Tracking reactive intermediates in phosphine-promoted reactions with ambiphilic phosphino-boranes†‡

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The ambiphilic phosphino-borane *i*-Pr_2P(*o*-C_6H_4)$BMes_2$ affords stable versions of key zwitterionic intermediates by reactions with diethyl azodicarboxylate or PhNCO.

Over the past 20 years, derivatives combining donor and acceptor functionalities, so-called ambiphilic compounds, have attracted increasing interest. In particular, combinations of phosphine and borane moieties have been studied as π-conjugated materials,[1] as metal-free systems capable of dihydrogen activation and transfer,[2] and as versatile ligands for transition metals.[3]

In order to further exploit phosphino-borane (PB) compounds,[4] we recently investigated their potential for the stabilisation of highly reactive adducts of phosphines. For example, the Staudinger reaction between PhN_3 and PB compound *i*-Pr_2P(*o*-C_6H_4)$BMes_2$ (**1**) was shown to give a phosphazide with a high thermal stability as a result of intramolecular $N_\alpha \rightarrow B$ interactions. Notably, this compound exhibits unprecedented photoisomerization behavior, in which an $N_\alpha \rightarrow B$ interaction is converted to an $N_\beta \rightarrow B$ coordination.[5]

Following the spectacular synthetic developments reported recently in phosphine-promoted reactions,[6] we were intrigued by the possibility of using PBs such as **1** for the stabilisation of key intermediates in similar reactions. In this regard, zwitterionic intermediates **A** and **B** (Fig. 1), resulting from the nucleophilic addition of phosphines to azodicarboxylates and isocyanates, respectively, were chosen as representative targets. On the one hand, "Huisgen zwitterions" **A** are generally accepted as the first intermediates in phosphine-promoted reactions of azodicarboxylates, including the famous Mitsunobu reaction,[7–9] as well as C–C and C–N bond-forming reactions.[10] However, the transient formation of compounds of type **A** has so far only been substantiated by ^{31}P NMR and FTIR spectroscopy, as well as chemical trapping.[11] On the other hand, phosphines are well-known catalysts for the cyclo-oligomerisation of isocyanates, but very little is known about the mechanism of this reaction.[12–15] Verkade *et al.* detected the 1 : 1 adduct between a proazaphosphatrane and PhNCO by ^{31}P NMR.[12] In addition, Horváth *et al.* recently reported 1 : 2 adducts between tri(*n*-butyl)phosphine and *n*-alkyl isocyanates, which were characterised *in situ* by NMR spectroscopy.[13]

Here, we report the ability of PB compound **1** to afford stable versions of key zwitterionic intermediates **A** and **B** by reaction with diethyl azodicarboxylate (DEAD) and PhNCO, respectively. Adducts **2** and $\mathbf{3_O}$ have both been characterized structurally, and DFT calculations have substantiated the selectivity and reversibility of the fixation of the isocyanate.

PB **1**[5] reacted with DEAD in toluene to afford a single product, but a large excess of DEAD (5 equiv.) was necessary to achieve complete conversion in a reasonable time at room temperature (Scheme 1).† After work up, the resulting compound, **2**, was isolated in 65% yield as a white solid. The derivatization of the phosphorus centre was apparent from the low field shift of the ^{31}P NMR signal (from +5.5 ppm in **1** to +60.4 ppm in **2**), while the high field shift of the ^{11}B NMR signal (from +75.0 ppm in **1** to −0.8 ppm in **2**) indicated a change from tri- to tetra-coordinate boron. In addition, the formation of a 1 : 1 adduct was demonstrated by mass spectrometry (MH^+ found at m/z = 617). The spectroscopic

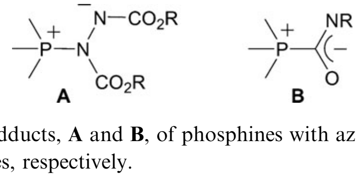

Fig. 1 1 : 1 adducts, **A** and **B**, of phosphines with azodicarboxylates and isocyanates, respectively.

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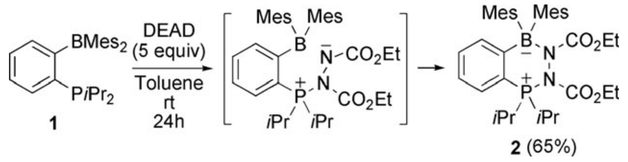
‡ Crystal data for **2**. $C_{36}H_{50}BN_2O_4P$, M = 616.56, triclinic, space group $P\bar{1}$, a = 12.2517(12), b = 16.8989(17), c = 17.0838(17) Å, α = 86.287(2), β = 77.074(2), γ = 89.524(2)°, V = 3440.1(6) $Å^3$, Z = 4, μ(Mo Kα) = 0.120 mm^{-1}, T = 173(2) K, crystal size 0.6 × 0.5 × 0.2 mm^3, 17 368 reflections collected (11 517 independent, R_{int} = 0.0779), 843 parameters, R_1 [$I > 2\sigma(I)$] = 0.0569, wR_2 [all data] = 0.1469, GOF = 0.937, largest differential peak and hole: 0.336 and −0.315 e $Å^{-3}$. CCDC 682859.

Crystal data for $\mathbf{3_O}$. $C_{39.50}H_{51}BNOP$, M = 597.59, monoclinic, space group $P2_1/c$, a = 10.5050(14), b = 18.114(3), c = 18.875(3) Å, α = 90, β = 101.404(3), γ = 90°, V = 3520.7(8) $Å^3$, Z = 4, μ(Mo Kα) = 0.108 mm^{-1}, T = 173(2) K, crystal size 0.6 × 0.4 × 0.2 mm^3, 17 251 reflections collected (5941 independent, R_{int} = 0.0810), 425 parameters, R_1 [$I > 2\sigma(I)$] = 0.0693, wR_2 [all data] = 0.1720, GOF = 1.045, largest differential peak and hole: 0.554 and −0.432 e $Å^{-3}$. CCDC 682860.

For crystallographic data in CIF or other electronic format see DOI: 10.1039/b805161e



Scheme 1 Formation of 1 : 1 adduct **2** from PB **1** and DEAD.

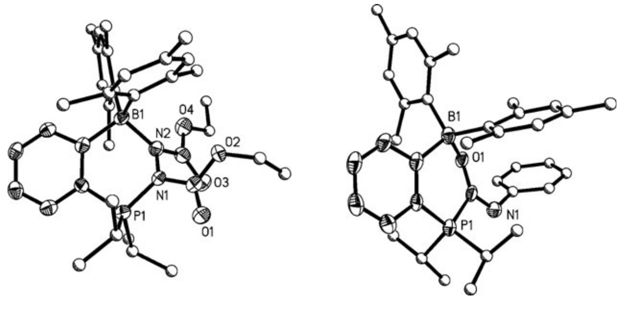
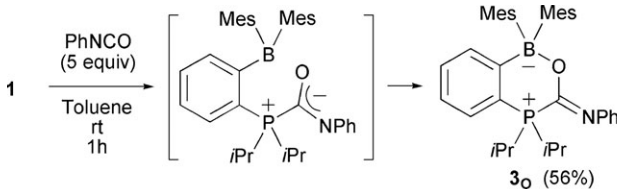


Fig. 2 Molecular views of **2** (left) and $\mathbf{3_O}$ (right) in the solid state (thermal ellipsoids at 50% probability). The isopropyl, mesityl, ethyl and phenyl groups are simplified, with the hydrogen atoms and solvate molecules omitted for clarity. For **2**, only one of the two independent molecules present in the asymmetric unit is shown.



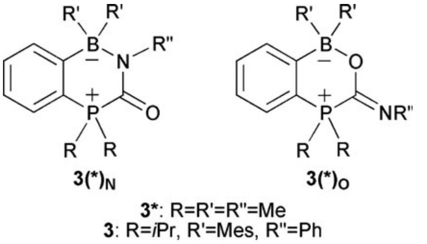
Scheme 2 Formation of 1 : 1 adduct $\mathbf{3_O}$ from PB **1** and PhNCO.

data for **2** support a zwitterionic structure combining phosphonium and borate units, which was unambiguously confirmed by an X-ray diffraction analysis (Fig. 2).‡ Two molecules with very similar geometries were found within the unit cell. The short N···B distance (1.66 Å) and the noticeable pyramidalization of the boron environment ($\Sigma B_\alpha \sim 337°$) confirm the ability of the borane moiety of **1** to interact with an electron rich centre maintained in close proximity, despite the steric constraints imposed by the two mesityl groups.

Having established that PB **1** is capable of stabilising reactive intermediates in phosphine-promoted transformations, an evaluation of its scope was of interest. To this end, the reaction of **1** with PhNCO was investigated. Treatment of **1** with an excess (5 equiv.) of PhNCO in toluene at room temperature afforded within 1 h a single compound that exhibited ^{31}P and ^{11}B NMR signals at +1.2 and +4.7 ppm, respectively (Scheme 2). The selective formation of a 1 : 1 adduct was indicated by mass spectrometry (MH$^+$ found at m/z = 562). At this stage, two isomeric structures, $\mathbf{3_O}$ and $\mathbf{3_N}$ (resulting from the addition of **1** to the C=O and C=N bonds of PhNCO, respectively), had to be considered. Neither the ^{13}C NMR chemical shift for the central carbon atom of the PhNCO unit (doublet, 150.6 ppm, $^1J_{PC}$ = 120 Hz),[16] nor the IR band observed at 1616 cm^{-1} were sufficient to discriminate between $\mathbf{3_O}$ and $\mathbf{3_N}$. However, the identity of the adduct was unambiguously established by an X-ray diffraction study (Fig. 2).‡ As expected, the phosphorus atom is bonded to the central carbon atom of the PhNCO moiety. The C···N distance (1.29 Å) is typical for a C=N double bond, and the phenyl group at the nitrogen is *trans* to the phosphonio group in order to minimize steric constraints. In addition, the boron strongly interacts with the oxygen atom (O···B distance = 1.60 Å; boron pyramidalization = 341°).

In order to gain more insight into the selective formation of the 1 : 1 adduct $\mathbf{3_O}$, DFT calculations were carried out at the B3PW91/SDD(P),6-31G** (other atoms) level of theory (Table 1).† The model adduct, **3***, resulting from the reaction of the permethylated PB with MeNCO was first investigated. Two minima, $\mathbf{3^*_N}$ and $\mathbf{3^*_O}$, featuring N→B and O→B interactions, respectively, were located on the potential energy surface (Fig. 3). In contrast with experimental observations, isomer $\mathbf{3^*_N}$, resulting from the addition to the C=N bond of the isocyanate, was found to be favoured energetically by about 8 kcal mol^{-1} over $\mathbf{3^*_O}$. In order to estimate the influence of steric factors on the selectivity, the two isomers of actual adduct **3** were then studied. Here, the optimized geometry of $\mathbf{3_O}$ reproduced very well the structure found experimentally. In addition, $\mathbf{3_O}$ was predicted to be about 13 kcal mol^{-1} more stable than $\mathbf{3_N}$, thereby confirming the key role of the sterically

Table 1 Experimental and theoretical[a] data for adducts $\mathbf{3_N}$, $\mathbf{3_O}$, $\mathbf{3^*_N}$ and $\mathbf{3^*_O}$: selected bond lengths, bond and torsion angles, and relative energies



Adduct		C···O/Å	C···N/Å	N···B or O···B/Å	ΣB_α (°)	PCCB (°)	ΔE/kcal mol^{-1}
$\mathbf{3_O}$	X-Ray	1.294(4)	1.292(4)	1.601(4)	340.8	12.1	—
$\mathbf{3^*_N}$	DFT	1.238	1.319	1.615	329.0	0.0	0
$\mathbf{3^*_O}$	DFT	1.289	1.281	1.583	335.7	2.3	+8.3
$\mathbf{3_N}$	DFT	1.234	1.340	1.670	326.7	14.1	0
$\mathbf{3_O}$	DFT	1.289	1.287	1.582	341.5	8.0	−12.8

[a] At the B3PW91/SDD(P),6-31G** (other atoms) level of theory.

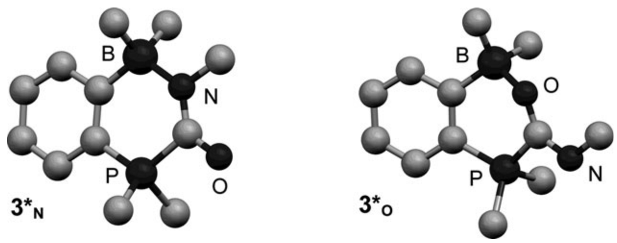


Fig. 3 Optimized structures of $\mathbf{3^*_N}$ and $\mathbf{3^*_O}$.

demanding substituents of **1** in the selective addition to the C=O double bond (a higher steric congestion can be reasonably anticipated in $\mathbf{3_N}$ *vs.* $\mathbf{3_O}$).

In line with the large excess of PhNCO required to achieve good yields of $\mathbf{3_O}$, the formation of $\mathbf{3_O}$ is predicted to be almost athermic (at 25 °C, $\Delta H = 0.7$ kcal mol^{-1} leading to $\Delta G = 18.9$ kcal mol^{-1}, as a result of an important entropic effect). This also suggests that the fixation of the isocyanate might be reversible, and indeed, crystals of $\mathbf{3_O}$ slowly release **1** and PhNCO upon dissolution,[17] as indicated by ^{31}P NMR and IR spectroscopic monitoring.

In conclusion, PB **1** has been shown to react readily with DEAD and PhNCO to afford isolable examples of the zwitterionic 1 : 1 adducts **A** and **B**, as a result of intramolecular stabilisation by the Lewis acid moiety. These results extend the synthetic application of ambiphilic compounds to the stabilisation of reactive intermediates. Variation of the electrophilic partner is currently under investigation,[18,19] as is the modulation of the ambiphilic probe.

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