# Epimerization of an Optically Active Hexaco-ordinated Phosphorus Compound: Kinetic Studies

By **Max Koenig, Alain Klaébé, Aurelio Munoz,** and **Robert Wolf,** * Equipe de recherche du C.N.R.S. No. 82, Laboratoire des hétérocycles du phosphore et de l'azote, Université Paul Sabatier, 31077 Toulouse Cedex, Fance

The phenomenon of second-order asymmetric transformation often encountered for optically active spirophosphoranes has made possible the isolation of the optically pure hexaco-ordinate phosphorus compound (2). It was possible to follow the epimerization of the hexaco-ordinate phosphorus atom by n.m.r. spectroscopy and polarimetry for dimethyl sulphoxide solutions. The values of $\Delta G^{\ddagger}$ (21.3 kcal mol^{-1}) are very close to those observed for pentaoxyspirophosphoranes.

RESULTS

The process (Scheme 1) by which (+)-mandelic acid reacts with the pentaco-ordinate substrate (1) to produce compound (2) has already been described.[1] After 20 h the yield is 80%.
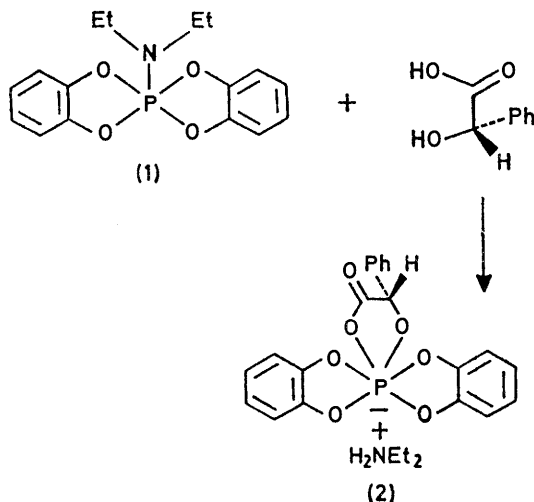
SCHEME 1

The ^{31}P n.m.r. spectrum of compound (2) (c 0.636M in Me$_2$SO; reference 85% H$_3$PO$_4$) shows a broad signal at δ +90 p.p.m. which after proton decoupling, divides into two singlets separated by 0.5 p.p.m. The spectrum of a sample kept in a sealed tube for one month at room tempera-

ture did not alter. In the ^{1}H n.m.r. spectrum (100 MHz; c 0.343M in [^{2}H$_6$]Me$_2$SO; 35°) the proton linked to the chiral carbon of mandelic acid can be observed after 3 min in the form of two doublets. This confirms the existence of two diastereoisomers A and B with n.m.r. parameters δ_A 5.33 ($^3J_{\text{H-C-O-P}}$ 7.8 Hz) and δ_B 5.19 ($^3J_{\text{H-C-O-P}}$ 7.2 Hz). The ratio of the two diastereoisomers B : A is 45 : 55. At 18 °C the initial ratio of isomer B to A is 25 : 75. This ratio increases with time to stabilize at the value B : A = 44 : 56. The variation of this ratio with time enables the kinetics of epimerization to be followed.

The interconversion between the isomers observed at 18° was confirmed by dynamic ^{1}H n.m.r. spectroscopy. At 120° the doublets A and B coalesce (broad, unresolved singlet) and at 150° the HC*Ph signal is a doublet, δ 5.22 ($^3J_{\text{H-C-O-P}}$ 8.4 Hz). The free energy of activation of the transformation, calculated according to Eyring's formula,[2] gives $\Delta G^{\ddagger}$ 20.5 ± 0.4 kcal mol^{-1}.

Polarimetry.—A solution in Me$_2$SO of crystalline (2) has a rotation which varies with time until it reaches a stable value not equal to zero. This mutarotation allowed a kinetic study of the phenomenon. In the temperature (291—308 K) and concentration ranges (0.029—0.343M) used, the kinetic data (Tables 1 and 2) fit equation (1)

$$(\alpha_t - \alpha_\infty) = (\alpha_0 - \alpha_\infty)\,(e^{-k_{\text{app}}t}) \qquad (1)$$

where α_0 is the rotation at the time zero, α_∞ the rotation at equilibrium, α_t the rotation at time t. Although the rate

[1] A. Munoz, G. Gence, M. Koenig, and R. Wolf, *Bull. Soc. chim. France*, 1975, 1433.
[2] G. Binsch, *Topics Stereochem.*, 1968, **3**, 97.

constant increases with concentration (Table 2), a first-order dependence, with respect to solute, is observed strictly up to 5—7 half-lives. The variations observed both in the n.m.r. and by polarimetry arise from the same phenomenon,

TABLE 1

Apparent rate constants k_{app} of epimerization of (2) at different temperatures

T/K	$10^3[(2)]/M$	$10^3 k_{app}/s^{-1}$	$t_{1/2}/s$	$\Delta G^{\ddagger}_{app}/$ kcal mol^{-1}
293	28.6	0.717 2	966	21.35
298	26.1	1.271 8	544	21.39
303	28.0	2.496	277	21.35
308	32.7	4.52	153	21.35

TABLE 2

Variation of k_{app} with concentration

T/K	$10^3[(2)]/M$	$10^3 k_{app}/s^{-1}$	$t_{1/2}/s$	$\Delta G^{\ddagger}_{app}/$ kcal mol^{-1}
291	29	0.567	1 221	21.34
291	343	2.859	242	20.40

the existence, in solution, of equilibrium (2) between the two hexaco-ordinate diastereoisomers. Measurement of

$$A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B \qquad K_e = k_1/k_{-1} \qquad (2)$$
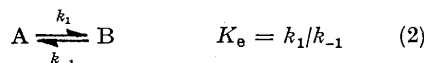
the equilibrium constant K_e (Table 3) makes it possible to obtain the microscopic rate constants k_1 and k_{-1} (Table 4).

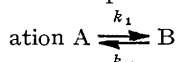The equilibrium constants were determined by integration of the doublets for A and B in the n.m.r. spectra. We

TABLE 3

Variation of equilibrium constant K_e with temperature *

T/K	291	308	330	358	ΔH_0 +0.509 ± 0.060 kcal mol^{-1}
$K_e = B/A$	0.799	0.839	0.885	0.941	ΔS_0 +1.3 ± 0.18 cal K^{-1} mol^{-1}

* $[(2)] = 0.343M$

TABLE 4

Rate constants and activation parameters of the transformation $A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B$

T/K	$K_e = B/A^a$	$10^3 k_1/s^{-1}$	$10^3 k_{-1}/s^{-1}$	$\Delta G^{\ddagger}_1$ $^b/$ kcal mol^{-1}	$\Delta G^{\ddagger}_{-1}$ $^b/$ kcal mol^{-1}
293	0.803 8	0.319	0.397	21.83	21.70
298	0.815 7	0.571	0.700	21.86	21.74
303	0.827 4	1.130	1.365	21.83	21.72
308	0.838 8	2.062	2.458	21.83	21.72

^{a} Interpolated data. ^{b} Mean values of the other activation parameters are $\Delta H^{\ddagger}_1$ 21.54, $\Delta H^{\ddagger}_{-1}$ 21.04 kcal mol^{-1}, $\Delta S^{\ddagger}_1$ −0.95, $\Delta S^{\ddagger}_{-1}$ −2.2 cal K^{-1} mol^{-1}.

assumed that the equilibrium constant values are not affected, to a first approximation, by the difference between the polarimetric and n.m.r. concentrations. This is justified given the low value of ΔH_0 and the accuracy of measurement of K_e. This has been checked using a new polarimetric method (temperature jump [3]) which leads to

more accurate values of ΔH_0 at the polarimetric concentrations.

DISCUSSION

The [31]P n.m.r. chemical shift of compound (2), given the environment of the central atom, indicates unequivocally that the phosphorus atom is hexaco-ordinated.[4-10] Hexaco-ordination arises from the branching of the three bidentate ligands used in the synthesis. The observation of two diastereoisomers implies the existence of a second chiral centre in addition to that in mandelic acid. Given the nature of the other ligands, this chirality is necessarily linked to the geometry of the compound. Allcock and Bissell [11] determined, by X-ray diffraction, the structure of a similar chiral compound, triethyl-ammonium tris-(o-phenylenedioxy)phosphate which is an almost perfect octahedron. The octahedral geometry and the chirality arising from the three bidentate ligands (helices Δ and Λ) give a good explanation of the diastereoisomerism (Scheme 2).
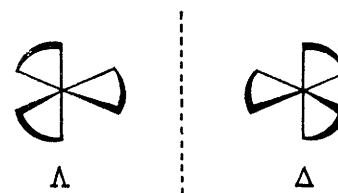
SCHEME 2

The variation of the ratio of the diastereoisomers and of the change in rotation which becomes constant at a value not equal to zero entails: (i) the transformation of one diastereoisomer into the other on starting from a system not at equilibrium (crystalline phase); (ii) the configurational lability of one and only one of the chiral centres.[12] Indeed, if both these centres were labile, the rotation at equilibrium would be nil. The non-rupture of the C–H bond is supported in the dynamic n.m.r. spectrum by the persistence of the coupling constant $^3J_{H-C-O-P}$ at 150° after coalescence of the two doublets. The chiral carbon centre being configurationally stable, the epimerization observed is a direct consequence of the lability of the hexaco-ordinate skeleton.

The same property is evident for a similar compound (3) which does not have a chiral ligand (Scheme 3). The two methyl groups of the acid are diastereotopic (δ_1 1.30, δ_2 1.42) thus demonstrating the chirality of the hexaco-ordinate structure, i.e. the existence of two helices Δ and Λ.[13] The coalescence of the methyl signals observed at 140 ± 5° ($\Delta G^{\ddagger}$ 21.7 ± 0.3 kcal mol^{-1}) is characteristic of rapid exchange between the two enantiomers.

In consequence the kinetic parameters (Table 4) are

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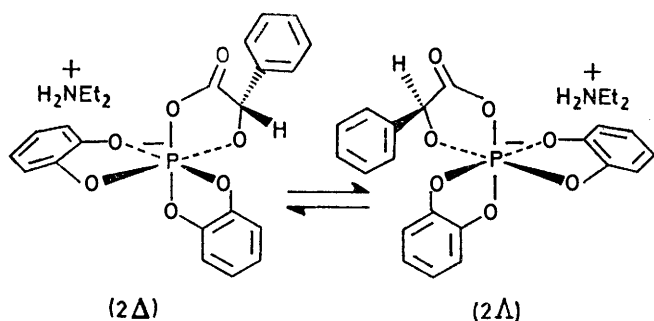[11] H. R. Allcock and E. C. Bissell, J. Amer. Chem. Soc., 1973, 95, 3154.
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those for an epimerization of the skeleton unit in a system which tends towards an equilibrium between the two helixes (2Δ) and (2Λ) (Scheme 4).


(3 Δ)   **(3 Λ)**

SCHEME 3

(2 Δ)   **(2 Λ)**
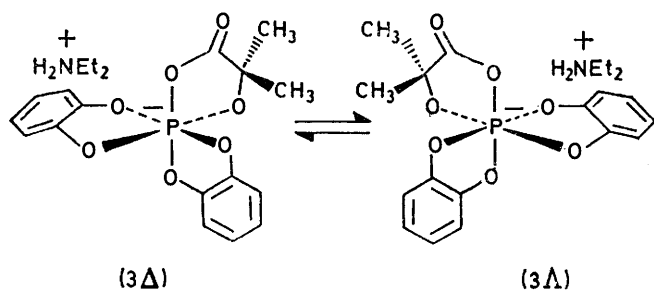
SCHEME 4

The kinetics in the Me_2SO at 18° measured by n.m.r. and polarimetry at the same concentration (0.343M) give identical apparent rate constants (within experimental error): k_{app} 2 × 10^{-3} ± 1 × 10^{-3} s^{-1}, n.m.r.; 3.06 × 10^{-3} ± 0.05 × 10^{-3} s^{-1}, polarimetry. Thus the extrapolation to time zero of the intensity of the doublets A and B given by n.m.r., based on the rate constant obtained from polarimetry indicates that the isolated isomer is

(4 Δ)   **(5 Λ)**
$[\alpha]_{589}^{25}$ −580·9° $[\alpha]_{573}^{24}$ −1930°
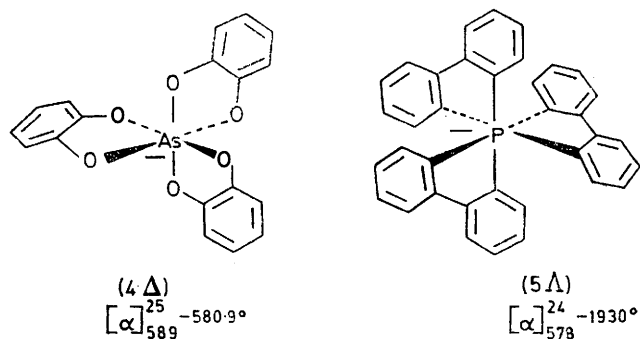
SCHEME 5

optically pure within experimental error; the value of $[\alpha_0]$ is that of the specific rotation $[\alpha_A]$ of the pure

* There are two examples of optically pure molecules similar to those studied here whose complete configuration has been determined (Scheme 5) (common cation K$^+$). The first is the arsenic compound (4), whose helical structure obtained by X-ray c.d. measurements is Δ, $[\alpha]_{589}^{25}$ −580.9°.[14,15] The second (5) has a central phosphorus atom and its helical structure, established by c.d. is Λ, $[\alpha]_{578}^{24}$ −1 930°.[16,17] These results mean that it is not possible to relate simply the sign of rotation to a given helical structure.

diastereoisomer A. $[\alpha_A]_{546}^{18}$ is 245° (c 0.343M, Me_2SO) and as $[\alpha_\infty]_{546}^{18}$ is +91° and K_e 0.799, the specific rotation of the other diastereoisomer $[\alpha_B]_{546}^{18}$ is −102°.* This model presents the phenomenon of second-order asymmetric transformation [12,18] which was predicted given the coexistence in the same molecule of two chiral units, the one configurationally stable and the other labile, and given the value of the epimerization barrier of the latter.

Mechanism.—One can distinguish in the literature two types of isomerization mechanisms: (i) regular isomerization, a monomolecular process without bond breakage and (ii) irregular isomerization, an intra- or intermolecular process going through a change of co-ordination. The regular isomerization (mechanism I) envisaged by Bailar [19] (Scheme 6) (see also Ray and Dut [20]) and observed by Pignolet,[21] was demonstrated by Eaton et al.[22] at low temperature for aluminium and cobalt complexes. In this latter case the low temperature process is one of inversion of absolute configuration (Δ ⇌ Λ) which proceeds by a trigonal–twist mechanism. In opposition to these results leading to a regular mechanism one can propose irregular isomerization hypotheses: (i) a transition through a pentaco-ordinate form,[23] a pseudo-rotation with [24] or without interaction of the solvent and ring reclosing (mechanism II, Scheme 7); (ii) a partial or total interaction between a molecule of solvent and a

Λ   Δ
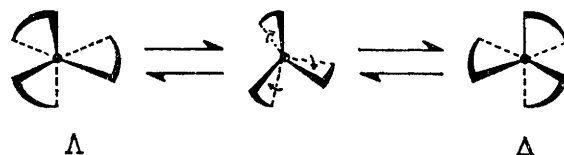
SCHEME 6

hexaco-ordinated structure to give a heptaco-ordinate intermediate [25] (mechanism III); (iii) a process of exchanges between ligands bringing to bear an intermolecular mechanism (mechanism IV). These hypotheses can be evaluated in the light of the following experimental results: (i) the rate reaction laws are first order; (ii) in the ^{31}P n.m.r. spectrum it was not possible to detect an intermediate (penta- or hepta-co-ordinate); (iii) the rate constant increases by a factor of five when the concentration increases by a factor of 12; (iv) the

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activation entropy is low. The fact that an intermediate was not detected does not rule out any of the proposed mechanisms. The first-order reaction laws and the low value of $\Delta S^{\ddagger}$ argue for putting aside mechanisms III and IV and favour mechanisms I and II. In the latter, the rate-determining step would be pseudorotation of the pentaco-ordinate form.

However, the results already obtained in the study of regular isomerization of pentaco-ordinate phosphorus compounds [26] or in the case of ionic molybdenum complexes [27] have shown that variation of concentration has

connected with the interaction between the carboxylate anion and the pentaco-ordinate phosphorus intermediate. The isomerization of R_2NPF_4 in the presence of Me_2O observed by Eisenhut et al.[24] supports this view.

EXPERIMENTAL

Compound (2) was formed by treating (1) (0.01 mol) dissolved in benzene (30 ml) with (+)-mandelic acid (0.01 mol) dissolved in ether (20 ml) at room temperature. Crystals precipitated slowly and after 20 h diethylammonium 4-oxo-5-phenyl-1,3,2-dioxaphospholebis-(2-spiro-2'-benzo-1,3,2-dioxaphosphol)ate (80%) was collected (Found: C, 60.3; H,
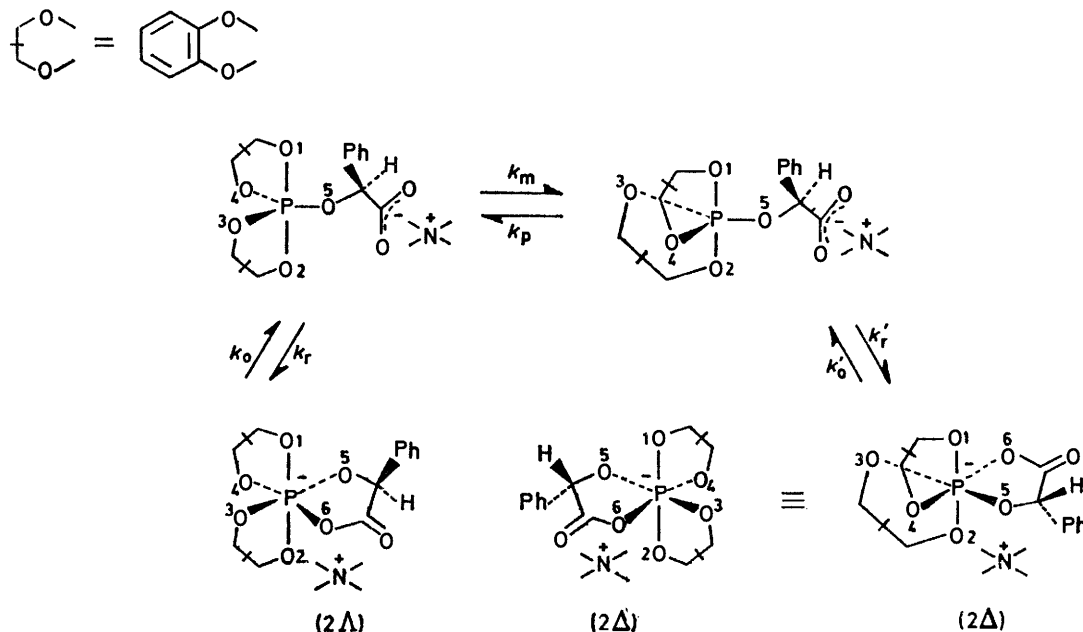
SCHEME 7

little effect on the values of the rate constants. If these results were to be applied to hexaco-ordination of phosphorus they would make an isomerization of a regular kind (mechanism I) unlikely.

Epimerization (Scheme 7) after transition through a pentaco-ordinate intermediate explains the experimental data. Indeed the epimerization barriers found in the literature for pentaoxyspirophosphoranes are of the same order of magnitude.[28] In this case the rate-determining step is a regular skeletal rearrangement whilst the higher rate constant would be that of reclosing (the failure to detect an intermediate in n.m.r. entailing $k_r \gg k_0$).

The lowering of the epimerization barrier with increase of concentration would be due to (i) to the variation of the ionic strength which facilitates bond breaking resulting in charge separation [29] and (ii) to an autocatalytic process

5.55; N, 2.9; P, 6.55. $C_{24}H_{26}NO_7P$ requires C, 61.15; H, 5.55; N, 2.9; P, 6.6%), $\lambda_{max.}$ 283 (ε 8 800) and 197 nm (118 000).

60 and 100 MHz ^1H n.m.r. spectra were taken with Varian T60 and HA100 instruments with tetramethylsilane as internal standard. ^{31}P N.m.r. spectra (24.3 MHz) were taken with a Perkin-Elmer R10 and Bruker WP60 instruments with 85% H_3PO_4 as external standard. N.m.r. data are given in the text. Polarimetric measurements ($\pm 0.002°$) were taken with a Perkin-Elmer 141 instrument in a temperature controlled cell (± 0.02 °C). The equilibrium constants at different temperatures were determined by integration of n.m.r. signals with a Dupont 310 curve resolver and statistical treatment of the data by the least-squares method using a Hewlett–Packard 20 calculator. Kinetic data were treated using the LSG program [30] on a IRIS 80 computer.

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