



# Dynamic $^1\text{H}$ NMR study around the heteroaryl–carbon and carbon–carbon single bonds and also around carbon–carbon double bond in a particular phosphorous ylide involving a 2-methyl indole

Sayyed Mostafa Habibi-Khorassani\*, Malek Taher Maghsoodlou, Ali Ebrahimi, Fatemeh Vasheghani Farahani, Elahe Mosaddeg, Mohammad Amin Kazemian

Department of Chemistry, Faculty of Sciences, University of Sistan and Baluchestan, PO Box 98135-674, Zahedan, Iran Department of Chemistry, Iran

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## ABSTRACT

For the first time, a series of separate dynamic  $^1\text{H}$  NMR effects are reported at different temperatures within a particular phosphorous ylide involving a 2-methyl indole namely dimethyl 2(*N*-2-methyl indole-1-yl)-3-(triphenyl phosphoran ylidene) butandioate. These effects are attributed to restricted rotation around the heteroaryl–carbon and carbon–carbon single bonds and also around carbon–carbon double bond. Rotational energy barrier ( $\Delta G^\ddagger$ ) for their interconversion process of rotational isomers equals  $(55.33, 49.91 \text{ and } 70.16) \pm 2 \text{ kJ mol}^{-1}$ , respectively.

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## 1. Introduction

Development of simple routes for widely used organic phosphorous compounds from readily available reagents is one of the major tasks in organic chemistry.<sup>1</sup> Phosphorous ylides are important systems in organic chemistry because of their application in the synthesis of organic products,<sup>2–30</sup> especially in the synthesis of naturally occurring products with biological and pharmacological activities.<sup>31–40,22,23,41–43</sup> Some of these compounds exhibited dynamic  $^1\text{H}$  NMR effect that affords good information regarding the interchangeable process of rotational isomers that provide important kinetic data. Herein, we wish to describe this effect in reaction between dimethyl acetylenedicarboxylate **1** and 2-methyl indole **2** in the presence of triphenylphosphine for generating a particular phosphorous ylide **3**, synthesis of which has been reported previously.<sup>19</sup>

## 2. Results and discussion

The  $^1\text{H}$ ,  $^{13}\text{C}$  and  $^{31}\text{P}$  NMR spectra of ylide **3** are consistent with the presence of two isomers<sup>19</sup> (see Fig. 1). The ylide moiety of these compounds is strongly conjugated with the adjacent carbonyl group and rotation around the heteroaryl–carbon and

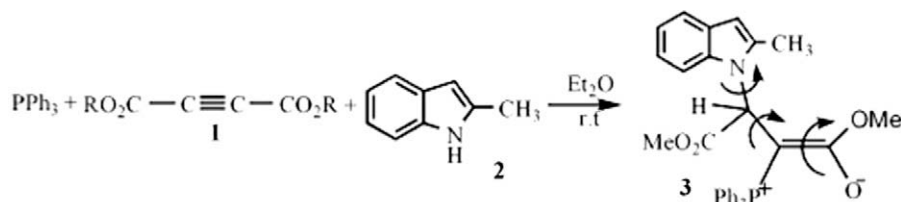
carbon–carbon single bonds and also around the partial carbon–carbon double bond in the 3-*Z* and 3-*E* rotational isomers is slow on the NMR time scale at ambient temperature (see Fig. 2). Herein, the  $^1\text{H}$  NMR spectra of three exhibit two doublets for methine proton ( $\text{H}-\text{C}=\text{C}=\text{P}$ ,  $^3J_{\text{PH}}$ ) at  $\delta = 5.15$  and 5.10 ppm, for the major and minor geometrical isomers, respectively. Effects of dynamic  $^1\text{H}$  NMR around each bond will be followed according to the following discussion:

### 2.1. Dynamic effect for the 3-*Z* isomer (Fig. 3, entry I), as a result of restricted rotational process (a, III and e, V) around the heteroaryl–carbon and carbon–carbon single bonds at 283 K and 228 K, respectively

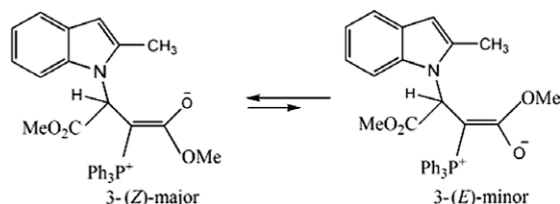
The  $^1\text{H}$  NMR spectrum for the 3-*Z* (Fig. 3, a, I and III) showed a resonance arising from methine proton ( $\text{H}-\text{C}=\text{C}=\text{P}$ ,  $^3J_{\text{PH}}$ ) that is appreciably broadened in comparison with a corresponding doublet that was measured at room temperature. This resonance coalescence occurred at approximately 10 °C (283 K) which is relevant to restricted rotational process around heteroaryl–carbon single bond. Moreover, when the temperature was considerably reduced under zero, another coalescence occurred at –45 °C (228 K) which is related to the rotational process (Fig. 3, c, I and V) around the carbon–carbon single bond. Investigation of  $^1\text{H}$  NMR spectra of 3-*Z* at variable temperature allowed us to calculate the rotational energy barrier ( $\Delta G^\ddagger$ ) for both the restricted rotational processes around the

\* Corresponding author. Tel./fax: +98 5412450995.

E-mail address: [smhabibius@yahoo.com](mailto:smhabibius@yahoo.com) (S.M. Habibi-Khorassani).



**Figure 1.** Synthesis of particular dimethyl (*N*-2-methyl indole-1-yl)-3-(triphenyl phosphoran ylidene) butandioate **3** from reaction between **1** and **2** in the presence of triphenylphosphine involving three possible dynamic  $^1\text{H}$  NMR effects around heteroaryl–carbon and carbon–carbon single bonds and also around carbon–carbon double bond.



**Figure 2.** Two rotational interchangeable processes of two isomers (*Z* and *E*) for ylide **3** involving a 2-methyl indole.

**Table 1**

Selected  $^1\text{H}$  chemical shifts (at 500.1 MHz, in ppm,  $\text{Me}_4\text{Si}$ ) and activation parameters of phosphorus ylide **3** involving a 2-methyl indole, in  $\text{CDCl}_3$ , for rotation around the heteroaryl–carbon single bond in the (*Z*)-isomer, (major, III)

$T_c$ (K)	$\delta$ (ppm)	$\nu\Delta$ (Hz)	$\Delta G^{\#42-44}$ (kJ/mol)	$k_c^{42-44}$ ( $\text{s}^{-1}$ )	$\Delta H^{\#43}$ (kJ/mol)	$\Delta S^{\#43}$ (kJ/mol)
283	5.32, 5.00	157.53	$55.33 \pm 1$	349.82	17.80	-0.13

heteroaryl–carbon (see Table 1) and also around carbon–carbon single bonds (see Table 2). Using the expression  $k_c = \pi\Delta\nu/\sqrt{2}$ , first-order rate constants were calculated for both bond rotational processes. Application of the absolute rate theory with a transmission coefficient ( $k$ ) of one gave free Gibbs rotational energy barrier with respect to the experimental data values of  $\Delta H^{\#}$  and  $\Delta S^{\#45,46}$  which were calculated for each process. These are reported in Tables 1 and 2. Effect of temperature on the rate constant was investigated on the basis of measurement of different chemical shifts in a series of other separate experiments. The results were too small so that the changes in first-order rate constant and Gibbs free energy barrier are negligible in comparison with the results obtained at  $-10^\circ\text{C}$ .<sup>42</sup>

## 2.2. Dynamic effect for the 3-*E* isomer (Fig. 3, entry II) as a result of restricted rotational processes (b, IV and d, VI) around the heteroaryl–carbon and carbon–carbon single bonds at 268 K

The  $^1\text{H}$  NMR spectrum for the 3-*E* (Fig. 3, b, II and IV) showed a resonance arising from methine proton ( $\text{H}-\text{C}=\text{C}=\text{P}$ ,  $^3J_{\text{PH}}$ ) that is

**Table 2**

Selected  $^1\text{H}$  chemical shifts (at 500.1 MHz, in ppm,  $\text{Me}_4\text{Si}$ ) and activation parameters of phosphorus ylide **3** involving a 2-methyl indole, in  $\text{CDCl}_3$ , for rotation around the carbon–carbon single bond in the (*Z*)-isomer, (major, V)

$T_c$ (K)	$\delta$ (ppm)	$\Delta\nu$ (Hz)	$\Delta G^{\#}$ (kJ/mol)	$k_c$ ( $\text{s}^{-1}$ )
228	5.76, 5.75	7.58	$49.91 \pm 1$	16.83

appreciably broadened in comparison with a corresponding doublet that was measured at room temperature. This resonance coalescence occurred at approximately  $-5^\circ\text{C}$  (268 K) which is relevant to restricted rotational process around heteroaryl–carbon single bond. For this process, activation parameters involving  $k$ ,  $\Delta H^{\#}$ ,  $\Delta S^{\#}$  and  $\Delta G^{\#}$  were calculated according to the procedure that was same as that reported for the 3-*Z* isomer. The results are summarized in Table 3.

Moreover, by decreasing temperature to  $-100^\circ\text{C}$ , coalescence occurred which is related to the rotational process (Fig. 3, d, II and VI) around the carbon–carbon single bond. The available experimental data for this rotation are not suitable for obtaining thermodynamic parameters.

## 2.3. Dynamic effect for the 3-*Z* and 3-*E* rotational isomers as a result of restricted rotational processes (Fig. 3, e, I and II) around the partial carbon–carbon double bond at 332 K

The  $^1\text{H}$  NMR spectrum for the 3-*Z* and the 3-*E* (Fig. 3, e, I and II) showed a resonance arising from methine proton ( $\text{H}-\text{C}=\text{C}=\text{P}$ ,  $^3J_{\text{PH}}$ ) that is appreciably broadened in comparison with a corresponding two doublet that was measured at ambient temperature. This resonance coalescence occurred at approximately  $59^\circ\text{C}$  (332 K) which is relevant to restricted rotational process around carbon–carbon double bond. For this process, activation parameters involving  $k$ ,  $\Delta H^{\#}$ ,  $\Delta S^{\#}$  and  $\Delta G^{\#}$  are given in Table 4.

**Table 3**

Selected  $^1\text{H}$  chemical shifts (at 500.1 MHz, in ppm,  $\text{Me}_4\text{Si}$ ) and activation parameters of phosphorus ylide **3** involving a 2-methyl indole, in  $\text{CDCl}_3$ , for rotation around the heteroaryl–carbon single bond in (*E*)-isomer, (minor, IV)

$T_c$ (K)	$\delta$ (ppm)	$\nu\Delta$ (Hz)	$\Delta G^{\#}$ (kJ/mol)	$k_c$ ( $\text{s}^{-1}$ )	$\Delta H^{\#}$ (kJ/mol)	$\Delta S^{\#}$ (kJ/mol)
268	5.28, 4.92	180.04	$51.97 \pm 1$	399.79	101.75	0.18

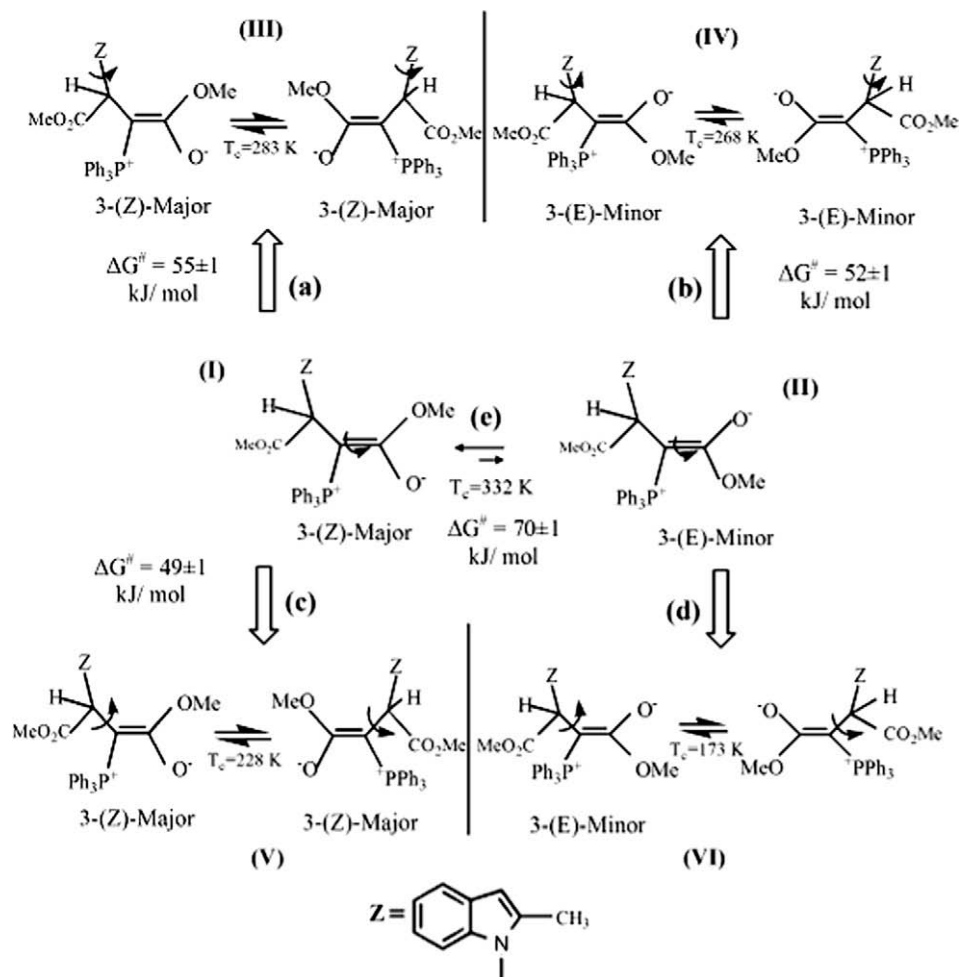
**Table 4**

Selected  $^1\text{H}$  chemical shifts (at 500.1 MHz, in ppm,  $\text{Me}_4\text{Si}$ ) and activation parameters of phosphorus ylide **3** involving a 2-methyl indole, in  $\text{CDCl}_3$ , for rotation around the carbon–carbon double bond, (I, II)

$T_c$ (K)	$\delta$ (ppm)	$\Delta\nu$ (Hz)	$\Delta G^{\#}$ (kJ/mol)	$k_c$ ( $\text{s}^{-1}$ )	$\Delta H^{\#}$ (kJ/mol)	$\Delta S^{\#}$ (kJ/mol)	$\Delta G^{\#38}$ (kJ/mol)
332	5.10, 5.15	27.50	$70.16 \pm 1$	61.07	63.66	0.02	0.56

$$\Delta G^{\#} = -RT_c \ln k, \quad k_c = \frac{\pi\Delta\nu}{\sqrt{2}}, \quad \Delta G^{\#} = 4.57T_c [9.97 + \log \frac{T_c}{\Delta\nu}], \quad \Delta H^{\#} = -R \times 2.303 \times \frac{\Delta \left[ \log \frac{k_c}{T_c} \right]}{\Delta \left[ \frac{1}{T_c} \right]}$$

$$\Delta S^{\#} = \frac{\Delta H^{\#} - \Delta G^{\#}}{T_c}$$



**Figure 3.** Interchangeable process of rotational isomers for ylide **3**. (a) Restricted rotational process (III, 283 K) around the heteroaryl–carbon single bond [entry (I)]. (b) Restricted rotational process (IV, 268 K) around the heteroaryl–carbon single bond [entry (II)]. (c) Restricted rotational process (VI, at temperature lower than 173 K) around the carbon–carbon single bond [entry (II)]. (e) Restricted rotational process (I, II, 332 K) around the carbon–carbon double bond.

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