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Original Investigations

A Comparison of Various MO Methods for Predicting Regioselectivity in Diels–Alder Reactions

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Various semiempirical MO methods for predicting regioselectivity in Diels–Alder reactions are compared in order to examine their reliability. They are the frontier molecular orbital method using CNDO/2, HMO and MNDO molecular orbitals and the HMO approach on pericyclic reactions presented by Tang.

Keywords: Regioselectivity – Diels–Alder reactions.

1. Introduction

The frontier molecular orbital (FMO) method has been valuable in predicting regioselectivity of organic reactions [1, 2]. Houk [3] presented some rules for estimating frontier orbital energies and coefficients of dienes and dienophiles with various kinds of substituents. However, these rules cannot be applied in all cases, so that a suitable molecular orbital method has to be chosen for evaluating the energies and coefficients. As pointed out by Houk, various molecular orbital methods do not provide identical results even qualitatively. As a specific example, the HOMO coefficients of Z-substituted olefins, obvious disagreement has been found [3, 4]. The methods used by Houk et al. [4] were CNDO/2, INDO and EH. Alston et al. [5] chose the INDO method. The simple HMO method was also adopted [6]. The MNDO method [7] was published after Houk's work. It gives good estimates of heats of formation, equilibrium geometries, ionization potentials and dipole moments. However, it has not been applied to the FMO method for predicting regioselectivity. It is worthwhile to discuss which methods are comparatively adequate to the prediction of regioselectivity.

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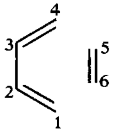
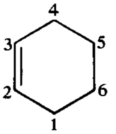
Tang [8] presented a method for studying pericyclic reactions. In Tang's method, the HMO matrix of the reaction system is a linear function of the reaction coordinate ξ. For example, the HMO matrix of the reactants of the butadiene-ethylene cycloaddition is



$$\begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix}, \qquad \xi = 0,$$

and that of the product is



$$\begin{bmatrix} 0 & 0 & 0 & 0 & 0 & \sigma \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \sigma & 0 \\ 0 & 0 & 0 & \sigma & 0 & 0 \\ \sigma & 0 & 0 & 0 & 0 & 0 \end{bmatrix}, \qquad \xi = 1,$$

in which $\sigma = 1.34$ is the resonance integral of a σ-bond formed in the reaction. Consequently, the HMO matrix as a function of ξ will be

$$\begin{bmatrix} 0 & 1-\xi & 0 & 0 & 0 & \sigma\xi \\ 1-\xi & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1-\xi & 0 & 0 \\ 0 & 0 & 1-\xi & 0 & \sigma\xi & 0 \\ 0 & 0 & 0 & \sigma\xi & 0 & 1-\xi \\ \sigma\xi & 0 & 0 & 0 & 1-\xi & 0 \end{bmatrix}$$

The method can be used to estimate the energy change along the reaction path and then the activation energy, so that it might be used to predict regioselectivity. In this work, calclations have also been carried out using Tang's method in comparison with the FMO.

Computations were done using programs written by the author.

2. Computational Details

The MO methods used in this work are HMO, CNDO/2 and MNDO. The EH method was not adopted for it overestimates change distribution for molecules with heteroatoms, as pointed out by Houk et al. [4]. The results of INDO differ little from CNDO/2 for closed-shell molecules, so it was not included in this work.

The chosen HMO parameters based on the proposal by Streitwieser [9] are listed in Table 1. Streitwieser has proposed no parameter for the C≡N bond, but $k_{CN} = 1$ for an aromatic CN bond. Assuming that the bond parameter is

Table 1. Chosen HMO parameters

	Colulomb integral $\alpha_A = \alpha + h_A\beta$		Resonance integral $\beta_{A-B} = k_{A-B}\beta$
C=C CC(aromatic) C—C C—C(σ)	$h_C = 0$		$k_{C=C} = 1.1$ $k_{CC} = 1$ $k_{C-C} = 0.9$ $k_{C-C(\sigma)} = 1.474$
C—Me	$h_C = -0.2$,	$h_{Me} = 2$	$k_{C-Me} = 0.7$
C≡N	$h_C = 0.05$,	$h_N = 0.5$	$k_{C\equiv N} = 1.4$
CHO	$h_C = 0.1$,	$h_{\dot{O}} = 1$	$k_{C=\dot{O}} = 1$
COOH, COOMe	$h_C = 0.2$, $h_{\ddot{O}} = 2$,	$h_{\dot{O}} = 1$, $h_{Me} = 2$	$k_{C=\dot{O}} = 1$ $k_{C-\ddot{O}} = 0.8$ $k_{O-Me} = 0.5$
C—Cl	$h_C = 0.1$,	$h_{Cl} = 2$	$k_{C-Cl} = 0.4$

proportional to the overlap integral, the C≡N bond parameter is chosen to be 1.4. The O—Me bond in methyl acrylate has little effect on the C=C π-bond, and its bond parameter is chosen to be 0.5 discretionally. In Tang's method, the resonance integral of the C—C σ-bond formed in the reaction was set to be 1.34 times that of the C=C π-bond. Since the resonance integral of C=C has

Table 2. Comparison between predicted and experimental regioselectivities

		CNDO–FMO		HMO–FMO		Tang's method				
Reaction	Experi-mental	Donor	Adduct	Donor	Adduct	Energy in transition state (in β)				Adduct
1+2	*o* [13]	diene	*o*	diene	*o*	*m*	12.891	*o*	12.909	*o*
1+6	*o* [13, 14]	diene	*o*	diene	*o*	*m*	21.291	*o*	21.307	*o*
1+8	*o* [13]	diene	*o*	diene	*o*	*m*	12.981	*o*	12.987	*o*
1+12	*o* [6]	diene	*m*	diene	*m*	*m*	27.215	*o*	27.188	*m*
1+10	*o* [13]	diene	*o*	diene	*o*	*m*	17.5583	*o*	17.5595	*o*
3+4	*o* [13]	diene	*m*	diene	*m*	*m*	21.256	*o*	21.251	*m*
3+10	*o* [13]	diene	*o*	olefin	*o*	*m*	21.535	*o*	21.537	*o*
5+10	*o* [13]	diene	*o*	diene olefin	*o*	*m*	25.670	*o*	25.672	*o*
7+4	*p* [13]	diene	*p*	diene	*p*	*p*	18.9624	*m*	18.9631	*m*?
7+6	*p* [14]	diene	*p*	diene	*p*	*p*	22.4076	*m*	22.4075	*p*?
7+10	*p* [13]	olefin	*m*	olefin	*p*	*p*	17.79866	*m*	17.79862	*p*?
9+2	*p* [13]	diene	*p*	diene	*p*	*p*	12.886	*m*	12.879	*p*
9+4	*p* [13]	diene	*p*	diene	*p*	*p*	17.274	*m*	17.268	*p*
9+10	*p*[13]	diene	*p*	diene	*p*	*p*	17.5459	*m*	17.5457	*p*?
9+6	*p* [13, 14]	diene	*p*	diene	*p*	*p*	21.285	*m*	21.280	*p*
11+6	*p* [14]	diene	*p*	diene	*p*	*p*	20.9086	*m*	20.9091	*m*?
13+6	*p* [14]	diene	*p*	diene	*p*	*p*	25.5281	*m*	25.5274	*p*?

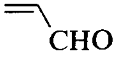
been adopted to be 1.1β instead of 1β used by Tang, the resonance integral of such a σ-bond is set to be $1.34 \times 1.1\beta = 1.474\beta$. According to Tang, all the parameters change as a linear function of the reaction coordinate ξ, which changes from 0 of the reactant to 1 of the product. It results in an energy-ξ curve, whose maximum is referred to as the energy of the transition state.

The standard geometrical parameters [11] were used to construct models in CNDO/2 and MNDO calculations. The COH angle in carboxyl group was set to be 107°, and the C—Cl bond length was set to be 1.72 Å. The *sp* basis set was used for Cl atom in CNDO/2 calculations.

3. Results and Discussion

Typical dienes and dienophiles were selected as examples to perform HMO and CNDO/2 calculations. A comparison between predicted regioselectivity and observation is given in Table 2, where the molecules are numbered as follows:


(1)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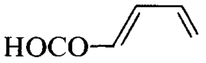
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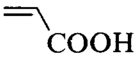
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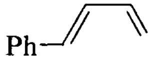
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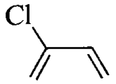
(6)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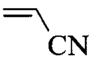
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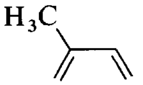
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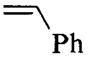
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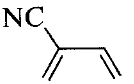
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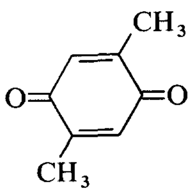
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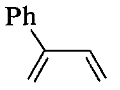
(13)

There are three cases in which the CNDO/2 predictions are at odds with experiment. The first, the adduct of the reaction (7)+(10) is predicted to be meta, whereas the HMO calculation predicts the right adduct.

The second case is the reaction (1)+(12), for which the HMO prediction is also wrong. Anomaly of this kind was discussed by Houk et al. [10]. Taking propylene and hydride ion without overlap between them as a model of the complex (1)+(12), they showed that the LUMO of propylene changes in polarization under the influence of the donor (H^-) – the greater coefficient of the substituted carbon becomes the less one. In this work, a unit negative point charge was taken in place of the hydride ion at a distance of 1.15 Å from the center of the double bond of propylene. The CNDO/2 results also indicate that the negative point charge polarizes the LUMO toward the unsubstituted terminus, although the CNDO/2 LUMO of propylene has a larger coefficient at the unsubstituted carbon atom when the point charge is absent (Table 3). Thus, the point charge model using CNDO/2 can also serve to explain the anomaly in the cases of methyl-substituted olefins, such as in the reaction (1)+(12), according to Houk's concepts.

The third case is the reaction (3)+(4) which was taken as a typical example in illustrating the regioselectivity of cycloaddition of a Z-substituted olefin to a $1-Z$-substituted diene [2]. However, the CNDO/2 as well as HMO data show that the HOMO coefficient of (3) is larger at the substituted terminus. The MNDO data show the same behavior. Thus, all three MO methods give the wrong predictions in this case (see Table 4).

According to Houk's concepts, the effect of the olefin acting as an acceptor was considered. A unit positive point charge was placed at a distance of 1.15 Å from the center between C_1 and C_4 of (3) and at an angle of 120° from the plane of the π-system. The results do show a polarization toward the unsubstituted terminus (Table 4). However, the effect is so small that we suspect other effects may be important. Thus, the interaction between the two carboxyl groups must be substantial and may be the main effect leading to the ortho-adduct.

Table 3. The effect of a negative point charge on the LUMO of propylene

	LUMO coefficient	
	substituted terminus	unsubstituted terminus
without a point charge	0.645	−0.668
with a point charge	0.508	−0.605

Table 4. The FMO terminal coefficients of (3) and (4)[a]

	HOMO of (3)	LUMO of (4)
HMO	(0.543, −0.537)	(0.229, −0.590)
MNDO	(0.565, −0.543)	(0.479, −0.667)
CNDO/2	(0.486, −0.460)	(0.424, −0.621)
CNDO/2 with a point charge	(0.352, −0.343)	

[a] The first value in parentheses is the coefficient of the substituted terminus.

Table 5. Inadequate MNDO results in comparison with CNDO/2 and HMO ones[a]

	MNDO	CNDO/2	HMO
HOMO of (11)	0.533, −0.561	0.593, −0.505	0.584, −0.553
HOMO of (2)	0.691, 0.646	0.487, 0.575	0.578, 0.594
HOMO of (4)	0.693, 0.643	0.341, 0.424	0.569, 0.586
HOMO of (6)	0.688, 0.643	0.297, 0.375	0.565, 0.581
HOMO of (8)	0.653, 0.652	0.381, 0.568	0.574, 0.645

[a] Values are the terminal coefficients, in which the first is that of the terminus near the substituent.

MNDO gives inadequate results listed in Table 5 in comparison with those given by CNDO/2 and HMO. The HOMO of 2-cyanobutadiene (11) has the opposite polarization. As a result, for reactions involving (11) such as (11)+(6) in Table 2, MNDO will predict the wrong adduct. The HOMOs of Z-substituted olefins, (2), (4), (6), and (8), also have the opposite polarization, and the addition of such olefins to dienes with low-lying LUMO will also be predicted incorrectly. As pointed out by Houk [3], MINDO/2 results of the HOMO coefficients for Z-substituted olefins are opposite to those of CNDO/2, INDO and *ab initio* SCF, and photoelectron spectra support the latter calculations. CNDO/2 parameters were chosen to fit the orbital energies and coefficients roughly with those of *ab initio* calculations, while MNDO parameters as well as MINDO ones were chosen to fit calculations with experimental heats of formation, equilibrium geometries, dipole moments, and ionization potentials without fitting the coefficient neither with *ab initio* calculations nor with ESR informations. As a rational result, MNDO is much better than CNDO/2 in heats of formation, geometries, etc., but worse in coefficients and in FMO prediction of regioselectivity.

Tang's method [8], as shown in Table 2, is not very good in predicting regioselectivity. Thus, we can realize that regioselectivity must be controlled by the early stage in the reaction path. The large–large interaction leads to a stronger σ-bonding in the transition state than the small–small one, while such a difference has been neglected in Tang's method.

4. Conclusions

HMO and CNDO/2 are better than MNDO in prediction of regioselectivity in Diels–Alder reactions. Tang's method is not so good as the FMO method in such prediction.

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