

Application of nonmetallic frustrated cations in the activation of small molecules

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The concept of nonmetallic frustrated cations has been used in the small molecule activation. The *in situ* generated ambiphilic phosphinoborinium cation activated phenyl isocyanate, diisopropylcarbodiimide, and acetonitrile under very mild conditions without any catalyst, yielding single-, double-, or mixed-activation products. Furthermore, the mechanisms of the reactions of the phosphinoborinium cation with small molecules were elucidated using density functional theory calculations.

Introduction

The formation and breaking of chemical bonds are key steps in the activation of abundant and stable molecules, and represent critical challenges in chemical synthesis and catalysis, as well as for the chemical industry. To date, the activation of strong chemical bonds has been generally achieved using transition metals (TMs).^[1–4] The ability of these species to activate small molecules is closely linked to their electronic structure, where partially filled *d* orbitals of appropriate symmetry can interact with the frontier molecular orbitals of the substrate. The chemistry field known as “main-group metallomimetics”^[5–7] provides novel synthetic strategies using systems containing only globally available, earth-abundant elements of the *s* and *p* blocks. The discovery of frustrated Lewis pairs (FLPs) opened a new avenue in the application of main-group compounds for small molecule activation. FLPs are a combination of a Lewis acid and a Lewis base, where steric hindrance or a dissociative equilibrium prevents the formation of a classical Lewis acid–base adduct.^[8–10] Consequently, free acceptors (Lewis acids, usually boranes) and donors (Lewis bases, mostly phosphorus, nitrogen, carbon, and oxygen compounds) can simultaneously interact with a third (activated) molecule.^[11]

Within the main group of compounds capable of activating small molecules, low-coordinated boron compounds have attracted particular attention.^{[12],[13]} Among them, two-coordinate borinium cations $[R_2B]^+$ are especially noteworthy.^[14,15] The low coordination number of the B atom and the intrinsic electron deficiency make these species the most electron-poor boron compounds available. Despite these attractive features, only a few studies have reported the

activation of small molecules by two-coordinate borinium cations acting as strong Lewis acids (Scheme 1A). The acidic properties of Shoji's cation $[Mes_2B]^+$ are demonstrated by its reaction with CE_2 ($E = O, S$). The observed cleavage of the double $C=E$ bond leads to the formation of an aroyl cation.^{[16],[17]} The same cation undergoes twofold 1,2-carboration reactions with two 2 equiv of diphenylacetylene, yielding a two-coordinate cation bearing two substituted vinyl groups at the boron center.^[18] Moreover, Shoji's cation was utilized by the Stephan group for the activation of HD and Et_3SiH , generating the unstable borenium–mesitylene adduct $[MesB(E)(C_6Me_3H_2E)]^+$ ($E = H, D$) and the $[MesB(\mu-H)_2(\mu-Mes)BMes]^+$ cation, respectively.^[19] The $[MesBNiPr_2]^+$ borinium cation possessing mixed substituents reacts with isothiocyanate and carbodiimides, resulting in B–C insertion to afford nitrilium and borenium amidinate salts.^[20] The amino-substituted $[(iPr_2N)_2B]^+$ cation acts as a hydroboration agent toward alkyne, nitrile, ketone, and diazomethane (Scheme 1A).^[21] It should be noted that, despite the electron-donor properties of N atoms they do not interact directly with the small molecules, which can be attributed to the strong π -interactions between N and B.

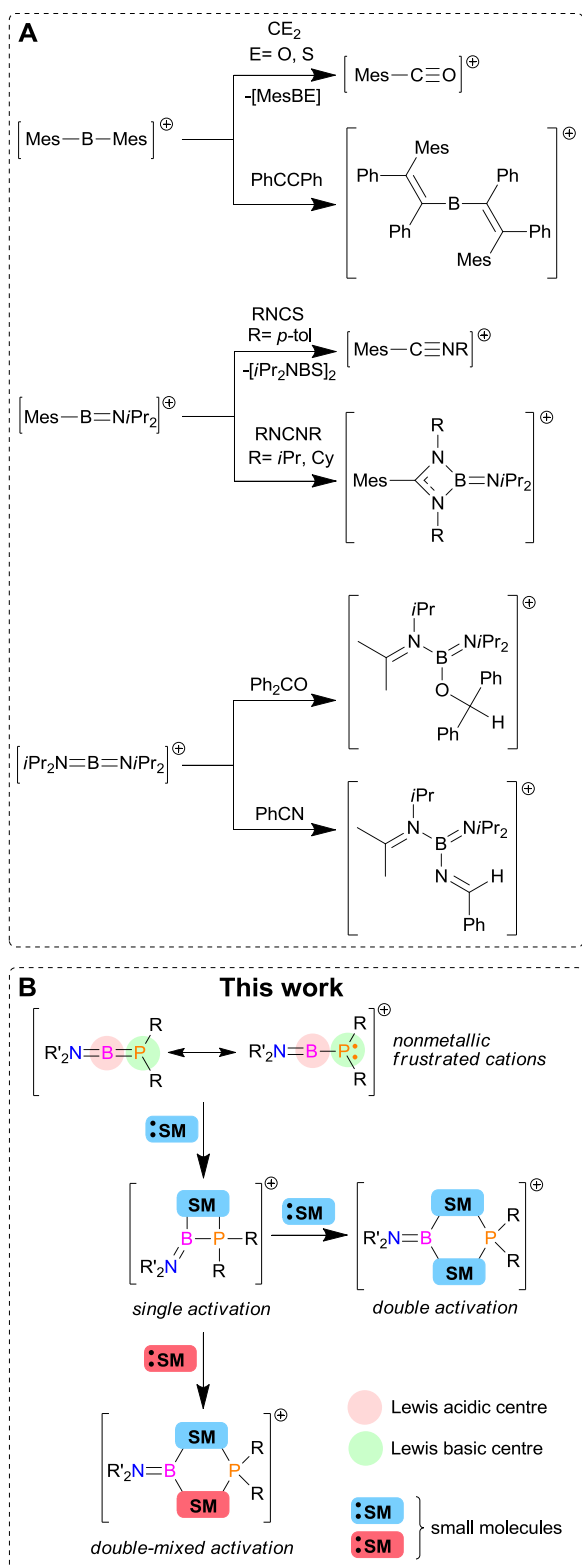
To date, among cationic species, the concept of frustrated Lewis pairs has been limited to transition metal cations, in particular to Zr(IV) compounds.^[22–30] To the best of our knowledge, no previous reports on nonmetallic frustrated cations (NFCs) are available; to fill this gap, we aimed to synthesize these reactive and ambiphilic species.

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Electronic Supplementary Information (ESI) available: Experimental, crystallographic, spectroscopic and computational details.



Scheme 1. Examples of borinium cations used in the activation of small molecules (A). Concept of nonmetallic frustrated cations (NFCs) (B).

Our group is investigating low-coordinate, ambiphilic B–P bond systems exhibiting high reactivity toward inert molecules.^[31–35] Within this research program, we introduced a P–B moiety into the structure of borinium cations, where the boron atom is substituted by amino and phosphanyl groups (Scheme 1B).

According to our hypothesis, strong π -interactions will only be present between B and N atoms, whereas the side-by-side overlapping of empty and filled valence orbitals of B and P atoms is not effective, owing to the different orbital shapes and energies. Therefore, the B–P bond possesses only partial double bond character and the phosphorus atom retains Lewis basic properties. NFCs are thus expected to be ideal small molecule activators because of the following reasons (Scheme 1B): i) in contrast to the known borinium cations, NFCs have both Lewis acidic and basic properties, and can serve as electron pair donors and/or acceptors (mimicking TMs); ii) the proximity of the B and P reactive centers will facilitate reactions with small molecules and promote the formation of thermodynamically stable cyclic systems; iii) the coordinative unsaturation and electron deficiency of the B atom will favor the addition of small molecules; moreover, a single NFC should be able to activate more than just one small molecule, or even two different molecules.

Results and discussion

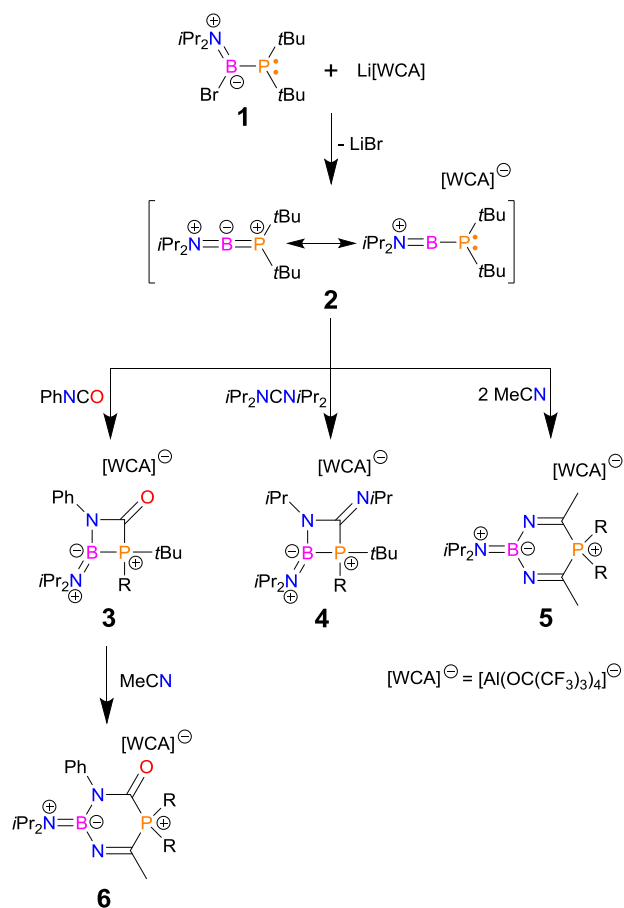
Encouraged by the results of our recent preliminary studies on phosphinoborinium cations,^[36] we decided to apply these species in the activation of small molecules and experimentally verify the concept of NFCs. The 2^+ NFC was generated *in situ* by Br^- abstraction from $i\text{Pr}_2\text{NB}(\text{Br})\text{PtBu}_2$ (**1**)^[33] using the lithium salt of the weakly coordinating anion $[\text{Al}(\text{OC}(\text{CF}_3)_3)_4]^-$ (WCA)^[37] in dichloromethane (Scheme 2). We tested the reactivity of 2^+ toward phenyl isocyanate, diisopropylcarbodiimide, and acetonitrile. A dichloromethane solution of a small molecule was added dropwise to an equimolar suspension of precursor **1** and $\text{Li}[\text{WCA}]$ in dichloromethane at -70°C . Then, the mixture was allowed to warm to room temperature and stirred overnight. The progress of the reactions was monitored by ^{11}B and ^{31}P NMR spectroscopy. Generally, the reactions of 2^+ with small molecules proceeded smoothly and cleanly, giving only one activation product. The LiBr precipitate was separated by filtration. The analytically pure salts **3**, **4**, **5**, and **6** were isolated by solvent evaporation and layering from of the resulting oil with pentane (**3**), by crystallization from a concentrated CH_2Cl_2 solution (**4**) or from $\text{CH}_2\text{Cl}_2/\text{pentane}$ solution at low temperature (**5**, **6**). The addition of 1 equiv of PhNCO to 2^+ afforded the three-coordinate borenium cation **3**⁺ bearing a four-membered BPCN ring. This species produced a broad doublet at 28.7 (bd, $^1J_{\text{BP}} = 119.3$ Hz) ppm in the ^{11}B NMR spectrum and a broad multiplet at 66.8 ppm in the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum. These data are consistent with the presence of a three-coordinate B atom and a direct B–P bond in the resulting activation product. Single-crystal X-ray structural analysis of salt **3** confirmed the formation of a four-membered ring and new B1–N1 and P1–C1 bonds between 2^+ and the PhNCO moiety (Figure 1).

Similar to the synthesis using PhNCO , the reaction of 2^+ with an equimolar amount of $i\text{PrNCN}i\text{Pr}$ also gave the four-membered cyclic borenium cation **4**⁺ (Scheme 2). The NMR spectroscopic signatures of **4**⁺ [^{11}B NMR: δ 27.4 ppm (bd, $^1J_{\text{BP}} = 106.4$ Hz); $^{31}\text{P}\{^1\text{H}\}$ NMR: δ 69.2 ppm (bm)] are very similar to those

observed for **3⁺**. These data suggested that the addition of a carbodiimide molecule to **2⁺** proceeded in a similar way to that observed for the reaction utilizing PhNCO. The X-ray diffraction analysis of the obtained colorless crystals of **4** (yield: 61%) confirmed this assumption (Figure 1).

We then explored the possibility to activate two molecules with one NFC. To this end, we reacted **2⁺** with 2 equiv of PhNCO or *i*PrNCN/*i*Pr. However, the monitoring of the progress of these reactions by NMR spectroscopy revealed only the formation of the single activation products **3⁺** and **4⁺** described above, respectively. We suspected that steric hindrance prevented the addition of a second molecule. Therefore, we decided to use a smaller molecule in the following experiments. The reaction of **2⁺** with 2 equiv of CH₃CN afforded the double-activation product **5⁺** (Scheme 2). The ¹¹B NMR spectrum of **5⁺** displayed a singlet in a similar range as that observed for **3⁺** and **4⁺**, with a chemical shift of 22.6 ppm. In contrast to the borenium cations described above, the ³¹P{¹H} NMR spectrum of **5⁺** consists of an upfield-shifted singlet at -32.7 ppm. The lack of ¹¹B NMR signal splitting and of a broad ³¹P{¹H} resonance suggested the absence of the B-P bond in **5⁺**. The X-ray diffraction analysis of **5** revealed the formation of a double-activation product (Figure 1). The *i*Pr₂NB and *t*Bu₂P fragments are connected by two CH₃CN moieties, forming a six-membered BNPCPN ring.

As the next step to assess the reactivity of the NFCs, we performed the activation of two different molecules using one NFC. For this purpose, **2⁺** was reacted successively with 1 equiv of PhNCO and 1 equiv of CH₃CN (Scheme 2). Similar to the borenium cations discussed above, the obtained cation **6⁺** exhibits ¹¹B NMR resonance at 26.6 ppm (s). Interestingly, the ³¹P{¹H} NMR spectrum shows a sharp singlet at 10.9 ppm (s) where the chemical shift is between those observed for **3⁺** (66.8 ppm) and **5⁺** (-32.7 ppm). The incorporation of two different small molecules into the structure of **6⁺** was further confirmed by X-ray diffraction analysis (Figure 1). The structure of **6⁺** resembles that of cation **5⁺**; however, in the case of **6⁺**, one CH₃CN moiety is replaced by a PhNCO fragment. The high reactivity of **2⁺** prevented its isolation as crystalline salt. In contrast to our previously reported [Cy₂NBP*t*BuPh]⁺ species,^[36] **2⁺** does not tend to dimerize, because of the bulkier phosphanyl group. Upon heating a suspension of **1** and Li[WCA] from -70 to 25 °C, very broad downfield ¹¹B and ³¹P{¹H} NMR signals appeared at 67.5 and 51.5 ppm, respectively, which could be attributed to monomeric **2⁺**. These signals disappeared within 1 h at room temperature, accompanied by an increase in the intensity of other signals, probably originating from solvent activation products (see ESI).



Scheme 2. Reactivity of borinium frustrated cation with small molecules. Synthetic details: solvent CH₂Cl₂; temperature from -70 to 25 °C; yields: 3–56%, 4–61%, 5–50%, 6–41%. The bulk purity of the products was confirmed by elemental analysis.

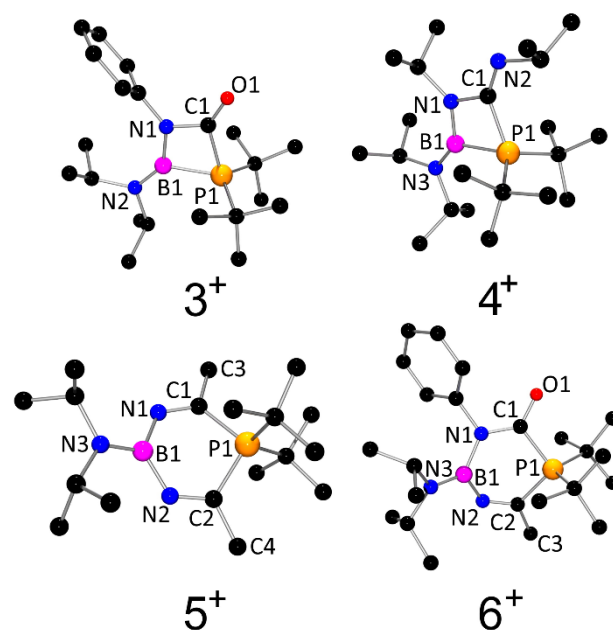


Figure 1. X-ray structures of cations **3⁺**, **4⁺**, **5⁺**, and **6⁺**. Counterions and H atoms are omitted for clarity.

To obtain further insight into the electronic structure of **2⁺** and its reactivity toward PhNCO and CH₃CN, we performed density functional theory (DFT) calculations. The optimized structure of **2⁺** and its frontier molecular orbitals (MOs) are shown in Figure 2. The short B-N and B-P distances of 1.327 and 1.796 Å, respectively, are indicative of π -interactions along N-B-P bonds. They are consistent with the planar geometry around the B atom ($\Sigma_B = 360^\circ$) and the flattened pyramidal geometry of the phosphanyl group ($\Sigma_P = 335^\circ$). The N-B-P bonds are slightly bent, with an angle of 167.8°. Taking into account these

structural features, the electronic structure of 2^+ can be described by the two resonance Lewis structures presented in Scheme 2. The HOMO and LUMO mainly results from the overlap of the empty p -orbital of the B atom with the lone electron pair of the P atom. The second empty p -orbital of the B atom is involved in an analogous interaction with the N atom (HOMO-1, LUMO+1).

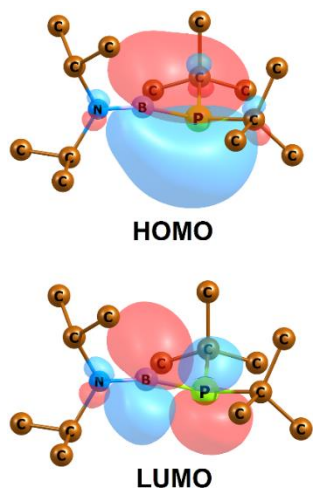


Figure 2. Optimized structure and frontier MOs of 2^+ .

According to the Gibbs free energy profile, the reaction of 2^+ with PhNCO proceeds *via* only one transition state (TS), with an energy barrier of 16.0 kcal/mol (Figure 3A). The initial step involved a nucleophilic attack of the PhNCO atom on the B atom, which led to the N–B bond formation and the elongation of C–N and B–P bonds. After crossing the TS, no intermediate structure is observed, but the C–P bond formation is barrierless. The final product is 39.0 kcal/mol lower in energy than the substrates.

The activation of two CH_3CN molecules by 2^+ involved two first-order saddle points (TS1–TS2) and three intermediate products (IP1–IP3) (Figure 3B). The first step of the reaction is the barrierless formation of a cation–acetonitrile adduct (IP1). Next, the nucleophilic attack of the P atom on the CH_3CN atom leads to a four-membered cycle (IP2) through TS1 (0.7 kcal/mol). The second CH_3CN molecule interacts with IP2 to form a new N–B bond, accompanied by the cleavage of the B–P bond (IP3); finally, a six-membered ring is generated as a result of the C–P bond formation after crossing TS2 (-13.0 kcal/mol). The reaction of 2^+ with CH_3CN is exergonic, with $\Delta G_{298} = -30.2$ kcal/mol.

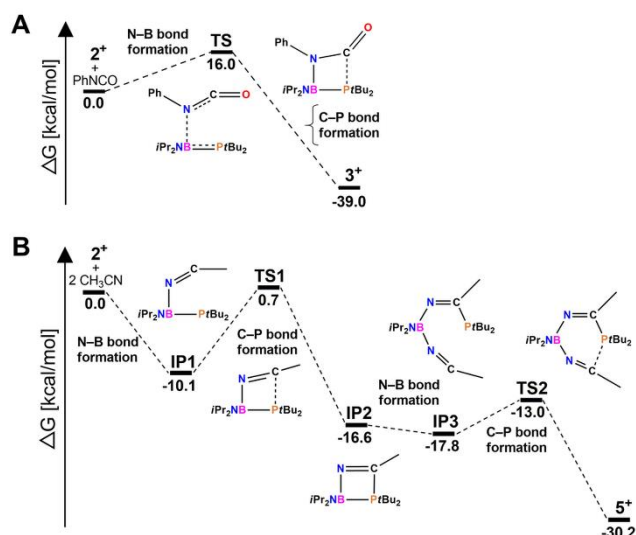


Figure 3. $\omega\text{B97xD}/6\text{-311++G(d,p)}$ Gibbs free energy profiles for the reactions of 2^+ with PhNCO (A) and CH_3CN (B).

Conclusions

The present results confirmed the applicability of NFCs in the activation of small molecules. Their versatile reactivity results from unique features such as the low coordination number of boron, the electron deficiency, and the combination of Lewis acidic and basic properties. Taking into account that the steric and electronic properties of NFCs can be easily tuned by the selection of appropriate substituents, these properties will enable to translate their reactivity into reversible reactions. This will be the first step toward the discovery of new catalytic reactions involving NFCs as intermediates.

Author Contributions

K.K.-L.: funding acquisition, conceptualization, investigation, visualization, writing – original draft; M.C.: formal analysis, writing – original draft; J.C.: investigation, formal analysis; R.G.: supervision, conceptualization, writing – original draft.

Conflicts of interest

There are no conflicts to declare

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