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A New Reaction Pathway in Organophosphorus Chemistry: Competing $S_N 2$ and AE' Pathways for Nucleophilic Attack at a Phosphorus–Carbon Cage Compound**

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The S_N2 character of nucleophilic-substitution reactions at carbon atoms and other first-row centers is well-established, both experimentally and theoretically.^[1] For phosphorus^[2] and second-row atoms in general,^[3] where expansion of the octet is possible, there is evidence that, at least in the gas phase, nucleophilic substitution proceeds instead via an additionelimination (AE) pathway featuring a hypervalent intermediate. Herein, we use a combination of temperature-dependent ³¹P NMR spectroscopy and density functional theory to show that both S_N2- and AE-type pathways contribute simultaneously to chloride exchange in the tricyclic phosphoruscarbon cage 1a (Scheme 1). In a series of recent papers, we have demonstrated the synthetic potential of 1a, which reacts with the Lewis acid AlCl₃ (in CH₂Cl₂) to give the novel nido ionic species $[3,5-tBu_2-1,2,4-C_2P_3][AlCl_4]$ (2).^[4] In contrast, alkali metals and magnesium react with 1a at room temperature in THF to form, selectively and in quantitative yield, $M[3,5-tBu_2-1,2,4-C_2P_3]$ (3; M = Li, Na, K, or $Mg_2(\mu-Cl)_3$ - $(thf)_6$, which contain the important aromatic C_2P_3 anion.^[4,5]

In the course of monitoring the reduction of 1a with lithium in $[D_8]$ THF by in situ ³¹P NMR spectroscopy, we were surprised to observe that, whilst the characteristic resonance

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Scheme 1. $\bullet = CtBu$; M = Li, Na, K, or $Mg_2(\mu-Cl)_3(thf)_6$.

of **1a** at $\delta = -302.2$ ppm remained relatively sharp throughout the course of the reaction, the resonances at $\delta = 234.7$ and -121.4 ppm were significantly broadened. Similar broadening of these two resonances was also observed when small amounts of either LiCl or nBu_4NCl were added to a solution of **1a** in [D₈]THF. Moreover, when the solution of **1a** in [D₈]THF containing 0.05 equivalents of nBu_4NCl was cooled from 325 K to 255 K, the two broad resonances at $\delta = 234.7$ and -121.4 ppm became sharpened, and the line shape of the resonance at $\delta = -302.2$ ppm also showed significant changes (Figure 1).

To fully rationalize these observations, it was clear that knowledge of the precise topology of 1a was required. Previously, Binger, Regitz, and co-workers had assigned the structure of **1a** simply on the basis of three ³¹P NMR resonance signals at $\delta = 234.7$, -121.4, and -302.2 ppm, which relate to the three magnetically distinct environments of P^1 , P^2 , and P^3 (Scheme 1), respectively, in the tricyclic cage.^[6] The computed ³¹P NMR chemical shifts (at the B3LYP/6-311G^{**} level of theory) of $\delta = 354$ (P¹), -93.4 (P^2) , and -298.6 ppm (P^3) for the model compound $ClP_3(CH)_2$ (1a') are fully consistent with this assignment. However, all attempts to confirm the structure of 1a by single-crystal X-ray diffraction have been unsuccessful. Fortunately, we have been able to support this structural assignment by the serendipitous preparation and crystallographic characterization of 1b (Figure 2), the iodo analogue of 1a, formed by the reaction of 1a with $[SmI_2(thf)_2]$. The very similar ³¹P{¹H} NMR characteristics of **1b** ($\delta = 248.7, -101.8$ and -241.3 ppm in [D₈]toluene at 298 K) and 1a provide convincing evidence that the two species are isostructural.

To probe the dynamic processes associated with chloride exchange, the ³¹P{¹H} NMR spectra of **1a** were simulated using the gNMR suite of programs.^[7] Critically, the accurate simulation of all three resonances in the ³¹P NMR spectra over the range of temperatures and concentrations employed





Figure 1. Variable-temperature ${}^{31}P{}^{1}H$ NMR spectra of $1a/nBu_4NCI$ in $[D_8]THF$. Spectra are shown in 10K increments.



Figure 2. X-ray crystal structure of **1b**. Selected bond lengths [Å] and angles [°]: P(1)-I(1) 2.561(1), P(2)-P(3) 2.154(1), P(1)-C(1) 1.826(2), P(1)-C(6) 1.832(2), P(2)-C(1) 1.862(2), P(2)-C(6) 1.862(1), P(3)-C(1) 1.911(2), P(3)-C(6) 1.917(2); C(1)-P(2)-P(3) 56.27(7), C(1)-P(2)-C(6) 74.52(10), C(1)-P(3)-C(6) 72.24(1), C(1)-P(1)-I(1) 104.67(7), C(1)-P(1)-C(6) 76.17(10).

could only be achieved when two distinct dynamic processes were invoked, one involving the exchange of P¹ and P² and the other involving the exchange of P² and P³. The simulations yielded activation parameters of $\Delta H^{\pm} = 37.7 \pm 0.8 \text{ kJ mol}^{-1}$ and $\Delta S^{\pm} = -73.1 \pm 2.7 \text{ J mol}^{-1} \text{K}^{-1}$ for the P¹ \leftrightarrow P² exchange process and $\Delta H^{\pm} = 37.3 \pm 4.3 \text{ kJ mol}^{-1}$ and $\Delta S^{\pm} = -90.1 \pm$ 14.1 J mol⁻¹ K⁻¹ for the P² \leftrightarrow P³ exchange. The negative ΔS^{\pm} values imply that both processes are associative, a conclusion that is also consistent with the linear dependence of both rates of exchange on the concentrations of both chloride anion and **1a**. The activation parameters indicate that the two processes are competitive within the temperature regime employed and that the P¹ \leftrightarrow P² exchange becomes more favored at higher temperatures.

The origin of these experimental observations was revealed when density functional theory was employed to explore the potential-energy surface for the nucleophilic attack of a chloride ion on the model compound $\text{ClP}_3(\text{CH})_2$ (**1a**', Figure 3).^[8] The topology of **1a**' offers five distinct trajectories for nucleophilic attack by a chloride ion (Scheme 2), each of which was probed explicitly. For trajec-



Figure 3. Potential-energy surface for nucleophilic attack on 1a' by a Cl⁻ ion. Interatomic separations are given in Å.

tory (a), the potential-energy surface shows a classic S_N^2 -type profile in which a $C_{2\nu}$ -symmetric transition state TS_a connects two degenerate precursor intermediates I_a . The S_N^2 character of this pathway contrasts markedly with chloride exchange at the related species ClPH₂, for which Radom and co-workers reported an AE mechanism with a $C_{2\nu}$ -symmetric intermediate rather than a transition state.^[2d] The significant difference between ClPH₂ and the tricyclic species 1a' can be traced to the different acceptor orbitals available in each case. In the case of ClPH₂, the only available acceptor orbital is $\sigma^*(P-Cl)$, and interaction of this orbital with a chloride lone pair of electrons leads directly to the hypervalent $C_{2\nu}$ -symmetric intermediate. In tricyclic ClP₃(CH)₂, in contrast, a second



Scheme 2. Conceptual trajectories and resultant transition states/intermediates for nucleophilic attack of Cl^- on 1a'.

acceptor orbital, $\sigma^*(P^2-P^3)$, is available to accommodate the chloride lone pair. In fact, the P³–Cl² separation in I_a (2.85 Å) is actually shorter than the P¹–Cl² separation (3.43 Å), suggesting that the major interaction in I_a is between the chloride ion and the $\sigma^*(P^2-P^3)$ orbital rather than the $\sigma^*(P^1-Cl^1)$ orbital.

A further ramification of this interaction is that introduction of a Cl⁻ ion via trajectory (e) also results in the formation of I_a . Indeed trajectories (a) and (e) proved to be indistinguishable as the calculated reaction coordinate is a hybrid of these two conceptual pathways. Progression along the reaction coordinate from I_a towards the transition state TS_a enhances overlap of the chloride lone pair of electrons with the $\sigma^*(P^1-Cl^1)$ orbital, but only at the cost of reduced overlap with the $\sigma^*(P^2-P^3)$ orbital, and the competition between the two acceptor orbitals leads to an S_N2-type, rather than an AEtype, profile. Trajectory (b), in contrast, gives a classic AEtype potential-energy surface which features only a $C_{2\nu}$ symmetric intermediate I_{b} . In comparison to TS_{a} , the P²-P³ bond in $I_{\rm h}$ is substantially elongated ($I_{\rm h}$ 2.43 Å, $TS_{\rm a}$ 2.18 Å) while both P–Cl bonds in I_b are shorter (I_b 2.37 Å, TS_a 2.57 Å), thus suggesting that the primary charge transfer interaction in this case is again between the chloride lone pair of electrons and the $\sigma^{*}(P^{2}\!\!-\!\!P^{3})$ orbital. The attack of a chloride ion at the remote P^2 center, as opposed to the one bound to chloride (P1), marks a subtle distinction from previous examples of the AE mechanism, in which the entering and leaving groups are bound to the same center. The distinction is, in fact, reminiscent of that between the well-known $S_N 2$ and $S_N 2'$ pathways^[9] in carbon-centered nucleophilic-substitution reactions. By analogy, we propose that trajectory (b) represents the first example of an AE'-type mechanism in a phosphorus compound.

The presence of two distinct pathways for nucleophilic attack corresponding to trajectories (a) and (b) is sufficient to explain fully the observed ³¹P NMR spectra: trajectory (a) or (e) leads to exchange of P² and P³, while trajectory (b) leads to exchange of P¹ and P². Scheme 2 suggests that there are two other possible trajectories, (c) and (d), but we have been unable to locate any stationary points for these cases: both result in the expulsion of chloride. The unique stability of **I**_b,

as distinct from the putative intermediates arising from trajectories (c) and (d), is a consequence of the stabilization of the negative charge on P³ by delocalization into *both* $\sigma^*(P-Cl)$ orbitals (see HOMO of **I**_b, inset in Figure 3). In contrast, attack along trajectories (c) or (d) would direct either one (trajectory (c)) or both (trajectory (d)) of the $\sigma^*(P-Cl)$ orbitals away from the negatively charged phosphorus center, thus preventing effective delocalization of the negative charge.

In summary, the ³¹P NMR spectra of solutions containing **1a** and Cl⁻ ions, in conjunction with a detailed analysis of the potential-energy surface for nucleophilic attack on **1a**' by a Cl⁻ ion, have revealed the presence of competing S_N2- and AE'-type mechanisms for chloride exchange. The much greater complexity of this transformation as compared to nucleophilic attack at monophosphorus systems can be traced to the presence of the low-lying $\sigma^*(P-P)$ orbital in the valence manifold which strongly perturbs the trajectories of the incoming nucleophile. Such an effect has not been previously observed, and we are presently exploring the implications of this interesting finding.

Experimental Section

All experimental procedures were performed under an atmosphere of nitrogen or argon by using standard Schlenk-line and glovebox techniques.

NMR studies were performed on either a Bruker AMX 300 spectrometer (operating frequencies 300.13 MHz (¹H), 121.49 MHz (³¹P)) or a Bruker AV 500 spectrometer (operating frequencies 500.13 MHz (¹H), 202.47 MHz (³¹P)). All NMR studies were performed in [D₈]THF (0.5 mL), and the required concentration of chloride anion was obtained by adding the appropriate amount of a 2.26×10^{-3} M stock solution of *n*Bu₄NCl in THF. Spectra were simulated over a range of temperatures by using the gNMR suite of programs, and the resulting rate constants in the temperature range 325 K to 285 K were used to generate Eyring plots from which activation parameters were extrapolated.

Single-crystal X-ray diffraction data for **1b**: $C_{10}H_{18}IP_3$, $M_r =$ $358.05 \text{ g mol}^{-1}$, crystal dimensions $0.34 \times 0.05 \times 0.04 \text{ mm}^3$, orthorhombic, space group $P2_12_12_1$, a = 6.2694(4), b = 13.2771(9), c = 13.2771(9)17.2491(12) Å, V = 1435.81(17) Å³, Z = 4, $\rho_{calcd} = 1.656$ Mg m⁻³, F-(000) = 704, $\mu Mo_{K\alpha} = 2.531 \text{ mm}^{-1}$, $\theta = 1.94$ to 29.05° , 15466 measured reflections, 3798 independent reflections, $R_{\text{int}} = 0.0295$, $-8 \le h \le 8$, $-18 \le k \le 18, -23 \le l \le 23, R_1(l > 2\sigma) = 0.0203, wR_2(l > 2\sigma) = 0.0399,$ $R_1(\text{all data}) = 0.0243$, $wR_2(\text{all data}) = 0.0408$, GOF = 1.015. Diffraction data were collected at 115 K on a Bruker Smart Apex diffractometer with $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å) by using a SMART CCD camera. Diffractometer control, data collection, and initial unit-cell determination were performed with SMART (version 5.625, Bruker-AXS). Frame integration and unit-cell refinement were carried out with SAINT+ (version 6.22, Bruker AXS). Absorption corrections were applied by SADABS (version 2.03, Sheldrick). Structures were solved by direct methods with SHELXS-97 (Sheldrick, 1997) and refined by full-matrix least squares with SHELXL-97 (Sheldrick, 1997). All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed by using a riding model and included in the refinement at calculated positions. CCDC-293160 contains 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.

All calculations were carried out with the Gaussian 03 series of programs. $^{[10]}$ Geometry optimizations were performed with the



B3LYP functional^[11] in conjunction with the 6-31 + G(d,p) basis set^[12] The optimized stationary points were characterized as minima by analytic vibrational-frequency calculations at the same level of theory. Shielding parameters (σ) were calculated by using the GIAO formalism^[13] and converted to chemical shifts (δ) using the relation $\delta = 328.5 - \sigma$, where 328.5 is the absolute shielding parameter for the ³¹P NMR reference standard 85% H₃PO₄.^[14]

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