ChemComm

Cite this: *Chem. Commun.*, 2012, **48**, 11739–11741

www.rsc.org/chemcomm

COMMUNICATION

Anomalous Staudinger reaction at intramolecular frustrated P–B Lewis pair frameworks†

Annika Stute, Lukas Heletta, Roland Fröhlich,‡ Constantin G. Daniliuc,‡ Gerald Kehr and Gerhard Erker*

Received 18th September 2012, Accepted 15th October 2012
DOI: 10.1039/c2cc36782c

The FLP-mesityl azide addition products 5, formed by FLP-addition to the terminal azide nitrogen atom, undergo N–N bond cleavage in an unusual variant of the Staudinger reaction upon thermolysis or photolysis to give an internally borane stabilized [P]═NH phosphinimine and a dimethylindazole derivative.

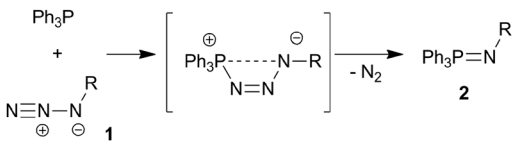
H. Staudinger reported in 1919 about the formation of phosphinimines (iminophosphoranes) by treatment of tertiary phosphanes with organic azides.[1] Since then the "Staudinger reaction" has been a valuable synthetic method for the preparation of phosphinimines and of various follow up products.[2] It has been a useful method for the synthesis of amines from azides,[3] but more importantly it has provided an invaluable tool in chemical biology where it is used for the preparation of bio-conjugates under very mild "biotic" conditions ("Staudinger ligation").[4]

The phosphinimines **2** are formed in the Staudinger reaction by transfer of an N–R unit from the N_3–R azide reagent **1** to the phosphane with thermodynamically favorable elimination of dinitrogen (see Scheme 1).[5] We have now found an anomalous course of the Staudinger reaction[6] where the N_2 elimination is avoided by formation of an indazole derivative to give an unsubstituted Ar_2RP═NH phosphinimine. This remarkable alternative to the "normal" Staudinger reaction has been observed eventually by reacting some intramolecular vicinal frustrated phosphane–borane Lewis pairs[7,8] with mesityl azide.[9]

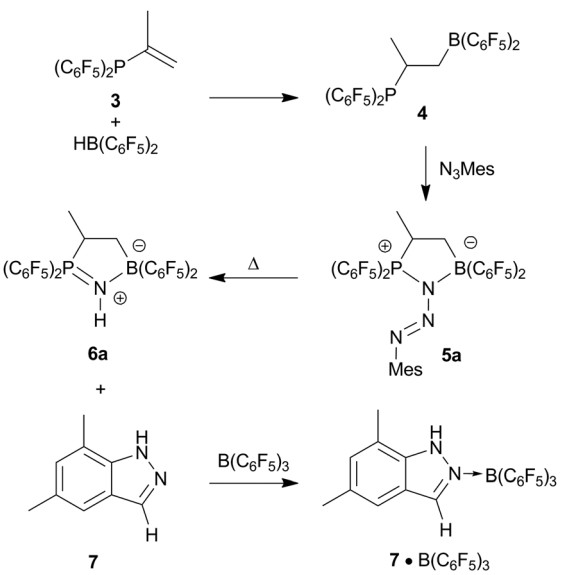
For this study we reacted bis(pentafluorophenyl)-2-propenylphosphane (**3**) with Piers' borane [$HB(C_6F_5)_2$]. This resulted in a clean hydroboration reaction with anti-Markovnikov orientation to yield the intramolecular vicinal frustrated Lewis pair **4**. Compound **4** is an example of an electronically controlled FLP without any appreciable interaction between its Lewis acid and Lewis base components.[9c,10] It features a ^{11}B NMR signal at δ = 67.8, typical of a strongly Lewis acidic planar-tricoordinate boron center (^{31}P NMR of **4**: δ = −32.5).

Compound **4**, *in situ* generated in *n*-pentane, reacted rapidly with mesityl azide. After 1 h at room temperature the product **5a** had precipitated and was isolated as a white solid in *ca.* 60% yield. The X-ray crystal structure analysis of **5a** revealed that the FLP **4** has undergone 1,1-addition to the terminal nitrogen atom of the mesityl azide reagent to form a five-membered heterocycle (see Scheme 2).[11] Both the P1–N1 and B1–N1 bonds in **5a** are rather long (see Table 1). The N–N–N bond lengths are alternating. The N2═N3 double bond is *trans*-disubstituted (dihedral angle N1–N2–N3–C51 174.8°) (see Fig. 1). The heterocyclic ring is non-planar, it shows a typical cyclopentane-like conformation.

In solution compound **5a** features heteroatom NMR signals at δ = 18.1 (^{31}P) and δ = −5.9 (^{11}B). Due to the chiral center inside the five-membered heterocycle we have observed the ^{19}F NMR signals of pairs of diastereotopic C_6F_5 substituents at both boron and phosphorus (for details see the ESI†).



Scheme 1



Scheme 2

Organisch-Chemisches Institut, Universität Münster, Corrensstraße 40, D-48149 Münster, Germany. E-mail: erker@uni-muenster.de

† Electronic supplementary information (ESI) available: Text and figures giving further experimental and spectroscopic details and CIF files giving crystallographic data for **5a**, **5b**, **6a**, **6b** and **7·B(C$_6$F$_5$)$_3$**. CCDC: 902225–902229. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2cc36782c

‡ X-ray crystal structure analysis.

Table 1 Selected structural parameters of compounds **5** and **6**[a]

Compound	**5a**	**6a**	**5b**	**6b**
P1–N1	1.651(2)	1.583(3)	1.687(2)	1.609(2)
B1–N1	1.594(2)	1.586(5)	1.600(4)	1.564(3)
N1–N2	1.378(2)	—	1.368(3)	—
N2–N3	1.255(2)	—	1.255(3)	—
P1–N1–B1	114.9(1)	115.4(3)	116.2(2)	116.2(2)
C1–P1–N1	97.0(1)	100.2(2)	95.1(1)	96.2(1)
C2–B1–N1	98.9(1)	100.4(3)	99.1(2)	100.5(2)
P1–C1–C2–B1	47.0	36.5	43.5	44.9

[a] Bond lengths in Å, angles in degrees.

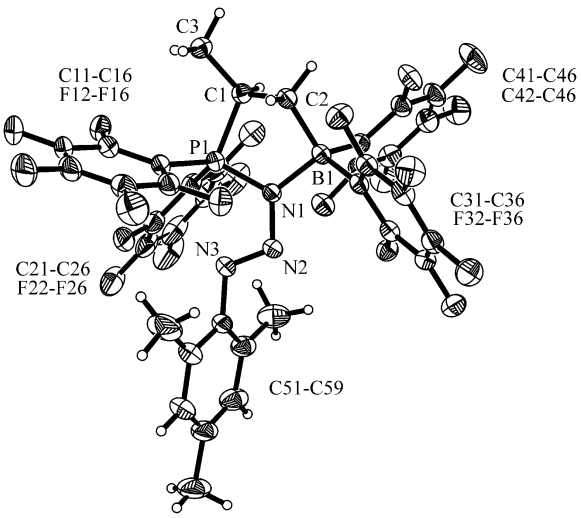


Fig. 1 A view of the molecular structure of compound **5a** (thermal ellipsoids are shown with 30% probability).

The FLP–mesityl azide adduct **5a** was then thermolyzed in the solid at 150 °C for 1 h. During that period of time a white solid had sublimed which was collected (see below). The remaining residue was worked up chromatographically to give the five-membered heterocyclic FLPNH product **6a** in 75% yield. (**6a** was also obtained by photolysis of **5a** in dichloromethane, for further details see the ESI†). The compound was identified by X-ray diffraction (see Fig. 2 and Table 1). The structure features a five-membered heterocyclic core that contains an unsubstituted NH functionality. The P1–N1 bond in **6a** is markedly shorter than the corresponding P–N linkage in its precursor **5a**, indicating a substantial [P]═NH phosphinimine character[12] of the product **6a**. In solution, compound **6a** exhibits a ^{31}P NMR resonance at δ = 36.6 and an ^{11}B NMR signal at δ = −4.8, typical of tetracoordination at boron. Compound **6a** also shows the typical ^{19}F NMR signals of two pairs of diastereotopic C_6F_5 substituents at the heterocyclic core structure.

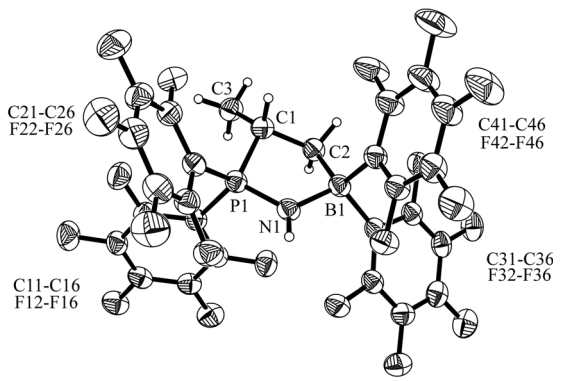


Fig. 2 Molecular structure of compound **6a** (thermal ellipsoids are shown with 30% probability).

The sublimed co-product (see above) was isolated and identified spectroscopically as the dimethylindazole derivative **7** (for details see the ESI†).[13] This was confirmed by an X-ray crystal structure analysis of its adduct with the Lewis acid $B(C_6F_5)_3$, which was isolated in 80% yield and characterized spectroscopically (see the ESI†) and by X-ray diffraction (see Fig. 3, N2–B1: 1.599(3) Å).

A similar overall reaction was observed starting from the FLP **8** and mesityl azide. Compound **8** contains a markedly more nucleophilic phosphane Lewis base. It is a weakly interacting intramolecular vicinal P–B FLP, as we had previously shown.[8a] It reacted with mesityl azide in *n*-pentane (1.5 h, r.t.) to give the 1,1-addition product **5b**, isolated in 68% yield (see Scheme 3). The X-ray crystal structure analysis of **5b** showed a similar five-membered heterocyclic structure as found for **5a** (for details see Table 1 and the ESI†). In solution, compound **5b** features an ^{11}B NMR resonance at δ = −5.9 and a ^{31}P NMR signal at δ = 54.6.

Compound **5b** was slowly decomposed upon UV irradiation (HPK 125, Pyrex filter) in a dichloromethane solution at ambient temperature. After 4 d the reaction was complete and we isolated the corresponding FLPNH product **6b** in 87% yield.

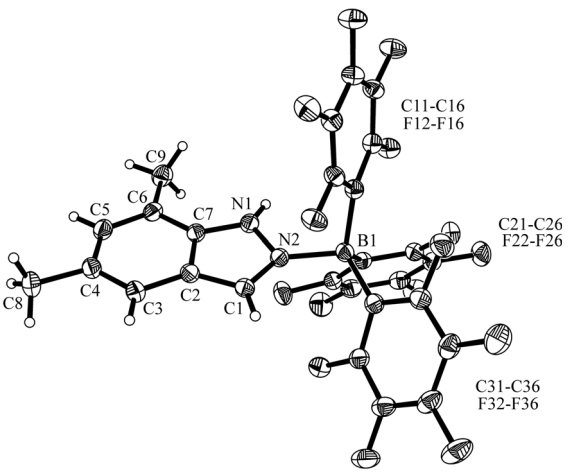
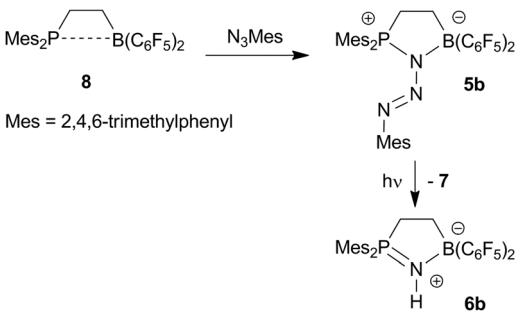
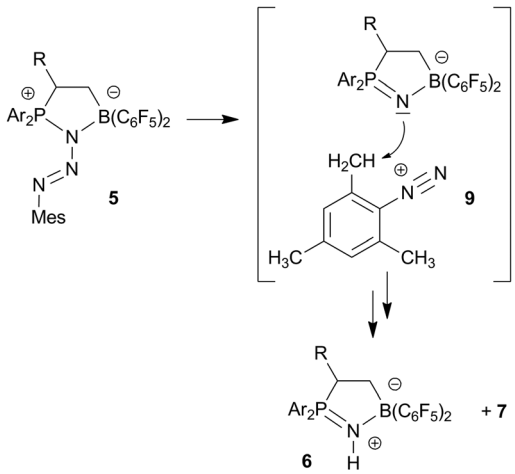


Fig. 3 A view of the molecular structure of the **7**·**B(C$_6$F$_5$)$_3$** adduct (thermal ellipsoids are shown with 30% probability).



Scheme 3



Scheme 4

It was again formed together with the indazole derivative **7** (thermolysis of **5b** also gave **6b** + **7**, but not as cleanly, see the ESI†). Compound **6b** shows a single set of ^{19}F NMR features of the pair of C_6F_5 substituents at boron and the $^{1}H/^{13}C$ NMR signals of the mesityl substituent pair at phosphorus. The [P]═NH ^{1}H NMR signal occurs at δ = 2.80 (d) with a $^{2}J_{PH}$ = 12.1 Hz coupling constant. Compound **6b** shows the core heteronuclei NMR resonances at δ = −4.6 (^{11}B) and δ = 50.7 (^{31}P), respectively. The compound was characterized by X-ray diffraction (for details see the ESI† and Table 1).

Although a detailed mechanistic picture of this unusual FLP variant of the Staudinger reaction will require additional experimental evidence, the observed reactions may be rationalized by the pathway that is schematically depicted in Scheme 4. This would involve initial heterolysis of the N–N single bond in the azide adducts **5** to generate the ion pairs **9**.[14] Deprotonation at the benzylic position of the mesityl substituent would directly lead to the internally N→B stabilized phosphinimines[15] **6** and open a viable pathway for the formation of the indazole derivative **7** (see Scheme 4).

The reaction of the two examples of the intramolecular vicinal FLPs **4** and **8** with mesityl azide followed by thermolysis or photolysis, respectively, has opened pathways to an unusual variant of the Staudinger reaction. This indicates the power that the active Lewis acid–Lewis base combination, as it is characteristic of frustrated Lewis pair chemistry, has to influence reactivity and to lead to new chemical reactions.[16]

Financial support from the European Research Council is gratefully acknowledged.

Notes and references

1 H. Staudinger and J. Meyer, *Helv. Chim. Acta*, 1919, **2**, 635–646.

2 Review articles on the Staudinger reaction: (*a*) Y. G. Gololobov, I. N. Zhmurova and L. F. Kasukhin, *Tetrahedron*, 1981, **37**, 437–472; (*b*) E. F. V. Scriven and K. Turnbull, *Chem. Rev.*, 1988, **88**, 297–368; (*c*) Y. G. Gololobov and L. F. Kasuhkin, *Tetrahedron*, 1992, **48**, 1353–1406.

3 E. g.: K. J. Wallace, R. Hanes, E. Anslyn, J. Morey, K. V. Kilway and J. Siegel, *Synthesis*, 2005, **12**, 2080–2083.

4 (*a*) E. Saxon and C. R. Bertozzi, *Science*, 2000, **287**, 2007–2010; (*b*) M. Köhn and R. Breinbauer, *Angew. Chem.*, 2004, **116**, 3168–3178 (*Angew. Chem., Int. Ed.*, 2004, **43**, 3106–3116).

5 (*a*) J. E. Leffler and R. D. Temple, *J. Am. Chem. Soc.*, 1967, **89**, 5235–5246; (*b*) W. Q. Tian and Y. A. Wang, *J. Org. Chem.*, 2004, **69**, 4299–4308; (*c*) F. L. Lin, H. M. Hoyt, H. van Halbeek, R. G. Bergmann and C. R. Bertozzi, *J. Am Chem. Soc.*, 2005, **127**, 2686–2695.

6 Ph_3PNMes: (*a*) A. T. Katritzky, N. M. Khashab and S. Bobrov, *Helv. Chim. Acta*, 2005, **88**, 1664–1675; See however: (*b*) S. Bittner, M. Pomerantz, Y. Assaf, P. Krief, S. Xi and M. K. Witczak, *J. Org. Chem.*, 1988, **53**, 1–5; (*c*) P. Molina, C. Lopèz-Leonardo, J. Llamas-Botía, C. Foces-Foces and C. Fernandez-Castaño, *J. Chem. Soc., Chem. Commun.*, 1995, 1387–1389; (*d*) J. Kovács, I. Pintér, M. Katjár-Peredy and L. Somsák, *Tetrahedron*, 1997, **53**, 15041–15050.

7 Review: D. W. Stephan and G. Erker, *Angew. Chem.*, 2010, **122**, 50–81 (*Angew. Chem., Int. Ed.*, 2010, **49**, 46–76).

8 (*a*) P. Spies, G. Erker, G. Kehr, K. Bergander, R. Fröhlich, S. Grimme and D. W. Stephan, *Chem. Commun.*, 2007, 5072–5074; (*b*) P. Spies, G. Kehr, K. Bergander, B. Wibbeling, R. Fröhlich and G. Erker, *Dalton Trans.*, 2009, 1534–1541; (*c*) K. V. Axenov, C. M. Mömming, G. Kehr, R. Fröhlich and G. Erker, *Chem.–Eur. J.*, 2010, **16**, 14069–14073; (*d*) S. Schwendemann, R. Fröhlich, G. Kehr and G. Erker, *Chem. Sci.*, 2011, **2**, 1842–1849.

9 See for a comparison: (*a*) M. W. P. Bebbington, S. Bontemps, G. Bouhadir and D. Bourissou, *Angew. Chem.*, 2007, **119**, 3397–3400 (*Angew. Chem., Int. Ed.*, 2007, **46**, 3333–3336); (*b*) C. M. Mömming, G. Kehr, B. Wibbeling, R. Fröhlich and G. Erker, *Dalton Trans.*, 2010, **39**, 7556–7564; (*c*) A. Stute, G. Kehr, R. Fröhlich and G. Erker, *Chem. Commun.*, 2011, **47**, 4288–4290.

10 (*a*) C. Rosorius, G. Kehr, R. Fröhlich, S. Grimme and G. Erker, *Organometallics*, 2011, **30**, 4211–4219; (*b*) C. Appelt, H. Westenberg, F. Bertini, A. W. Ehlers, J. C. Slootweg, K. Lammertsma and W. Uhl, *Angew. Chem.*, 2011, **123**, 4011–4014 (*Angew. Chem., Int. Ed.*, 2011, **50**, 3925–3928); (*c*) S. Roters, C. Appelt, H. Westenberg, A. Hepp, J. C. Slootweg, K. Lammertsma and W. Uhl, *Dalton Trans.*, 2012, **41**, 9033–9045; (*d*) C. Appelt, J. C. Slootweg, K. Lammertsma and W. Uhl, *Angew. Chem.*, 2012, **124**, 6013–6016 (*Angew. Chem., Int. Ed.*, 2012, **51**, 5911–5914).

11 M. W. P. Bebbington and D. Bourissou, *Coord. Chem. Rev.*, 2009, **253**, 1248–1261.

12 (*a*) M. Grün, K. Harms, R. Meyer zu Kocker and K. Dehnicke, *Z. Anorg. Allg. Chem.*, 1996, **622**, 1091–1096; (*b*) F. Heshmatpour, D. Nunhar, R. Garbe, S. Wocadlo, W. Massa, K. Dehnicke, H. Goesmann and D. Fenske, *Z. Anorg. Allg. Chem.*, 1995, **621**, 443–450. See also: (*c*) L. Braun, G. Kehr, R. Fröhlich and G. Erker, *Inorg. Chim. Acta*, 2008, **361**, 1668–1675; (*d*) K. Spannhoff, R. Rojas, R. Fröhlich, G. Kehr and G. Erker, *Organometallics*, 2011, **30**, 2377–2384.

13 (*a*) P. Molina, A. Arques and M. V. Vinader, *J. Org. Chem.*, 1990, **55**, 4724–4731; (*b*) P. Molina, A. Arques, I. Cartagena and R. Obón, *Tetrahedron Lett.*, 1991, **32**, 2521–2524; P. Molina, C. Conesa, A. Alías, A. Arques, M. D. Velasco, A. L. Llamas-Saiz and C. Foces-Foces, *Tetrahedron*, 1993, **49**, 7599–7612.

14 For a remotely related intramolecular C–H-activation pathway see: (*a*) C. Dell'Erba, M. Novi, G. Petrillo and C. Tavani, *Tetrahedron*, 1992, **48**, 325–334; (*b*) C. Dell'Erba, M. Novi, G. Petrillo and C. Tavani, *Tetrahedron*, 1994, **50**, 3529–3536.

15 (*a*) R. Appel and F. Vogt, *Chem. Ber.*, 1962, **95**, 2225–2231; (*b*) W. K. Holley and G. E. Ryschkewitsch, *Phosphorus, Sulfur Silicon Relat. Elem.*, 1990, **53**, 271–284; (*c*) O. Alhomaidan, E. Hollink and D. W. Stephan, *Organometallics*, 2007, **26**, 3041–3048; (*d*) N. Kano, K. Yanaizumi, X. Meng and T. Kawashima, *Heteroat. Chem.*, 2012, **23**, 429–434; (*e*) M. Möhlen, B. Neumüller, A. Dashti-Mommertz, C. Müller, W. Massa and K. Dehnicke, *Z. Anorg. Allg. Chem.*, 1999, **625**, 1631–1637.

16 See e.g. (*a*) C. M. Mömming, E. Otten, G. Kehr, R. Fröhlich, S. Grimme, D. W. Stephan and G. Erker, *Angew. Chem.*, 2009, **121**, 6770–6773 (*Angew. Chem., Int. Ed.*, 2009, **48**, 6643–6646); (*b*) E. Otten, R. C. Neu and D. W. Stephan, *J. Am. Chem. Soc.*, 2009, **131**, 9918–9919; (*c*) A. J. P. Cardenas, B. J. Culotta, T. H. Warren, S. Grimme, A. Stute, R. Fröhlich, G. Kehr and G. Erker, *Angew. Chem.*, 2011, **123**, 7709–7713 (*Angew. Chem., Int. Ed.*, 2011, **50**, 7567–7571).