Tetrahedron Letters, Vol. 33, No. 8, pp. 1049-1052, 1992
Printed in Great Britain

0040-4039/92 $3.00 + .00
Pergamon Press plc

A NEW ACCESS TO PHOSPHAINDOLIZINES BY [3+2] CYCLOADDITION OF AZOMETHINE YLIDES ONTO PHOSPHAALKYNES[1]

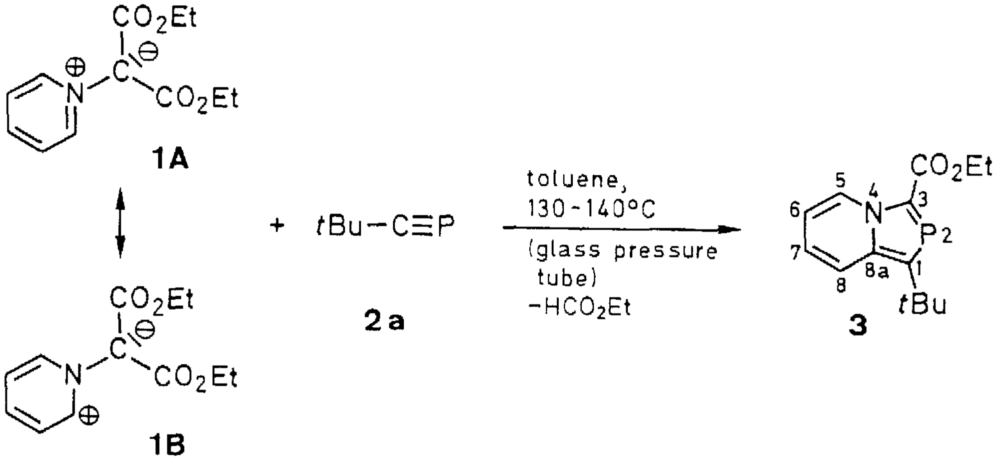
Uwe Bergsträßer, Andreas Hoffmann, and Manfred Regitz*

Fachbereich Chemie der Universität Kaiserslautern, Erwin-Schrödinger-Stasse, D-6750 Kaiserslautern,
Federal Republic of Germany

Abstract: Azomethine ylides such as **1** and **4** in which the nitrogen atom is incorporated in a six-membered heterocyclic ring undergo regiospecific [3+2] cycloadditions with the phosphaalkynes **2a** and **b** at 130-140 °C to furnish the phosphaindolizines **3** and **5a-c** after elimination of ethyl formate or hydrogen cyanide, respectively. In contrast, dipoles of the type **6** react unspecifically with the phosphaalkyne **2a** to yield the regioisomers 7 and **8**.

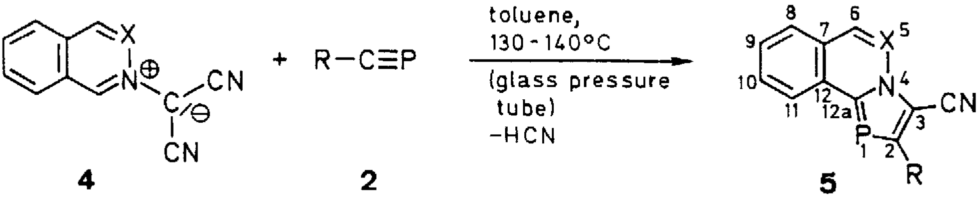
Phospholes with a λ^3,σ^2-phosphorus and other heteroatoms in the ring system play an important role in the development of the chemistry of low coordinated phosphorus[2,3]. 1,3-Azaphospholes, which are a structural component of all the phosphaindolizines to be discussed here, have been prepared by cyclocondensation[4], by O/P exchange in oxazolium salts with tris[trimethylsilyl]phosphine[5], and by [3+2] cycloadditions of mesoionic compounds to phosphaalkynes[6] or of nitrile ylides to phosphaalkenes[7]. In both the latter procedures, elimination reactions follow the actual ring-forming reaction.

With the previously unknown reaction of azomethine ylides of the types **1**, **4**, and **6** with phosphaalkynes **2**, we now describe a new and generally applicable synthesis of the title compounds.



When the pyridinium ylide **1** is heated with the phosphaalkyne **2a**, a regiospecific [3+2] cycloaddition[8] reaction takes place and is followed, under the harsh reaction conditions employed, by an elimination of ethyl formate to furnish the [1,3]azaphospholo[1,5-*a*]pyridine **3** (30% yield). The ^{31}P-NMR chemical shift (δ = +162.4) as well as the ^{13}C-NMR signals of the azaphosphole ring and their respective coupling constants [δ = 133.4 ($^{1}J_{C,P}$ = 47.3 Hz, C3); 155.1 ($^{1}J_{C,P}$ = 45.1 Hz, C1); 142.1 ($^{2}J_{C,P}$ = 9.2 Hz, C8a)] agree very well with the values for the independently prepared methyl derivative (**3**; Me in place of *t*Bu)[9].

Isoquinolinium and phthalazinium methylides (**4a** and **b**, respectively) react similarly with the phosphaalkynes **2a** and **2b** via [3+2] cycloaddition and elimination (in this case of hydrogen cyanide which, however, necessitates the addition of triethylamine) and the condensed 1,3-azaphospholes **5a-c** are obtained (25-40% yield).



4	a	b
X	CH	N

2	a	b
R	*t*Bu	CMe$_2$Et

5	a	b	c
X	CH	N	CH
R	*t*Bu	*t*Bu	CMe$_2$Et

These reactions are also regiospecific although the dipole orientation is the reverse of that in the reactions **1** + **2a** → **3**.

The constitution of **5b** - and thus the direction of addition of **4b** to **2a** - has been confirmed unequivocally by an X-ray structure analysis (Fig. 1)[10].

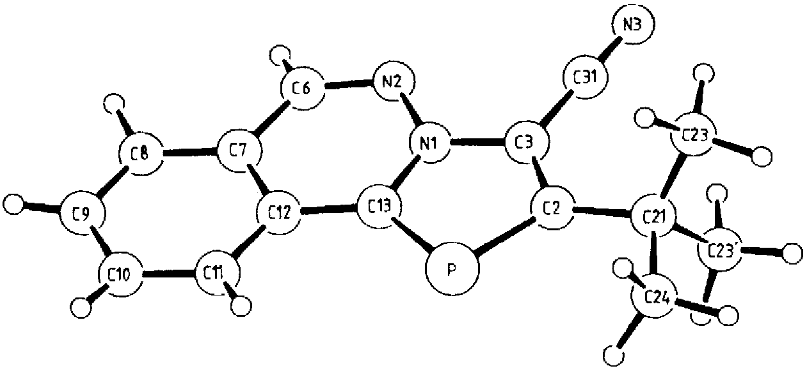


Fig. 1. Crystal structure of the phosphaindolizine **5b**. - Selected bond lengths [Å] and bond angles [°]

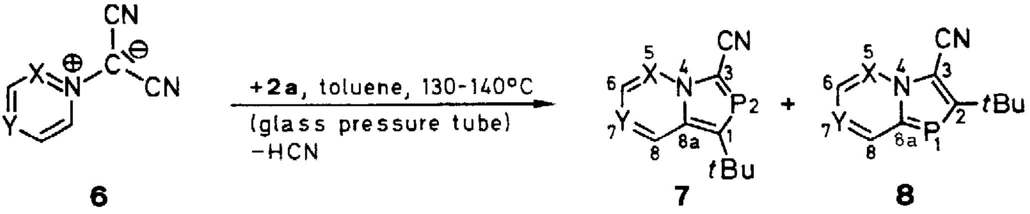
Bond lengths					
N2 -N1	1.375(4)	C3 -C31	1.419(5)	C7 -C12	1.392(5)
P -C2	1.754(3)	C7 -C6	1.428(5)	N1 -C3	1.372(4)
N2 -C6	1.286(4)	P -C13	1.734(4)	C31 -N3	1.140(5)
C12 -C13	1.431(5)	C3 -C2	1.371(5)	C2 -C21	1.533(5)
N1 -C13	1.365(4)				

Bond angles					
C13 -P -C2	89.9(2)	C12 -C13 -P	131.2(3)	C21 -C2 -C3	124.7(3)
C3 -C2 -P	111.5(3)	C13 -N1 -C3	114.0(3)	C3 -C31 -N3	178.6(4)
C2 -C3 -N1	112.9(3)	N1 -C13 -P	111.8(2)	N2 -N1 -C3	119.4(3)
C31 -C3 -N1	117.6(3)	C13 -N1 -N2	126.5(3)	C12 -C13 -N1	117.1(3)
C21 -C2 -P	123.8(2)	C31 -C3 -C2	129.5(3)		

The bond lengths for P-C2 and P-C13 [1.754(3) and 1.734(4) Å, respectively] are intermediate between those of P/C single and P/C double bonds and are indicative of electron delocalization in the phosphorus-containing heteroaromatic ring. The bond angle C13-P-C2 [89.9(2)°] is in the region characteristic for 1,3-azaphospholes[2].

When the ^{31}P- and ^{13}C-NMR data of the 1,3-azaphosphole systems of **5a-c** are considered, it is seen that they all lie in narrow absorption ranges [^{31}P: δ = +72.9 to +83.3; ^{13}C: δ = 104.9-109.7 ($^2J_{C,P}$ = 5.5-6.1 Hz, C3); 153.9-161.8 ($^1J_{C,P}$ = 42.3-59.9 Hz, C12a); 172.8-175.3 ($^1J_{C,P}$ = 54.3-55.3 Hz, C2)]. In conjunction with the crystal structure analysis of **5b**, these data confirm that the products **5a-c** all belong to the same structural type.

Although the pyridinium, pyridazinium, and 1,4-diazinium dicyanomethylides **6a-c** all react with the phosphaalkyne **2a** in the manner described above (the elimination of HCN is again promoted by the addition of 1 mol of NEt_3), the primary step is completely non-selective so that 1:1 mixtures of **7a-c** with **8a-c** are formed (40-60% yield).



6-8	**a**	**b**	**c**	**d**	**e**	**f**	**g**	**h**	**i**
X	CH	N	CH	CH	CH	CH	CH	CH	CH
Y	CH	CH	N	CMe	C*t*Bu	O*i*Pr	C−CO_2Me	C−C≡N	C−COPh

When donor-substituents were introduced into the 4 position of **6a**, is was found that a methyl group had no effect on the product ratio (**7d**:**8d** = 50:50) whereas *tert*-butyl and isopropoxy groups favoured the formation of the isomer **7** (**7e**:**8e** = 80:20; **7f**:**8f** = 100:0). Acceptor substituents exhibited neutral effects (**7g-i**:**8g-i** = 50:50)[11]. The product mixtures can be separated by MPLC (Merck silica gel 60, 0.015-0.049 mm, ether/pentane, 2:1), as has been demonstrated for the example **7a/8a**.

Acknowledgements: We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for generous financial support.

References and Notes

1. Organophosphorus Compounds; Part 54. For Part 53, see: Breit, B.; Memmesheimer, H., Boese, R.; Regitz, M. *Chem. Ber.* **1992**, *125*, in press.
2. Schmidpeter, A.; Karaghiosoff, K. in *Rings, Clusters and Polymers of Main Group and Transition Elements* (Roesky, H. W., ed), Elsevier, Amsterdam 1989, pp. 307-343.
3. Schmidpeter, A. in *Multiple Bonds and Low Coordination in Phosphorus Chemistry* (Regitz, M., Scherer, O. J., eds.), Thieme, Stuttgart 1990, pp. 258-286.
4. See, e.g., Issleib, K.; Vollmer, R.; Oehme, H.; Meyder, H. *Tetrahedron Lett.* **1978**, *19*, 441-444; Issleib, K.; Vollmer, R. *Z. Anorg. Allg. Chem.* **1981**, *481*, 22-32; Heinicke, J.; Tzschach, A. *Tetrahedron Lett.* **1982**, *23*, 3643-3646.
5. See, e.g., Märkl, G.; Dorfmeister, G. *Tetrahedron Lett.* **1986**, *27*, 4419-4442 as well as *Tetrahedron Lett.* **1987**, *28*, 1089-1092.
6. Rösch, W.; Richter, H.; Regitz, M. *Chem. Ber.* **1987**, *120*, 1809-1813; Fuchs, E. P. O.; Hermesdorf, M.; Schnurr, W.; Rösch, W.; Heydt, H.; Regitz, M.; Binger, P. *J. Organomet. Chem.* **1988**, *338*, 329-340; see also Regitz, M. in Ref.[3], pp. 73-74.
7. Märkl, G.; Troetsch-Schaller, I.; Hölzl, W. *Tetrahedron Lett.* **1988**, *29*, 785-788; Regitz M.; Burkhardt, B. unpublished results with RC(OTms)=PTms, University of Kaiserslautern, 1989.
8. Reviews on the cycloaddition reactivity of phosphaalkynes: Regitz, M.; Binger, P. *Angew. Chem.* **1988**, *100*, 1541-1565; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1484-1508; Regitz, M. *Chem. Rev.* **1990**, *90*, 191-213.
9. Cyclocondensation of pyridinium salts with PCl_3: Bansal, R. K.; Karaghiosoff, K.; Gupta, N.; Schmidpeter, A.; Spindler, C. *Chem. Ber.* **1991**, *124*, 475-480. Further examples of this methodology are given therein.
10. $C_{15}H_{14}N_3P$. M = 267.3 g·mol^{-1}, orthorhombic. Pnma (No.62), a = 13.844(4), b = 6.948(2), c = 13.780(2) Å, V = 1325.5(6) Å^3, Z = 4, $d_{calc.}$ = 1.339 g cm^{-3}, absorption coefficient μ = 1.9 cm^{-1}. The measurements were performed with an Enraf-Nonius CAD4 diffractometer with monochromatic Mo K_α radiation; 1116 independent reflections [h: 0 -> +16; k: 0 -> +7; l: 0 -> +16] with $4.0° \le 2\theta \le 50°$, of which 985 with $I > 2\sigma(I)$ were observed; number of parameters 134. The structure solution [SHELX-86] and the subsequent refinement by direct methods [SHELX-76] converged at R = 0.0474 and R_W = 0.0470. Further details such as atomic coordinates, tables of bond lengths and bond angles, as well as temperature factors are available on request from The Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, U.K.
11. Phosphaindolizines of the structural type **8a** were also obtained by O/P exchange in oxazolium salts: Märkl, G.; Pflaum, S. *Tetrahedron Lett.* **1987**, *28*, 1511-1514.

(Received in Germany 27 November 1991)