One-pot Synthesis of a New Class of Fused 2,4-Diimino-1,3-diazetidines by an Aza-Wittig/[2 + 2] Cycloaddition of Carbodiimides Process

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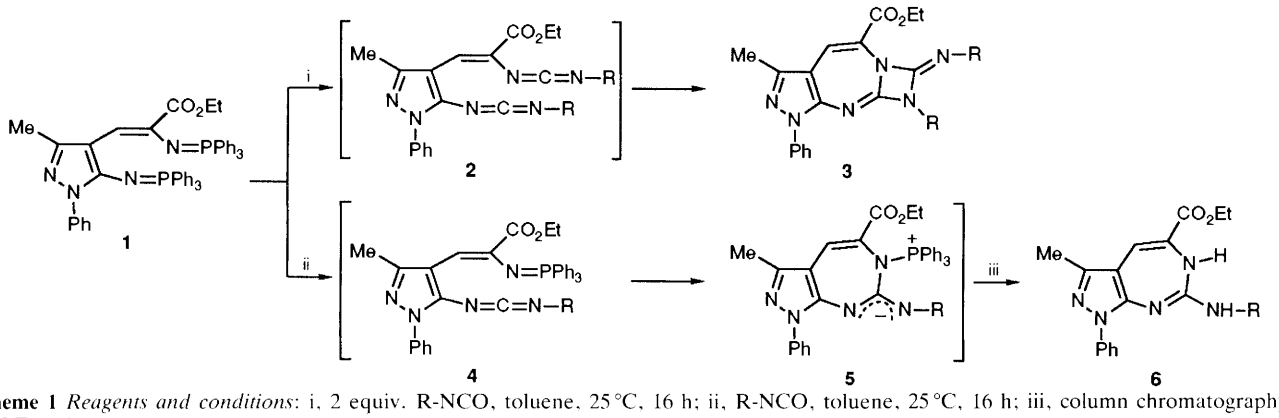
The new [5.7.4]tricyclic ring system **3** is synthesized in a one-pot reaction from bis(iminophosphorane) **1** and two equivalents of aryl isocyanate; compound **1** also reacts with one equivalent of isocyanate to give the bicyclic [1,3]diazepine **6**; the crystal structure of compounds **3** and **6** are determined.

Iminophosphorane-mediated syntheses of heterocyclic ring systems have developed remarkably in recent years, which is obviously linked to the rapid progress in the preparation of functionalized iminophosphoranes. While relevant examples involving iminophosphoranes have been reported,[1] the chemistry of bis(iminophosphoranes) remains almost unexplored. This type of compound is expected to have synthetic potential as a result of the ability to react with reagents having two functionalities or with two separate reagents with the same or different functionality. In this context, we have recently shown that bis(iminophosphoranes) derived from the condensation products between *o*-azidobenzaldehyde and *o*-azidoaniline or ethyl azidoacetate are valuable building blocks for the preparation of structurally complex heterocyclic rings.[2]

Herein, we describe the first use of bis(iminophosphoranes) for the synthesis of heterocycles by a tandem aza-Wittig/[2+2] cycloaddition reaction for the first time. Starting compound **1**, is readily prepared in 55% yield by condensation of 5-azido-4-formyl-3-methyl-1-phenyl(1*H*)pyrazole[3] with ethyl azidoacetate at −25 °C followed by treatment with triphenylphosphine in dry dichloromethane at 0 °C.

When compound **1** is treated with two equivalents of aryl isocyanates in dry toluene at room temperature, the fused heterocycles **3** are obtained in a tandem reaction.

In this reaction sequence the bis(iminophosphorane) **1** apparently reacts initially with the isocyanate to give the intermediate bis(carbodiimide) **2** as aza-Wittig product. In the last reaction step an intramolecular [2+2] cycloaddition between the two carbodiimide moieties leads to the tricyclic



Scheme 1 *Reagents and conditions*: i, 2 equiv. R-NCO, toluene, 25 °C, 16 h; ii, R-NCO, toluene, 25 °C, 16 h; iii, column chromatography, AcOEt–n-hexane

Table 1 1,3-Diazeto[1′,2′-*a*]pyrazolo[3,4-*d*][1,3]diazepines **3** and pyrazolo [3,4-*d*][1,3]diazepines **6**

Compound[a]	R	Yield(%)	M.p./°C
3a	Ph	60	150–151
3b	*p*-MeC_6H_4	66	190–191
3c	*p*-$MeOC_6H_4$	50	143–144
3d	*p*-ClC_6H_4	68	223–224
6a	Et	65	168–169
6b	Pr	60	163–164
6c	Ph	65	199–200
6d	*p*-MeC_6H_4	53	174–175

[a] All new compounds described here had spectral and microanalytical properties in agreement with the assigned structures.

system **3**. Considering the number of steps involved in this one-pot reaction the yields 50–68% obtained are very good.

Despite its apparent simplicity, the [2+2] cycloaddition of carbodiimides is rare; it has only been reported[4] that diphenylcarbodiimide in the presence of tri-n-butylphosphine undergoes dimerization through a [2+2] cycloaddition process to give 2,4-diimine-1,3-diazetidine; cyclic carbodiimides undergo a similar type of cyclization at high temperatures.[5]

Compound **1** also reacts with one equivalent of alkyl or arylisocyanates at room temperature to give directly the fused diazepines **6** in fair yields† (53–70%). The formation of **6** can be understood by an initial aza-Wittig type reaction between the iminophosphorane moiety directly linked to the heterocyclic ring and the isocyanate to give a carbodiimide intermediate **4**, which undergoes cyclization by nucleophilic attack of the nitrogen atom of the β-styryliminophosphorane group on the central carbon atom of the carbodiimide to give **5**, which by hydrolytic cleavage leads to **6**. This assumption is in accord with recent results obtained in our laboratory[2a,6] that clearly show that an aryliminophosphorane group is more reactive than a β-styryliminophosphorane one in an aza-Wittig type reaction towards isocyanates. That conversions **1** → **3** and **1** → **6** are reasonably general in nature is indicated by examples given in Table 1.

Molecular structure of compounds **3b** (R = 4-Me-C_6H_4) and **6b** (R = Pr), with the atom numbering schemes used in the X-ray analysis‡ are shown in the ORTEP[7] drawings of Fig. 1 and 2.

The main differences between the two molecules were confined to the geometry of the seven-membered ring and to the different coplanarity of the ester group and the phenyl ring at N(1) with respect to the fused-rings system, giving rise to an overall conformation of compound **6** rather flat: boat–sofa conformation[8] slightly distorted, and double bonds at C(5)–C(6), C(4)–C(12) and C(10)–N(11) in **3** *vs.* an almost planar ring and delocalization, mainly of the C=N bond in **6**; the ester group and the phenyl ring are rotated by 38.1(4) and 35.4(4)° in **3**, but in **6** are twisted just –6.6(7) and –21.8(6)°, respectively (see Figs. 1 and 2), as measured by the C(5)–C(6)–C–O and N(2)–N(1)–C–C torsion angles.

Molecules of compounds **6** are related in pairs by crystallographic inversion centres; the dimer is formed *via* hydrogen bonds between the N–H of the side chain and the carbonyl of the ester group.

In conclusion, this work shows that the easily available bis(iminophosphorane) **1** undergoes a one-pot process to

† *Spectroscopic data* for **3b**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.02 (t, 3H, ^3J 7.1 Hz, *Me*–CH_2O), 2.25 (s, 3H, Me–C_3), 2.30 (s, 3H, Me–Ar), 2.31 (s, 3H, Me–Ar), 3.58 (q, 2H, ^3J 7.1 Hz, Me–*CH*$_2$O), 6.29 (s, 1H, H-4), 6.97 (d, 2H, ^3J 8.2 Hz), 7.11 (d, 2H, ^3J 8.2 Hz), 7.13 (d, 2H, ^3J 8.3 Hz), 7.32 (t, 1H, ^3J 7.2 Hz), 7.44 (t, 2H, ^3J 7.1 Hz), 7.74 (d, 2H, ^3J 7.9 Hz), 7.82 (d, 2H, ^3J 8.4 Hz); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 11.98 (Me–C_3), 13.66 (*Me*–CH_2O), 20.79 (Me–Ar), 20.91 (Me–Ar), 61.49 (Me–*CH*$_2$O), 105.54 (C_{3a}), 114.47 (C_4), 118.19 (=CH), 122.94 (=CH), 123.13 (C_5), 123.79 (=CH), 127.03 (=CH), 128.48 (=CH), 129.37 (=CH), 129.51 (=CH), 133.09 (q), 133.94 (q), 134.42 (q), 137.95 (C_7), 138.32 (q), 141.26 (q), 143.97 (C_{9a}), 148.98 (C_3), 151.12 (C_{8a}), 162.17 (C=O); El-MS: *m/z* 516 (M^+, 10%), 222 (100).

Compound **6b**: ^{1}H NMR (200 MHz, [$^2H_6$]DMSO): δ 0.74 (t, 3H, ^3J 7.1 Hz, *Me*–CH_2–CH_2–NH), 1.14 (t, 3H, ^3J 6.9 Hz, *Me*–CH_2O), 1.34 (sext, 2H, ^3J 7.2 Hz, Me–*CH*$_2$–CH_2–NH), 1.89 (s, 3H, Me–C_3), 2.97 (td, 2H, $^3J_{CH_2}$ 6.4 Hz, $^3J_{NH}$ 5.9 Hz, Me–CH_2–*CH*$_2$–NH), 4.07 (q, 2H, ^3J 7.0 Hz, Me–*CH*$_2$O), 6.19 (s, 1H, N_6–H), 6.34 (s, 1H, H-4), 7.08 (t, 1H, ^3J 6.9 Hz, H_p), 7.20–7.30 (m, 3H, H_m, NH), 7.65 (d, 2H, ^3J 8.0 Hz, H_o); ^{13}C NMR (50.3 MHz, [$^2H_6$] DMSO): δ 11.37 (*Me*–C_3), 11.51 (*Me*–CH_2–CH_2–NH), 14.13 (*Me*–CH_2O), 22.17 (Me–*CH*$_2$–CH_2–NH), 43.29 (Me–CH_2–*CH*$_2$–NH), 61.10 (Me–*CH*$_2$O), 103.30 (C_{3a}), 114.17 (C_4), 122.30 (C_o), 122.51 (C_5), 125.26 (C_p), 128.05 (C_m), 139.16 (C_i), 146.88 (C_3), 150.29 (C_{8a}), 154.05 (C_7), 162.92 (C=O); El-MS: *m/z* 353 (M^+, 71%), 278 (100).

‡ *Crystal data* for **3b**: monoclinic, $P2_1/a$, a = 14.7427(8), b = 14.3907(8), c = 13.5177(6) Å, β = 104.516(4)°, V = 2776.3(3)Å^3, D_c = 1.236 g cm^{-3}, Z = 4, crystal dimensions 0.33 × 0.33 × 0.10 mm, ω–2θ scan, θ_{max} = 65°, μ(Cu-Kα) = 6.06 cm^{-1}, 4728 independent reflections, $R(R_w)$ = 0.054(0.063) for 3306 [$I > 3\sigma(I)$] observed reflections. Min., max. final ΔF peaks ±0.17 e Å^{-3}.

For **6b**: monoclinic, $P2_1/c$, a = 12.0044(3), b = 12.6065(3), c = 12.8634(3)Å, β = 109.547(2)°, V = 1834.5(1)Å^3, D_c = 1.280 g cm^{-3}, Z = 4, crystal dimensions 0.37 × 0.17 × 0.07 mm, ω–2θ scan, θ_{max} = 60°, μ(Cu-Kα) = 6.61 cm^{-1}, 2707 independent reflections, $R(R_w)$ = 0.081(0.091) for 1866 [$I > 3\sigma(I)$] observed reflections. Min., max. final ΔF peaks ±0.62 e Å^{-3}.

Philips PW1100 diffractometer, Cu-Kα radiation, graphite monochromator. XRAY80[9] computer program. The structures were solved by direct methods SIR88.[10] Refinement on F_o with two block/full matrix. Anisotropic thermal model for the non-hydrogen atoms while H atoms, obtained unambiguously from difference Fourier synthesis were refined isotropically. In spite of the high thermal values of the C atoms of the ester group in **3b** (Fig. 1), and the Pr chain in **6b** (Fig. 2), no disorder models could be obtained. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

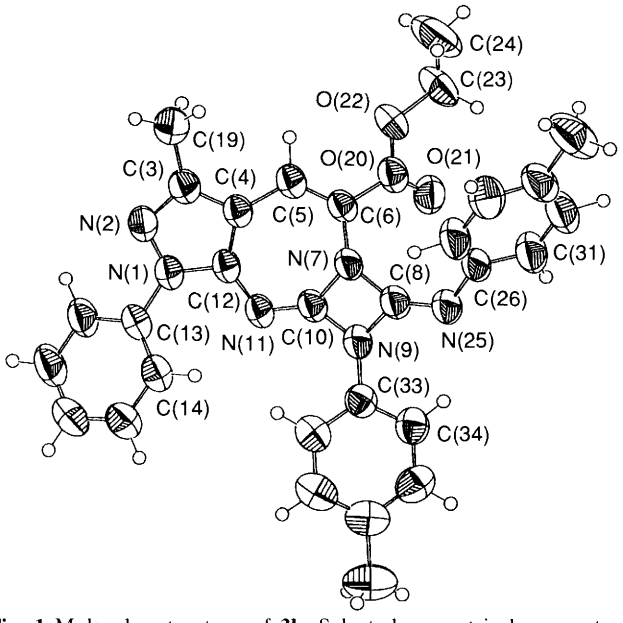


Fig. 1 Molecular structure of **3b**. Selected geometrical parameters (Å;°): C(4)–C(5) 1.455(3), C(5)–C(6) 1.335(4), C(6)–N(7) 1.421(4), N(7)–C(10) 1.417(3), C(10)–N(11) 1.265(3), N(11)–C(12) 1.391(4), C(12)–C(4) 1.376(4), N(7)–C(8) 1.439(4), C(8)–N(9) 1.418(4), N(9)–C(10) 1.389(3), C(8)–N(25) 1.250(3), C(4)–C(5)–C(6)–N(7) −6.8(4), C(5)–C(6)–N(7)–C(10) 41.8(4), C(6)–N(7)–C(10)–N(11) −40.9(5), N(7)–C(10)–N(11)–C(12) 1.4(5), C(10)–N(11)–C(12)–C(4) 19.1(4), N(11)–C(12)–C(4)–C(5) 0.5(5), C(12)–C(4)–C(5)–C(6) −17.5(5), N(2)–N(1)–C(13)–C(18) 35.4(4), C(5)–C(6)–C(20)–O(22) 38.1(4), C(6)–N(7)–C(8)–N(25) 49.1(6), N(7)–C(8)–N(25)–C(26) −0.8(6), C(8)–N(25)–C(26)–C(27) 42.8(5), N(11)–C(10)–N(9)–C(33) −17.6(5) and C(10)–N(9)–C(33)–C(38) −4.1(5).

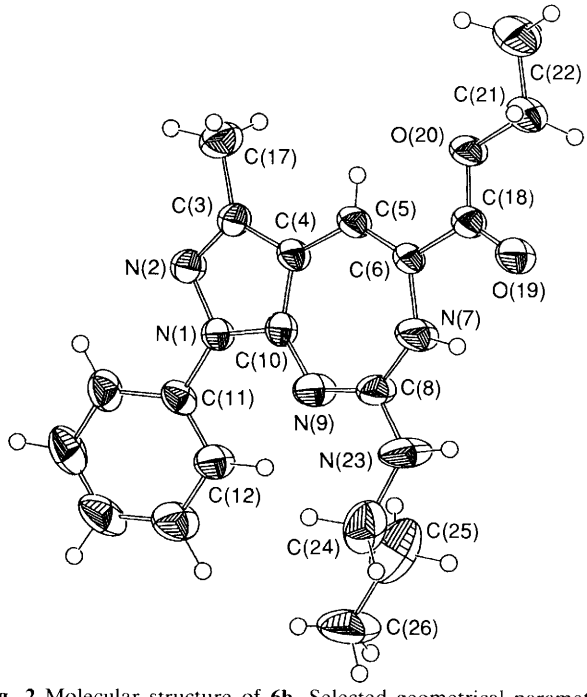


Fig. 2 Molecular structure of **6b**. Selected geometrical parameters (Å;°): C(4)–C(5) 1.451(6), C(5)–C(6) 1.331(7), C(6)–N(7) 1.402(7), N(7)–C(8) 1.337(7), C(8)–N(9) 1.294(6), N(9)–C(10) 1.348(6), C(10)–C(4) 1.385(6), C(4)–C(5)–C(6)–N(7) −1.3(9), C(5)–C(6)–N(7)–C(8) −1.8(10), C(6)–N(7)–C(8)–N(9) 0.4(11), N(7)–C(8)–N(9)–C(10) 5.5(9), C(8)–N(9)–C(10)–C(4) −8.9(9), N(9)–C(10)–C(4)–C(5) 4.9(9), C(10)–C(4)–C(5)–C(6) 1.2(8), N(2)–N(1)–C(11)–C(16) −21.8(6), C(5)–C(6)–C(18)–O(20) −6.6(7), N(9)–C(8)–N(23)–C(24) −3.0(9) and N(23)–H(23)···O(19)($-x$, $1-y$, $-z$) 0.92(7), 2.01(7), 2.929(6), 176(7).

afford the previously unreported fused 1,3-diazetidines **3** and fused [1,3]diazepines **6**.

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