# IMPORTANT ROLE OF THE σ-π CONCERTED ELECTRON REORGANIZATION

IN THE RING-OPENING REACTION OF HETEROCYCLIC COMPOUNDS

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Abstract: It is emphasized that the simultaneous σ- and π-electron reorganization plays an important role in the σ-bond cleavage. On the basis of this stereoelectronc factor, the reaction course of heterocyclic compounds can successfully be predicted.

Behavior of electrons in chemical reactions is very important for the microscopic understanding of reaction mechanism. We would like to emphasize here the importance of the σ-π concerted electron reorganization for the prediction of the site selectivity in the ring-opening reaction of heterocyclic compounds. Although the concept described here can be applied to many reactions other than the ring-opening reactions of heterocyclic compounds, the small ring compounds are good examples to illustrate the importance of this concept, since their molecular structures are rigid and the electron behavior during the reaction process can easily be visualized. The compound I, β-lactam, is an important intermediate in penicillin chemistry.[1] There are two possibilities in the ring-opening reaction of I; the C-N bond cleavage to give the compound II and the C-C bond cleavage to
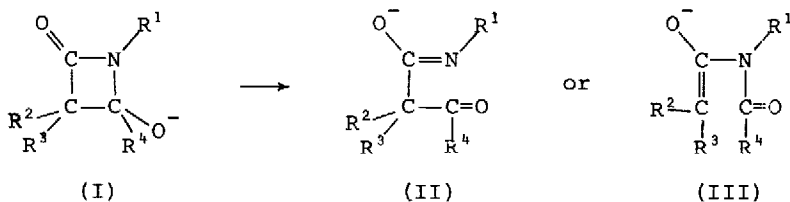
| (I) | (II) | (III) |

give the compound III.

This site selectivity may simply be understood on the basis of the bond strength; that is, the C-N bond is weaker than the C-C bond. However, the problem is not so simple. The MINDO/3[2] calculation gives that the compound III is more stable than II by 2 kcal/mol,[3] and this indicates that the formation of III is preferable or comparable to the formation of II, if the site selectivity is predicted on the basis of the energy difference between the reactant and the product. This is a wrong prediction. Only the formation of II has experimentally been observed,[1] and the theoretical MINDO/3 results[4] shown in Fig. 1 also predict the formation of II. Although the potential curves given in Fig. 1 can elucidate the observed site selectivity in the ring-opening reaction of I, it is shown here that the examination of the electron behavior during the reaction process can also fully explain this selectivity without energy calculation.

The C-C bond breaking process, I→III, may be expressed by a two-stage mechanism, I→V→VI. It is noted that the lower energy of III comes from the large stabilization of the negative charge produced at the carbon atom
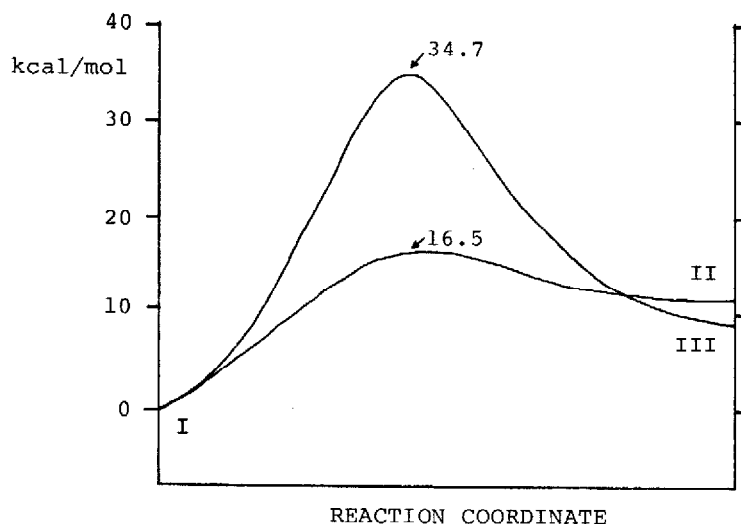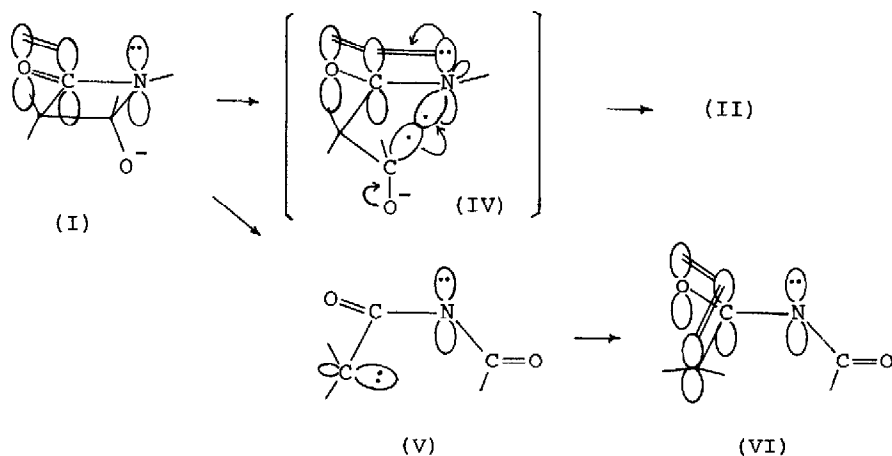

REACTION COORDINATE

Fig. 1 Potential energy variations calculated by MINDO/3. The reaction coordinate is the NCC and CCC angles for the I→II process,and the CNC and NCC angles for the I→III process. These values were changed discontinuously form I to II or from I to III. $R^1=R^2=R^3=R^4=H$.

(I) → [(IV)] → (II)

(V) → (VI)

by the carbonyl group, and this stabilization is achieved completely by the 90° of the bond rotation about the C-C bond. Because in reality the C-C bond breaking and the C-C bond rotation occur concertedly, the negative charge developing at the carbon atom is not largely stabilized at the transition state; the C-C bond rotation is not completed at the transition state and the overlap between the negative charge and the carbonyl π-system is small. The I→III process is thus unfavorable from the stereoelectronical point of view and will have high activation energy. On the other hand, during the C-N bond breaking, the localization of the σ-electrons at the N atom is accompanied by the delocalization of the π-lone pair electrons at the N atom into the carbonyl π-system (IV).[5] The maximum stabilization by this reorganization of the π-system is expected *at any point* of the I→II process including the transition state. This process is stereoelectronically favorable and will proceed easily.

The term "stereoelectronic control" has been used for the cases in which the σ-bond break is accelerated by the interaction of the σ-bond being broken with the adjacent p orbital.[6] The present concept is different from this, since, in the present case, the σ-bond cleavage is assisted by the reorganization of the electrons in the *different*(π) space.

There remains a question whether the semi-empirical MINDO/3 method can or cannot predict correctly the small energy difference between II and III.

The present argument is not affected by this uncertainty, since the site selectivity of I is determined by the stability of the system at its transition state and not by the stability of the products. Thus the present concept is clearly different from the simple resonance concept applied to the stability of the reaction products.

The concept described here is very useful for the prediction of the site selectivity and the microscopic understanding of the reactions of heterocyclic compounds. The application of the present concept to some other reactions as well as more detailed results for the ring-opening reaction of I will be reported elsewhere.

References and Notes

1) S. Wolfe, S.L. Lee, J.B. Ducep, G. Kannengiesser, and W.S. Lee, Can. J. Chem., 53, 497(1975) and references cited therein.

2) R.C. Bingham, M.J.S. Dewar, and D.H. Lo, J. Am. Chem. Soc., 97, 1285 (1975).

3) 3) In the energy calculations, all the geometrical parameters of I, II, and III ($R^1=R^2=R^3=R^4=H$) were optimized.

4) All the molecular parameters were optimized at each point of the reaction coordinate. The bond breaking of the present system is ionic one, and the potential curves were obtained by MINDO/3 without CI.

5) The importance of the π-lone pair electrons in the acyl migration mechanism has been pointed out by Curtin and Miller: D.Y. Curtin and L.L. Miller, J. Am. Chem. Soc., 89, 637(1967).

6) P. Deslongchams and R.J. Taillerfer, Can. J. Chem., 53, 3029(1975) and references cited therein; S. David, O. Einstein, W.J. Hehre, L. Salem, and R. Hoffmann, J. Am. Chem. Soc., 95, 3806(1973) and references cited therein; W.C. Agosta and S. Wolff, J. Am. Chem. Soc., 99, 3355(1977); D.G. Gorenstein, J.B. Findlay, B.A. Luxon, D. Kar, ibid., 99, 3473(1977).