Optically Active Five-co-ordinated Phosphoranes. Apicophilicity of the Amino-group compared with Hydrogen: a Comparative Kinetic Study. Influence of the Activation Entropy

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Two diasteroisomeric pairs of optically active spirophosphoranes have been synthesized, which differ only in the nature of the monodentate phosphorus substituent: H for (1) and PhNH for (2). A kinetic study of the isomerization (epimerization) of each of these pairs has been carried out by polarimetry. The difference in apicophilicity of the exocyclic ligand fails to explain the small difference between the barriers observed for (1) and (2). An accurate determination of the activation parameters shows that in these cases the variation in the isomerization barrier is essentially due to entropy factors.

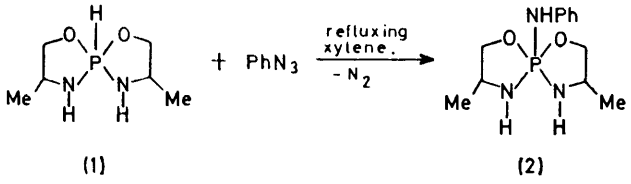
THE study of the molecular flexibility of pentacovalent phosphorus compounds has developed rapidly since 1964,[1] from both the theoretical [2] and the experimental [3] point of view. Results in this area since 1973 have been reviewed by Luckenbach [4] and by Holmes.[5] Among the more recent contributions on the factors controlling the mechanism of stereolability, Trippett's [6] is distinguished by the introduction of a quantitative parameter: the apicophilicity. By this term Trippett defines the trend for a ligand to occupy an apical site in a structure with a trigonal bipyramidal geometry (TP). Trippett's elegant models have been chosen because the measure of the free energy of activation ($\Delta G^{\ddagger}$) of a particular isomerization of a phosphorane (in the above geometry) corresponds to the difference between the energy of a single activated form (or a structure close to this form) bearing the group being studied in an apical position and that of the isoenergetic ground states in which this ligand is in an equatorial position; from measurements by dynamic n.m.r. spectroscopy of the corresponding activation parameters for many different compounds, Trippett has constructed a relative scale of apicophilicity for many groups linked to five-co-ordinated phosphorus.[7] On this scale, amino-substituents have low apicophilicity, much less than alkoxy-groups and hydrogen: the difference between values for NR_2 and H is estimated to be *ca.* 7 kcal mol^{-1}.†

The comparative study reported here deals with the isomerization barrier of optically active anilinospirophosphoranes compared with their *P*-unsubstituted counterparts, and leads to unexpected results when using the apicophilicity scale. We point out that the activation parameter $\Delta G^{\ddagger}$, when used alone, fails to account for the results obtained in the compounds studied here.

† 1 cal = 4.184 J.

RESULTS

The reaction of phenyl azide with the spirophosphorane (1) leads to the anilinospirophosphorane (2) as a mixture of two optically active diastereoisomers which are in equilibrium in solution (Schemes 1 and 2).[8,9] The phosphorus



(1) (2)

SCHEME 1

atom is substituted by two ligands derived from (+)-alaninol [(2*S*)-2-aminopropan-1-ol] in these compounds. This equilibrium is a result of the stereolability of the spiro-structure. For (1), as for (2), one of the two optically pure diastereoisomers can be isolated, through a second-order asymmetric transformation, by slow crystallization. On dissolution of the isolated product, its epimer is formed until equilibrium is reached. This transformation can be followed by ^{1}H n.m.r. spectroscopy or polarimetry. Using polarimetry, the transformation was followed kinetically by the variation in rotation of the solution with time (mutarotation). The kinetics observed are first-order

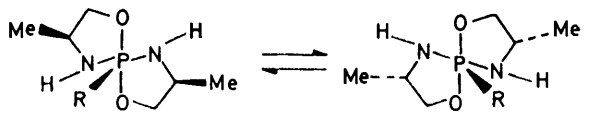
TABLE 1

Kinetic and activation parameters for (1) in benzene

T/K	10^2[(1)]/M	$10^5 k_{app.}$/s^{-1}	$10^5\sigma$/s^{-1} [a]	$\Delta G^{\ddagger}$/kcal mol^{-1}	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}
287.9	6.25	38.5	1.5	21.33		
290.5	6.53	52.70	0.9	21.34		
293.5	5.19	71.9	4	21.39	19.45 [b]	−6.52 [b]
293.5	24.27	71.8	0.7	21.39		
297.2	6.02	114.2	5	21.39		
306.1	5.57	308.5	23	21.44		

[a] Standard deviations for $k_{app.}$ given by the L.S.G. program (see Experimental section). [b] Mean values at the given temperatures.

with respect to the solute; large variations in concentration (×10) have no influence on this order, and the kinetic constants are independent of concentration. The activation parameters which were calculated are in Tables 1—4. Table 4 also gives the kinetic parameters for compounds (3) and (4) which are closely related to (2). However, it is interesting to compare directly the isomerization



(1) R = H
(2) R = PhNH

SCHEME 2

activation parameters for (1) and (2) because they differ only in the nature of the monodentate ligand (H or PhNH).

TABLE 2

Kinetic and activation parameters for (2) in benzene

T/K	10^2[(2)]/ M	$10^5 k_{app.}$/s^{-1}	$10^5\sigma$/s^{-1} [a]	$\Delta G^{\ddagger}$/kcal mol^{-1}	$\Delta H^{\ddagger}$/kcal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}
293.8	4.86	2.46	0.04	23.38		
307.7	2.82	9.96	0.1	23.66		
317.0	2.53	25.95	4	23.79	17.99 [b]	−18.35 [b]
324.0	2.66	46.79	0.6	23.95		

[a] Standard deviation for $k_{app.}$ given by the L.S.G. program.[21]

DISCUSSION

The isomerization of *P*-unsubstituted spirophosphoranes has been shown to follow a regular process [9,10] as is the case for compound (1); to our knowledge there are no reports of a systematic mechanistic study of (2) and related compounds, but two experimental findings strongly suggest that the isomerization of (2), (3), and (4) must be regular: (i) the negative value of the activation entropy (Tables 2 and 3), and (ii) the insensitivity of the isomerization barrier to variation in polarity of the solvent (Table 4). We note that, for spirophosphoranes, intramolecular isomerization without bond breaking occurs by a mechanism belonging to the permutational mode M(1).[11] In this mode, Berry [12] pseudorotation (PR) is the mechanism which best describes this isomerization type.

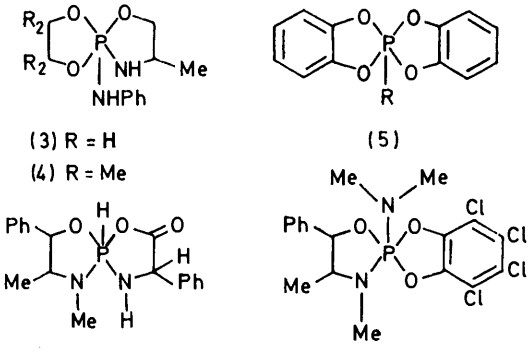
TABLE 3

Comparative activation parameters for (1) and (2) in benzene with their standard deviations σ

Products	$\Delta G^{\ddagger}$ kcal mol^{-1}	$\Delta H^{\ddagger}$ kcal mol^{-1}	$\sigma(\Delta H^{\ddagger})$	$\Delta S^{\ddagger}$ cal mol^{-1} K^{-1}	$\sigma(\Delta S^{\ddagger})$
(1)	21.39	19.45 [a]	0.1	−6.5 [a]	0.2
(2)	23.49	17.99 [b]	0.3	−18.3 [b]	1

[a] Mean values in the temperature range 288—310 K. [b] Mean values in the temperature range 293—323 K.

As a working assumption, in order to obtain information on the activated form through which the isomerization proceeds, we have used the topological representation in Scheme 3, which is best suited to the phenomenon under study and compounds (1) and (2).[13,14] Using the hypothesis of a pseudorotation (PR) process, Scheme 3 shows the four different ways possible to pass from the TP (12) in a ground state to its enantiomer ($\bar{1}\bar{2}$)



(3) R = H
(4) R = Me
(5)
(6)
(7)

Three of these involve five steps and pass through high-energy trigonal bipyramids (TP) ($4\bar{5}$) [or (35)] and (25) [or ($1\bar{5}$)]; the fourth way, with seven PR steps misses TP (45) but involves the state (25) or ($1\bar{5}$) (see Scheme 4).

The most destabilized stereoisomers ($4\bar{5}$) and (25) do contain the substituent R in an apical position but they are at different energy levels; as a consequence the isomerization paths are inequivalent. So, at a first analysis, our models do not agree over the transition state, as far as the apicophilicity of the group R is concerned. However, it seems to us more accurate to discuss the relative stability of the transition states. According to the Berry mechanism, the transition state

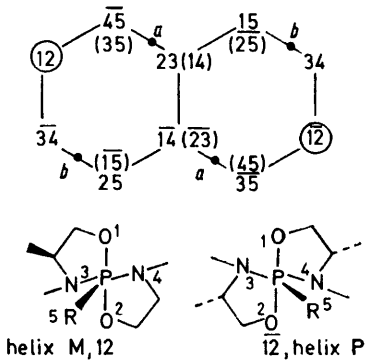
TABLE 4

Activation parameters for the isomerizations of (3) and (4) in benzene and pyridine and their standard deviation σ

	Benzene					Pyridine				
Solvent	$\Delta G^{\ddagger}$ kcal mol^{-1}	$\Delta H^{\ddagger}$ kcal mol^{-1} [a]	$\sigma(\Delta H^{\ddagger})$	$\Delta S^{\ddagger}$ cal K^{-1} mol^{-1} [a]	$\sigma(\Delta S^{\ddagger})$	$\Delta G^{\ddagger}$ kcal mol^{-1}	$\Delta H^{\ddagger}$ kcal mol^{-1} [a]	$\sigma(\Delta H^{\ddagger})$	$\Delta S^{\ddagger}$ cal K^{-1} mol^{-1} [a]	$\sigma(\Delta S^{\ddagger})$
(3)	21.47	18.68 [b]	0.4	−9.3 [b]	1.2	21.25	21.08 [c]	0.32	−0.58 [c]	1.1
(4)	20.16	11.97 [d]	0.5	−27.3 [d]	1.6	20.80	20.6 [d]		−0.67 [d]	

[a] Mean values in the temperature ranges specified. [b] 288—310 K. [c] 288—303 K. [d] 283—288 K.

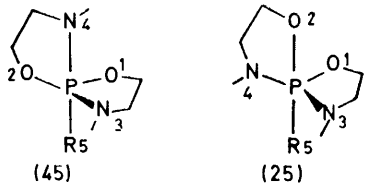
is considered to adopt a square pyramidal (SP) geometry between two TP intermediates. The topological representation then shows that the transition states with the highest energy are the SP states (a) and (b) (Scheme 4).

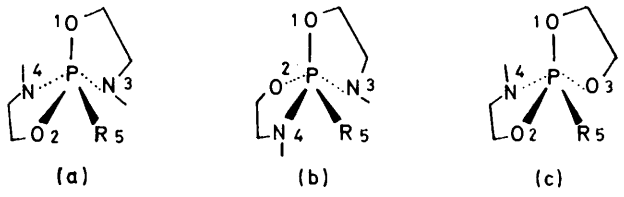


SCHEME 3

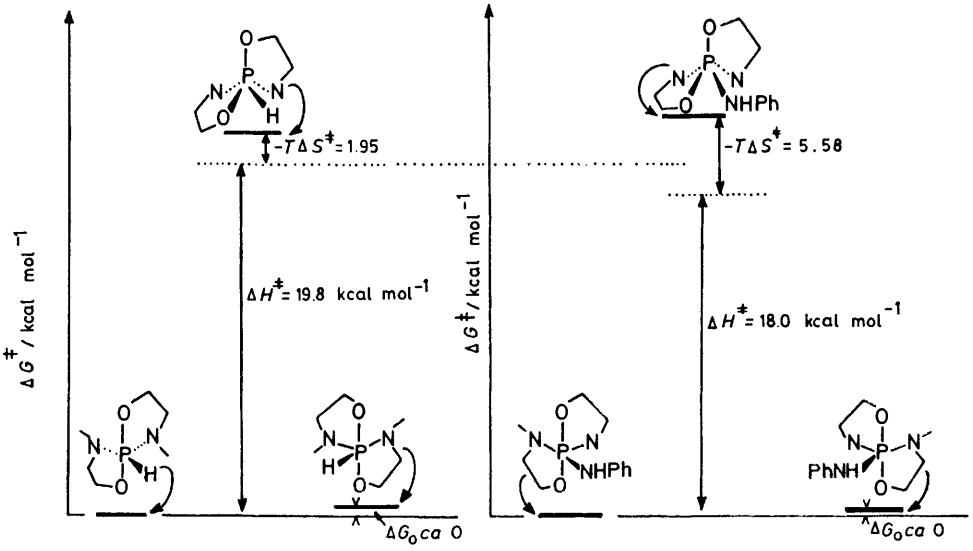
For these two SP states, the exocyclic substituent R (numbered 5) occupies a basal position; one of the rings spans dibasal positions and the other is linked to a basal nitrogen and a polar oxygen. This structure is also the one Holmes *et al.*[15] arrive at, from their calculations on the molecular deformations in the isomerization processes, as the transition state with the highest energy. As was the case for the TP intermediates (4̄5) and (25) these SP transition states (a) and (b) are not isoenergetic. For (a) the ligand R is in a *trans*-position with respect to a nitrogen atom; in (b) it is *trans* to oxygen. We cannot ascertain whether one of these two structures would be of higher energy; nevertheless it is probable that the interactions of the lone pairs of the two basal atoms (oxygen and nitrogen) with R could be major factors leading to an energy difference. We believe that these differences in energy can be neglected, however, owing to the relative magnitude of the activation parameters. We suggest that these two activated forms may be considered to be isoenergetic, so, the isomerization pathways are equivalent and our models are similar to those of Trippett. It is noteworthy, in the case of compounds (3) and (4), that the only activated form is the SP structure (c) (Scheme 4).

The foregoing arguments allow the direct comparison of compounds (1) and (2), in which the ligand H is replaced by the PhNH group. The activation parameters in Table 3 show that this substitution in passing from (1) to (2) increases the isomerization barrier ($\Delta\Delta G^{\ddagger}$) by 2 kcal mol^{-1}; the direction of this variation could have been foreseen using Trippett's apicophilicity scale but the magnitude of the variation is clearly smaller than expected. In fact, if one takes into account activation enthalpies ($\Delta H^{\ddagger}$), the direction of the variation is opposite: $\Delta H^{\ddagger}$ is smaller for (2) than for (1) ($\Delta\Delta H^{\ddagger}$ = 1.45 kcal mol^{-1}). The entropy term $T\Delta S^{\ddagger}$ at 300 K





SCHEME 4



SCHEME 5

is 1.9 kcal mol^{-1} for (1) and 5.6 kcal mol^{-1} for (2); this last value is therefore very important, and thus the entropy factor plays a decisive role in determining the value of the isomerization barrier (Scheme 5).

We propose the following interpretation of these data and the direction of their variation.

(a) A smaller activation enthalpy parameter for (2) than for (1) would be the result of a greater deformation of the TP ground state for (2) towards the SP geometry of the transition state.[16] This structural deformation might arise from the relatively higher steric hindrance of the anilino-ligand in the equatorial plane in (2) than the hydrogen in (1). Thus, the extents of deformation towards the SP geometry (D%) of the six spirophosphoranes in Table 5, calculated following Muetterties's

TABLE 5

Extent of deformation (D%) towards SP geometry of spirophosphoranes of type (5) [a]

R	H	F	Ph	Ad [b]	Me	Ph
D%	3	64.8	72.1	73	82.4	87.7

[a] From ref. 16. [b] Adamantyl.

criterion,[17] show that the deformation increases roughly with the bulkiness of the monodentate ligand R.

The results [10,18] of two X-ray crystal structure determinations exemplify the effect of the replacement of hydrogen by a dimethylamino-group on the extent of deformation (Table 6).

Application of these arguments to compounds (3) and (4), for which $\Delta\Delta H^{\ddagger} = 6.7$ kcal mol^{-1}, indicates that the deformation is greater for (4) than for (3).

(b) The difference in activation entropy between (1) (−6.5 cal mol^{-1} K^{-1}) and (2) (−18.6 cal mol^{-1} K^{-1}) shows that it is this parameter which controls the relative height of the isomerization barriers between (1) and (2).* How can this variation be interpreted?

TABLE 6

Comparative extents of deformation (D%) towards SP geometry for the spirophosphoranes bearing hydrogen (6) or a dimethylamino-group (7) as monodentate ligand

Compound	(6)	(7)
D%	8.9 [a]	18 [b]

[a] From ref. 18. [b] From ref. 10.

The activation entropy ($\Delta S^{\ddagger}$) is considered by Binsch [19] to be a sum of terms, one of which is the partial rotation entropy of the ligand R ($\Delta S^{\ddagger}_{R}$); $\Delta S^{\ddagger}_{R}$ is the difference in the rotation entropy for the ligand R in the excited state and the ground state of the molecule. This term depends on the numbers of degrees of freedom of the group R; in compound (1), the H ligand shows a single rotational degree of freedom in its ground and excited states. In contrast, compound (2), containing the PhNH substituent, has at least three rotational degrees of freedom (if the hydrogen atoms linked to the aromatic ring are not taken into account).

Now, if we compare for (2) the relative position of the monodentate equatorial ligand PhNH in the ground state (TP) and its basal location in the activated state with SP geometry, it is very likely that the P–NHPh rotations would be much more hindered in the activated structure (see Scheme 4).

The same arguments can explain the large value of the activation entropy for (3) and (4) (Table 4). Moreover, the difference $\Delta\Delta S^{\ddagger}$ (9.3 cal mol^{-1} K^{-1}) for the isomerization of compounds (3) and (4) in benzene will be due to rotations of the anilino-group in the excited state. These rotations would be much more hindered in (4) than in (3), owing to intereactions between the NHPh ligand and the Me substituent in the dioxaphospholan ring. In pyridine solution we have obtained small values for both compounds ($\Delta S^{\ddagger}$ *ca.* 0) (Table 4); this effect can be explained by the fact that in pyridine solution the rotations of the anilino-group are already hindered in the ground state by hydrogen bonds between solvent and the NH proton.† Formation of these strong hydrogen bonds has been detected by ^{1}H n.m.r. spectroscopy and evidence for them presented elsewhere.[20]

EXPERIMENTAL

100-MHz ^{1}H N.m.r. spectra were recorded with a Varian HA 100 instrument for C_6D_6 solutions with tetramethylsilane as internal standard, and 24.3 MHz ^{31}P n.m.r. spectra with a Perkin-Elmer R10 instrument, with 85% H_3PO_4 as external standard.

The rates of the epimerization M ⇌ P were obtained from the linear plot of $\ln(\alpha_t - \alpha_\infty)$ against time, where α_t is the optical rotation of the solution at time t. and α_∞ the rotation after more than ten half-lives. The kinetic parameters were obtained using the L.S.G. program [21] with an Iris 80 computer or the same program adapted to a Tectronix 4051 computer equipped with a graphic system.

Polarimetric measurements were taken with a Perkin-Elmer 141 instrument with an accuracy of ±0.002° in a temperature-controlled cell (±0.02 °C). Error limits were evaluated by a method reported previously.[22] The Tables show the standard deviations given by the L.S.G. program.

Compound (1) was prepared refluxing tris(dimethylamino)phosphine (1 equiv.) with (+)-alaninol [(2*S*)-2-aminopropan-1-ol] (2 equiv.) in benzene under nitrogen. The dimethylamine generated was titrated to follow the progress of the reaction. After completion of the reaction the mixture was cooled, when the spirophosphorane (1) crystallized as white needles. The ^{1}H n.m.r. spectrum of a solution of the product in benzene at *ca.* 6 °C shows the presence of only one diastereoisomer: δ 7.10 (d, $J_{H\text{-}P}$ 731.4 Hz, P–H) and 0.86 (d, $J_{H\text{-}C\text{-}C\text{-}H}$ 4.0 Hz, CMe); ^{31}P n.m.r.: δ −56 p.p.m., and this single diastereoisomer was obtained following the slow crystallization as a result of a second-order asymmetric transformation. This diastereo-

* Our results serve to stress the importance of the activation entropy term, which is seldom considered in the literature. G. Buono (Thèse, Université Marseille III, 1977) and J. R. Llinas work (Thèse, Université Marseille II, 1979) have recently determined high values of $\Delta S^{\ddagger}$ for monocyclic and spirophosphoranes.

† For instance for (3) we observe a deshielding for the N–H protons in pyridine (see Experimental section): δ(pyridine) −δ(toluene) 1.60 for PhNH and 1.90 for ring NH. This effect reflects the formation of the hydrogen bonds between pyridine and the product.

isomer gives in solution the other diastereoisomer [δ 7.26 (d, J_{H-P} 729.3 Hz, P–H) and 0.76 (d, $J_{H-C-C-H}$ 4.0 Hz, CMe); ^{31}P n.m.r.: δ −56 p.p.m.] by slow epimerization at the chiral phosphorus centre.

Compound (2) was synthesized by refluxing (1) (1 equiv.) and phenyl azide in xylene during 10 h. The progress of the reaction was followed by the evolution of nitrogen, and the product was purified by crystallization from benzene. As for (1), one diastereoisomer was obtained as a result of a second-order asymmetric transformation: ^1H n.m.r.: δ 0.78 (d, $J_{H-C-C-H}$ 5.5 Hz, CMe), 4.7 (d, J_{H-N-P} 7 Hz, PhNH), and 2.76 (d, J_{H-N-P} 14.5 Hz, ring NH); ^{31}P n.m.r. δ −49.3 p.p.m. The other diastereoisomer is formed following epimerization at phosphorus: ^1H n.m.r.: δ 0.84 (d, $J_{H-C-C-H}$ 6 Hz, CMe), 4.7 (d, J_{H-N-P} 7 Hz, PhNH), and 2.76 (d, J_{H-N-P} 14.5 Hz, ring NH); ^{31}P n.m.r.: δ −49.3 p.p.m.

Compounds (3) and (4) were prepared in the same way as (2) and show the second-order asymmetric transformation phenomenon; compound (3): ^1H n.m.r. (C_7D_8) for the isolated diastereoisomer: δ 0.69 (d, $J_{H-C-C-H}$ 5.6 Hz, N–CMe), 4.6 (d, J_{H-N-P} 8 Hz, PhNH), and 2.69 (d, J_{H-N-P} 20 Hz, ring NH; ^{31}P n.m.r.: δ −46.2 p.p.m.; ^1H n.m.r. spectrum for the diastereoisomer formed by epimerization: δ 0.73 (d, $J_{H-C-C-H}$ 5.7 Hz, N–CMe), 4.6 (d, J_{H-N-P} 8 Hz, PhNH), and 2.69 (d, J_{H-N-P} 20 Hz. ring NH); ^{31}P n.m.r.: δ −46.2 p.p.m.; ^1H n.m.r. spectrum for a mixture (*ca.* 1 : 1) of the two diastereoisomers in [$^2H_5$]pyridine solution: δ 1.22 (d, $J_{H-C-C-H}$ 6.0 Hz, N–CMe), 1.16 (d, $J_{H-C-C-H}$ 6.0 Hz, N–CMe), 6.20 (d, J_{H-N-P} 8.0 Hz, PhNH), and 4.59 (d, J_{H-N-P} 20 Hz, ring NH); compound (4): ^1H n.m.r. spectrum for the isolated diastereoisomer: δ 0.75 (d, $J_{H-C-C-H}$ 5.4 Hz, N–CMe), 4.78 (d, J_{H-N-P} 8 Hz, PhNH), and 2.72 (d, J_{H-N-P} 20 Hz, ring NH); ^{31}P n.m.r.: δ −48.0 p.p.m.; ^1H n.m.r. spectrum for the other diastereoisomer: δ 0.84 (d, $J_{H-C-C-H}$ 5.4 Hz, N–CMe), 4.78 (d, J_{H-N-P} 8 Hz, PhNH), and 2.72 (d, J_{H-N-P} 20 Hz, ring NH); ^{31}P n.m.r.: δ −48.0 p.p.m.

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