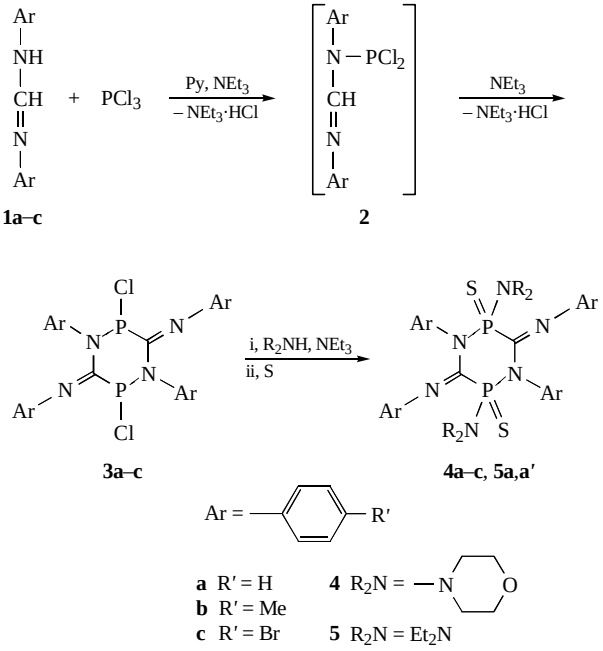
Novel heterocyclizations of *N*,*N*′-diarylformamidines: 1,4,2,5-diazadiphosphorinanes

Gennady V. Oshovsky,* Alexander M. Pinchuk, Alexander N. Chernega, Igor I. Pervak and Andrey A. Tolmachev

Institute of Organic Chemistry, National Academy of Sciences of Ukraine, 253660 Kyiv, Ukraine. Fax: +7 044 543 6843; e-mail: oshovsky@carrier.kiev.ua

The heterocyclization of *N*,*N*′-diarylformamidines with phosphorus trichloride to form 1,4,2,5-diazadiphosphorinanes was found to proceed *via* the key stage of aliphatic electrophilic ylide substitution at the formamidine carbon atom.

The first examples of aliphatic electrophilic substitution at the formamidine carbon atom in reactions with trivalent phosphorus halides were found recently.[1] There is no published data on similar reactions of formamidines with other electrophilic agents. C-Substitution in N,N,N′-trisubstituted formamidines is an extension of well-studied N-phopshorylation of *NH*-amidines.[2] In this work, we report a novel approach to *N*,*N*′-diarylformamidines as N,C-bifunctional compounds, in which classical substitution at the nitrogen atom is followed by the formation of a bond with the formamidine carbon atom. This is a new feature of using formamidines in syntheses of heterocyclic compounds. Using a model reaction of the title compounds with phosphorus trichloride, we implemented a new promising synthesis of 1,4,2,5-diazadiphosphorinane[3] (Scheme 1).



Scheme 1

The first step of the reaction leads to N-phosphorylated[2] amidines **2**. Compounds **2** are transformed into **3** only in a basic medium (a mixture of pyridine and NEt_3).† This fact suggests that the transformation occurs *via* the ylide mechanism[4] of electrophilic C-substitution at the HCXY moiety (X, Y = NR, N, S, O) of heterocyclic compounds and is similar to acylation[5] and phosphorylation[6] of azoles.

The transformation of **2** into **3** can be easily monitored by ^{31}P NMR. This process is considerably slower than the formation of **2** from amidine and PCl_3. The ^{31}P NMR spectrum of **3** exhibits two signals as a result of two possible isomers of **3**. These isomers are interconvertable in solution; it is likely that this conversion is caused by the presence of trace acids.‡

The mixture of isomers **3** reacts smoothly with secondary amines and sulfur leading to a mixture of stable isomers **5**. The difference in solubility allows the separation of stable isomers **5a** and **5a′**. X-ray analysis confirmed the structure of **5a′** (Figure 1).§,¶ Compound **5a′** corresponds to the *cis* isomer, and the diazadiphosphorinane ring has a boat conformation in crystals.

The second isomer **5a** is *trans*. Both *cis* and *trans* isomers are sterically hindered. Judging from very wide signals in the ^1H NMR spectra corresponding to Ar bonded to endocyclic nitrogen and amide moieties at phosphorus,†† one can conclude that the energy difference between conformers of each isomer should be insignificant. This is not surprising, because the 1,4,2,5-diazadiphosphorinane ring involves sp^2 carbons. Therefore, there is a dynamic equilibrium between the conformers, instead of an excess of one of them, in contrast with less sterically hindered phosphaheteroannelated cyclohexanes.[7]

† *General method for the synthesis of* **3**, **4a–c**, **5a**,**a′**: 0.005 mol of an amidine was dissolved in 10 ml of pyridine and 0.0125 mol of NEt_3; next 0.005 mol of PCl_3 was added to this reaction mixture cooled to –70 °C. The reaction mixture was allowed to stand for 7 h at room temperature. Next, (A) to prepare compounds **3**, the reaction mixture was filtered and evaporated to dryness. By-products were extracted with dry acetonitrile (up to 100 ml). (B) To prepare compounds **4a–c**, **5a**, 0.015 mol of NEt_3 was added to the reaction mixture, and, after cooling to –50 °C, 0.006 mol of a secondary amine was added. The reaction mixture was allowed to stand for 1 h, then 0.005 mol of S was added. After standing for 2 h, the precipitate was filtrered off and washed three times with hot benzene; the solvent was evaporated to dryness in a vacuum, and by-products were extracted with acetonitrile (up to 100 ml). The solid residue was recrystallised from toluene (crystallisation from dioxane is also acceptable). To prepare **5a′**, the acetonitrile extract was evaporated to dryness, and the product was crystallised from octane and ethyl acetate.

‡ **2b** (R = Me): $\delta_{^{31}P}$ = 152.3 ppm (Py); **3b** $\delta_{^{31}P}$ = 67.31 (prevailing isomer), $\delta_{^{31}P}$ = 67.61 (minor isomer), yield of the isomers mixture 42%. The yields of isomers strongly depend on the temperature and the nature of substituents at phosphorus and of aryl substituents at nitrogens.

§ To confirm the structure of isomers **4a**, **4b** and **5a**, mass spectroscopy (molecular desorption) was used: **4a**, 690±5 (calc. 686.48); **4b**, 747±5 (calc. 742.85); **5a**, 660±5 (calc. 658.78). Elemental analysis corresponds to the calculated data to within 0.25%.

¶ *Crystallographic data for* **5a′**. A crystal of compound **5a′** as a transparent prism (crystal dimensions 0.16×0.34×0.62 mm) was grown from ethyl acetate, $C_{34}H_{40}N_6P_2S_2$, M = 658.80, monoclinic, a = 8.723(3), b = 38.29(1), c = 10.938(5) Å, β = 109.06(3)°, V = 3453.4 Å^3 (by the least-squares refinement of the setting angles for 24 automatically centered reflections), space group $P2_1$, Z = 4, D_c = 1.27 g cm^{-3}, μ = = 2.70 cm^{-1}. 'Enraf-Nonius CAD4' diffractometer was used, $\omega/2\theta$ scan mode with the ω scan width 0.71 + 0.34tg θ, ω scan speed 1.7–6.7 ° min^{-1}, graphite-monochromated MoKα radiation (λ = 0.71069 Å), 6338 reflections were measured ($2 < \theta < 30°$), 5473 unique (merging R = 0.017), giving 4044 with $I > 3\sigma(I)$. The structure was solved using direct methods, full-matrix least-squares refinement against F with all non-hydrogen atoms in anisotropic approximation (793 variables, observations/variables = 5.1). All crystallographic calculations were carried out using the CRYSTALS program package. Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. For details, see *Mendeleev Commun*., Issue 1, 1999. Any request to the CCDC for data should quote the full literature citation and the reference number 1135/37.

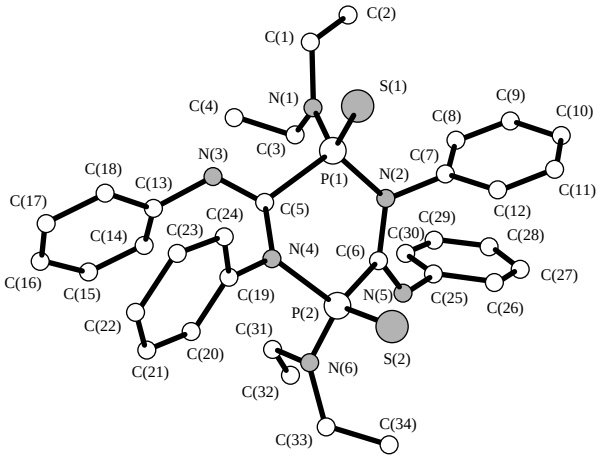
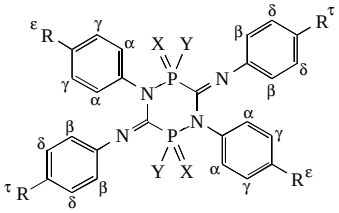


Figure 1 Crystal structure of 1,4,2,5-diazadiphosphorinane **5a′**. Selected bond lengths (Å): P(1)–S(1) 1.924(3), P(2)–S(2) 1.915(3), P(1)–N(1) 1.643(7), P(1)–N(2) 1.712(6), P(2)–N(4) 1.706(6), P(2)–N(6) 1.638(7), P(1)–C(5) 1.856(8), P(2)–C(6) 1.828(8); selected bond angles (°): N(2)–P(1)–C(5) 101.1(3), N(4)–P(2)–C(6) 102.0(3), C(5)–N(3)–C(13) 122.2(7), C(6)–N(5)–C(25) 125.9(7). The C(5)–P(1)–N(2)–C(6) and C(5)–N(4)–P(2)–C(6) groups are planar to within 0.06 Å, and the dihedral angle between these planes is 39.5°.

†† *Spectral data*:



3b (prevailing isomer): ^{1}H NMR (C_6D_6) δ: 7.43 (d, 4H, α, $J_{\alpha\gamma}$ 7.2 Hz), 6.76–6.92 (m, 12H, βγδ), 1.96 (s, 12H, ετ, Me).

4a: yield 56%, mp 302–303 °C. ^{1}H NMR (C_6D_6) δ: 7.45 (br. s, 4H, α), 7.015 (d, 4H, β, $J_{\beta\delta}$ 7.5 Hz), 6.90 (t, 4H, δ), 6.70 (t, 2H, τ, $J_{\tau\delta}$ 7.2 Hz), 6.63 (br. s, 6H, γε), 3.36, 3.08 and 2.72 (br. s, 16H, Y = NR_2). ^{31}P NMR (pyridine) δ: 67.2.

4b: yield 49%, mp 295–296 °C. ^{1}H NMR (C_6D_6) δ: 7.45 (br. s, 4H, α), 7.06 (d, 4H, β, $J_{\beta\delta}$ 8.1 Hz), 6.77 (d, 4H, δ), 6.62 (br. s, 4H, γ), 3,40, 3.16 and 2.83 (br. s, 16H, Y = NR_2), 2.00 and 1.84 (s, 12H, ετ). ^{31}P NMR (pyridine) δ: 68.4.

4c: yield 37%, mp > 350 °C. ^{1}H NMR (C_6D_6) δ: 7.29 and 7.10 (br. s, 8H, αγ), 7.22 and 6.62 (d, 8H, βδ, $J_{\beta\delta}$ 7.8 Hz), 3.37, 3.21 and 3.06 (br. s, 16H, Y = NR_2). ^{31}P NMR (benzene) δ: 57.3.

5a (*trans*): yield 48%, mp 260–262 °C. ^{1}H NMR (C_6D_6) δ: 7.52 and 7.43 (br. s, 4H, α), 7.07 (d, 4H, β, $J_{\beta\delta}$ 7.2 Hz), 6.91 (t, 4H, δ, $J_{\tau\delta}$ 7.2 Hz), 6.8–6.6 (br. s, 8H, γετ), 3.39 and 3.18 [br. s, 8H, Y = NR_2:(CH_2)], 0.58 [br. s, 12H, Y = NR_2:(Me)]. ^{31}P NMR (C_6D_6) δ: 61.42.

5a′ (*cis*): yield 12%, mp 208–209 °C. ^{1}H NMR (C_6D_6) δ: 7.72 (br. s, 4H, α), 6.9–7.2 (br. s, 6H, γε), 6.99 (t, 4H, δ), 6.82 (t, 2H, τ, $J_{\tau\delta}$ 7.5 Hz), 6.40 (d, 4H, β, $J_{\beta\delta}$ 6.8 Hz), 3.42 [br. s, 8H, Y = NR_2:(CH_2)], 1.15 [br. s, 12H, Y = NR_2:(Me)]. ^{31}P NMR (MeCN) δ: 60.72.

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