Selective Oxidation of an Active Intramolecular Amine/Borane Frustrated Lewis Pair with Dioxygen

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Ⓢ *Supporting Information*

ABSTRACT: Oxidation reactions are rarely encountered in frustrated Lewis pair (FLP) chemistry. We describe the selective reaction of an amine/borane FLP with molecular oxygen. The trimethylene-bridged amine/borane frustrated Lewis pair was prepared by hydroboration of *N*-allyl-tetramethylpiperidine with Piers' borane [HB-$(C_6F_5)_2$]. The intramolecular N/B system undergoes a variety of typical FLP reactions. It is a very active hydrogen splitting reagent at ambient conditions. Its reaction with dioxygen takes place rapidly at ambient conditions to give a tetrahydroisoxazolium/borate salt. A possible pathway of its formation is proposed and supported by DFT calculations.

Frustrated Lewis pair (FLP) chemistry[1] has seen some remarkable developments in the recent years. The inter- or intramolecular combinations of nonquenched main group element Lewis acids and bases has led to activation or binding of a variety of small molecules. Most notable is the heterolytic cleavage of dihydrogen[2] especially by a variety of amine or phosphane/borane combinations and the use of many such systems as catalysts for metal-free hydrogenation of a variety of unsaturated organic substrates.[3] Some such hydrogen activation procedures with, e.g., intramolecular P/B FLPs proceed with remarkably high reaction rates.[4] Frustrated Lewis pairs were shown to undergo selective reactions with quite a variety of substrates. They were shown to sequester environmentally problematic gases such as carbon dioxide, sulfur dioxide or some nitrogen oxides,[5] but they also add to olefinic and acetylenic substrates, to organic carbonyl compounds and many other reagents.[6] Frustrated Lewis pair chemistry has successfully been used to actually find a variety of new chemical reactions.[7]

It is noteworthy that examples of oxidation reactions are rather seldomly encountered in this manifold of FLP reactions.[8] In case of the P/B FLP systems, exposure to oxidants (or related reagents) has invariably led to phosphine oxide formation (or formation of the respective P=S or P=NR products).[9] We have now synthesized a new reactive intramolecular N/B FLP and found that it cleanly and selectively reacted with dioxygen. The FLP chemistry and the outcome of this unusual FLP oxidation reaction will be described and discussed in this report.

Tetramethylpiperidine was N-allylated with allyl bromide, KI, and base in DMF at 150 °C. We prepared the trimethylene-bridged N/B FLP **2** by treatment of the resulting bulky allyl amine **1**[10] with Piers' borane [HB(C_6F_5)$_2$][11] (see Scheme 1).

Scheme 1. Synthesis of the N/B FLP 2 and Protonation Reactions
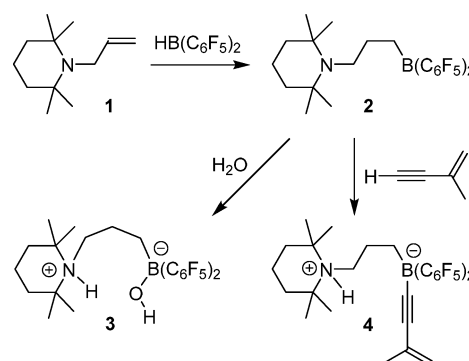
Compound **2** was isolated as a yellow crystalline solid from the pentane reaction mixture at low temperature and obtained in 86% yield. It shows an ^{11}B NMR signal at δ 73.5 ppm and a ^{19}F NMR spectrum featuring three resonances in a 2:1:2 intensity ratio of the *o*, *p*, and *m*-C_6F_5 fluorine atoms with $\Delta\delta^{19}F_{m,p}$ = 13.2 ppm. These NMR features indicate the presence of a planar tricoordinate borane geometry. The X-ray crystal structure analysis (single crystals were obtained from pentane at −35 °C) confirmed an open FLP structure with a free amine Lewis base and a free borane Lewis acid (see Figure 1). The C_3-bridge of compound **2** shows an antiperiplanar/gauche conformational orientation.

The new amine/borane system **2** undergoes a variety of typical FLP reactions[1,3] (see Schemes 1−3). It reacts with H_2O to give the [N]H⁺/[B]OH⁻ product **3** (isolated in 89% yield; ^1H NMR, δ 11.70 ppm (NH); ^{11}B NMR, δ −1.5 ppm). It deprotonates a terminal alkyne such as the methylbutenyne example to give the respective [N]H⁺/[B]alkynyl⁻ product **4** (isolated in 93% yield). Both the products were characterized spectroscopically, by C,H,N-elemental analysis and by X-ray diffraction (for details including the depicted molecular structures see the Supporting Information (SI)).
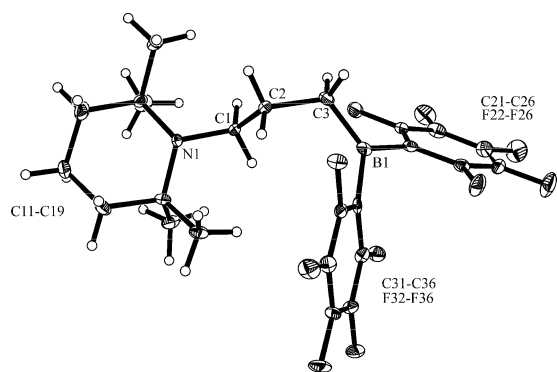
Figure 1. A view of the molecular structure of the N/B FLP **2** (thermal ellipsoids are shown at the 50% probability level). Selected bond lengths (Å) and angles (°): N1−C1 1.471(4), C1−C2 1.523(4), C2−C3 1.539(4), C3−B1 1.544(5); C1−N1−C11 114.3(2), C1−N1−C15 114.0(2), C11−N1−C15 118.3(2), C3−B1−C21 121.3(3), C3−B1−C31 121.7(3), C21−B1−C31 117.0(3), $\sum$N1^{CCC} 346.6°, $\sum$B^{CCC} 360.0°.

Scheme 2. Reaction of the N/B System 2 with Additional Piers' Borane
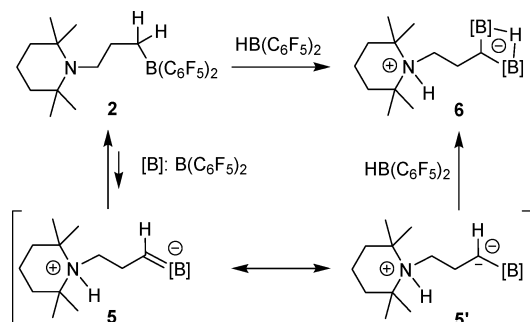
Scheme 3. H$_2$ and D$_2$ Splitting Reactions of the N/B System 2
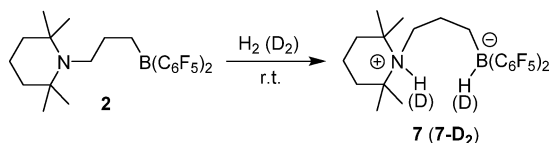
The FLP **2** undergoes an unusual subsequent reaction with HB(C$_6$F$_5$)$_2$. Compound **2**, in situ generated by the rapid HB(C$_6$F$_5$)$_2$ addition to the allyl amine **1** at rt in dichloromethane, slowly adds another equivalent of Piers' borane [HB(C$_6$F$_5$)$_2$] (6 h, rt) to eventually give the zwitterionic product **6**, isolated in 86% yield as a white solid (see Scheme 2). The compound shows a broadened ^{1}H NMR 1:1:1 intensity triplet of the [N]H$^+$ ammonium cation moiety at δ 3.61 ppm [$^1J_{(14N,1H)}$ = 49.4 Hz] and a broad [B]$_2$(μ-H) ^{1}H NMR signal at δ 2.72 ppm [with a corresponding ^{11}B NMR resonance at δ −19.3 ppm]. The methine CH unit bridging the pair of boranes gives rise to NMR signals at δ 1.11 ppm (^{1}H NMR) and δ 10.9 ppm (^{13}C NMR), respectively. The X-ray crystal structure analysis of compound **6** (see Figure 2) shows the ammonium unit at one end of the C$_3$-chain. Carbon atom C3 has the geminal pair of B(C$_6$F$_5$)$_2$ moieties bonded to it, which is bridged by a hydride. The connecting N1−C1−C2−C3 unit is found in a maximally extended antiperiplanar conformation.
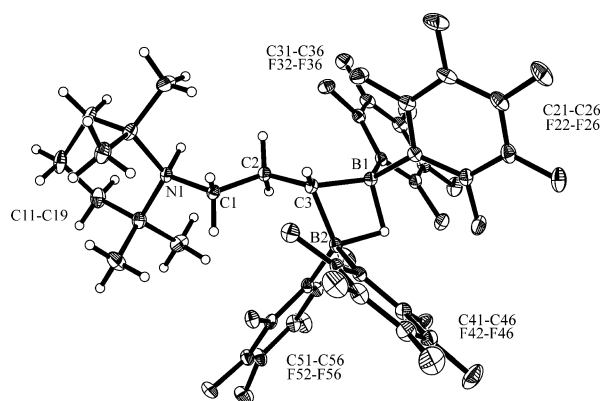

Figure 2. A view of the zwitterionic compound **6** (thermal ellipsoids are shown at the 15% probability level). Selected bond lengths (Å) and angles (°): N1−C1 1.532(5), C1−C2 1.506(6), C2−C3 1.508(6), C3−B1 1.596(6), C3−B2 1.593(7), B1−B2 1.942(7); C1−N1−C11 113.0(3), C1−N1−C15 113.2(4), C11−N1−C15 117.4(3), C3−B1−C21 122.3(4), C3−B1−C31 115.3(4), C21−B1−C31 111.1(4), C3−B2−C41 116.7(9), C3−B2−C51 118.7(4), C41−B2−C51 114.3(7).

C−H bonds α-positioned to boranes are acidic, especially when they are adjacent to the B(C$_6$F$_5$)$_2$ group featuring a pair of strongly electron withdrawing pentafluorophenyl substituents. We had recently shown that R-CH$_2$B(C$_6$F$_5$)$_2$ boranes are almost as CH acidic as cyclopentadienes.[12] The resulting carbanions show strong stabilization by charge delocalization with the adjacent borane Lewis acid, so that the few isolated examples of this general class of compounds have convincingly been rather described as borata-alkenes.[13] We assume that the α-CH$_2$ hydrogens in FLP **2** are just CH acidic enough to allow deprotonation by the internal amine base in an endothermic equilibrium situation to make the zwitterionic borata-alkene isomer **5/5'** available as a reactive intermediate. Since trapping by HB(C$_6$F$_5$)$_2$ has previously been demonstrated being a favored pathway in borata-alkene chemistry,[12,13f] we assume that the product **6** was formed in this way by scavenging the reactive borata-alkene isomer **5, 5'** of the FLP **2** by excess Piers' borane (see Scheme 2).

The FLP **2** is a very reactive hydrogen activator. It cleaves dihydrogen almost instantaneously at close to ambient conditions. From a competition experiment we learned that it is ca. 8 times more reactive toward H$_2$ than the vicinal P/B FLP Mes$_2$PCH$_2$CH$_2$B(C$_6$F$_5$)$_2$[2b,4c] (for details see the SI). When compound **2** was exposed to H$_2$ (2.0 bar) at rt in pentane solution, the product **7** of heterolytic dihydrogen splitting precipitated after ca. 5 min reaction time. It was isolated as a white solid in 95% yield (see Scheme 3). The X-ray crystal structure analysis showed that a zwitterionic compound had been formed exhibiting the ammonium cation and the −B(H)(C$_6$F$_5$)$_2$ anion unit at the terminal carbon atoms (C1 and C3) of the C$_3$-chain. Both the nitrogen atom N1 and the boron atom B1 show pseudotetrahedral coordination geometries [$\sum$N1^{CCC} 343.3°, $\sum$B1^{CCC} 333.2°]. The bridging trimethylene unit shows a double gauche conformational orientation, which orients the [N]−H$^+$/[B]−H$^−$ hydrogens toward each other ([N]−H⋯H−[B] separation: 1.719 Å). In solution (toluene-d_8) compound **7** shows a ^{11}B NMR doublet at δ −19.1 ppm ($^1J_{BH}$ = 75 Hz) and a single set of ^{19}F NMR resonances of the −B(H)(C$_6$F$_5$)$_2$ group with a typical small borate anion-like *m,p*-chemical shift difference of $\Delta\delta^{19}F_{m,p}$ = 3.0 ppm.

Reaction of the FLP **2** with dideuterium (1.0 bar) gave the respective [N]D$^+$/[B]D$^-$ product **7-D$_2$** (isolated in 89% yield). It shows ^{2}H NMR signals at δ 7.72 ([N]D$^+$) and δ 3.07 ppm ([B]D$^-$), respectively (in toluene).

Quite remarkable is the selective reaction of the N/B FLP **2** with dioxygen. The amine/borane system was exposed to O$_2$ (1.0 bar) in pentane solution at rt. Within 5 min, a white precipitate of the product **8** was formed, which was isolated in 85% yield (see Scheme 4). The X-ray crystal structure analysis

Scheme 4. Reaction of the FLP 2 with Dioxygen
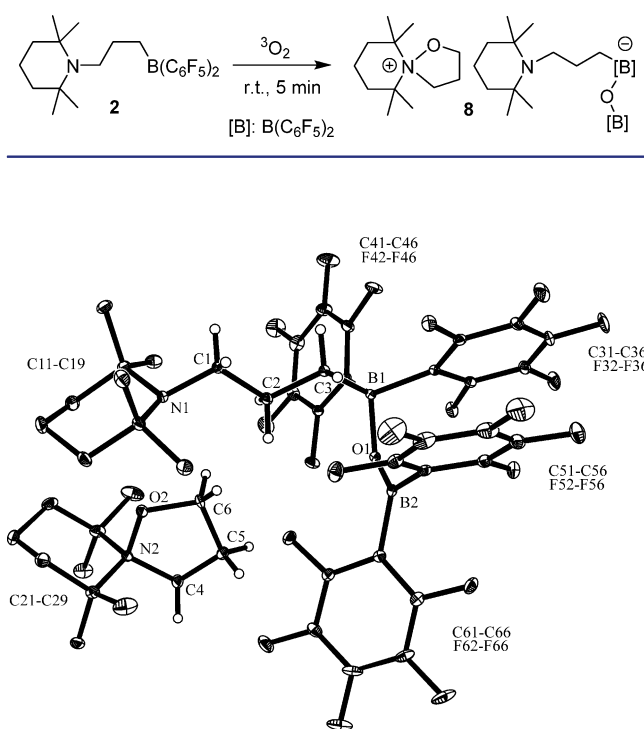
of **8** revealed the formation of a salt (see Figure 3). The tetrahydroisoxazolium type cation of **8** contains both a newly formed nitrogen−oxygen and a carbon−oxygen bond. The counteranion features the framework of **2** to which the negatively charged [O−B(C$_6$F$_5$)$_2$]$^-$ building block had been added. This resulted in the formation of a nonlinear [B]−O−[B] unit which contains both a tetracoordinated borate anion and a tricoordinate OB(C$_6$F$_5$)$_2$ unit ($\sum$B1^{CCO} = 324.8°, $\sum$B2^{CCO} = 360.0°). The unchanged tetramethylpiperidinyl unit is found at the other end of the C$_3$-chain of the anion.

The NMR spectra of **8** show the ^{1}H/^{13}C NMR signals of the pair of tetramethylpiperidine substituents (for details see the SI). We have monitored a pair of typical ^{11}B NMR resonance of the anion of **8** at δ 0.6 (tetracoordinated borate) and δ 34.5 ppm (tricoordinated borane), respectively.

We assume that the reaction of the N/B FLP **2** with triplet dioxygen is initially following the radical chain mechanism as it

Figure 3. A projection of the molecular structure of the salt **8** (thermal ellipsoids are shown at the 30% probability level; hydrogen atoms are partly omitted for clarity). Selected bond lengths (Å) and angles (°): N1−C1 1.476(2), C1−C2 1.526(2), C2−C3 1.536(2), C3−B1 1.626(2), B1−O1 1.525(2), O1−B2 1.311(2), N2−C4 1.526(2), C4−C5 1.503(10), C5−C6 1.534(10), C6−O2 1.499(5), N2−O2 1.451(1); O1−B1−C31 109.5(1), O1−B1−C41 106.2(1), C31−B1−C41 109.2(1), C51−B2−C61 116.4(1), O1−B2−C61 119.2(1), O1−B2−C51 124.4(1), B1−O1−B2 131.3(1).

is often found for the oxygenation of alkylboranes (see Scheme 5).[14,15] Our study was supported by DFT calculations to

Scheme 5. A Possible Mechanistic Pathway for the Oxidation of FLP 2 with DFT Calculated Gibbs Energies $\{\Delta G(298 \text{ K})\}$ in kcal mol^{-1} at the PW6B95-D3/def2-TZVP(COSMO-RS, toluene)//TPSS-D3/def2-TZVP Level of the Theory for the Individual Reaction Steps
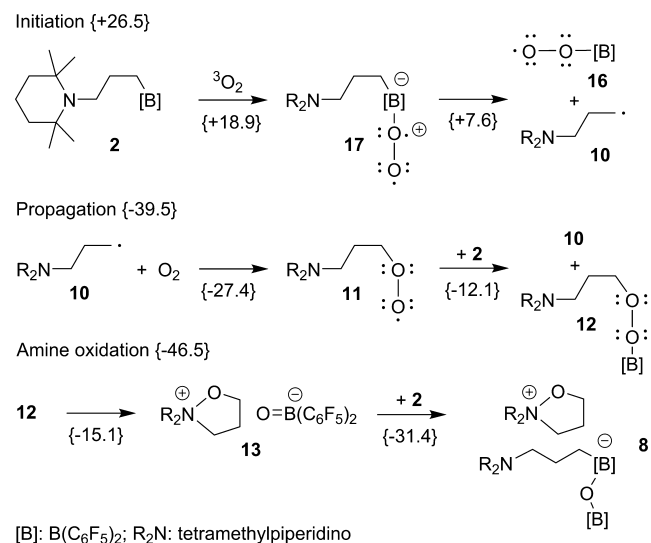
characterize the thermodynamics of the reaction scheme. The structures were optimized at the dispersion-corrected TPSS-D3 level of theory,[16a−c] in conjunction with the def2-TZVP basis set.[16d,e] Accurate electronic energies were obtained from single point calculations at the PW6B95-D3 level[16b,c,f] with the same basis set. The COSMO-RS (Conductor-like Screening Model for Real Solvents) solvation model[16g,h] was used to compute the solvation Gibbs free energies with toluene as the solvent (for computational details, see the SI). The results show that the initiation sequence is an endergonic process with a Gibbs free energy of $\Delta G(298 \text{ K})$ = +26.5 kcal mol^{-1}, a value that is similar to that calculated for the often used reaction of triethylborane with ^{3}O$_2$ to generate the ethyl radical and ·O−O−BEt$_2$ (calc +19.9 kcal mol^{-1}).[15] The propagation step of our sequence to form the alleged borylperoxide intermediate **12** is strongly exergonic (−39.5 kcal mol^{-1})[15] as is the subsequent actual amine oxidation with extrusion of the good [O═B(C$_6$F$_5$)$_2$]$^-$ leaving group and its stabilization by addition to the Lewis acid function of another equivalent of FLP **2** to eventually give the observed product **8**. The amine oxidation process is again strongly exergonic with a calculated Gibbs energy of −46.5 kcal mol^{-1}. We should note, however, that none of the intermediates have so far been observed experimentally and, consequently, confirmation of this reaction scheme will need further studies.[17]

We conclude that the simple HB(C$_6$F$_5$)$_2$ hydroboration reaction of the allyl amine **1** derived from the bulky tetramethylpiperidine building block provides an easy entry to the reactive N/B FLP **2**. This is an open frustrated Lewis pair that does not show a direct Lewis acid/Lewis base interaction, neither in the solid state nor in solution. Consequently, the system is a very active hydrogen splitting reagent. It is prone to deprotonation at the α-position to boron by the amine base to generate in situ its ammonium/borata-alkene isomer **5**, which we could trap with Piers' borane. A remarkable chemical feature

of the FLP **2** is its selective reaction with dioxygen which eventually leads to the formation of the tetrahydroisoxazolium borate salt **8** by amine oxidation in combination with extrusion of the favorable $[O=B(C_6F_5)_2]^-$ leaving group (which was then trapped by compound **2**). This may actually indicate a prominent role of the negatively charged $[O=B(C_6F_5)_2]^-$ moiety similar to the often utilized analogous role of the neutral $OPPh_3$ group.[18] Our study shows that our N/B FLP can selectively react in a rather specific way with dioxygen under mild conditions by a pathway that eventually leads to internal oxidation of the amine Lewis base.

◼ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b00325.

> Experimental and computational details and characterization data (PDF)
> Crystallographic data (CIF)
> Structure data files (ZIP)

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Notes
The authors declare no competing financial interest.

◼ ACKNOWLEDGMENTS

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