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Dalton Transactions

COMMUNICATION

Cycloaddition Reactions of (C$_6$F$_5$)$_2$BN$_3$ with Dialkyl Acetylenedicarboxylates

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The 1,3-dipolar cycloaddition reactions of the electron deficient boron azide, (C$_6$F$_5$)$_2$BN$_3$ (1) with the electron-poor acetylenes RO$_2$CC≡CCO$_2$R (R = Me, Et) afforded the new *mono*- and *bis*-1,2,3-triazole derivatives 5 and 6.

"Click reactions" including the synthesis of 1,2,3-triazoles from the cycloaddition reaction between an azide and an alkyne were first described in 2001 by Kolb, Finn and Sharpless.[1-5] Such reactions have found broad utility in organic synthesis including pharmaceutical chemistry, polymer synthesis and material science as these reactions are rapid and offer high yields with no waste by-product. Typically Cu or Ru salts are used to catalyse the azide-alkyne cycloaddition.[6-11] Nonetheless, uncatalysed click reactions have been known to be affected at elevated temperatures for over 100 years although such reactions frequently result in mixtures of 1,4- and 1,5-regio-isomers.[12]

Boron azide compounds (R$_2$BN$_3$)[13-20] can be readily synthesised from salt elimination reactions of R$_2$BCl with NaN$_3$ or the substitution reactions of R$_2$BCl with Me$_3$SiN$_3$. Nonetheless, applications of boron azides are relatively scarce. Boron azides have been used as precursors to borylnitrenes,[21-26] and the boron azides R$_2$BN$_3$ [R = C$_6$F$_5$ (1), Cy (2)] were employed in Staudinger phosphine oxidations affording boron-substituted phosphinimine derivatives.[27] More recently, (C$_6$F$_5$)$_2$BN$_3$ was shown to undergo aromatic C-H activation of benzene and toluene when reacted with boron substituted alkynes.[28] In 2012, Curran *et al.* reported the reactivity of the electron-rich NHC-boryl azide 3 with electron-deficient alkynes, alkenes and nitriles,[29] while Bettinger *et al.* have reported that although the boryl azide, 2-azido-4,4,5,5-tetramethyl-1,3,2-dioxaborole (pinBN$_3$, 4)[30] reacts with cyclooctyne, it does not react with electron-poor acetylenes such as MeO$_2$CC≡CCO$_2$Me. Previously we have described the cycloadditions of more electron deficient boron azides with alkynes.[27, 31-32] For example, the boron azide Cy$_2$BN$_3$, generated *in situ*, undergoes catalyst-free cycloadditions generating novel boron-substituted heterocycles.[32] The varying reactivity of boron azides with RO$_2$CC≡CCO$_2$R described to date (Scheme 1) prompted us to probe the room

temperature catalyst-free reaction of the electron deficient (C$_6$F$_5$)$_2$BN$_3$ with dialkyl acetylenedicarboxylates. In this manuscript we show that the reactivity of (C$_6$F$_5$)$_2$BN$_3$ (Scheme 2) with alkynes is markedly different to that of Cy$_2$BN$_3$ (Scheme 1).
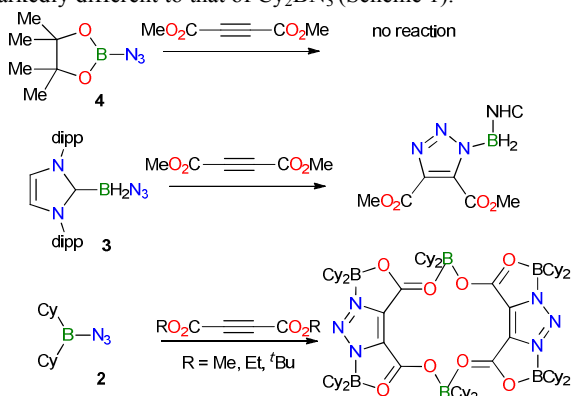
Scheme 1 Reactions of boron azides with dialkyl acetylenedicarboxylates.
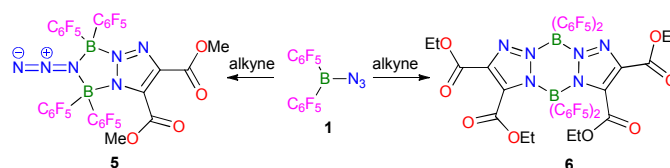
Scheme 2. Synthesis of 5 and 6.

The boron azide (C$_6$F$_5$)$_3$BN$_3$ (1) was synthesised in high yield *via* the method reported by Klapötke in 2000[20] from the 1:1 stoichiometric reactions of the chloroborane (C$_6$F$_5$)$_2$BCl[33] with trimethylsilyl azide. To avoid storage of the potentially explosive boron azide, 1 was prepared and subsequently reacted *in situ* with electron deficient acetylenes RO$_2$CC≡CCO$_2$R (R = Me, Et). In the initial case, the room temperature stoichiometric reaction of 1 with MeO$_2$CC≡CCO$_2$Me over 48h afforded a green solution. Removal of

the solvent resulted in a dark green oil which was recrystallised from a pentane/toluene solution to afford a small crop of large colourless crystals of **5** (Scheme 2). X-ray diffraction confirmed the identity of **5** as a bicyclic system bearing one triazole C_2N_3 ring fused to a B_2N_3 ring (Fig. 1). The triazole ring is essentially planar (max. deviation from planarity 0.002 Å). However the B_2N_3 ring deviates from a planar structure with the azide functionality lying out of the plane (the nitrogen atom bridging the boron atoms lies 0.225 Å from the ring plane) with the azide bent out of the ring plane by 165.1°. Two of the C_6F_5 groups adopt a near coplanar geometry (9.0° from coplanar) with ring centroid···centroid distances of just 3.44 Å, falling at the shorter end of the range observed for other C_6F_5···C_6F_5 π−π contacts (3.23 − 4.47 Å).[34] The resulting structure of **5** is comparable to those previously reported from reactions of Cy_2BN_3 with EtC≡CCOMe or $Ph_2P(=O)C≡CH$ which led to the formation of similar fused triazole and B_2N_3 rings.[32]

It is noteworthy that the boron azide **1** is known to exist in the solid state as a 1,1-azide-bridged dimer with a 4-membered B_2N_2 core.[20] Thus it is tempting to suggest that **5** arises from the 1,3-dipolar cycloaddition of one azide fragment of the dimer **1** with the alkyne affording the 1,2,3-triazole fragment. In this fashion the bridging coordination of a second equivalent of azide between the boron centres is maintained. However, $[(C_6F_5)_2BN_3]_2$ is known to dissociate in solution,[20] and a reaction pathway involving monomeric $(C_6F_5)_2BN_3$ is more likely and discussed further below.
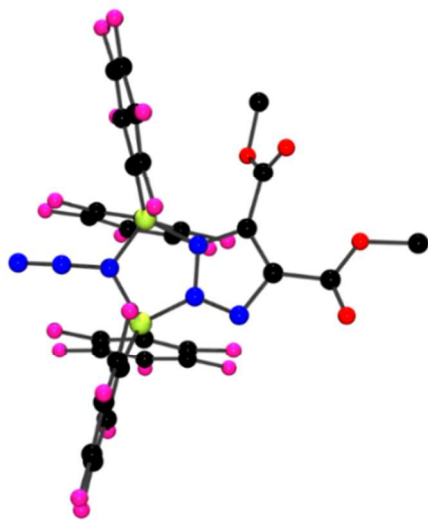

Fig. 1. POV-ray depiction of **5**. C: black, N: Blue, O: red, B: yellow-green, F: pink. H atoms omitted for clarity.

The corresponding reaction of **1** with $EtO_2CC≡CCO_2Et$ resulted in a dark red solution after stirring for 48h at room temperature. Removal of the solvent led to an oil which could be recrystallised from hexane over several months to give large colourless crystals of **6** (Scheme 2). The structure of **6** was determined by X-ray diffraction (Fig. 2). In contrast to **5**, the structure of **6** is comprised of a fused tricyclic system constructed from two 5-membered triazole rings bridged by two boron atoms leading to a central 6-membered N_4B_2 ring. Whilst the triazole rings are planar (max. deviation from planarity 0.004 Å and 0.009 Å) the central ring adopts a boat geometry due to the tetrahedral boron atoms. This has the effect of creating a molecular butterfly-type geometry with the triazole wings inclined by 138.4°

with respect to each other. Notably the two axially-disposed C_6F_5 rings are nearly parallel (7.2°) with a centroid···centroid separation of 3.45 Å, similar to that in **5**. It is interesting to note that **6** is not a centrosymmetric triazole dimer, suggesting that the thermodynamically favoured polar dimer is formed on prolonged exposure of the analogue of **5** to alkyne. Both **5** and **6** were fully characterised by NMR, mass spectroscopy and elemental analysis. Multinuclear NMR data for **5** reveal that its structure appears intact in solution as shown by a peak in the ^{11}B NMR spectrum around 0 ppm with no evidence for dissociation at room temperature to regenerate free triazole and $(C_6F_5)_2BN_3$ (δ = 43.9 ppm).[20]
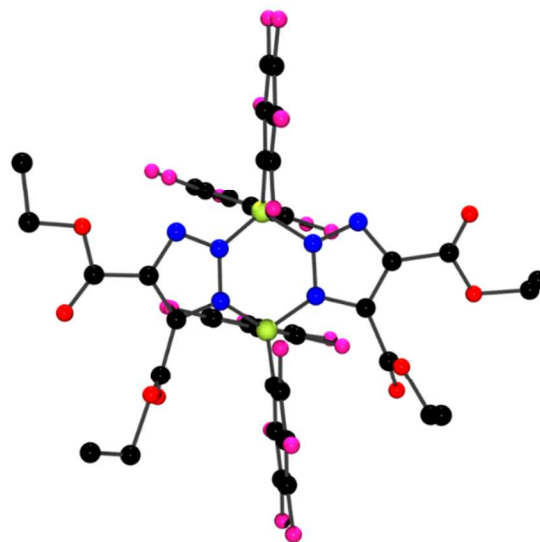

Fig. 2. POV-ray depiction of **5**. C: black, N: Blue, O: red, B: yellow-green, F: pink. H atoms omitted for clarity.

The chemistry of these boron-azide/triazole systems seems to be determined by the Lewis acidity of the boron centre which affords some degree of aggregation particularly in the solid state structures of these compounds. DFT studies[35] (B3LYP/6-311G*) indicate that reaction of the alkyne $MeO_2CC≡CCO_2Me$ and monomeric $(C_6F_5)_2BN_3$ occurs through interaction of the alkyne HOMO with the LUMO of the azide forming the anticipated 5-membered triazole ring, **I1** (ΔH = -200 kJ/mol) (see ESI). The Lewis acidity of boron and Lewis basicity of the central nitrogen atom of the triazole ring prompt capture of free $(C_6F_5)_2BN_3$ affording **5** (ΔH = -79 kJ/mol) (Scheme 3).
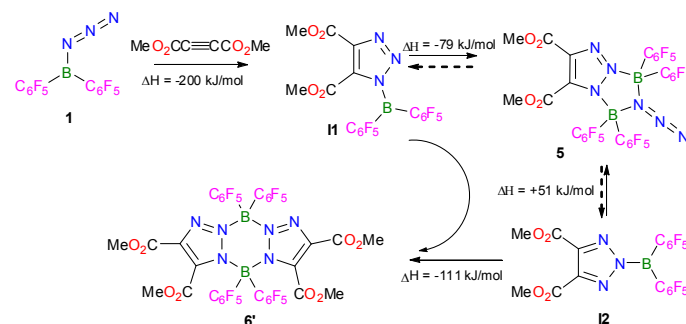
Scheme 3 Potential route for the synthesis of **5** and **6**.

Whilst formation of **5** appears to occur *via* a simple two-step process, the mechanism of formation of the polar dimer **6** is less evident. One plausible mechanism involves the dissociation of **5** regenerating $(C_6F_5)_2BN_3$ and intermediate **I2**, effectively affording a 1,2-migration of the $B(C_6F_5)_2$ moiety. Calculations reveal this is a low energy transformation ($\Delta H = +51$ kJ/mol). Reaction of **I2** with **I1** would afford the polar dimer **6'** (Scheme 3) ($\Delta H = -111$ kJ/mol).

The isolation of both 1:1 and 2:1 products based on a 1:1 stoichiometric reaction presumably reflects subtle differences in the stereo-electronics of the reaction chemistry such that the rate constant for formation compound **6** from intermediates **I1** and **I2** is comparable with that for formation of **5** from **I1** and unreacted $(C_6F_5)_2BN_3$. Both are associated with a Lewis acid-base aggregation process. In addition, given the low recovered yields (14% and 22% respectively), the isolation of 1:1 and 2:1 adducts may in part be driven by the relative solubilities of **5** and **6** under differing recrystallisation conditions. This does not preclude other species being present in solution as the isolated products were just the least soluble under the recrystallization conditions employed.

Previously, theoretical studies by Bettinger showed that tricoordinate boron azides act as ambiphilic 1,3-dipoles, whilst electron rich, NHC-stabilised tetracoordinate boron azides react preferentially with electron deficient alkynes.[30] Both Cy_2BN_3 and $(C_6F_5)_2BN_3$ act as electron-poor azides but reveal differing reactivity towards acetylenedicarboxylates. In this regard it is also noteworthy that Bettinger found that $PinBN_3$ does not react with acetylenedicarboxylates. Thus the unique products **5** and **6** appear to reflect the increased Lewis acidity of the B centre in **1**.

Conclusions

In conclusion, the boron azide $(C_6F_5)_2BN_3$ **1** reacts with dialkyl acetylenedicarboxylates to give mono and bis-triazole derivatives **5** and **6**. However, whilst these reactions are providing new insights into boron-azide cyloaddition chemistry, the low recovered yields and apparent diversity of reactivity preclude them from being described as conventional azide/alkyne "click reactions". These products contrast sharply with those derived from known "click" products derived from other boron azides and alkyl acetylenedicarboxylates. The subtly differing reactivity of $(C_6F_5)_2BN_3$ and Cy_2BN_3 towards alkyne carboxylates poses questions about the structure-reactivity relationships in these boron azides which can be potentially met through studies of other boron azides, R_2BN_3, as well as computational studies. Such efforts will be the subject of future publications.

Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental details, NMR data, DFT calculations and details of the crystal structure determination of **5** and **6**. CCDC 1041090 and 1041089. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b000000x/

‡ **Caution:** Covalent azides are potentially explosive and reactions were performed on a small scale behind blast shields.

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TOC Graphics

Catalyst-free Cycloaddition Reactions