JOURNAL OF PHYSICAL ORGANIC CHEMISTRY, VOL. 2, 225–231 (1989)

# THEORETICAL STUDY OF PYRAZOLE ELIMINATION OF *N*-ALKYL PYRAZOLES

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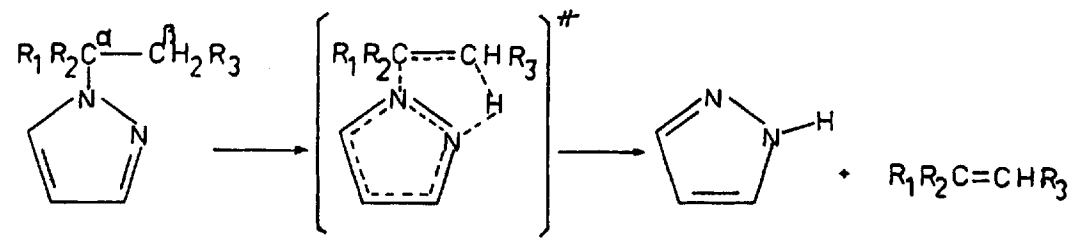
## ABSTRACT

The gas-phase pyrazole elimination of *N*-alkyl pyrazoles has been studied using MNDO semi-empirical molecular orbital (MO) theory with complete geometry optimization of all stationary points. We found that the activation energies ($E_a$) of the concerted processes are around 80 kcal/mol, 25 kcal/mol higher than experimental values. But the differences in $E_a$ between compounds with different substituents are in good agreement with the experimental ones.

## INTRODUCTION

We have recently reported that *N*-alkyl pyrazoles undergo thermal elimination reactions in gas-phase affording pyrazole and the corresponding olefin[1] (Scheme 1). Besides, we have reported the activation parameters for *N*-ethyl, *N-sec*-butyl, *N-tert*-butyl and *N*-ethyl-3,5-dimethyl pyrazole which support a unimolecular process through a five-membered cyclic transition state. In addition the experimental results show a low sensitivity of the activation energy to α and β carbon substitutions by alkyl groups.[2]



I: $R_1 = R_2 = R_3 = H$ II b: $R_1 = R_3 = H$; $R_2$ $C_2H_5$

II a: $R_1 = H$; $R_2 = R_3 = CH_3$ III: $R_1 = R_2 = CH_3$; $R_3 = H$

Scheme 1. Reaction mechanism for the elimination reaction of *N*-alkyl pyrazoles

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0894–3230/89/030225–07$05.00 *Received May 1988*

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Since these reactions belong to a new class of gas-phase thermal elimination through a transition state which is midway from alkyl halides and carboxylic esters (four- and six-membered transition states respectively) it was interesting to explore a theoretical approach for the reaction coordinate of these reactions. Here we report the results of a MNDO calculation for the reaction coordinate of *N*-ethyl [**I**], *N-sec*-butyl [**II**] and *N-tert*-butyl pyrazole [**III**].

## PROCEDURE

All calculations were carried out with a TANDY 1200–3000 personal computer by using the MNDO semi-empirical molecular orbital procedure described by Dewar *et al.*[3]

Standard initial values were used for the geometry parameters of the molecules.[4]

RHF calculations were carried out with complete geometry optimization with no geometrical constraints using the standard gradients methods.

## RESULTS AND DISCUSSION

In all cases the $\Delta H^{\neq}$ calculated values are around 25 kcal/mol higher than the experimental ones. We think that this is due to the overestimation of non-bonded repulsions in crowded systems inherent in the MNDO methods.[5] Nevertheless it has been recently reported[6,7] that the MNDO has a tendency to overestimate repulsive interactions between atoms when the distance between them is 1·5–2 times the length of a corresponding covalent bond.

Table 1. Calculated and experimental values for the $\Delta H^{\neq}$ and $E_a$ resp. (all values in kcal/mol)

a.

| Compound | | $\Delta H^{\neq}$ (calc.) | $\Delta H^{\neq}$ (app.) | $\Delta$ ($\Delta H^{\neq}$) |
|---|---|---|---|---|
| **I** | | 83·60 | 83·60 | 3·1 |
| **II** | **IIa** | 77·25 | 80·50 | |
| | **IIb** | 82·67 | | 1·6 |
| **III** | | 78·91 | 78·91 | |

b.

| Compound | $E_a$ (exp.) | $\Delta$ ($E_a$) |
|---|---|---|
| **I** | 56·0 | 1·8 |
| **II** | 54·2 | 1·2 |
| **III** | 53·0 | |

On the other hand, we have performed a calculation of Cl—H elimination from ethyl chloride giving a $\Delta H^{\neq} = 96{\cdot}1$ kcal/mol against an experimental value of around 60 kcal/mol.[8] The difference, around 36 kcal/mol, is consistent with the difference found between experimental and calculated values of $\Delta H^{\neq}$ for *N*-alkyl pyrazoles considering that the transition state in the first case is a four-membered ring rather than a five-membered ring in the pyrazole elimination from *N*-alkyl pyrazoles..

However, the differences in $\Delta H^{\neq}$ for **I**, **II** and **III** agree quite well with the activation energy previously reported for the same compounds (Table 1).

In the case of **II**, there are two alternative elimination pathways, either through a methylene hydrogen (**IIa**) or through a methyl hydrogen (**IIb**) (Table 1a); both possibilities have been calculated obtaining different $E_a$ values and these do not agree very well with the experimental results which are in a statistical ratio 2:3 for the 2-butene and 1-butene respectively. We have no experimental evidence on geometric isomers distribution for the 2-butene formation. The calculations of **IIa** were carried out only for the *trans* isomer and perhaps the difference in energy may be attributed to the contribution of the *cis* isomer. Thus we can not obtain, at present, further advances in comparing these theoretical results with the experimental ones.

The apparent $E_a$ of **II** has been calculated as the weighted average of the **IIa** and **IIb** results.

In addition we found that α-carbon atoms are highly positive charged, meanwhile the β-carbon atoms are negatively charged (see Table 2); hence the transition states must be highly polarized. These results agree with those proposed by Benson *et al.*[9] for four-center cyclic transition states in HX elimination from alkyl halides and for six-membered cyclic transition states.[10]

Table 2. Calculated charges for α and β carbon atoms

| Compound | α-carbon | β-carbon |
|---|---|---|
| **I** | 0·26 | −0·50 |
| **IIb** | 0·22 | −0·45 |
| **III** | 0·17 | −0·45 |

Maccoll *et al.*,[11] Barton *et al.*[12] and Benson *et al.*[9] have studied in detail the kinetics of HX eliminations from a large number of differently substituted bromides and chlorides showing that the $E_a$, and therefore the rate constant, are very sensitive to the substitution on the α-carbon atom.

A similar behavior can be clearly envisaged from our results comparing the $\Delta H^{\neq}$ values obtained for **I**, **IIb** and **III** (with secondary, tertiary and quaternary α-carbon atoms resp.) which are 83·60, 82·67 and 78·91 kcal/mol respectively.

On the other hand, the optimized geometries for **I**, **II** and **III**, their transition states and products are shown in stick figures form and in spheres form in Figure 1 and Figure 2 respectively. (For further geometry parameters information ask the authors.)

A plot of energy vs. reaction coordinate for **I**, **II** and **III** is shown in Figure 3. From this figure it can be seen that the transition state is highly asynchronic and is placed at a point where the N—H bond length is near the equilibrium value for pyrazole, in agreement with the

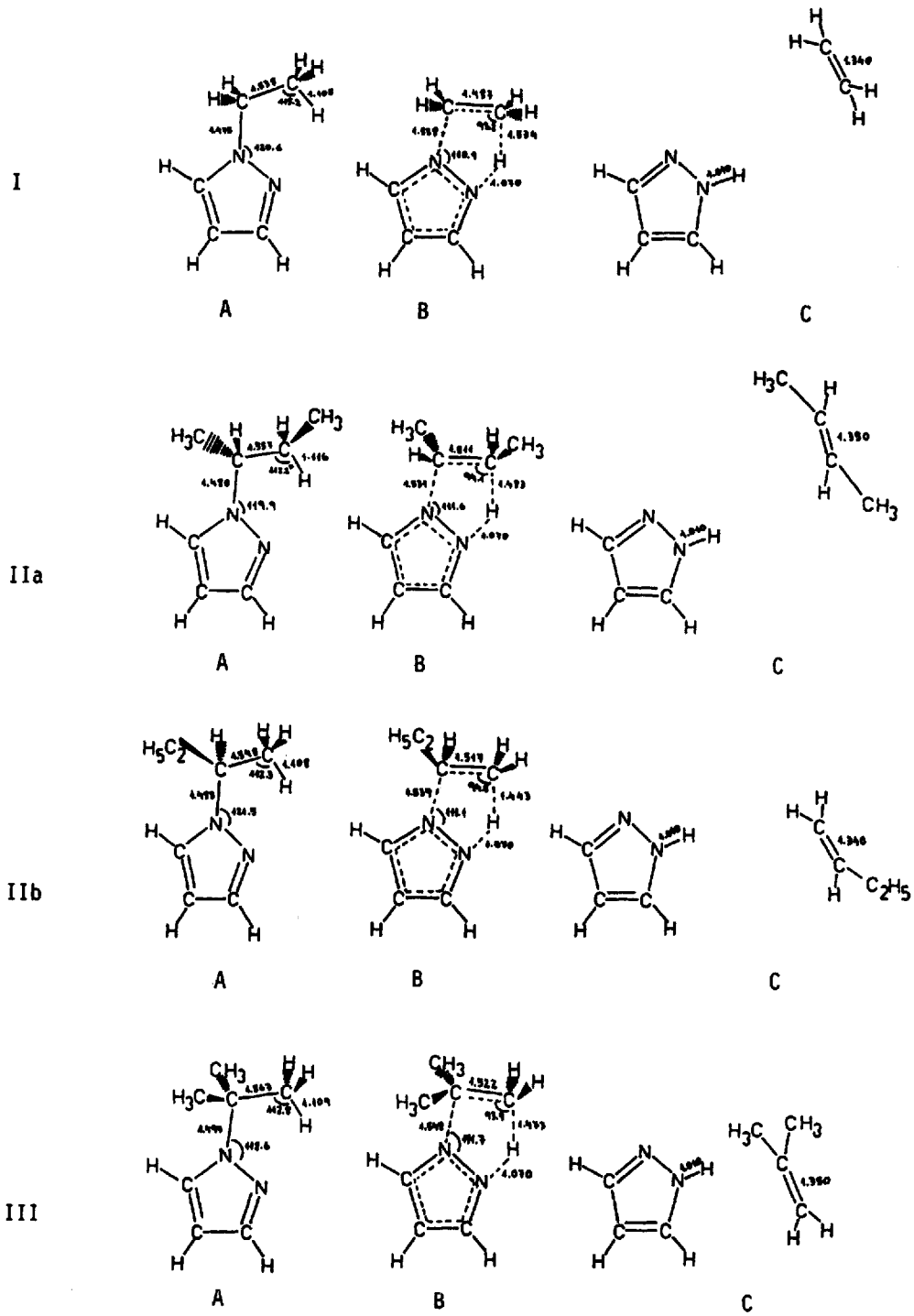


Figure 1. Optimized geometries for **I**, **II**, and **III**. A, Reactants; B, Transition states; C, Products. (in stick form)

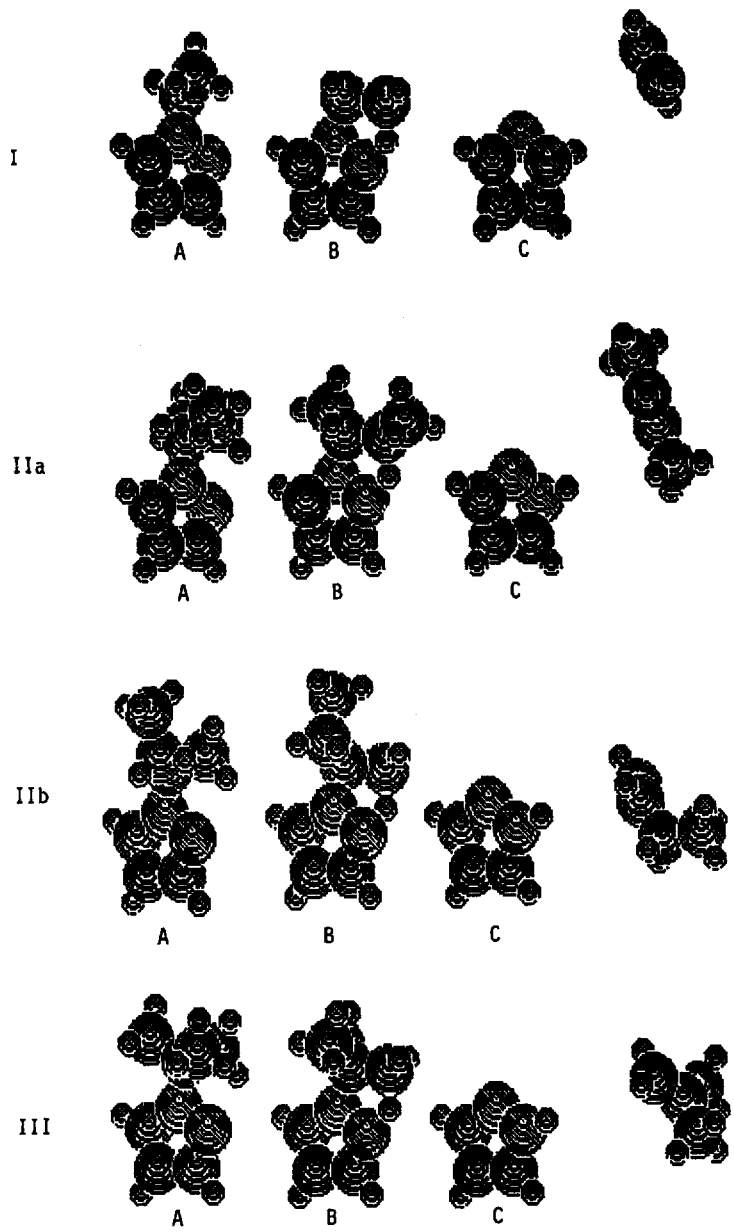


Figure 2. Optimized geometries for **I**, **II**, and **III**. A, Reactants; B, Transition states; C, Products. (in spheres form)

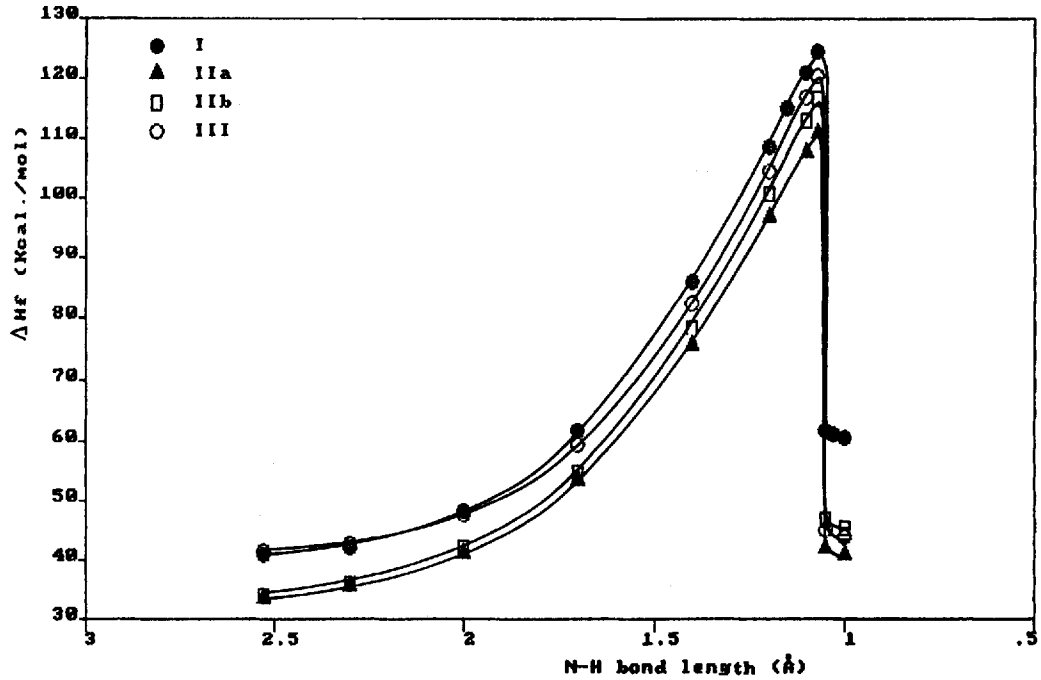


Figure 3. Calculated enthalpy profile

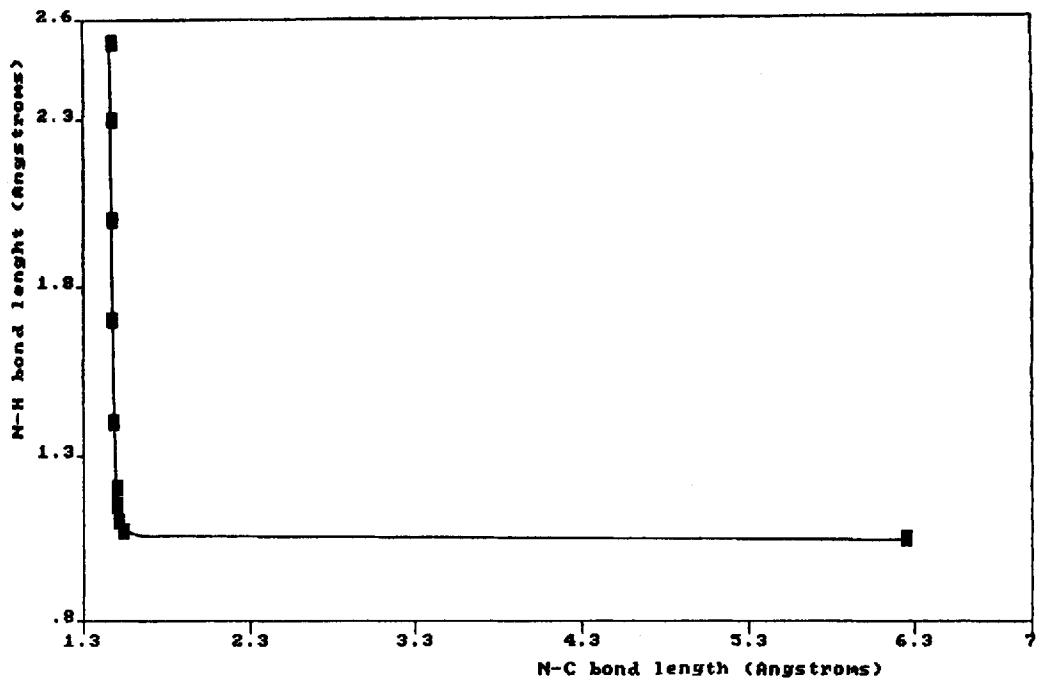


Figure 4. Contour diagram for *N*-ethyl pyrazole

results of Dewar *et al.*[6] where they found a tendency of MNDO to predict unsymmetrical geometries for the transition states of pericyclic reactions. This fact can be clearly envisaged in Figure 4 where the N—H bond length is plotted vs. the C—N one.

ACKNOWLEDGMENTS

This work is sponsored by the Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) (PID 3–016200/85), and partially supported by the Consejo de Investigaciones Científicas y Tecnológicas de Córdoba (CONICOR).

L. M. Phagouapé and G. E. Davico are recipients of a fellowship from the Consejo Nacional de Investigaciones Científicas y técnicas (Argentina).

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