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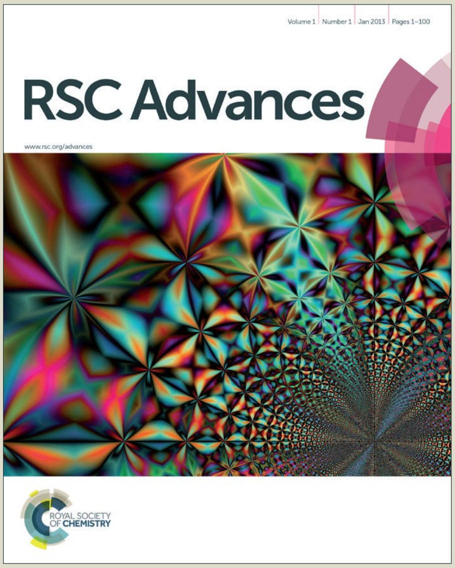

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Variable temperatures ^{1}H NMR technique on the kinetics and thermodynamic parameters of equilibrium between the Z and E isomers in a stable phosphorus ylide involving an imidazole

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Abstract

Analysis of ^{1}H NMR spectra in a special ylide involving an imidazole at variable temperatures has been employed to study the kinetics of the interchangeable process in the equilibrium between the two Z- and E-isomers of a stable phosphorus ylide. Activation data (k_{-1}, k_1, k_{total}, E_{a1}, E_{a-1}, $E_{a\,(total)}$, $\Delta H^{\ddagger}$, $\Delta G^{\ddagger}$, $\Delta S^{\ddagger}$) and thermodynamic parameters (K_e, ΔH°, ΔG° and ΔS°) for the forward and reverse steps of the opposing reaction were obtained by means of variable temperatures ^{1}H NMR technique and T-jump method. The ^{1}H NMR results indicate that the interchangeable process of rotational isomers follows first-order kinetics with respect to both the forward and reverse reactions. The process was also entropy controlled.

Keywords

^{1}H NMR; Ylide; Kinetics; Imidazole; Geometrical Isomer

1. Introduction

Organophosphorus compounds have broad biological, industrial and pharmacological applications [1-9]. They are used in organic synthesis as useful reagents and also as ligands in a number of transition metal catalysts [10]. The phosphorus ylides represent an outstanding achievement of the chemistry of the twentieth century [11, 15]. Phosphorus ylides are a class of special type of zwitterions, which bear strongly nucleophilic electron rich carbanions. The electron distribution around the $P^+–C^-$ bond and its consequent chemical implications have been probed and assessed through theoretical, spectroscopic and crystallographic investigations. These are accessible compounds which can be obtained from cheap chemical reagents using simple methods. This accessibility of phosphorus ylides is the reason for the intensive studies of their chemical properties that have led to the wide extension of the ylides both in preparative chemistry and in industrial fine organic synthesis [16-20].

These compounds usually exist as a mixture of two geometrical isomers (Z and E), although some of these exhibit only one isomer. In our previous works, a fully joint experimental and theoretical investigation of the kinetics and a mechanistic study regarding phosphorus ylides was made possible using UV spectrophotometry method [21-24]. However, determining the kinetic parameters for the interchangeable process between the Z- and E-isomers is not practical using UV techniques, due to this process being considerably fast. In addition, methods like stopped-flow technique are not suitable for use in investigating the kinetics of the two Z and E-rotational isomers due to the spectrum of both isomers being identical in the range of 190 and 400 nm, hence, ^{1}H NMR technique was employed. Because protons are very sensitive to environmental electronic effects and their ^{1}H NMR spectra can provide unambiguous structural assignments. The chemical shifts of the two Z- and E rotational isomers in the relevant ylide are different in the ^{1}H NMR spectra. Thus, the variable temperature ^{1}H-NMR technique has been used for the kinetics investigation of this process. The purpose of this work is to utilize the ^{1}H NMR technique to obtain a complete set of thermodynamic and activation parameters in a rotational interchangeable process between the Z- and E-isomers of ylide **3**. In our previous work, we have reported several kinetic investigations of phosphorus ylides using the ^{1}H NMR technique [25-27].

2. Experimental

Synthesis of the reaction between dimethyl acetylendicarboxylate **1** and imidazole **2** in the presence of triphenylphosphine for the generation of phosphorus ylide **3** involving the two Z- and E-geometrical isomers (Figure 1) has been reported earlier [28].

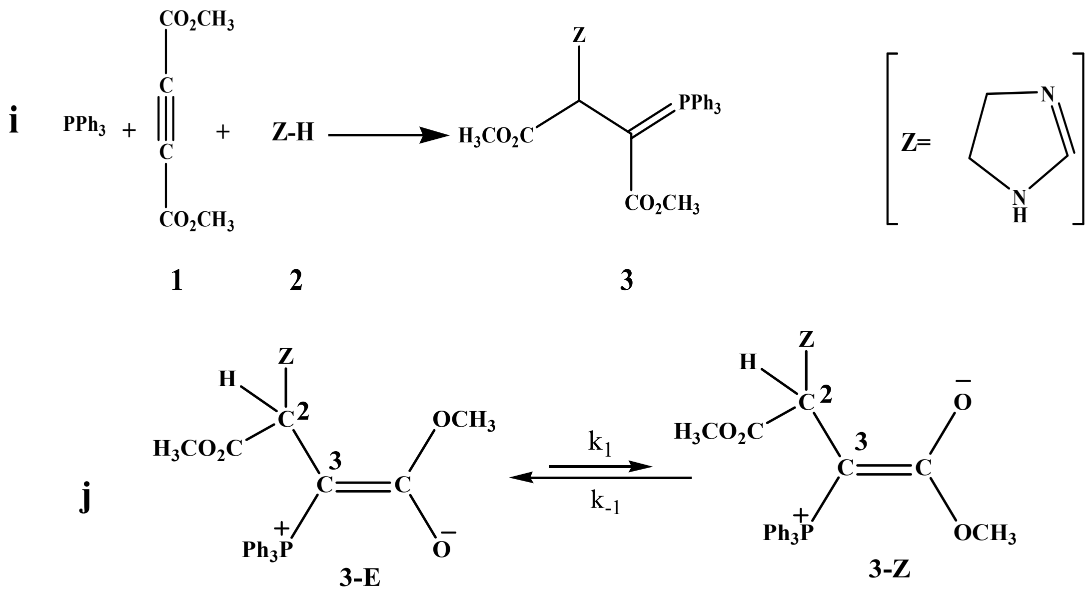

Figure 1. i) Synthesis of the reaction between dimethyl acetylendicarboxylate **1** and imidazole **2** in the presence of triphenylphosphine for the generation of phosphorous ylide [28] **3. j**) Interchangeable process between the two rotational isomers such a **3**-E and **3**-Z

In order to measure kinetic and thermodynamic parameters for the interchangeable process between the two **3**-Z and **3**-E rotational isomers, consisting of one elementary reaction and its reverse (Figure 1(j)), a study of the kinetics of the reaction was undertaken using the variable-temperature ^{1}H-NMR technique (T-jump method). For each kinetics experiment, first an aliquot from a freshly made solution of compound **3** (in $CDCl_3$) was pipetted into a capillary ^{1}H NMR tube. The temperature was kept at -30 °C (243 K) for a few minutes, allowing the ^{1}H NMR spectrum of **3** to give the corresponding equilibrium concentrations of each rotational isomer at the first equilibrium state at -30 °C (243 K) from the integrated peaks. The temperature was then suddenly jumped to -20 °C (253 K) and the ^{1}H NMR spectrum was then recorded every 12 s until the completion of the reaction (second equilibrium state).

A change in temperature from low (-30 °C) to high (-20 °C) reduces the time interval needed for reaching the second equilibrium state. In each step several scans were recorded. Thus, before the completion of the reaction, the concentration of each isomer, as the reaction proceeded in $CDCl_3$, could be obtained from its corresponding integral at each stage. All concentrations are relevant to the non-equilibrium state of the equilibrium reaction (before the second equilibrium state). When the measurement of a corresponding integral is held constant, the opposing reaction will be in a second equilibrium state.

2.1. Materials and methods

Dimethyl acetylendicarboxylate, triphenylphosphine, and imidazole were purchased from Fluka (Buchs, Switzerland) and used without further purification. Extra-pure solvents $CDCl_3$ and ethyl acetate were obtained from Merck (Darmstadt, Germany). ^{1}H NMR spectra were recorded at 500.1 MHz on a Bruker DRX-500 Avance instrument with $CDCl_3$ as a solvent.

3. Results and Discussion

Changes in the concentration of each isomer (for example, the E-isomer) can be calculated from the difference between its initial integrated peak of the E-isomer in the first equilibrium state [-30 °C, i.e., corresponding to the initial concentration of E-isomer (a)] and its integrated peak in the non-equilibrium state at each stage. These are reported in Table **1** as a typical example, for all investigated time during the temperature jump from 20 °C (293 K) to 30 °C (303 K).

Table 1. Values of concentration of E isomer at various times investigated at 30 ˚C (303 k) during the temperature jump from 20 ˚C (293 K) to 30 ˚C (303 K)

t / s	300	312	324	336
x_E mol / lit	0.002	0.032	0.047	0.060
ln (m-x_E)	-2.8	- 3.5	-4.2	- 6.9

In Table 1, X_E corresponds to the difference between the integrated peak of the E-isomer at the first equilibrium state and its corresponding points in the non-equilibrium state (30 °C) at all investigated times for the **J** step of the reaction shown in Figure 1. This behavior is kinetically simple and provides a classic example of an opposing first-order reaction, with the mechanism consisting a first-order elementary forward reaction (k_1) and its first-order reverse (k_{-1}). So the rate law and its integral form can be written: in equations 1-7, a and b refer to the initial concentrations of the two Z- and E- isomers at the first equilibrium state (Equation 1).

$$\text{First equilibrium}: \underset{\mathbf{a}}{\mathbf{E}} \rightleftharpoons \underset{\mathbf{b}}{\mathbf{Z}} \qquad \mathbf{(1)}$$

$$\text{second equilibrium}: \underset{\mathbf{a-x}}{\mathbf{E}} \rightleftharpoons \underset{\mathbf{b+x}}{\mathbf{Z}} \qquad \mathbf{(2)}$$

$$\frac{dx}{dt} = k_1\,(a - x) - k_{-1}\,(b + x) \qquad (3)$$

$$\ln(m - x) = -(k_1 + k_{-1})t + \ln m \qquad (4)$$

$$\text{Or } \ln\frac{m}{m-x} = (k_1 + k_{-1})t \qquad (\mathbf{5})$$

$$m = \frac{k_1 a - k_{-1} b}{k_1 + k_{-1}} \qquad (6)$$

$$\text{Slope} = -(k_1 + k_{-1}), \qquad k_{total} = k_1 + k_{-1} \qquad (\mathbf{7})$$

We can plot the left-hand side of equation 4 against time (t) to obtain the value of the total rate constants k_{total} = k_1 + k_{-1} from the slope. This plot is shown in Figure 2 using the experimental data at 30 ˚C (303 K).

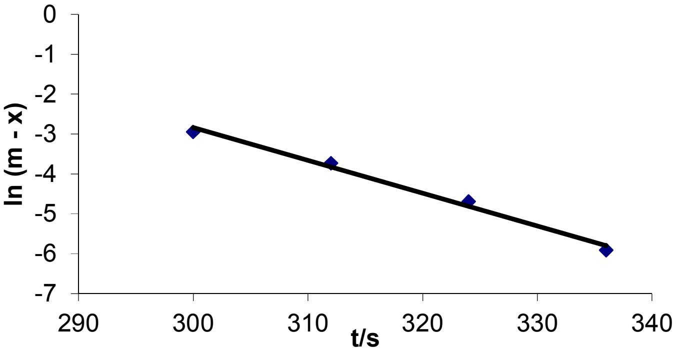

Figure 2. The plot of ln (m-x) versus time (t) for the forward and reverse reactions (opposing reaction) at 30 ˚C (303 K) in the interchangeable process between the two **3**-E and **3**-Z rotational isomers.

The experimental data provided a linear plot that explicitly confirms first-order kinetics. Thus, the interchangeable process of the rotational isomer follows first-order kinetics with respect to the forward and reveres reactions in the present opposing reaction. On the other hand, the equilibrium constant of an elementary reaction is equal to the ratio of the rate constants of the forward and reverse reactions. This relation (equation 8) has been employed for an elementary reaction which is shown in Figure 1(j).

$$K_e = \frac{k_1}{k_{-1}} \qquad (\mathbf{8})$$

The equilibrium constant at each temperature (here, 30 ˚C) is obtainable and is in proportional to the ratio of the NMR integrated peak of the **3**-Z isomer to that of the **3**-E isomer in ylide **3** when the reaction has reached its second equilibrium state after temperature increase. Using equations 7 and 8, gave satisfactory values for the forward rate constant (k_1) and reverse rate constant (k_{-1}) at the temperature of 30˚C. To confirm the above observations, further experiments were performed under conditions similar to these used in the previous experiments at several temperatures. The value of the rate constant for the forward and the reverse reactions and also the equilibrium constant in the present opposing reaction are reported in Table 2.

Table 2. The values of k_{-1}, k_1, k_{total} (k_{1+} k_{-1}) and K_e for the opposing reaction at different temperatures.

T / K	k_1/min^{-1}	k_{-1}/min^{-1}	k_{total}/min^{-1}	K_e
253	0.002	0.04	0.046	0.049
273	0.005	0.09	0.095	0.052
303	0.006	0.10	0.11	0.056
323	0.008	0.14	0.15	0.062

The results show that the interchangeable process proceeds faster at higher temperatures and a kinetics investigation of such an equilibrium can be followed by the variable-temperature ^{1}H NMR technique (temperature jump method). As can be seen (Table 2), at ambient temperature, both the forward and reverse reactions are merely fast, hence investigating for obtainable kinetic parameters is only possible by making a disturbance in the equilibrium state.

Arrhenius equation is best in describing the reaction kinetic constant (k) of this work:

$$k=A \exp(-E_a/RT) \qquad (9)$$

Where: A is frequency factor, E_a is activation energy of reaction, R is general gas constant (8.314 J K^{-1} mol^{-1}) and T is reaction temperature in Kelvin.

In the temperature range studied, the dependence of the first-order rate constant of the forward (k_1), reverse (k_{-1}) and the rate constant of the overall reaction on the reciprocal temperature is consistent with the Arrhenius equation, which gives the activation energies of the forward (E_{a1}), reverse (E_{a-1}) and also overall opposing reactions ($E_{a\ total}$), respectively. These are reported in Figures 3, 4 and 5, respectively. The activation energies are compiled in Table 3.

$$\ln k = \ln A - \frac{E_a}{RT} \qquad (10)$$

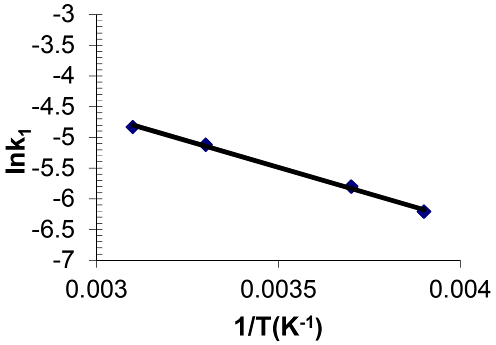

Figure 3. Dependence of the first-order rate constant of the forward reaction (ln k_1) on reciprocal temperature for the opposing reaction

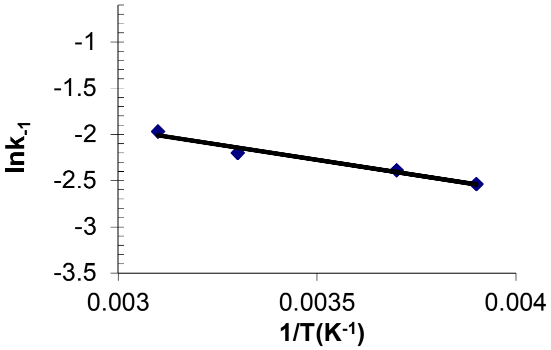

Figure 4. Dependence of the first-order rate constant of the reverse reaction (ln k_{-1}) on reciprocal temperature for the opposing reaction **(Figure 1, j)**

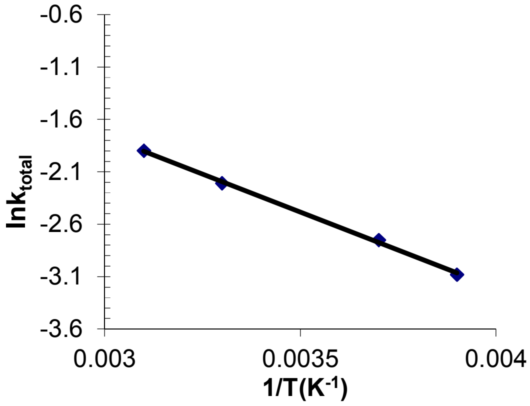

Figure 5. Dependence of the first-order rate constant of the overall reaction (ln k_{total}) on the reciprocal temperature for the opposing reaction

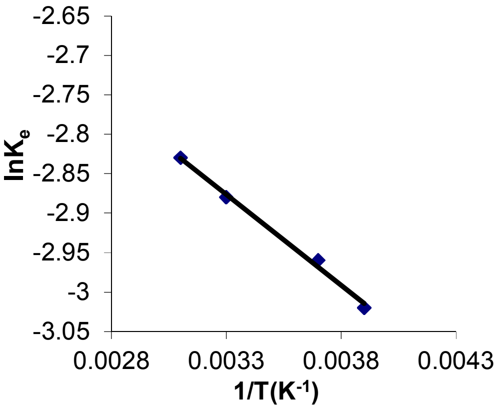

Figure 6. Dependence of equilibrium constant (ln K_e) on the reciprocal temperature for the opposing reaction **(Figure 1, j)**

Table 3. Activation energies involving forward, reverse and overall reactions for the interchangeable process in the opposing reaction between the two Z- and E- rotational isomers.

	E_{a1} / kJ.mol^{-1}	E_{a-1} / kJ.mol^{-1}	$E_{a\ total}$ / kJ.mol^{-1}
Opposing reaction	12.22	10.02	10.4

Where the slope of the line is equivalent to the negative activation energy (E_a) divided by the gas constant, R, and the extrapolation of the line back to the y-intercept yields the value for ln A. The two activation energies of the forward and the reverse of any elementary opposing reaction and the enthalpy change (ΔH°), are linked to each other as per equation 11. ΔH° and the equilibrium constant (K_e) can be written as equation 12;

$$\Delta H^{\circ} = E_{\mathrm{forward}} - E_{\mathrm{reverse}} \tag{11}$$

$$\Delta H^{\circ} = 12.22 - 10.02 = 2.2$$

$$\ln K_e = \frac{-\Delta H^{\circ}}{R}\left(\frac{1}{T}\right) + C \tag{12}$$

From equation 12, the enthalpy change (ΔH°=1.8 kJ.mol^{-1}), can be obtained from the slope of the plot (ln K_e on reciprocal temperature), as shown in Figure 6. As can be seen, the values of ΔH°, obtained using the two methods, are in good agreement.

With respect to the K_e and ΔH°, changes in the entropy and Gibbs free-energy can be calculated for the overall opposing reaction. The results are reported in Table 4.

$$\Delta G^{\circ} = -RT\ln K_e^{\circ} \tag{13}$$

$$\Delta S^{\circ} = \frac{\Delta H^{\circ} - \Delta G^{\circ}}{T} \tag{14}$$

Table 4. Thermodynamic parameters for the interchangeable process between the two rotational isomers in opposing reaction (Figure 1, j).

	ΔH°/ kJ.mol-1	ΔG°/ kJ.mol-1	ΔS°/ kJ.mol-1K-1
Opposing reaction	1.75	7.5	-.019

Now the activation parameters such as $\Delta H^{\ddagger}$, $\Delta G^{\ddagger}$ and $\Delta S^{\ddagger}$ can be calculated using the Eyring equation 15 at the relevant temperature for the interchangeable process between the two isomers. The results for the forward and reverse reactions at 303 K are shown in Table 5. The values obtained on the basis of the Eyring equation indicate that the negative activation entropy is related to a greater degree of ordering in the transition state than the initial state. These results (Table 5) suggest that the transition state in a forward reaction (k_1) is ordered more effectively stabilized than the transition state in a reverse reaction (k_{-1}). Furthermore, both the activation enthalpy and Gibbs free energy are at their lowest for the reverse reaction (k_{-1}) in relation to the forward reaction (k_1), which means that the reaction occurs more conveniently for the reverse reaction (Z→E). As a result, the equilibrium tend to proceed into the left-side direction (more generation of E-isomer).

$$k = \frac{k_B \times T}{h} \times (RT)^{-\Delta n} \times e^{-\frac{\Delta H^\ddagger}{RT}} \times e^{\frac{\Delta S^\ddagger}{R}} \qquad (15)$$

Table 5. Activation parameters for the interchangeable process between the two rotational isomers at 30 ˚C (303 K), (Figure 1.j)

Forward reaction	$\Delta H^\ddagger$ ($kJ.mol^{-1}$)	$\Delta G^\ddagger$ ($kJ.mol^{-1}$)	$\Delta S^\ddagger$ ($J.mol^{-1}.K^{-1}$)	$T\Delta S^\ddagger$ ($kJ.mol^{-1}$)
T=303 K	9.70	19.30	-320	-9.69
Reverse reaction	$\Delta H^\ddagger$ ($kJ.mol^{-1}$)	$\Delta G^\ddagger$ ($kJ.mol^{-1}$)	$\Delta S^\ddagger$ ($J.mol^{-1}.K^{-1}$)	$T\Delta S^\ddagger$ ($kJ.mol^{-1}$)
T=303 K	7.50	16.30	-290	-8.79

Comparing the magnitudes of $\Delta H^\ddagger$ and $T\Delta S^\ddagger$ for reverse reaction clearly shows that the $T\Delta S^\ddagger$ value is considerably larger than the corresponding enthalpy value. Hence, one could arrive at the conclusion that the interchangeable process between the two rotational isomers is entropy controlled [29-30]. Experimentally, the overwhelming contributions to the value of $\Delta G^\ddagger$ result from the large decrease in the entropy of the reaction. The activation energy E_a and the activation enthalpy $\Delta H^{\neq}$ are related with each other as follows:

$$E_a = \Delta H^\ddagger + RT \qquad (16)$$

The value of the activation energy which is obtained using equation 16 agrees with the value from the Arrhenius equation.

3. Conclusion

Using the ^{1}H-NMR technique, we have made a kinetic investigation of the interchangeable process in the equilibrium between the two Z- and E-isomers of a stable phosphorous ylide containing an imidazole as an opposing reaction at variable temperatures. The results show that the interchangeable process of the rotational isomers follows first-order kinetics with respect to the forward and reverse reactions. Activation parameters such as (k_{-1}, k_1, k_{total}, Ea_1, Ea_{-1}, Ea_{total}, $\Delta H^{\ddagger}$, $\Delta G^{\ddagger}$ and $\Delta S^{\ddagger}$) and thermodynamic parameters (K_e, ΔH°, ΔG°, and ΔS°) were obtained for the forward (k_1), reverse (k_{-1}) and overall reactions. The overall reaction is not remarkably endothermic, because the enthalpy is not very high (ΔH° = 1.8 kJ mol^{-1}). In addition, the Gibbs free energy for the overall opposing reaction is very small and positive (ΔG° = 7.5 kJ mol^{-1}), close to zero. This explains why the interchangeable process between the Z and E isomers is an equilibrium state. Comparing the magnitudes of $\Delta H^{\ddagger}$ and $T\Delta S^{\ddagger}$ shows that the reverse process is entropy controlled. We recommend the use of ^{1}H NMR technique as a standard technique to study interchangeable processes in such isomers in the future.

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