6**·(**6**/**7**)], and **8** has been deposited at the CCDC under accession numbers 2431184, 2431182, 2431179, 2431181, 2431190, 2431186, and 2431178 and can be obtained from **https://www.ccdc.cam.ac.uk/**

Conflicts of interest

There are no conflicts to declare.

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