Phospholes

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Observation of a Thermally Induced Bora-Nazarov Cyclization at a Phosphole Framework**

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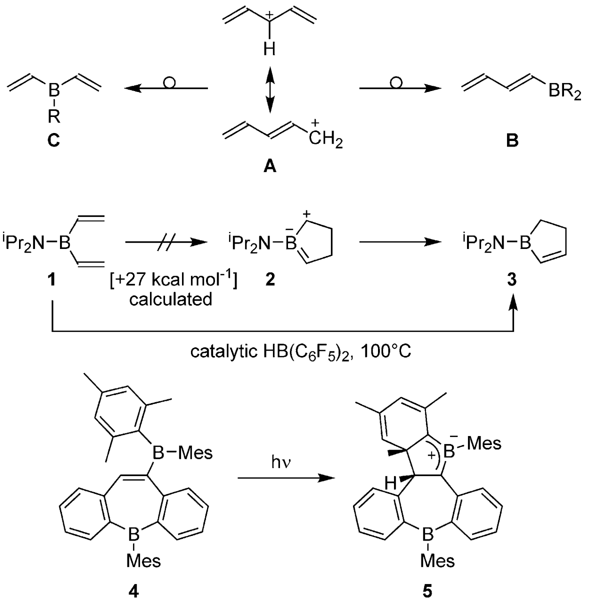
Abstract: *The reaction of the bis(enynyl)phosphanes* ***6a,b*** *with the electrophilic borane reagents R−B(C_6F_5)$_2$ (R = C_6F_5, CH_2CH_2Ph, CH_3) gave phospholes cleanly in a 1,1-carboboration reaction sequence. Depending on the steric bulk, the resulting 2,5-alkenylphospholes underwent a thermally induced bora-Nazarov type cyclization. The equilibrium situation of these examples of a bora-Nazarov type cyclization was investigated in detail by NMR spectroscopy, X-ray crystal structure analysis, and DFT calculations.*

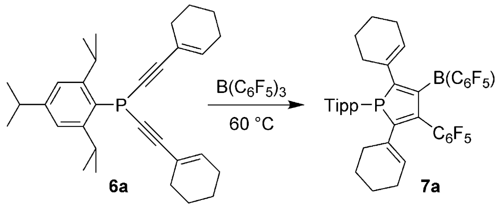
The thermally induced ring-closure of suitably substituted pentadienyl cations (**A**; Scheme 1) is the basis of a variety of synthetically important reactions.[1] The Nazarov cyclization, that is, the acid-catalyzed formation of conjugated cyclopentenones from bis(alkenyl)ketones, is a most prominent example of this important reaction type.[2] Formal substitution of the carbocation by a boron center in the 1- (**B**) or 3-position (**C**) of the pentadienyl system would provide a neutral isolobal analogue which might also be able to undergo this fundamental type of ring-closure reactions. To the best of our knowledge there have been surprisingly few attempts to verify this analogy experimentally, especially in view of the increasing importance of unsaturated boron-containing five-membered heterocycles for example, in organic materials chemistry.[3,4]



Scheme 1. HB(C_6F_5)$_2$ catalyzed and photoinduced bora-Nazarov cyclization.

A recent combined DFT/experimental study had shown that the formation of the ring-closed product **2** from the divinylborane starting material **1** is thermodynamically unfavorable, but we were able to achieve the **1**→**3** isomerization in a different way, namely catalyzed by HB(C_6F_5)$_2$.[4c] Yamaguchi et al. recently described a genuine bora-Nazarov example, namely formation of **5** by photochemically induced ring-closure of the dimesitylboryl-substituted dibenzoborepin **4** (Scheme 1).[5] We have now found an example of a facile ring-closure reaction of a 1-borylbutadiene system (**B**), which is a different approach to experimentally realizing a bora-Nazarov type reaction.

We prepared the bis(alkynyl)phosphane **6a** by treatment of 2,4,6-triisopropylphenyldihalogenophosphane (TippPX_2, X = Cl, Br) with the alkynyllithium reagent derived from cyclohexenylacetylene.[6] Treatment with one molar equivalent of B(C_6F_5)$_3$ in pentane at 60 °C (4 h) gave the phosphole **7a** (Scheme 2) as an orange solid in 91% yield. The X-ray crystal structure analysis (Figure 1) showed a pentasubstituted phosphole bearing the bulky 2,4,6-triisopropylphenyl (Tipp) group at phosphorus, a single C_6F_5 substituent at carbon atom C4, and the remaining B(C_6F_5)$_2$ unit adjacent at C3.



Scheme 2. Formation of phosphole **7a** by a 1,1-carboboration reaction sequence from the bis(alkynyl)phosphane **6a**.

The cyclohexenyl substituents at the phosphole α-carbon atoms C2 and C5 are both rotated from full conjugation with

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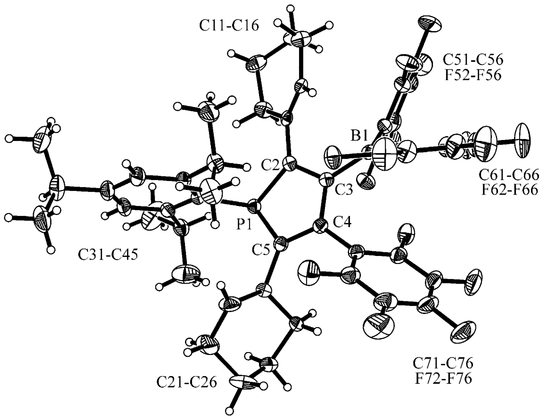


Figure 1. A view of the molecular structure of the phosphole **7a** (ellipsoids are set at 30% probability).[17]

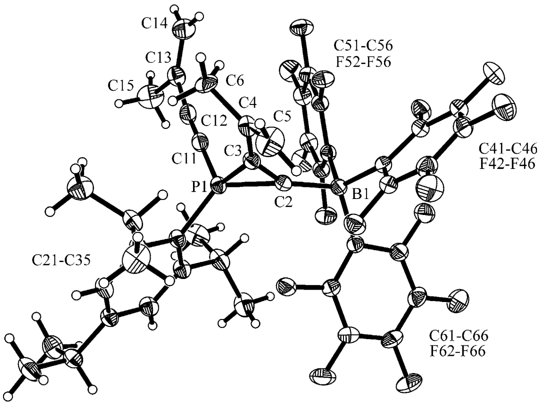
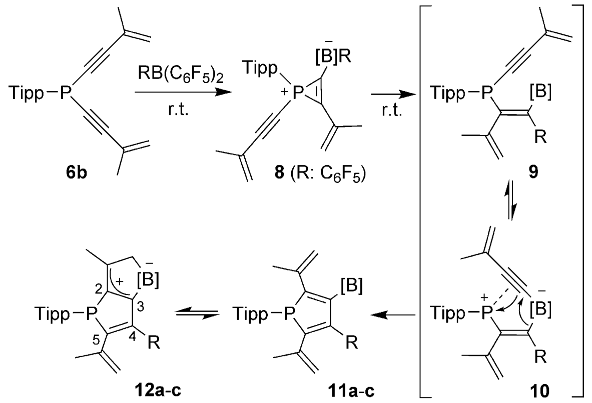


Figure 2. A view of the molecular structure of the phosphirenium borate **8** (ellipsoids are set at 30% probability). Selected bond lengths (Å) P1-C2 1.776(2) Å, P1-C3 1.738(2) Å, C2-C3 1.333(2) Å.[17]

the central phosphole π-system (θ C3-C2-C11-C12 −40.8(2)°; C4-C5-C21-C22 112.0(2)°). The phosphole system is slightly non-planar (angle between the C2-P1-C5 and C2-C3-C4-C5 planes: 14.7°) and the phosphorus atom features a trigonal-pyramidal coordination geometry (ΣP^{CCC} 318.1°). The boron atom B1 is planar tricoordinate (ΣB^{CCC} 360.0°). The boryl group is rotated by −44.5(3)° (θ C4-C3-B1-C61) out of the C2-C3-C4-C5 plane. The separation between B1 and the sp^2-CH carbon atom (C12) of the proximal cyclohexenyl substituent is large (2.920 Å), indicating that there is no interaction between these two centers of the 1-boryldiene subunit in compound **7a**. Consequently, compound **7a** shows a ^{11}B NMR resonance at δ 59 (in C_6D_6) and $\Delta\delta^{19}F_{p,m}$ = 13.1 ppm, both typical of a Lewis acidic, planar tricoordinate $RB(C_6F_5)_2$ situation (for further details, see the Supporting Information).

We then reacted the analogously prepared[6] Tipp-bis(methylbutenynyl)phosphane **6b** with a small series of $RB(C_6F_5)_2$ reagents (R = C_6F_5, CH_2CH_2Ph, CH_3). The reaction of **6b** with the parent Lewis acid $B(C_6F_5)_3$ at RT gave the phosphirenium borate **8** in 87% yield (Scheme 3). It was characterized by an X-ray crystal structure analysis (Figure 2 and the Supporting Information). In solution, compound **8** shows a very typical phosphirenium cation ^{31}P NMR signal[7] at δ −166.9 and a ^{11}B NMR borate resonance at δ −17.4 ($\Delta\delta^{19}F_{p,m} = 5.2$ ppm).



[B]: $B(C_6F_5)_2$; R: C_6F_5 (**a**), $-CH_2CH_2Ph$ (**b**), Me (**c**)

Scheme 3. Formation of the phospholes **11** and subsequent bora-Nazarov cyclization to **12**.

Compound **8** might be serving as an intermediate in the subsequent series of 1,1-carboboration reactions.[8] The initial products **9**[9,10] would then form **10** by alkynyl migration from phosphorus to boron followed by the final ring-closing step by intramolecular 1,1-alkenylboration (Scheme 3). In this series of reactions of three $R{-}B(C_6F_5)_2$ reagents with **6b**, we did not experimentally observe any of these intermediates (except **8**), but treatment of **6b** with any of the three boranes at elevated temperature (40°C to 75°C, 4 h to 1 h) gave the boryl-substituted phospholes **11a–c**.

The reaction of **6b** with $PhCH_2CH_2B(C_6F_5)_2$ (obtained by styrene hydroboration with Piers' borane $[HB(C_6F_5)_2]$)[11] was complete after 3 h at 45°C in pentane solution. Workup gave compound **12b** as a dark red solid in 83% yield. It was characterized by C,H elemental analysis, by spectroscopy, and by X-ray diffraction (single crystals were obtained from cyclopentane at −35°C). The X-ray crystal structure analysis (Figure 3) showed that the typical series of 1,1-carboboration reactions[12] were complete and the penta-substituted P-heterocycle was formed. It featured the former terminal alkynyl substituents at the α-carbon atoms C2 and C5, the

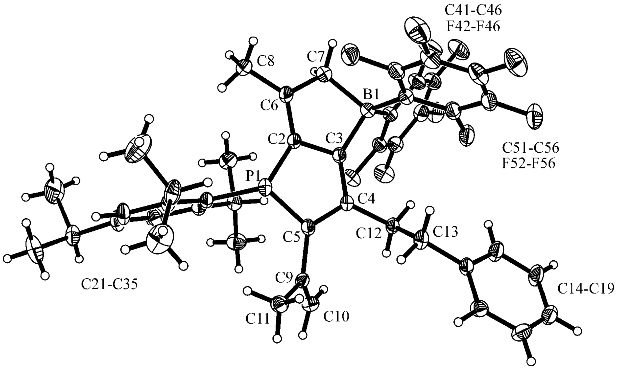


Figure 3. A view of the molecular structure of the cyclized product **12b** (ellipsoids are set at 15% probability).[17]

selectively shifted CH_2CH_2Ph substituent[13] at C4, and the remaining $B(C_6F_5)_2$ group at C3. However, in this case the probably initially formed phosphole **11b** had undergone a clean 1-borylbutadiene Nazarov-type ring-closure reaction at the phosphole framework to give the isomer **12b**.

The borane Lewis acid is found bonded to the former 2-propenyl methylene group (B1–C7 1.664(5) Å). The boron atom is tetra-coordinated (B1–C3 1.629(4) Å, angle C3-B1-C7 97.7(2)°). In the crystal, the C6–C7 bond in the newly formed five-membered borata heterocycle is in the C–C σ-bond range at 1.483(4) Å, whereas the adjacent C6–C2 bond is short (1.370(4) Å). The C2–C3 (1.427(4) Å), C3–C4 (1.406(4) Å), and C4–C5 (1.410(4) Å) linkages are all in a similar range, which indicates effective delocalization of the formal positive charge over this part of the phosphole framework. A natural population analysis (NPA)[14] revealed a marked increase of positive charge at carbon atoms C6 and C3 (and to some extend C5 as well) upon going from **11b** to **12b** and a marked charge increase at boron (no change at phosphorus; for details see the Supporting Information). The 2-propenyl substituent at C5 is rotated out of the phosphole π-plane (θ C4-C5-C9-C10 −45.2(2)°). The phosphorus atom itself seems not to be participating much in the delocalization (bond lengths P1–C2 1.781(3) Å, P1–C5 1.770(3) Å). It is oriented slightly out of the adjacent carbon plane.

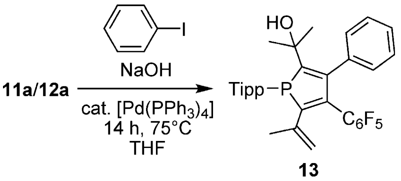
The deep red solution of compound **12b** shows a typical borate ^{11}B NMR signal at δ −8.9 (δ^{31}P −4.9). The $C7H_2$ methylene group bonded to boron features a ^{1}H NMR doublet in the saturated alkyl range at δ 2.89 with $^4J_{PH} =$ 5.6 Hz, δ^{13}C 56.7 (br). In contrast, the opposite olefinic methylene group $C10H_2$ shows the typical pair of ^{1}H NMR resonances at δ 5.02/4.71 (δ^{13}C 120.2). The remaining carbon framework shows very characteristic ^{13}C NMR resonances at δ 215.6, 160.3 (C6,2), 233.3 (br, C3), 153.1 (C4) and 193.0 (C5). Most of these signals are markedly different from those of its non-cyclized relative **7a** (e.g. δ^{13}C C11: 140.6, C2: 172.4, C3,4: 148.5, 125.9, C5: 156.2).

The reaction of **6b** with $MeB(C_6F_5)_2$ (40 °C, 4 h in C_6D_6) gave compound **12c** of methyl migration as the major product (87 %) besides a minor isomer and some starting material. From the mixture, the NMR analysis of **12c** revealed very similar spectroscopic features as compound **12b** (for example, ^{11}B: δ −10.2; for further details see the Supporting Information) so that we can assume a ring-closed bora-Nazarov structure as well.

The reaction of **6b** with the parent $B(C_6F_5)_3$ borane Lewis acid furnished a slightly different result. The reaction required 1 h at 75 °C (CD_2Cl_2) to go to completion. Since we could not isolate the product without decomposition, it was directly characterized spectroscopically from the reaction mixture (an isonitrile adduct of **11a** could be characterized by X-ray single-crystal structure analysis; see the Supporting Information). In CD_2Cl_2 solution, the compound showed markedly temperature-dependent NMR spectra. In D_2 dichloromethane, the ^{11}B NMR shift changed continuously from δ +16 at RT to δ −10 at 183 K. Similar changes were monitored for many of the ^{13}C NMR signals of the carbon framework of compound **11a/12a**, for example, C6 underwent a low field shift of $\Delta\delta^{13}C(6)_{299K,183K} = +26.9$ ppm upon going from RT to −90 °C; $\Delta\delta^{13}C(3)_{299K,183K} = +27.3$ ppm and $\Delta\delta^{13}C(5)_{299K,183K} = +14.2$ ppm. The critical $C7H_2$ methylene carbon atom underwent a marked transition to smaller chemical shift values in that temperature range of $\Delta\delta^{13}C7_{299K,183K} = -24.0$ ppm. We interpret this NMR behavior as originating from a rapid equilibration of the open and ring-closed isomers **11a** and **12a** on the NMR time scale, which is shifted markedly to the heterocyclic side with decreasing temperature. It seems that at 183 K we have observed almost the complete presence of the ring-closed bora-Nazarov product **12a** by NMR spectroscopy.

The bora-Nazarov situation in these systems was further analyzed by a DFT study. Relative Gibbs enthalpies (ΔG^{298}) of open and closed forms of **7a**, **11a/12a** and **11b/12b** were calculated by DFT (PW6B95-D3//TPSS-D3/def2-TZVP) in solution (CH_2Cl_2).[15] In all three cases, minimum structures were obtained for both isomers. In the **11b/12b** system, the ring-closed bora-Nazarov isomer was calculated to be favored by $\Delta G^{298} = -8.8$ kcal mol^{-1} (rel. **11b**: $\Delta G^{298} = 0$). In the related cyclohexenyl substituted example **7a**, the situation was reversed: here the open isomer (as experimentally observed) was calculated by 5.2 kcal mol^{-1} thermodynamically favored over the (not-observed) ring-closed structure. In the **11a/12a** case the calculated Gibbs enthalpies of both isomers are almost identical (ΔG^{298}(rel): open form **11a**: 0; closed form **12a**: −0.2 kcal mol^{-1}). For further details, including several other DFT calculated bora-Nazarov cyclization examples, see the Supporting Information.

Many unsaturated $B(C_6F_5)_2$ substituted carbo- and heterocycles are amenable to metal-catalyzed cross-coupling reactions,[8,16] and so is the bora-Nazarov product **12a**. However, here it takes a special route since it does not contain a free boryl substituent. Treatment of **12a** with iodobenzene in the presence of NaOH and 10 mol % of $[Pd(PPh_3)_4]$ catalyst eventually gave the product **13** (Scheme 4). Compound **13** was characterized by X-ray diffraction (for details, see the Supporting Information). We assume that its formation has involved a specific nucleophilic hydroxide attack at the positively charged carbon atom C6 of the bora-Nazarov product **12a** in the course of the Suzuki–Miyaura cross-coupling reaction.[16]



Scheme 4. Suzuki–Miyaura cross-coupling of the phosphole **11a/12a**.

We conclude that we have observed a genuine case of the 1-borylbutadiene Nazarov type cyclization reaction. This neutral analogue of the synthetically important pentadienyl cation cyclization is much less thermodynamically favorable. In our case it has made use of some extra delocalization of the resulting carbocation section of the zwitterionic products by the incorporated phosphole π-system. This has in some cases resulted in making the bora-Nazarov product so favorable that it has been observed as the only product experimentally (and by DFT calculations). In some cases this stabilization is not sufficient to offset adverse substituent effects and we have consequently only observed the open, non-cyclized isomer. In one case there seems to be close equilibrium situation with the open and closed form being almost isoenergetic; in this situation the equilibrium is markedly shifted with temperature and the closed bora-Nazarov product is favored at low temperatures. Our study has revealed some of the special requirements that are necessary to successfully observe the neutral Nazarov-type ring-closure reaction of 1-borylbutadiene systems. We will see how these findings will be used to find more general examples of this interesting and potentially useful transformation.

Keywords: 1,1-carboboration reactions · bora-Nazarov reaction · conjugated π-systems · cyclization · phospholes

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[17] CCDC 1054628 (**7a**), 1054629 (**8**), 1054630 (**11a**), 1054631 (**12b**), and 1054632 (**13**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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