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Novel reactions of phosphorus(III) azides and isocyanates: unusual modes of cycloaddition with dipolarophiles and an unexpected case of ring expansion†

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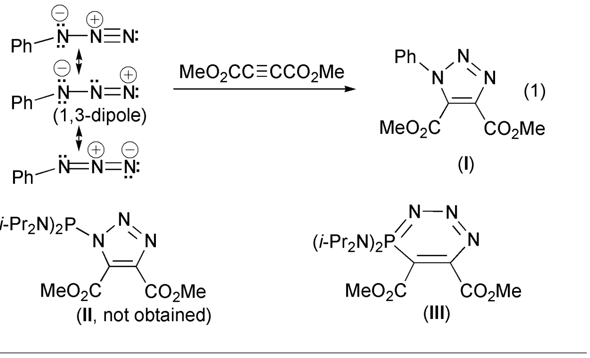
New modes of 1,3-dipolar cycloaddition are uncovered by the isolation of [CH$_2$(6-*t*-Bu-4-Me-C$_6$H$_2$O)$_2$]P{C(CO$_2$Me)C(CO$_2$Me)N[NP(N$_3$)(OC$_6$H$_2$-6-*t*-Bu-4-Me)$_2$CH$_2$]N} (3) and [CH$_2$(6-*t*-Bu-4-Me-C$_6$H$_2$O)$_2$]P{C(CO$_2$Me)C(CO$_2$Me)C(O)N} (4) on treating [CH$_2$(6-*t*-Bu-4-Me-C$_6$H$_2$O)$_2$]P-X [X = N$_3$ (1) and NCO (2)] with the dipolarophile MeO$_2$CC≡CCO$_2$Me; compound 4 undergoes an unprecedented ring expansion upon addition of 2-(methylamino)ethanol to afford the spirocycle [CH$_2$(6-*t*-Bu-4-Me-C$_6$H$_2$O)$_2$]P{OCH$_2$CH$_2$N(Me)CH(CO$_2$Me)CH(CO$_2$Me)C(O)N} (5).

1,3-Dipolar cycloaddition reactions constitute a large class of synthetically useful processes.[1] Organic azides (*e.g.* PhN$_3$) are valuable substrates in such cycloadditions, and behave typically as 1,3-(N,N) dipoles towards dipolarophiles such as MeO$_2$CC≡CCO$_2$Me (dimethyl acetylenedicarboxylate, DMAD) [eqn. (1)].[1a,2] On this basis, one could naively expect that treatment of a σ^3,λ^3-phosphorus azide [*e.g.* (*i*-Pr$_2$N)$_2$PN$_3$] with DMAD would lead to the cycloaddition product **II**; however, the novel heterocycle **III** featuring a *six*-membered ring is formed by 1,4-(P,N) dipolar addition of the acetylene.[3] It has also been shown that the classical reactivity of an organic functional group can be dramatically altered by the presence of a σ^3,λ^3-phosphorus substituent.[4]

In this context, two questions that arose in our mind were, (i) how general are the reactions leading to products such as **III**? (ii) how do the isoelectronic P(III) isocyanates, R$_2$P–N=C=O behave towards dipolarophiles? To address these questions, we chose the P(III) azide and isocyanate **1** and **2** respectively, which possess a sterically hindered eight-membered ring. The cyclic part contains two oxygens that could impart electronic effects different from those in (*i*-Pr$_2$N)$_2$PN$_3$. Similar systems were employed by us previously to explore subtle aspects of penta- and hexa-coordinate phosphorus chemistry.[5] Herein, we describe some interesting aspects of the reactivity of **1**‡ and **2**, that include their unusual behaviour towards the dipolarophile MeO$_2$CC≡CCO$_2$Me (DMAD)§ and a novel ring expansion reaction (Scheme 1).

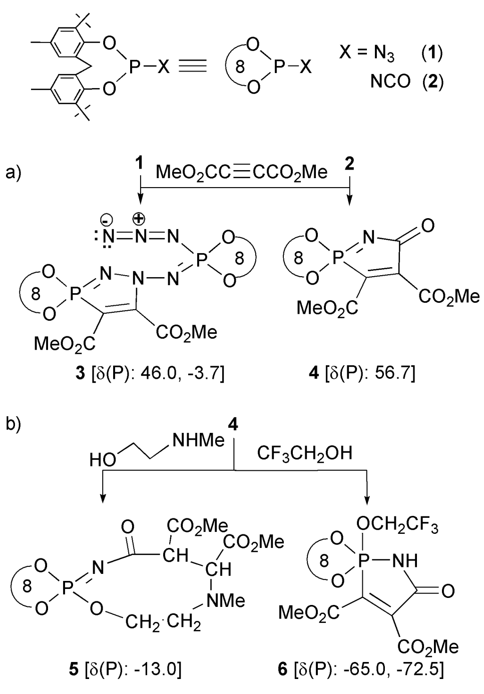
(i) Unlike an organic azide RN$_3$ or (*i*-Pr$_2$N)$_2$PN$_3$, our azide **1** *does not* behave like a 1,3-(N,N) or 1,4-(P,N) dipole towards the dipolarophile DMAD. The reaction involves one molecule of acetylene and two molecules of azide resulting in the practically exclusive formation of the 1,3-(P,N) heterocycle **3** containing an appended phosphazenyl azide residue! It may be noted that **3** is obtained in high yield irrespective of whether DMAD is added to the azide or *vice versa*.



(ii) For the first time, a convincing demonstration of the 1,3-(P,C) dipolar nature of a P(III) isocyanate is provided by the quantitative formation of **4**, in the reaction of **2** with DMAD. In contrast, it must be noted that treating an organic isocyanate R-NCO with DMAD could, logically, lead to 6-membered pyridone rings through a [2 + 2 + 2] cycloaddition, possibly *via* the unstable azetones.[6]

An unprecedented ring expansion (from *five* to *nine* membered) occurs upon addition of 2-(methylamino)ethanol to **4**, to yield **5**. A Michael-type [1,4] addition in which the amine attacks at the carbon adjacent to phosphorus is the key step; cleavage of the P–C bond occurs during subsequent attack by the hydroxy group on phosphorus. This reaction contrasts with the addition of 2,2,2-trifluoroethanol across the P = N bond of **4** resulting in the spirocyclic pentacoordinate phosphorane **6**.

The molecular structures of **3**–**6** have been determined by X-ray crystallography; those of **3** and **5** are shown in Figs. 1 and 2.[7]¶ It can be noted that the formal P–N *double bond* at the spiro-phosphorus in **3** [P(2)–N(6) 1.599(4) and P(4)–N(12) 1.612(4) Å; second molecule of the asymmetric unit not shown in Fig. 1] is slightly *longer* than the formal *single bond* in H$_2$NP[OC(CF$_3$)$_2$C(CF$_3$)$_2$O]$_2$ [1.590(8) Å],[8] thus posing an intriguing question on the nature of the P–N bond. A



Scheme 1

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† Electronic supplementary information (ESI) available: Platon diagrams with selected bond parameters for **4** and **6** and experimental details. See http://www.rsc.org/suppdata/cc/b1/b107087h/

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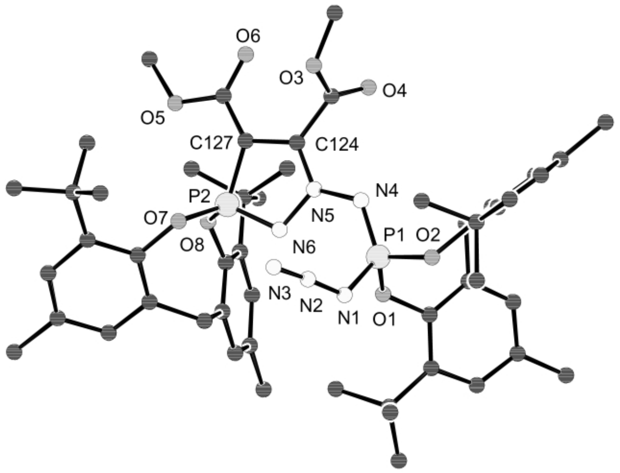

Fig. 1 Molecular structure of **3**·3/4CH$_3$CN; the solvent, second molecule in the asymmetric unit and hydrogen atoms are omitted. Selected distances: P(1)–N(1) 1.664(4), P(1)–N(4) 1.541(4), P(1)–O(1) 1.563(3), P(1)–O(2) 1.538(3), P(2)–N(6) 1.599(4), P(2)–O(7) 1.583(3), P(2)–O(8) 1.586(3), P(2)–C(127) 1.720(5), N(1)–N(2) 1.192(6), N(2)–N(3) 1.117(7), N(4)–N(5) 1.394(5), N(5)–N(6) 1.387(5), N(5)–C(124) 1.312(5), C(124)–C(127) 1.412(6) Å.

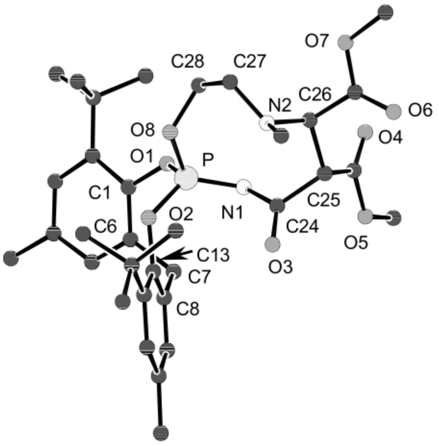

Fig. 2 Molecular structure of **5**·C$_6$H$_5$CH$_3$; the solvent and hydrogen atoms are omitted. Selected distances: P–N(1) 1.550(2), P–O(2) 1.566(2), P–O(1) 1.573(2), P–O(8) 1.580(2), O(8)–C(28) 1.457(2), N(1)–C(24) 1.370(2), N(2)–C(27) 1.467(3), N(2)–C(26) 1.471(3), C(24)–C(25) 1.533(3), C(25)–C(26) 1.539(3), C(27)–C(28) 1.510(3) Å.

rationalization can be put forth by assuming some phosphonium character for the spiro-phosphorus atom;[3] this would also explain the ready formation of the addition product **6** from **4** and CF$_3$CH$_2$OH.

Thus we have shown here that (i) the reaction of a P(III) azide with DMAD can lead to products other than that reported before and (ii) new heterocycles which are amenable for further exploration can be synthesised using P(III) isocyanates and DMAD. In this context, it may be noted that the isothiocyanate [CH$_2$(6-*t*-Bu-4-Me-C$_6$H$_2$O)$_2$]P-NCS also reacts with DMAD to give a heterocycle [*via* 1,3-(P,C) cycloaddition] which is similar to **4**.‖ This and related reactions are currently being investigated.

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Notes and references

‡ X-Ray structural data for this compound is available from the authors.

§ The reaction of some P(III) isocyanates with carbonyl compounds are reported.[9]

¶ Single crystal X-ray data were collected on an Enraf-Nonius MACH3 (compounds **3, 4** and **6**) or Stoe IPDS (compound **5**) diffractometer at 293 K using Mo-K$_\alpha$ (λ = 0.71073 Å) radiation. The structures were solved by direct methods and refined by full-matrix least squares method with the SHELXL-97 program.[7] *Crystal data*: **3**·3/4CH$_3$CN, C$_{107}$H$_{136.5}$N$_{13.5}$O$_{16}$P$_4$, M = 1991.68, triclinic, space group $P\bar{1}$, a = 14.616(4), b = 19.288(4), c = 23.112(8), α = 114.26(2), β = 103.91(2), γ = 96.55(2), V = 5597(3) Å^3, Z = 2, μ = 0.134 mm^{-1}, data/restraints/parameters: 19610/132/1374. R indices ($I > 2\sigma(I)$): R1 = 0.0658, $wR2$ = 0.1651, CCDC number 157568. See http://www.rsc.org/suppdata/cc/b1/b107087h/ for crystallographic files in .cif or other electronic format. **4**: C$_{30}$H$_{36}$NO$_7$P, M = 553.57, monoclinic, space group $P2_1/n$, a = 10.308(3), b = 17.604(4), c = 16.464(3), β = 107.14(2), V = 2854.9(11) Å^3, Z = 4, μ = 0.144 mm^{-1}, data/restraints/parameters: 5012/0/362. R indices ($I > 2\sigma(I)$): $R1$ = 0.0515, $wR2$ = 0.1247. CCDC 157569. **5**·C$_6$H$_5$CH$_3$, C$_{40}$H$_{53}$N$_2$O$_8$P, M = 720.81, triclinic, space group $P1$, a = 11.792(7), b = 12.580(7), c = 15.162(9), α = 110.66(6), β = 103.36(7), γ = 90.53(7), V = 2037(2) Å^3, Z = 2, μ = 0.118 mm^{-1}, data/restraints/parameters: 5850/0/480. R indices ($I > 2\sigma(I)$): $R1$ = 0.0423, $wR2$ = 0.1218. CCDC 157570. **6**.CH$_3$CN, C$_{34}$H$_{42}$F$_3$N$_2$O$_8$P, M = 694.67, triclinic, space group $P1$, a = 9.455(3), b = 10.861(3), c = 19.023(5), α = 93.24(2), β = 91.41(2), γ = 107.85(2), V = 1854.6(9) Å^3, Z = 2, μ = 0.138 mm^{-1}, data/restraints/parameters: 6520/0/454. R indices ($I > 2\sigma(I)$): $R1$ = 0.0605, $wR2$ = 0.1698. CCDC 157571.

‖ Diethyl acetylenedicarboxylate (EtO$_2$CC≡CCO$_2$Et) afforded products similar to **3** and **4**. The product of EtO$_2$CC≡CCO$_2$Et with **2** also underwent ring expansion and addition leading to compounds similar to **5** and **6**.

1 (*a*) F. A. Carey and R. J. Sundberg, *Advanced Organic Chemistry*, Part A: Structure and Mechanisms and Part B: Reactions and Synthesis, Plenum Press, New York, 1990, pp. 635–640 and pp. 300-306 respectively; (*b*) A. Padwa, *1,3-Dipolar Cycloaddition Chemistry*, vol. 1 and 2, Wiley Interscience, New York, 1984; (*c*) A. Padwa, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 4 (volume ed. M. F. Semmelhack), pp. 1069–1168; (*d*) J. Nakayama, A. Kimata, H. Taniguchi and F. Takahashi, *Chem. Commun.*, 1996, 205; (*e*) K. Banert and F. Köhler, *Angew. Chem., Int. Ed. Engl.*, 2001, **40**, 174; (*f*) J. S. Carey, *J. Org. Chem.*, 2001, **66**, 2526.

2 R. Huisgen, R. Knorr, L. Möbius and G. Szeimies, *Chem. Ber.*, 1965, **98**, 4014.

3 K. Bieger, J. Tejeda, R. Rèau, F. Dahan and G. Bertrand, *J. Am. Chem. Soc.*, 1994, **116**, 8087.

4 M. Granier, A. Baceiredo, M. Nieger and G. Bertrand, *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 1123.

5 (*a*) M. A. Said, M. Pülm, R. Herbst-Irmer and K. C. Kumara Swamy, *J. Am. Chem. Soc.*, 1996, **118**, 9841; (*b*) M. A. Said, M. Pülm, R. Herbst-Irmer and K. C. Kumara Swamy, *Inorg. Chem.*, 1997, **36**, 2044; (*c*) S. Kumaraswamy, C. Muthiah and K. C. Kumara Swamy, *J. Am. Chem. Soc.*, 2000, **122**, 964.

6 (*a*) N. E. Shore, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 5 (volume ed. L. A. Paquette), p. 1155; (*b*) M. A. Pericás, F. Serratosa, E. Valenti, M. Font-Altaba and X. Solans, *J. Chem. Soc., Perkin Trans. 2*, 1986, 961; (*c*) L. Gosez and J. Marchand-Brynaert in ref. 6(a), pp. 102–108; (*d*) F. P. Cossío, G. Roa, B. Lecea and J. M. Ugalde, *J. Am. Chem. Soc.*, 1995, **117**, 12306.

7 G. M. Sheldrick, *SHELX-97*, University of Göttingen, 1997.

8 W. Storzer, D. Schomburg and G. V. Röschenthaler, *Z. Naturforsch. B*, 1981, **36**, 1071.

9 (*a*) R. Francke and G. V. Röschenthaler, *Z. Anorg. Allgem. Chem.*, 1989, **572**, 135; (*b*) R. Francke, J. Heine and G. V. Röschenthaler, *Phosphorus, Sulfur, and Silicon*, 1990, **49/50**, 377.