Phosphorus Heterocycles

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A Truly Multifunctional Heterocycle: Iminophosphorane, N,P Chelate, and Dihydropyridine**

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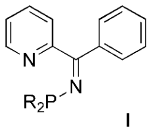
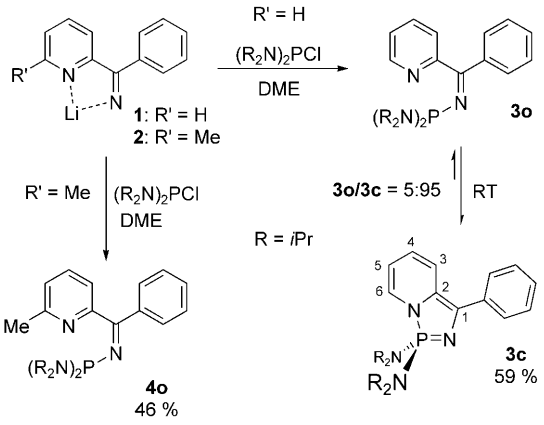
Bidentate ligands occupy a central position in coordination chemistry.[1] Their electronic and steric asymmetry can be harnessed to control reactivity at the chelated metal centre, often as a result of the differing *trans* influences exerted by the two donor components. Among such heteroditopic ligands, bidentate N,P chelates[2,3] are some of the most frequently used and have been shown to be beneficial in a number of applications such as allylic substitution,[4,5] olefin oligomerization,[6,7] and asymmetric hydrogenation.[8]

In this context, we have previously reported the synthesis and coordination chemistry of the κ^2-N,P-chelating pyridyl-*N*-phosphinoimines **I** (Scheme 1). In combination with sources of Pd^{II}, scaffold **I** (R = Ph) provides highly chemo- and regioselective initiators for direct alkene hydrocarboxylation in alcoholic media, which affords products that result from the coupling of two alkenes and two equivalents of carbon monoxide.[9] While exploring the stereoelectronic properties of ligands **I**, it was of interest to probe the effect of replacing the aryl substituents of phosphorus by σ-electron-withdrawing, π-basic amino groups.[10] Herein, we report the synthesis of such compounds and explore their unexpected, reversible intramolecular cyclization chemistry in solution. This unprecedented dynamic behavior has been probed using a combination of experiment and computation.



Scheme 1. Pyridyl-*N*-phosphinoimines **I**.

Reaction of *N*-lithiopyridylimines **1**[9] and **2** with equimolar quantities of bis(diisopropylamino)phosphine chloride[11] in 1,2-dimethoxyethane (DME), followed by extraction with hexane, afforded **3c** (59% yield) and **4o** (46% yield), respectively (Scheme 2). The ^{31}P NMR spectrum of compound **4o** shows a single resonance at $\delta = +71.3$ ppm, a chemical shift consistent with that for an *N*-bis(dialkylamino)phosphinoimine.[12] In contrast, the $^{31}P\{^1H\}$ NMR spectrum of **3** exhibits two singlet resonances: $\delta = +71.0$ ppm (**3o**), comparable to that for **4o**, and $\delta = +42.3$ ppm (**3c**), present in a ratio of **3o**/**3c** of 5:95, at 298 K.[13,14]



Scheme 2. Synthesis of closed cyclic iminophosphorane **3c**, its acyclic (open) valence tautomer **3o**, and open derivative **4o**.

Dark red single crystals of **3c** were grown from a hexane solution of **3**, and their bulk composition verified by solid-state ^{31}P NMR spectroscopy ($\delta^{31}P = +42.1$ ppm).[15] The structure of the unexpected product **3c** was elucidated by an X-ray diffraction study, which revealed it to be a closed, cyclic iminophosphorane (or, more formally, an anellated σ^4-$1\lambda^5$-[1,3,2]diazaphosphole) derivative (Figure 1).[16] The fused heterocycles A and B are both planar and form a dihedral angle of 4.7°. The rings comprise localized double (P=N2, C5=C6) and single (P–N1, C6–N1, C4–C5) bonds, with a significant degree of allylic character across the C1–C2–C3 unit of ring A. The two *exo*-cyclic P–N bonds show essentially single bond character.[17] This structure is in good agreement with both the ^{1}H and ^{13}C NMR spectroscopic data, which show a typical $^3J_{PH}$[18] coupling for H-C^6 of the 6-membered heterocycle (5.6 Hz) and characteristic nonconjugated alkenyl resonances for *endo*-cyclic carbons C^5 and C^4 (ca. $\delta = 110$ ppm).[15]

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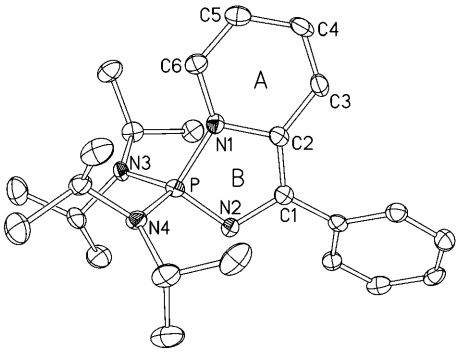
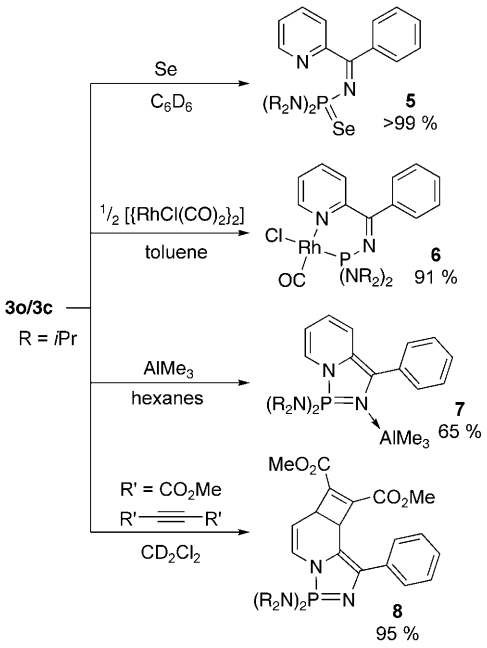


Figure 1. X-ray molecular structure of **3c**.[16] H atoms are omitted for clarity. Thermal ellipsoids are drawn at the 50% level. Selected bond lengths [Å] and angles [°]: P–N1 1.681(3), P–N2 1.589(3), N2–C1 1.399(4), C1–C2 1.376(4), C2–C3 1.420(4), C3–C4 1.353(4), C5–C6 1.336(4), N1-P-N2 97.41(14), P-N2-C1 109.6(2), P-N1-C2 108.0(2).

On dissolution of a crystalline sample of **3c** in toluene, both products **3o** ($\delta^{31}P = +71.0$ ppm) and **3c** ($\delta^{31}P = +42.3$ ppm) were observable by ^{31}P NMR spectroscopy in the same ratio (**3o**/**3c** = 5:95) as found for the crude reaction mixture at 298 K.[13,14] This is consistent with variable temperature ^{31}P NMR spectroscopic studies, which have clearly established that **3o** and **3c** may be regarded as interconverting valence tautomers in solution. On raising the temperature of a solution of **3** in toluene to 365 K the concentration of the open compound **3o** increased (**3o**/**3c** = 25:75), whereas on cooling to 225 K, **3o** virtually disappeared (< 2%).[15,19] In contrast, compound **4o** does not undergo such a tautomerization process, with a single ^{31}P NMR resonance at $\delta = +71.3$ ppm being observed across the temperature regime 225–365 K and upon prolonged heating at 335 K. Ring closure is presumed to be impeded in **4o** by the presence of the additional methyl substituent, which is consistent with the computational results (see below).

This intriguing **3o**/**3c** tautomerization process is without precedent, making it of interest to explore whether it would impact on the reactivity of **3**. A solution of **3** was treated with gray selenium, which resulted in the quantitative formation of the σ^4,λ^5-selenide derivative **5** (Scheme 3),[15] the ^{31}P NMR spectrum of which exhibits a characteristic resonance at $\delta = +55.1$ ppm ($|^1J_{SeP}| = 821$ Hz).[10] Clearly, reaction of selenium has occurred with the minor, open, valence tautomer **3o**. It was then tempting to probe reactions with a transition metal Lewis acid that could potentially react with both isomers **3o**/**3c**. Since both iminophosphoranes[20,21] and *N*-phosphinoimines[9] are established ligands for Rh(I), **3** was treated with 0.5 mole equivalents of $[\{RhCl(CO)_2\}_2]$ (Scheme 3). This gave rise to the Rh complex [RhCl(CO)(κ²-N,P-**3o**)] (**6**) in 91% yield ($\delta^{31}P = +117.8$ ppm $\{^1J_{Rh,P} = 209$ Hz$\}$) as a single isomer.[15] An X-ray diffraction study confirmed the structure of **6** (Figure 2), which is similar to that of its diphenylphosphino-substituted ligand analogue, [RhCl(CO)(κ²-N,P-**I**)].[9] The Rh centre of **6** adopts a slightly distorted square planar geometry with κ²-N,P-coordinated **3o**.

It is likely that the formation of complex **6**, which bears the open (**3o**) rather than the closed (**3c**) form of **3**, is driven



Scheme 3. Summary of the reactions of compounds **3o**/**3c**.

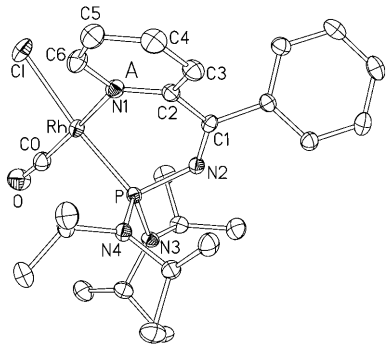


Figure 2. X-ray molecular structure of **6**.[16] H atoms are omitted for clarity. Thermal ellipsoids are drawn at the 50% level. Selected bond lengths [Å] and angles [°]: Rh–P 2.2060(6), Rh–N1 2.1532(19), Rh–C0 1.811(2), P–N2 1.7085(19), N2–C1 1.272(3), N1-Rh-P 84.98(5), Rh-N1-C2 127.45(14), Cl-Rh-C0 90.08(8).

by the formation of the chelate. Hence, in an attempt to observe the complexation of the closed tautomer **3c**, the reaction with a hard alkyl aluminum reagent was explored. Treatment of **3** with a stoichiometric quantity of $AlMe_3$ in hexanes afforded **7** in 65% yield (Scheme 3).[15] The ^{31}P NMR spectrum of complex **7** exhibits a single resonance at +46.6 ppm (cf. **3c**: $\delta^{31}P = +42.3$ ppm), together with observation of a $^3J_{PH}$ coupling of 6.4 Hz for H–C⁶. The ^1H NMR spectrum shows a single sharp resonance corresponding to an $AlMe_3$ fragment ($\delta = -1.18$ ppm). These data are clearly supportive of a closed heterocyclic structure for **7**, which was confirmed by a molecular structure determination (Figure 3). As for **3c**, **7** comprises an anellated σ^4-$1\lambda^5$-diazaphosphole ring, but with an $AlMe_3$ fragment bound through the *endo*-cyclic sp^2 N atom (Al-N2 1.9883(9) Å). This causes an elongation of the P=N2 bond by 0.04 Å, but otherwise little change in structure compared to **3c** is observed. Such κ¹-N

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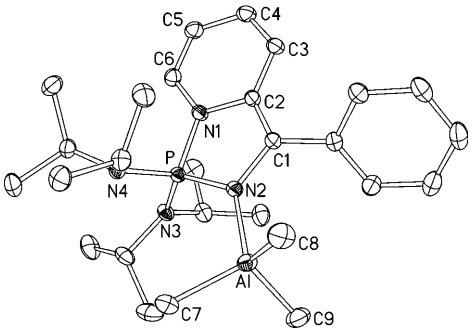

Figure 3. X-ray molecular structure of **7**.[16] H atoms are omitted for clarity. Thermal ellipsoids are drawn at the 50% probability level. Selected bond lengths [Å] and angles [°]: P–N1 1.6745(9), P1–N2 1.6308(9), N1–C2 1.429(1), N2–C1 1.436(1), C1–C2 1.360(1), C2–C3 1.438(1), C3–C4 1.358(2), C5–C6 1.3433(15), Al–N2 1.9883(9), N1-P-N2 95.70(4), P-N2-C1 109.46(7), P-N1-C2 109.97(7).

coordination of the $AlMe_3$ fragment is consistent with the localized *endo*-cyclic P=N bond of **3c**, and is entirely analogous to the reactions of classical iminophosphoranes in which hard Lewis acids bind to the N terminus of the P–N linkages.[22,23]

Since **3c** demonstrates reactivity analogous to iminophosphoranes, it was of interest to explore other reactions typical of this type of functional group, for example cycloaddition across the P=N bond.[23] Thus, a solution of **3c** in dichloromethane was treated with dimethyl acetylene dicarboxylate (DMAD) at room temperature. Over a period of 12 h, a new product **8** slowly formed and was isolated in 95% yield (Scheme 3).[15] However, the ^{31}P NMR spectrum of **8** clearly highlights that cycloaddition has not occurred at the P–N multiple bond, as a single resonance is observable at a chemical shift similar to that for **3c** (**8**: $\delta = +46.6$; **3c**: $\delta = +42.3$ ppm). Instead, a pseudo-[2+2] cycloaddition occurred at the localized C^3–C^4 double bond of the six-membered heterocycle, which is readily confirmed by a combination of ^1H, ^{13}C, and 2D NMR spectroscopy and mass spectrometry ($m/z = 554$). This reactivity perfectly mirrors the established chemistry of N-substituted 1,2-dihydropyridines, which behave as enamines in their reactions with DMAD to afford cyclobuta[*b*]pyridines.[24] It is reasonable to suggest that **3c** is prevented from undergoing cycloaddition across the P=N bond as a result of steric constraints imposed by the bulky diisopropylamino substituents.

As would be expected, the preference of pyridyl-*N*-phosphinoimines towards intramolecular cyclization is very sensitive to both the nature of the substituents of the phosphorus atoms and of the pyridyl moiety (see above). Indeed, reaction of **1** with alkyl or aryl chlorophosphines R_2PCl (R = Ph,[9] *i*Pr, cyclohexyl, and *t*Bu[25]) affords exclusively acyclic, open products. These observations are consistent with the diisopropylamino substituents rendering the phosphorus centre of **3o** more electrophilic and hence more susceptible to cyclization by reaction with the nucleophilic pyridine moiety, compared with its P-dialkyl and -diaryl analogues. However, the mechanism for the formation of the closed heterocycle **3c** could be envisaged as occurring by either a stepwise intramolecular nucleophilic attack of the pyridyl nitrogen of **3o** at phosphorus, or through a concerted 1,5-electrocyclization. Although a number of examples of intramolecular dative $N \rightarrow P^{III}$ interactions have been reported,[26–28] which can be regarded as "arrested" intermediates of a stepwise cyclization process, it was of interest to probe the course of ring closure for **3** in more detail.[15]

A computational study of compounds **3o,c** and **4o,c** was undertaken at the B3LYP/6-31G** level of theory.[15] The natural bond orbital (NBO) analysis and computed molecular orbitals and structure of **3c** are in good agreement with the experimentally observed iminophosphorane tautomer.[15] For the methylpyridine system **4**, *N*-phosphinoimine **4o**[29] and iminophosphorane **4c** are both minima on the hypersurface; however, **4c** is 20.2 kcal mol^{-1} (at 25 °C) higher in energy. This is consistent with only the open form **4o** being observed experimentally because of steric constraints imposed by the methyl substituent; this is supported by the calculated repulsion energies for **4o**/**4c**.[15] In contrast, the minima located for the closed **3c** and open **3o**[29] tautomers are at almost identical energies ($\Delta E = 3.0$ kcal mol^{-1} at 25 °C). These calculations support the existence of the **3o**/**3c** equilibrium in solution. No transition state was found, thus showing there to be no kinetic barrier to this thermodynamically allowed summarization process, which indicated that it is very likely that cyclization of **3o** takes place in a concerted manner.

In summary, it has been established both experimentally and theoretically that the pyridyl-*N*-phosphinoimine bearing diisopropylamino substituents at phosphorus, **3o**, exists in valence tautomeric equilibrium in solution with the closed anellated σ^4-$1\lambda^5$-[1,3,2]diazaphosphole derivative **3c**. The small energy difference between **3o** and **3c** means that **3** may react as an iminophosphorane, an N,P chelate, and a dihydropyridine depending on the reagents added. This study highlights that slight modifications of the P substituents may dramatically affect the chemical behavior of organophosphorus compounds and that incorporation of the bis(diisopropylamino)phosphino moiety is a powerful methodology for the stabilization of unusual, reactive species.[30,31]

Experimental Section

All reactions/manipulations were carried out under an atmosphere of dry nitrogen by using standard Schlenk and glovebox techniques.**3c**: Phenyllithium (1.8 M, 5.3 mL, 9.6 mmol) was added to a cooled (−78 °C) solution of 2-cyanopyridine (1.00 g, 9.6 mmol) in DME (50 mL). The mixture was stirred for 1 h before $(iPr_2N)_2PCl$ (2.56 g, 9.6 mmol) in DME (70 mL) was added. After stirring for 22 h at room temperature, volatile components were removed in vacuo and the product extracted with hexane. On cooling (−30 °C) red crystals of **3c** formed (2.33 g, 59%). $^{31}P\{^1H\}$ NMR (161.91 MHz, C_6D_6): $\delta = +42.3$ ppm (s); MS (FAB^+) m/z: 412 [M^+]. **3o**: $^{31}P\{^1H\}$ NMR (161.91 MHz, C_6D_6): $\delta = +71.0$ ppm (s). **4o**: An identical procedure to that used for the preparation of **3c** was employed, using 2-cyano-6-methyl-pyridine (0.50 g, 4.2 mmol), phenyllithium (1.8 M, 2.4 mL, 4.2 mmol), and $(iPr_2N)_2PCl$ (1.13 g, 4.2 mmol). **4o** was isolated as a brown solid (830 mg, 46%). $^{31}P\{^1H\}$ NMR (80.96 MHz, C_6D_6): $\delta = +71.3$ ppm; MS (EI^+) m/z: 426 [M^+]. **5**: A C_6D_6 solution of **3** (30 mg, 0.073 mmol) was treated with grey Se (58 mg, 0.73 mmol) and heated at 50 °C for 80 h. $^{31}P\{^1H\}$ NMR (80.96 MHz, C_6D_6): $\delta = +55.5$ ppm (s + satellites, $^1J_{Se,P} = 821$ Hz). **6**: A solution of **3** (198 mg, 0.5 mmol) in toluene (10 mL)was added to

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$[\{RhCl(CO)_2\}_2]$ (92 mg, 0.25 mmol) in toluene (10 mL). The mixture was degassed and stirred for 24 h. Volatile components were removed in vacuo to give **6** as a red-brown solid (252 mg, 91%). $^{31}P\{^1H\}$ (161.91 MHz, $CDCl_3$): $\delta = +117.8$ ppm (d, $^1J_{P,Rh} = 209$ Hz); MS (FAB^+) m/z: 550 $[M-CO^+]$; IR (KBr, $CDCl_3/CHCl_3$): $\nu(CO) = 1997\ cm^{-1}$.

7: A solution of $AlMe_3$ (25 mg, 0.35 mmol) in hexane (10 mL) was added to a solution of **3** (157 mg, 0.38 mmol, 1.1 equiv) in hexane (30 mL). After 1 h the precipitate was isolated by filtration, washed with hexane (3×4 mL) and dried in vacuo (116 mg, 65%). $^{31}P\{^1H\}$ NMR (80.95 MHz, CD_2Cl_2): $\delta = +46.6$ ppm (s).

8: DMAD (13 mg, 0.09 mmol) was added to a solution of **3** (38 mg, 0.09 mmol) in CD_2Cl_2 (0.8 mL). After 24 h, volatile components were removed in vacuo to afford **8** (95%). $^{31}P\{^1H\}$ NMR (161.91 MHz, CD_2Cl_2): $\delta = +46.6$ (s); MS (EI^+) m/z: 554 $[M^+]$.

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[15] See the Supporting Information for details.
[16] CCDC 686754 (**3c**), 686755 (**6**), and 686756 (**7**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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