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Theoretical studies of the intramolecular mechanism for the alkoxyphosphazene to alkoxyphosphazane transformation

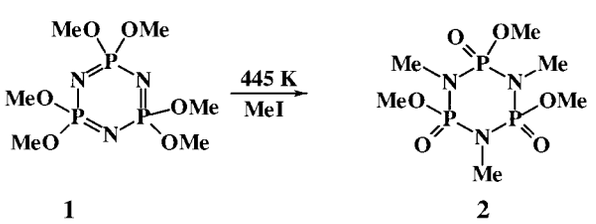
Stephen W. Doughty, Brian W. Fitzsimmons and Christopher A. Reynolds*

Department of Biological and Chemical Sciences, University of Essex, Wivenhoe Park, Colchester CO4 3SQ, UK

Semiempirical molecular orbital methods, and non-local density functional methods, have been used to study the minima and transition structures involved in the formation of six-membered ring alkoxycyclophosphazanes. These compounds show a marked conformational preference whereby two methoxy groups are above the ring and one is below (ααβ); the ααα form involving three methoxy groups pointing above the ring has not been observed experimentally. The free-energy calculations predict that the ααα is actually more stable than the ααβ compound, but the transition-structure calculations show that the energy barrier for the formation of the ααα compound is significantly higher than for the ααβ. Calculations involving demethylated compounds indicated that this selectivity arises due to steric effects in the transition structures. Indeed, there is significantly less distortion in the transition structure for the formation of the ααβ than for the ααα compound. Density functional calculations, using the Becke 88 exchange and the Lee–Yang–Parr correlation combination of functionals, were in broad agreement with semiempirical PM3 molecular orbital calculations.

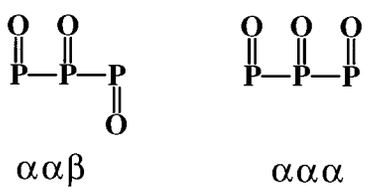
Thermally induced rearrangements involving the migration of alkyl groups are common throughout organophosphorus chemistry.[1] An illustrative example of this is provided by the alkoxyphosphazene ⟶ *N*-alkylphosphazane transformation,[2] as shown in Scheme 1 where the alkyl group is methyl. This product can be extracted from residues left after vacuum distillation of the phosphazene but a more convenient method is to heat the phosphazene in a sealed tube at 443 K in iodomethane. For example, 2,4,6-trimethoxy-1,3,5-trimethyl-2,4,6-trioxocyclotriphosphazane **2** is formed by heating hexamethoxycyclotriphosphazatriene **1** and methyl iodide; the methyl iodide functions as a catalyst.

Experimental X-ray data[3] show that compound **2** has a boat conformation with two methoxy groups pointing above the ring and one pointing below; this conformation is denoted ααβ. Here we wish to investigate, using computational methods, why the alternative arrangement with all three methoxy groups pointing above the ring, denoted ααα, has never been observed experimentally. The strategy followed was to determine the optimised structures on the potential-energy surface using molecular orbital methods, so as to determine the minimum energy for both the ααα and the ααβ forms. In addition, transition structures for the formation of both these conformations were determined. Consequently, some discussion of the mechanism is essential.

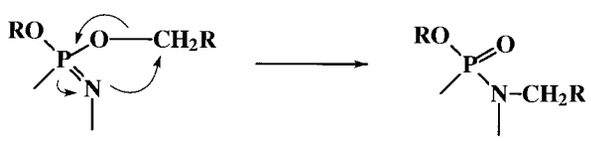


1 **2**

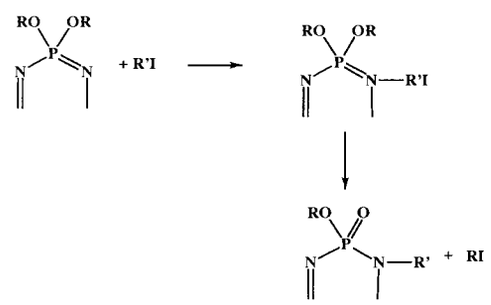
Scheme 1



ααβ ααα



Scheme 2

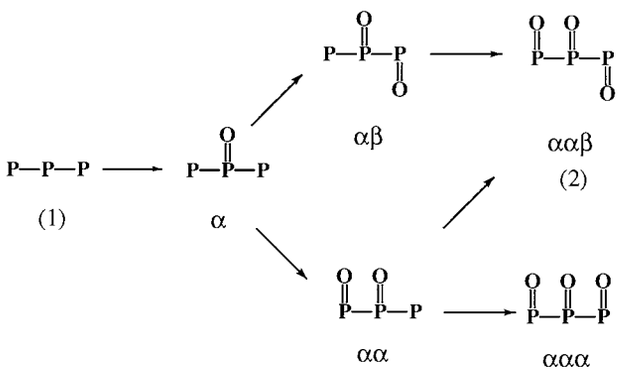


Scheme 3

It has been postulated that the rearrangement involves attack by the ring nitrogen atom on the α-carbon of the alkoxy group, either by an inter- or intra-molecular mechanism;[2] the latter is shown in Scheme 2 (see also Fig. 1), but since it may involve a strained ring other mechanisms need to be considered. The attack could also conceivably occur across the ring, but this is unlikely on steric grounds. An alternative mechanism, however, involves alkylation of a ring nitrogen by the alkyl halide catalyst (Scheme 3). The use of different alkyl halide catalysts leads to the formation of products containing mixed alkyl groups[4] and this provides evidence for an intermolecular mechanism, as does the observation that rearrangement is facilitated by excess of the corresponding alkyl halide catalyst. Using deuteriated starting products $[NP(OCD_3)_2]_3$ and $[NP(OMe)_2]_3$ leads to the production of cyclophosphazanes containing both methyl and deuteriomethyl units connected to the skeletal nitrogen atoms. The Gaussian distribution of molecular ions, detected by mass spectrometry, indicates scrambling between the methyl and trideuteriomethyl groups.[5] Similarly, the observations that reaction rates depend on the concentration of the phosphazane product and that cross-alkylation products have been detected[5] provide additional evidence for an intermolecular mechanism.

Table 1 Semiempirical PM3 energy and free-energy differences for the ααα and ααβ phosphazane forms, in kJ mol^{-1}; ΔH_f is the enthalpy of formation at 298 K. The angles τ_1, τ_2 and τ_3 refer to the N–P–O–C dihedral angle for rotation about the P–O bond

	ααα	ααβ
τ_1	42	−166
τ_2	−112	−88
τ_3	−88	−88
ΔH_f	−1663.6	−1670.7
ΔH_{298} (relative)	0	−7.1
ΔH_{448} (relative)	0	−7.9
ΔG_{448} (relative)	−15.1	0



Scheme 4

However, none of the experimental information rules out an intramolecular mechanism as an alternative pathway. Consequently, this initial study will concentrate on the intramolecular route. This intramolecular mechanism may well illustrate most of the important features pertinent to the formation of cyclophosphazanes and indeed it is important to investigate why the ααα compound is not formed by this route. As Scheme 4 shows, it is important to concentrate on the α ⟶ αα and the αα ⟶ ααα/ααβ steps in order to understand why the ααα form is not observed.

Methods

Conformational analysis and free-energy corrections

In order to determine the lowest-energy conformations of the phosphazanes a conformational search was carried out for rotation about the C–O bonds for each methoxy group, in increments of 30°. Full minimisation was performed at each increment of the torsional angles using the PM3 method[6] within the semiempirical molecular orbital program MOPAC;[7] the PM3 method was used as it is specifically parametrised for hypervalent phosphorus. The semiempirical methods predict the heat of formation at 298 K. To calculate the free energy of formation at 448 K, which corresponds to the reaction temperature, it was necessary to calculate second derivatives of the energy with respect to coordinates. The appropriate contributions to the enthalpy and entropy can then be calculated from the computed vibrational and rotational energy levels.[8]

Transition structures

The intramolecular transition structures were located using the conventional saddle-point algorithm implemented within the SADDLE option of MOPAC. In order to investigate the steric contribution of the methyl groups to the energy barriers, calculations were repeated on cyclophosphazanes containing only one methyl group, the migrating methyl group.

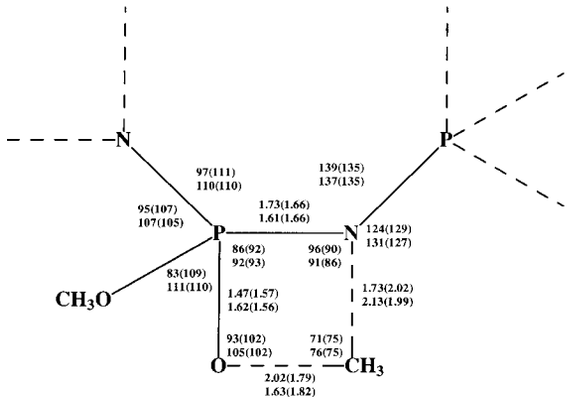


Fig. 1 Key structural features of the αα ⟶ ααβ and αα ⟶ ααα transition structures. The important geometric features for the αα ⟶ ααα transition structure are shown above those for the αα ⟶ ααβ transition structure. The corresponding features for the equilibrium structure are in parentheses. The key feature is that the key phosphorus atom has a more tetrahedral structure in the αα ⟶ ααβ transition structure (bond lengths in Å, angles in °)

Density functional calculations

It is generally considered that fully optimised transition-structure geometries are likely to be more reliable than the associated activation energies.[9] Consequently, all saddle points have been optimised using semiempirical methods. However, accurate energies were also calculated at these geometries using density functional methods[10] implemented within the CADPAC program.[11] This strategy of combining semiempirical geometries with density functional calculations to yield reliable energy differences has been used elsewhere[12] to calculate quinone electrode potentials *in solution* in good agreement with experiment. Density functional methods were chosen over alternative molecular orbital-based methods because non-local density functional methods in particular have recently been shown to give very good agreement with either experiment or high-level *ab initio* calculations in many applications,[13] including dissociation energies,[14] isomerisation energies[15] and energies of activation.[16] In this application, the Becke 88 exchange functional[17] and the Lee–Yang–Parr correlational functional[18] were used since this particular combination, denoted B-LYP, has been shown to give particularly good results in many problems, including energetics.[19] The functionals were integrated numerically over a large grid of about 163 000 points to ensure the integration was carried out accurately. While the absolute energies could be improved slightly by using a finer grid, the relative energies should be accurate within the B-LYP method.[12]

Results

The lowest-energy conformation of the phosphazanes, along with semiempirical (PM3) enthalpy and free-energy data, is shown in Table 1. Table 2 shows the semiempirical (PM3) and density functional (B-LYP) energies for the intramolecular transition structures. The key features of the transition structures for the αα ⟶ ααα and αα ⟶ ααβ transformations are shown in Fig. 1, but for simplicity the demethylated transition structures are not shown.

Discussion

The semiempirical PM3 molecular orbital calculations (Table 1) show that the heat of formation of the ααβ form at 298 K is marginally lower than for the ααα form. When free-energy corrections are applied to determine the enthalpy difference between the two forms at 448 K the ααβ form is still predicted to be the most stable. However, the entropy corrections show

Table 2 Semiempirical (PM3) and density functional (B-LYP) heats of formation (kJ mol^{-1}) and energies (Hartrees) for the minima and transition structures involved in the intramolecular formation of the ααα and ααβ forms of the phosphazane (1 Hartree = 2625.5 kJ mol^{-1}). For the semiempirical results, both the energy barrier for the individual reaction and that relative to the starting compound are shown

Structure		Semiempirical					Density functional		
Initial	Final	Initial	Final	Saddle point	$\Delta H^{\ddagger}$	Relative to start	Initial	Saddle point	$\Delta H^{\ddagger}$
Start	α	−1564.4	−1601.6	−1489.9	75	75	–	–	–
α	αβ	−1601.6	−1631.8	−1311.7	290	253	−1878.870 47	−1878.775 76	249
α	αα	−1601.6	−1631.8	−1310.8	291	254	−1878.870 47	−1878.771 61	260
αα	ααβ	−1631.8	−1670.7	−1417.1	215	147	−1878.885 68	−1878.808 67	202
αα	ααα	−1631.8	−1663.6	−1183.7	448	381	−1878.885 68	−1878.669 52	568
αβ	ααβ	−1631.8	−1670.7	−1483.2	149	81	–	–	–
$\alpha\alpha^{d}$*	ααβ	−1623.8	−1661.0	−1517.1	107	–	–	–	–
$\alpha\alpha^{d}$	ααα	−1625.9	−1660.6	−1511.7	114	–	–	–	–

* The d denotes energies for the reaction involving demethylated analogues.

that the ααα form actually has a lower free energy at 448 K. The calculated differences are small, suggesting that a mixture of products may be expected if the reaction were under thermodynamic control. Since the ααα compound is not observed experimentally, the implication is that the energy barrier for the formation of the ααα form is significantly higher than that for the ααβ form.

The results for the intramolecular transition structures are highly informative (Table 2). Clearly, the highest energy barrier by far (448 kJ mol^{-1}) is for the formation of the ααα product; relative to the starting compound, it is almost five times that of the lowest energy barrier to the ααβ product. Given such a clear difference in energy, it is unlikely that the semiempirical results could be qualitatively in error. Indeed, the semiempirical results are confirmed by the non-local density functional calculations which in most cases agree particularly well; this gives strong evidence that for these molecules the PM3 method is qualitatively reliable.

Insight into the origin of the differential energy barrier for the $\alpha\alpha \longrightarrow \alpha\alpha\alpha$ and the $\alpha\alpha \longrightarrow \alpha\alpha\beta$ reactions can be gained by examining the geometries of the two transition states. Examination of the transition structure O–C bonds (see Fig. 1) shows that the ααβ transition structure is early (bond length = 1.63 Å) while the ααα transition structure is late (bond length = 2.0 Å). Similar effects can be seen in the C–N bonds which are 2.13 and 1.73 Å respectively. The N–P–O bond angle also shows that the ααβ transition structure has to distort less from the equilibrium structure than does the ααα structure. Even more striking is the relative distortion at the phosphorus atom. In the ααα structure the phosphorus almost adopts a square-planar geometry, shown by the fact that most of the bond angles at it are close to 90°, whereas for the ααβ structure the phosphorus geometry is very much closer to the tetrahedral observed in the equilibrium structures.

These observations strongly suggest that steric forces are responsible for both the unusual distortion and the differential energy barriers. Consequently, the reaction involving demethylated analogues was studied. In this reaction only the migrating methyl group is retained; this is a different methyl group for the ααα and ααβ formation. (The slightly different energies for the two αα compounds given at the bottom of Table 2 are thus due to slight differences in conformational energy. While the methyl group is essential for stability experimentally, this is not the case in computational studies.) The results show that there is essentially no difference in the energy barrier for either reaction. We do not expect the substitution of methyl by hydrogen to have a large electronic effect. Consequently, these results strongly suggest that the ααα compound is not formed by an intramolecular mechanism because steric crowding of the methyl groups creates a large energy barrier. Although the intramolecular mechanism was initially not considered as likely as intermolecular mechanisms, the energy barrier found here is not too high, particularly when measured relative to the starting compound.

Conclusion

Semiempirical molecular orbital methods, and density functional methods, have been used to investigate why only the ααβ phosphazane **2**, and not the ααα form, is observed experimentally. Semiempirical molecular orbital calculations (PM3) show that the heat of formation of the ααβ form at 298 K is marginally lower than for the ααα form. When free-energy corrections are applied to determine the free-energy difference between the two forms at 448 K, the ααα form is actually predicted to be the most stable. However, the calculated differences are small, suggesting that a mixture of products may be expected if the reaction were under thermodynamic control. The implication is that the energy barrier for the formation of the ααα form is significantly higher than that for the ααβ form.

Calculations on the intramolecular transition structures support this as the energy barrier for the formation of the ααα compound is significantly higher than that for the ααβ product, implying that the reaction is indeed under kinetic control. These results have been verified by non-local density functional calculations which used a 6-31G* near-double-zeta-plus polarisation basis set and employed the B-LYP combination of functionals for exchange and correlation, confirming that the barrier for the intramolecular formation of the ααβ form is indeed much lower than for the formation of the ααα form. Calculations on demethylated cyclophosphazanes suggest that the differential energy barrier is steric in origin.

Acknowledgements

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