Determination of Thermodynamic and Kinetic Parameters for Equilibria between two Diastereoisomers by a Polarimetric Temperature-jump Method. The Application to Five- and Six-co-ordinate Phosphorus Compounds

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The usefulness of a polarimetric temperature-jump method for the determination of thermodynamic and kinetic parameters for equilibrium reactions between optically active compounds has been demonstrated for five- and six-co-ordinated phosphorus compounds. Even when the equilibrium constant (K_e) for the reaction cannot be accurately determined, it is shown that, with an approximate value of K_e at one temperature, the dependence of K_e on temperature (ΔH° and ΔS°) can be accurately determined using the above method.

IN an equilibrium between two optically active compounds A and B, where pure, but not necessarily enantiomerically pure, A (or B) is available, it may be possible to determine both the thermodynamic and activation parameters. Such experimental situations are frequently

$$A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B \qquad (1)$$

met for molecules having labile skeletons, for instance metal complexes,[1] organic molecules with high co-ordination numbers,[2] *etc.* This molecular lability could be due to two general types of mechanism:[3,4] (*i*) regular isomerization (without breaking and reforming bonds); (*ii*) irregular isomerization (with bond fission and reformation). Reactions taking place according to these two mechanisms are expected to show different entropies of activation ($\Delta S^\ddagger$): mechanism (*i*) is predicted to have small $\Delta S^\ddagger$ (*i.e.* close to zero), mechanism (*ii*) may have a substantial and positive activation entropy. Thus the determination of accurate activation parameters may enable the differentiation between the two mechanisms.

However, an accurate experimental determination of the activation parameters for reaction (1) in the conventional way is difficult because it is hard to measure accurately the temperature dependence of the equilibrium constant $K_e = [B]/[A]$. Where A (or B) is optically active by use of polarimetry it may be possible to accurately measure k_{app} ($= k_1 + k_{-1}$) at different temperatures. The equilibrium constant (K_e) on the other hand is not directly accessible from polarimetry if the specific rotation of A and B are not known. In the cases described below, n.m.r. spectroscopy can be used to determine K_e, but, because of the inaccuracy of this method when applied to dilute solutions (*i.e.* at the low concentrations of A and B at which the polarimeter experiments are made), the uncertainty in the thermodynamic parameters is too large.

In this paper we demonstrate that it is possible to accurately determine the temperature dependence of K_e (ΔH° and ΔS°) as well as that of k_1 and k_{-1} ($\Delta H_1^\ddagger$, $\Delta H_{-1}^\ddagger$, $\Delta S_1^\ddagger$, and $\Delta S_{-1}^\ddagger$). With an approximate value of K_e (*i.e.* obtained by n.m.r.) and polarimeter data from temperature-jump experiments on the reaction mixture, we can estimate the temperature dependence of K_e. The temperature dependence of the apparent rate constant (k_{app}) can be determined in the usual way or by employing Varytemp methods.[5]

The Phosphorus Compounds studied.—(*a*) Optically active spirophosphoranes of the type shown in equation (2) derived from (+)-ephedrine and 6-amino-*m*-cresol, quite readily epimerize in solution at room temperature and yield an equilibrium mixture of (1P) and (1M).[6,7] This rearrangement has been suggested to take place either

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[1] F. Basolo and R. G. Pearson, ' Mechanisms of Inorganic Reactions,' 2nd edn., Wiley, New York, 1967.

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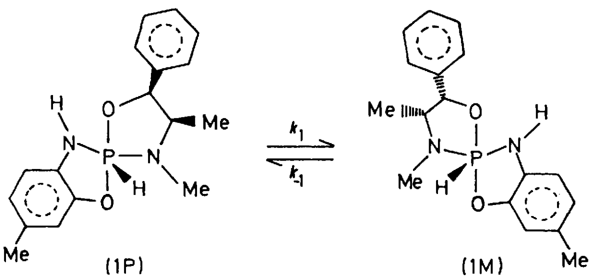
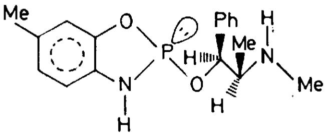
[7] A. Klaébé, A. Carrelhas Cachapuz, J. F. Brazier, and R. Wolf, *J.C.S. Perkin II*, 1974, 1668.

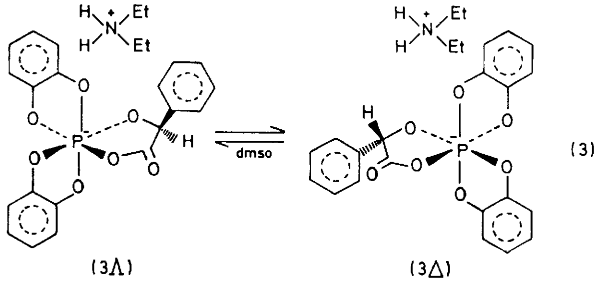
via a regular mechanism in which the phosphorus atom is five-co-ordinate throughout the reaction path, or by an irregular mechanism *via* a three-co-ordinate phosphorus intermediate of the type (2). (*b*) Optically active six-co-ordinate anions of the type (3) derived from catechol and (+)-mandelic acid epimerize in solution at room temperature and give an equilibrium mixture between (3Λ) and (3Δ).[8] This isomerization has been suggested to take place by a regular rearrangement (*i.e.* a trigonal twist mechanism) or by an irregular process, for instance *via* the intermediacy of a five-co-ordinate structure. A detailed discussion of this mechanism is included in ref. 9.



(1P) (1M) (2)



(2)

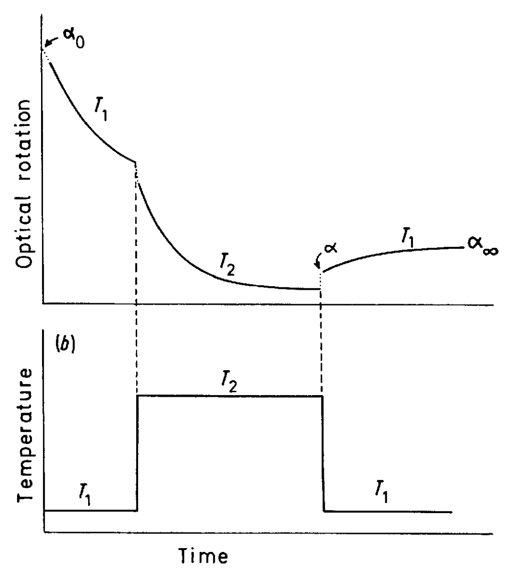


(3Λ) (3Δ) (3)

The two types of phosphorus compounds (1) and (3) can be easily obtained optically pure by a second-order transformation.[10-12] The present investigations were carried out with reaction mixtures initially containing optically pure (1P) or one of compounds (3) (*cf.* the Experimental section). The reactions were strictly first order and reversible in pyridine [equation (2)] or dimethyl sulphoxide (dmso) [equation (3)]. No significant deviations from straight-line plots of $\ln|\alpha_t - \alpha_\infty|$ against t were observed even after several half-lives.

Description of the Temperature-jump Method.—The reactions were studied in a 1-dm 1-cm³ Perkin-Elmer 141 polarimeter cell having a jacket for the thermostatting liquid. Two thermostats were employed, one maintained close to T_1 and the other close to T_2. After rapid preparation and introduction of the reaction mixture into the polarimeter cell, the initial rotation (α_0) at temperature T_1 was measured. The reaction was studied for one half-life at T_1, and then, by switching over to the other thermostat maintained close to T_2, a rapid jump in temperature of the reaction mixture to T_2 was obtained. The reaction was allowed to reach equilibrium at this new temperature (*ca.* 11 half-lives). The reaction mixture was then allowed to jump back to T_1. Within 1—2 min of the beginning of the jump the reaction mixture had reached thermal equilibrium at T_1. The jump $|T_2 - T_1|$ was sometimes as large as 25 °C. The changes in α and T are shown in the Figure (*a*) and (*b*). Thus after the jump from equilibrium at T_2 to T_1 the reaction mixture had the composition of the equilibrium mixture at T_2, and the relaxation of α to its new equilibrium value at T_1 was studied.

We now demonstrate that the temperature dependence of the equilibrium constant (K_e), *i.e.* $\Delta H^\ominus$ and $\Delta S^\ominus$, can be accurately determined from the following observed values, all obtained at the same temperature T_1, and from an approximate value of K_e (at T_1): (*a*) the initial rotation (α_0); (*b*) the optical rotation observed just after the jump (α); and (*c*) the equilibrium rotation (α_∞). Let α_A and α_B be the molar rotations of A and B respectively at T_1. In the expressions below, *a* and *b* represent concentrations. When the reaction has reached equilibrium



Variation of the optical rotation (*a*) and the temperature (*b*) with time for equation (1) with $\alpha_A > \alpha_B$, $T_2 > T_1$, and $\Delta H^\ominus > 0$. Changes in α as a result of the temperature jumps are shown schematically

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[12] J. F. Brazier, A. Cachapuz Carrelhas, A. Klaébé, and R. Wolf, *Compt. rend.*, 1973, **277**, 183.

at T_2, the equilibrium constant is K_2. During the rapid jump from T_2 to T_1, the composition of the reaction mixture is not significantly changed, *i.e.* $K_2 = b_2/a_2$, and the observed optical rotation (α) is as in equation (4).

$$\alpha = a_2\alpha_A + b_2\alpha_B \tag{4}$$

When the reaction has reached the new equilibrium at T_1, the equilibrium constant is $K_1 = b_1/a_1$ and the optical rotation α_∞ observed is as in (5). Initially at

$$\alpha_\infty = a_1\alpha_A + b_1\alpha_B \tag{5}$$

t_0 ($t = 0$) we have pure A at the concentration a_0. From equations (4)—(9), the measured values of α_0, α, α_∞, and a_0, an approximate K_1, the temperature dependence of K_e may be calculated, *i.e.* the change in K_e from K_1 to K_2 is accurately estimated. Thus we obtain equation

$$a_0 = a_1 + b_1 = a_2 + b_2 \tag{6}$$

$$\alpha_0 = a_0\alpha_A = (a_1 + b_1)\alpha_A = (a_2 + b_2)\alpha_A \tag{7}$$

$$K_1 = b_1/a_1 \tag{8}$$

$$K_2 = b_2/a_2 \tag{9}$$

(10) and hence (11). Since $\ln K_1 = -(\Delta H^\ominus/RT_1) +$

$$K_1/K_2 = [(\alpha_0 - \alpha_\infty) + K_1(\alpha - \alpha_\infty)]/(\alpha_0 - \alpha) \tag{10}$$

$$\ln K_1 - \ln K_2 = -\ln[(\alpha_0 - \alpha)/(\alpha_0 - \alpha_\infty)] + \ln[1 + K_1(\alpha - \alpha_\infty)/(\alpha_0 - \alpha_\infty)] \tag{11}$$

$(\Delta S^\ominus/R)$ and $\ln K_2 = -(\Delta H^\ominus/RT_2) + (\Delta S^\ominus/R)$, we obtain (12), by substitution (13) and (14).

$$\ln K_1 - \ln K_2 = (\Delta H^\ominus/R)[(T_1 - T_2)/T_1T_2] \tag{12}$$

$$\Delta H^\ominus = RT_1T_2/(T_1 - T_2)\{-\ln(\alpha_0 - \alpha)/(\alpha_0 - \alpha_\infty) + \ln[1 + K_1(\alpha - \alpha_\infty)/(\alpha_0 - \alpha_\infty)]\} \tag{13}$$

$$\Delta S^\ominus = R\ln K_1 + (\Delta H^\ominus/T_1) \tag{14}$$

It is easily seen that, compared with the n.m.r. technique, the above method is more convenient and accurate. The calculation of errors presented later shows that the method improves the accuracy of the values of $\Delta H^\ominus$ and $\Delta S^\ominus$ obtained by factors of four and two respectively. The improved precision depends on two factors: (*i*) the two equilibrated species A and B show very high and different specific rotations; (*ii*) the accuracy of the temperature measurements is much greater in polarimetry than in n.m.r. spectroscopy. The method could of course be used for any other property that can be accurately measured. It is interesting to note that, although the equilibrium constant (K_e) could not be accurately determined, its temperature dependence ($\Delta H^\ominus$ and $\Delta S^\ominus$) is surprisingly accurately estimated.

Determination of the Activation Parameters $\Delta H^\ddagger$ *and* $\Delta S^\ddagger$ *for the Epimerization.*—Conventionally, activation parameters are calculated from two or more rate constants determined at different temperatures in separate kinetic experiments. However, recently Varytemp methods have been developed, in which the activation parameters are determined in one kinetic experiment. The temperature is varied during the reaction either continuously or stepwise as above in the determination of the equilibrium temperature dependence. These methods are particularly useful in the study of reactions in which the conditions cannot be accurately reproduced: such situations are frequently met in acid, base, and enzyme catalysis. In the present applications the reproducibility of the reaction condition was only good in the case of the epimerization of (1P) to (1M) [equation (2)] and therefore the activation parameters obtained with the conventional procedure agree with those of the Varytemp method. Lack of reproducibility of conditions in the study of the reaction of 3Λ to 3Δ [equation (3)] is reflected in the large difference between the set of activation parameters measured with the two methods (Table 4).

The observed rate constant, $k_{obs.}$, in a constant-temperature experiment on reaction (1) is equal to the sum of the microscopic rate constants ($k_1 + k_{-1}$). Thus we have expressions (15) and (16). The activation enthalpy

$$\ln k_{obs.} = \ln(k_1 + k_{-1}) = \ln k_{-1} + \ln[1 + (k_1/k_{-1})] = \ln k_{-1} + \ln(K_e + 1) \tag{15}$$

$$\ln k_{-1} = \ln k_{obs.} - \ln(1 + K_e) \tag{16}$$

$\Delta H_{-1}^\ddagger$ may be calculated from a plot of $\ln\{[k_{obs.}/(1 + K_e)](\boldsymbol{h}/\boldsymbol{k}T)\}$ against $1/T$. The ordinate at $1/T = 0$ yields $\Delta S_{-1}^\ddagger$, the activation entropy. Furthermore, $\Delta H_1^\ddagger$ and $\Delta S_1^\ddagger$ may be estimated from $k_{obs.}$ and the quantities derived above.

EXPERIMENTAL AND RESULTS

(*a*) *Thermodynamic Parameters.*—The temperature-jump method was applied to the determination of the thermodynamic parameters of the epimerization (1) in pyridine and (3) in dmso. The values obtained can be compared with those from the conventional method in which the regression straight-line plot of $\ln K_e$ against $1/T$ leads to $\Delta H^\ominus$ and $\Delta S^\ominus$. The K_e values were obtained by ^{1}H n.m.r. spectroscopy (100 MHz) by integration of the low-field signals of the H–P doublets of the diastereoisomers (1P) [δ(H–P) 8.31 p.p.m., ^1J(H–P) 801.1 Hz] and (1M) [δ(H–P) 8.25 p.p.m., ^1J(H–P) 777.2 Hz]. For the couple (3Λ) and (3Δ), the *H*–C–Ph doublets appearing at δ 5.33 [^3J(HCOP) 7.8 Hz] and 5.19 p.p.m. [^3J(HCOP) 7.2 Hz] were integrated.* The n.m.r. probe temperature was measured before each integration using the O–H chemical shift of ethylene glycol with an accuracy of ±2 °C. The accuracy in the estimated K_e is at best between 2 and 5%. The $\Delta H^\ominus$ and $\Delta S^\ominus$ values are given in Tables 1 and 3.

The polarimetric temperature-jump method. The values of α_0 and α [Figure (*a*)] were obtained by extrapolation of plots at $\alpha(T_1)$ against t to t_0 and t_2. The extrapolations were computed using the L.S.G. program.[13] The computation also yielded the α_∞ value. These data, expressed as specific rotations, are given in Tables 1 and 3. The approximate value of the equilibrium constant K_e at T_1, needed for

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* The helicity of each diastereoisomer is known in the case of five-co-ordinate compounds.[7] For the six-co-ordinated compounds the helicity has not been determined.

[13] D. F. Detar, 'Computer Programs for Chemistry,' W. A. Benjamin, New York, 1968, vol. 1, p. 117.

the calculation, was obtained by n.m.r. spectroscopy as described above.

(b) *Kinetic Parameters*.—The kinetic parameters were obtained in two different ways. (*i*) The optically pure diastereoisomer was dissolved in a suitable solvent and the optical rotation was studied as a function of time at a fixed temperature. The kinetic parameters were determined from these data using the linear plot of $\ln(\alpha_t - \alpha_\infty)$ against *t*, or the L.S.G. program.[13] (*ii*) By use of the variations of the optical rotations with time in the temperature-jump experiment (Figure) and the L.S.G. program.[13] This gives the apparent rate constant at each of the temperatures (T_1 and T_2). The microscopic rate constants k_1 and k_{-1} together with the corresponding activation parameters are given in Tables 2 and 4.

TABLE 1

Thermodynamic parameters for (1P) $\rightleftharpoons$ (1M) in pyridine determined by the conventional method and the polarimetric temperature-jump method

Method	T_1/K	T_2/K	$\alpha_{0,m}$ [a]	α_m [a]	$\alpha_{\infty,m}$ [a]	K_e	$\Delta H^\ominus$/J mol^{-1}	$\Delta S^\ominus$/J K^{-1} mol^{-1}
Polarimetric temperature jump	280.3	303.0	601.2	85.32	76.30	1.345	−1 246 ± 200	−2.1 ± 1.5
	303.0	280.3	602.5	73.13	82.57	1.259	−1 280 ± 200	−2.5 ± 1.5
Conventional							−2 120 ± 1 340 [b]	−5.0 ± 5 [b]

[a] Specific rotation obtained at 436 nm with 0.0332 mol dm^{-3} solutions. [b] Average value of those calculated at T_1 and T_2.

TABLE 2

Activation parameters and rate constants for (1P) $\rightleftharpoons$ (1M) in pyridine determined by the conventional and polarimetric temperature-jump methods

Method	T/K	K_e	$k_{obs.}$	$10^{-5}k_1$	10^5k_{-1}	$\Delta G_1^\ddagger$	$\Delta G_{-1}^\ddagger$	$\Delta H_1^\ddagger$	$\Delta H_{-1}^\ddagger$	$\Delta S_1^\ddagger$	$\Delta S_{-1}^\ddagger$
			s^{-1}			kJ mol^{-1}				J K^{-1} mol^{-1}	
Polarimetric temperature jump	280.4	1.345	3.91	2.24	1.67	93.38	94.09	89.83 *	91.08 *	−12.5 *	−10.4 *
	302.9	1.259	75.5	42.07	33.42	93.67	94.30				
Conventional	280.5	1.345	3.79	2.17	1.61	93.51	94.22	90.71 *	92.88 *	−9.6 *	−4.6 *
	293.1	1.293	21.7	12.2	9.45	93.59	94.22				
	298.7	1.272	44.4	24.8	19.5	93.67	94.26				
	304.6	1.251	94.2	52.3	41.8	93.67	94.26				
	308.7	1.237	150.0	82.9	67.0	93.80	94.34				

* Average values of those at the given temperatures.

TABLE 3

Thermodynamic parameters for (3Λ) $\rightleftharpoons$ (3Δ) in dmso determined by the conventional and polarimetric-jump methods

Method	T_1/K	T_2/K	$\alpha_{0,m}$ [a]	α_m [a]	$\alpha_{\infty,m}$ [a]	K_e	$\Delta H^\ominus$/J mol^{-1}	$\Delta S^\ominus$/J K^{-1} mol^{-1}
Polarimetric temperature jump	293.0	310.7	284.3	94.02	98.45	0.804	1 830 ± 420	4.6 ± 2.3
Conventional							2 128 ± 1 460 [b]	5.4 ± 5.4 [b]

[a] Specific rotation obtained at 546 nm with 0.0261 mol dm^{-3} solutions. [b] Average value of those calculated at T_1 and T_2.

TABLE 4

Activation parameters and rate constants for (3Λ) $\rightleftharpoons$ (3Δ) in dmso determined by the conventional and the polarimetric temperature-jump methods

Method	T/K	K_e	$10^{-5}k_{obs.}$	$10^{-5}k_1$	$10^{-5}k_{-1}$	$\Delta G_1^\ddagger$	$\Delta G_{-1}^\ddagger$	$\Delta H_1^\ddagger$	$\Delta H_{-1}^\ddagger$	$\Delta S_1^\ddagger$	$\Delta S_{-1}^\ddagger$
			s^{-1}			kJ mol^{-1}				J K^{-1} mol^{-1}	
Polarimetric temperature jump	293.0	0.804	66.5	29.6	36.8	91.42	90.87	95.51 *	93.72 *	14.2	9.6 *
	310.7	0.839	645	294	351	91.12	90.71				
Conventional	291.0	0.799	56.7	25.2	31.5	91.17	90.62	90.04 *	87.95 *	−4.2 *	−9.2 *
	293.0	0.804	71.7	31.9	39.7	91.25	90.71				
	298.0	0.816	127.2	57.1	70.0	91.37	90.87				
	303.0	0.827	250	113	136.5	91.25	90.79				
	308.0	0.839	452	206	246	91.25	90.79				

* Average values of those at the given temperatures.

The synthesis of compounds (1) and (3) are described in refs. 7 and 9 respectively. The n.m.r. spectra were obtained with a Varian HA 100 spectrometer with $SiMe_4$ as internal standard. The relevant parameters have been given above. The integration of n.m.r. signals was made with a Dupont 310 curve resolver. Equilibrium data were treated by the least-squares method using a Hewlett-Packard 20 calculator. The L.S.G. program was processed on an IRIS 80 computer.

(*c*) *Calculation of Errors*.—The errors in conventional determinations of $\Delta H^\ominus$ were computed from expression (17) for relative error. Errors in determinations of $\Delta H^\ominus$ by the

$$\Delta(\Delta H^\ominus)/\Delta H^\ominus = (\Delta T_1/T_1) + (\Delta T_2/T_2) + (\Delta T_1 + \Delta T_2)/(T_1 - T_2) + \{[(\Delta K_1/K_1) + (\Delta K_2/K_2)](1/\ln K_1/K_2)\} \quad (17)$$

temperature-jump method were computed from expression (18) for the relative error; where $x = \alpha_0 - \alpha_\infty$ and $y = \alpha - \alpha_\infty$. The relative error in $\Delta S^\ominus$ using the two methods

$$\Delta(\Delta H^\ominus)/\Delta H^\ominus = (\Delta T_1/T_1) + (\Delta T_2/T_2) + (\Delta T_1 + \Delta T_2)/(T_1 - T_2) + \{\Delta x[(x + yK)^{-1} - (x - y)^{-1}] + \Delta y[K(x + yK)^{-1} + (x - y)^{-1}] + y\Delta K(x + yK)^{-1}\}[1/\ln(x + yK)(x - y)^{-1}] \quad (18)$$

is given by (19).

$$\Delta(\Delta S^\ominus)/\Delta S^\ominus = [R(\Delta K_1/K_1) + \{[\Delta(\Delta H^\ominus)/\Delta H^\ominus] + (\Delta T_1/T_1)\}T_1^{-1}\Delta H^\ominus]/[R \ln K + (\Delta H^\ominus/T_1)] \quad (19)$$

The results given in Tables 1 and 3 were computed from the following estimated errors:

Conventional method	ΔK_1	ΔK_2	ΔT_1	ΔT_2
(1P) $\rightleftharpoons$ (1M)	0.026	0.024	2	2
(3Δ) $\rightleftharpoons$ (3Λ)	0.04	0.047	2	2

Temperature jump method	ΔT_1	ΔT_2	$\Delta\alpha$	$\Delta K/K$
(1P) $\rightleftharpoons$ (1M)	0.05	0.2	0.005	0.1
(3Δ) $\rightleftharpoons$ (3Λ)	0.05	0.2	0.005	0.1

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