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PERTURBATIONAL ANALYSIS OF THE REGIOSELECTIVITY IN THE ACROLEIN DIMERIZATION

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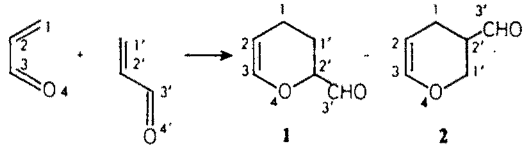
Abstract—Using intermolecular SCF-perturbation theory, the controlling factors determining the regioselectivity in the acrolein dimerization are derived by a rigorous decomposition of the interaction energy. This partitioning of the interaction energy is performed up to a level where a comparison with frontier orbital models is possible. The regioselectivity is found to be determined by orbital interactions occuring via the terminal atoms and atoms involved in secondary Woodward-Hoffmann interactions.

The dimerization of acrolein proceeds in a regiospecific way. Isomer **1** is formed exclusively, whereas regioisomer **2** has not been detected.[1] Several theoretical models have been used to rationalize this regioselectivity.



General reaction scheme of the acrolein dimerization.

Devaquet and Salem[2] applied the Intermolecular Orbital Theory, using SCF-π-orbitals for the interacting molecules and overlapping atomic orbitals. This approach predicts the experimentally observed regioisomer **1**. In the total interaction energies the electrostatic interactions are predominant and the energy contributions due to intermolecular MO-interactions are of minor importance. This finding does not agree with the generally accepted concept that (4 + 2)-cycloadditions are determined by orbital mixing.[3,4]

Einstein *et al.*[5] proposed a perturbational model restricted to the interacting frontier orbitals. According to this model terminal atoms possessing the largest LCAO coefficients in the frontier orbitals become bonded preferentially. The Hückel coefficients predict the observed regioisomer **1**. However, the relative magnitudes of the frontier orbital coefficients of the acrolein depend on the semiempirical method used as pointed out by Houk.[6]

Consequently, Alston and Shillady[7] investigated the influence of the applied wavefunctions for the acrolein on the predictive power of their frontier orbital model by using *ab initio* and semiempirical frontier orbital coefficients. In the model of Alston *et al.*[8] the regioselectivity is determined by the preferred bond formation between a definite pair of terminal atoms. This pair of atoms is selected by considering the product of the LCAO-coefficients in the frontier orbitals. If the bond formation between the terminal atoms is indiscriminative with respect to regioselectivity, secondary interactions decide which isomer is formed predominantly. Using this model the bond 1-1' should be formed faster than the 4-1' bond (see reaction Scheme) and the observed isomer **1** is predicted.[7] However, the secondary interactions modify this result. Comparing the LCAO-coefficients for the pairs 3-3' and 2-3', the 2-3' interaction predominates and points to the unobserved isomer **2**.[7]

Thus, some aspects, as the predominance of the electrostatic contributions[2] and the role of the secondary interactions[7] are still unsatisfactorily explained. Therefore the acrolein dimerization has been reinvestigated using the intermolecular SCF-perturbation theory parametrized in the CNDO/2 Scheme.[9]

Geometries and the perturbation method

Information on the course of dimerization is inferred by considering weakly interacting acrolein molecules, denoted R and S. As an example the *endo*-configurations leading to isomers **1** and **2**, with *cis*-acrolein as diene and *cis*-acrolein as dienophile are shown in Fig. 1. Bond angles and bond distances for acrolein are taken from Ref. 10. The molecular planes of the two acrolein molecules are assumed to be parallel with an intermolecular distance *r*. The terminal atoms where bond formation occurs are fixed in a plane being perpendicular to the molecular planes. The intermolecular distances between centres involved in bond formation are equal in all configurations considered. In the *exo*-configurations the dienophile S is rotated around the $C_{1'}$–$C_{2'}$ axis by 180°. The interaction energy ΔE and the perturbed one-electron density matrix of the weakly interacting reactants are analyzed by the technique developed.[9]

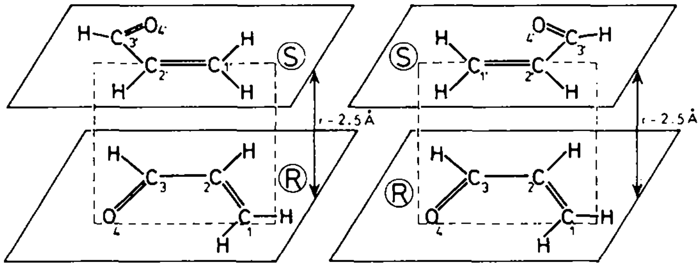
(a) ΔE is partitioned into electrostatic, steric, polarization and charge-tranfer terms.

(b) The interaction between the atomic centres is inferred from the diatomic contributions of ΔE.

(c) The diatomic parts of ΔE are resolved into contributions of pairs of interacting molecular orbitals.

The total interaction energies

The interaction energies $\Delta E = E^1 + E^2 + E^3$ between two acrolein molecules in the *endo*- and *exo*-approaches have been calculated at r = 2.5 A (Fig. 1). *Cis*- as well as *trans*-acrolein is used as dienophile S in the pre-reaction complexes of Fig. 1. The results are summarized in Table 1.



1 2

Fig. 1. Two cis-acrolein molecules in *endo*-configurations leading to the regioisomers 1 and 2.

Table 1. Interaction energies ΔE (kcal/mol) of two acrolein molecules at $r = 2.5$ Å.

S	isomer	endo	exo
cis	1	-16.30	-10.77
	2	-12.78	-11.06
trans	1	-15.24	-9.99
	2	-13.20	-11.19

The numerical values predict the *endo*-configurations to be more stabilized than the *exo*-configurations, in agreement with the general rule for (4+2) cycloadditions.[11] Moreover, the interaction energies for the *endo*-configurations indicate a predominance of the experimentally observed isomer **1**. The largest ΔE value (−16.3 kcal/mol) is calculated for the *endo*-configuration **1** containing *cis*-acrolein as diene and *cis*-acrolein as dienophile (Fig. 1).

Thus, the interaction energies support that isomer **1** is formed by the dimerization of two *cis*-acrolein molecules.

Due to the reaction conditions (150°),[1] the activation energy (2 kcal/mol)[12] for transforming *trans*- into *cis*-acrolein is easily available. The preferred dimerization of two *cis*-acrolein molecules is also supported by the result of Cárdenas[13] using cisoid and non-cisoid dienophiles in Diels–Alder reactions. The rate constants for the cycloadditions with cisoid dienophiles are found to be larger than those for non-cisoid dienophiles. Moreover, configuration **1** accords with the most favourable *endo*-approach for (4+2) cycloadditions as postulated by Salem.[14]

Since the largest ΔE value is calculated for the interaction of two *cis*-acrolein molecules the further analysis is restricted to the *endo*-configurations **1** and **2** shown in Fig. 1.

Decomposition of the total interaction energies

The observed regioselectivity may be determined by interactions characteristic for "charge" or "orbitally" controlled by numerical evaluation of the E^1_{el} and E^2 interaction energy ΔE into E^1_{el} (electrostatic), E^1_{st} (steric) and E^2 terms due to molecular orbital mixing,[9] the regioselectivity will be classified as "charge" or "orbitally" controlled by numerical evaluation of the E^1_{el} and E^2 interaction terms.

The decomposition of ΔE at $r = 2.5$ Å for the configurations **1** and **2** is performed in Table 2. The partitioning shows that differences ΔΔE, favouring isomer **1**, are mainly determined by ΔE^2. Therefore the interaction of molecular orbitals in configuration **1** is more favourable than in approach **2**.

Table 2. r-dependence of the total ΔE (kcal/mol) and the different interaction terms [9].

r [Å]	isomer	E^1_{el}	E^1_{st}	E^2	E^3	ΔE
2.5	1	-0.39	8.76	-20.41	-4.26	-16.30
	2	-0.29	8.93	-17.69	-3.74	-12.78
	$\Delta\|E^i\|$	0.10	0.17	2.72	0.53	3.52
3.0	1	-0.29	1.05	-3.61	-0.64	-3.49
	2	-0.21	1.08	-3.06	-0.56	-2.74
	$\Delta\|E^i\|$	0.08	0.03	0.55	0.09	0.75
3.5	1	-0.21	0.12	-0.55	-0.08	-0.72
	2	-0.15	0.12	-0.46	-0.07	-0.57
	$\Delta\|E^i\|$	0.06	0.00	0.08	0.01	0.15

Thus, the observed regioselectivity of the acrolein dimerization[1] is found to be "orbitally' controlled in the sense of Klopman.[15] This result is valid over the whole range of intermolecular distances *r* (Table 2).

In spite of the considerable net charges on the acrolein atoms (C_1: +0.0085; C_2: −0.0397; C_3: 0.2432; O_4: −0.2333), the electrostatic contributions E^1_{el} are almost negligible compared to the total ΔE values (Table 2). This conflicts with the results of Devaquet and Salem,[2] where 60–70% of the interaction energies are due to the electrostatic contribution. However, as for their method the electrostatic contributions point to the experimentally observed isomer **1**.

Role of the interacting centres

The purpose of the following analysis is to determine which pairs of interacting atoms are responsible for the observed regioselectivity. The procedure is based on the partitioning of E^2 into monoatomic and diatomic contributions $E_A{}^2$ and E^2_{AB} respectively.[9]

In Table 3 the interaction energy E^2 at $r = 2.5$ Å is decomposed into intra- and intermolecular energy contributions. $E^2_{intra\,R}$ and $E^2_{intra\,S}$ contain all E^2_{AB} where A and B denote atoms of R or S respectively. E^2_{inter} is the sum of all $E^2_{AB'}$ with A in the diene R and B′ in the dienophile S (Fig. 1). Table 3 shows that differences in the intermolecular contributions E^2_{inter} are responsible for favouring the *endo*-configuration **1**.

Table 3. Decomposition of the interaction energy E^2 (kcal/mol) into intra- and intermolecular contributions.

isomer	E^2	$E^2_{intra\,R}$	$E^2_{intra\,S}$	E^2_{inter}
1	-20.41	11.88	8.53	-40.82
2	-17.69	11.35	6.34	-35.37
$\Delta\lvert E^i\rvert$	2.72	0.53	2.19	5.44

The numerical values of the different diatomic $E^2_{AB'}$ indicate that the total E^2_{inter} is mainly determined by interactions between the terminal atoms, and atoms where secondary interactions occur, as proposed by Woodward and Hoffmann.[11] The numerical values of these important $E^2_{AB'}$ are summerized in Table 4. In configuration **1**, 87.4% of the total intermolecular terms are contained in the terminal interactions 1–1′, 4–2′ and in the secondary interaction 3–3′. In configuration **2**, 77.6% are contained in the pairs 1–2′, 4–1′ and 2–3′. Comparing the sums of the three diatomic contributions in configuration **1** and **2**, the predominance of regioisomer **1** is predicted (Table 4).

Table 4. $E^2_{AB'}$-values (kcal/mol) for the terminal atoms and the secondary interactions stabilizing the endo configurations 1 and 2

1			2		
A	B′	$E^2_{AB'}$	R	S	$E^2_{AB'}$
1	1′	-16.45	1	2′	-11.72
4	2′	-3.01	4	1′	-5.21
3	3′	-16.20	2	3′	-10.52
$\sum\limits_A \sum\limits_{B'} E^2_{AB'}$		-35.66	$\sum\limits_A \sum\limits_{B'} E^2_{AB'}$		-27.45

Thus, the observed regioselectivity is determined by the interactions 1–1′, 4–2′ and 3–3′ in configuration **1**. These interactions are more favourable than the corresponding contributions 1–2′, 4–1′ and 2–3′ of approach **2**.

If the electrostatic (E^1_{el}) and steric (E^1_{st}) contributions between the centres of configuration **1** are included into the discussion, the 3–3′ interaction in **1** is significantly diminished by the electrostatic terms (Table 5). The repulsive E^1_{el}-contributions are due to the positive net charges on the carbonyl C atoms 3 and 3′.

Table 5. $E^1_{AB'}$- and $E^2_{AB'}$-values (kcal/mol) of the terminal atoms and the secondary interaction in the endo approach 1

A	B′	E^1_{el}	E^1_{st}	E^2	$E^1 + E^2$
1	1′	0.01	1.63	-16.45	-14.81
4	2′	1.19	0.55	-3.01	-1.27
3	3′	7.62	1.76	-16.20	-6.83

The sum of the diatomic E^1 and E^2 values indicate an asymmetric bond formation on the beginning of the reaction coordinate (Table 5). The bond 1–1′ in configuration **1** should be formed faster than the bond 4–2′. This asymmetric bond formation is diminished by the 3–3′ interaction. The preferred bond formation between the centres 1–1′ is in agreement with an asymmetric reaction path for the acrolein dimerization as postulated by Devaquet and Salem.[2]

Role of the interacting molecular orbitals

In the following discussion the intermolecular $E^2_{AB'}$ characterizing the observed regioselectivity are analyzed with respect to the interacting molecular orbitals.

A critical examination of the $E^2_{AB'}$-values of Table 4 shows that they are almost completely approximated by the formula:[9]

$$E^2_{AB'} \approx 2 \sum_{\mu}^{A} \sum_{\nu}^{B'} P^1_{\mu\nu} \beta^1_{\mu\nu}. \qquad (1)$$

The intermolecular $P^1_{\mu\nu}$-elements of the perturbed bond order matrix are determined by the following expression:[9,16]

$$P^1_{\mu\nu} = 2 \sum_{i}^{R_{occ}} \sum_{j}^{S_{unocc}} a^1_{ij} C^0_{\mu i} C^0_{\nu j} + 2 \sum_{i}^{S_{occ}} \sum_{j}^{R_{unocc}} a^1_{ij} C^0_{\mu i} C^0_{\nu j}. \qquad (2)$$

The elements a^1_{ij} are the first order LCMO coefficients describing the mixing of the occupied and unoccupied orbitals i and j of R and S; the LCAO coefficients in the unperturbed orbitals i and j are denoted by $C^0_{\mu i}$ and $C^0_{\nu j}$.

Using eqn (1) the largest single contributions to the $E^2_{AB'}$ of Table 4 occur when μ and ν denote atomic orbitals being perpendicular to the molecular planes.

These 2_{p_z}–$2_{p_{z'}}$ contributions of the significant $E^2_{AB'}$ terms are summarized in Table 6. The percentage compared to the total $E^2_{AB'}$ is also recorded. Moreover, application of eqn (2) shows the $2_{p_z} - 2_{p_{z'}}$ parts of Table 6 to be completely determined by the mixing of the π-orbitals of the two *cis*-acrolein molecules.

In Table 7 the energy contributions of the interacting frontier orbitals to the 2_{p_z}–$2_{p_{z'}}$ part of the intermolecular $E^2_{AB'}$ of Table 4 are summarized. Comparing the values of column 4 and 6 in Table 7 for the terminal pairs 1-1′ and 1-2′, interaction 1-1′ predominates. However, the secondary interaction 3-3′ in configuration **1** is smaller than the 2-3′ contribution in approach **2**.

Thus, the same pattern as in the frontier orbital model of Alston *et al.*[7] is indicated by the values of Table 7 derived by the intermolecular SCF-perturbation theory.

The magnitude of the 1-1′ interaction points to the observed isomer **1**, but the secondary interactions favour the unobserved isomer **2**. This failure can be analyzed by comparing the role of the frontier orbitals in the terminal and secondary interactions of orientation **1** and **2**.

The calculated percentage values in column 5 and 7 of Table 7 show that the 2_{p_z}–$2_{p_{z'}}$ parts of the $E_{AB'}$ for the terminal pairs of 1-1′ in **1** and 1-2′ in **2** are characteristically determined by the frontier orbitals. For the secondary interactions 3-3′ in **1** and 2-3′ in **2** (Fig. 1) a different result is derived: only 44% of the 3–3′ interaction is determined by the frontier orbitals, but the same frontier orbitals contribute 75% to the 2-3′ value (Table 7). Thus, the incorrect prediction of the secondary interactions, considering the frontier orbitals only, is due to the different extent in determining the 3–3′ and 2–3′ contributions.

The performed analysis accords with the model of Alston *et al.*[7] that the regioselectivity is determined by localized interactions between the terminal atoms and atoms involved in secondary interactions. The restriction to the frontier orbitals is adequate for the terminal atom pairs. However, considering the frontier orbitals only seems not to be sufficient for the secondary interactions.

In all diatomic 2_{p_z}–$2_{p_{z'}}$ contributions of Table 7 the interaction of the diene-HOMO with the dienophile-LUMO is more pronounced than the mixing of the dienophile-HOMO with the diene-LUMO. The dienophile acts as the electron accepting component. The electron accepting properties of the dienophile are also indicated by the charge −0.0120 transferred from the diene R to the dienophile S. Use of eqn (23) in Ref. 9 shows that −0.0169 is due to the interaction of the diene-HOMO with the dienophile-LUMO. The back donated charge, transferred via the interaction of the dienophile-HOMO with the diene-LUMO, is 0.0036.

Thus, the analysis of the interactions between the centres determining the regioselectivity (Table 7) and the decomposition of the total transferred charge shows the predominance of the diene-HOMO dienophile-LUMO interaction. In this respect the acrolein dimerization may be classified as a "normal" Diels–Alder-reaction.[17]

Summary and conclusions

The performed partitioning of the interaction energy ΔE indicates the following factors to be responsible for the observed regioselectivity:

(a) The experimentally observed predominance of isomer **1** is determined by intermolecular orbital interaction. The electrostatic interactions are found to be unimportant for directing the reaction to isomer **1**.

(b) The molecular orbital mixing, determining the regioselectivity, occurs mainly via the terminal atoms and

Table 6. $2p_z$-$2p_{z'}$-contributions (kcal/mol) of the intermolecular $E^2_{AB'}$ terms determining the regioselectivity

	isomer **1**				isomer **2**		
A	B′	$2p_z$-$2p_{z'}$	%	A	B′	$2p_z$-$2p_{z'}$	%
1	1′	-10.12	61.5	1	2′	-6.75	57.6
4	2′	-2.67	88.8	4	1′	-4.39	84.2
3	3′	-8.26	51.0	2	3′	-5.96	56.6

Table 7. Energy contributions (kcal/mol) of the interacting frontier orbitals to the $2p_z$-$2p_{z'}$-part of the intermolecular $E^2_{AB'}$ determining the regioselectivity

	A	B′	R S HOMO → LUMO	%	R S LUMO ← HOMO	%
1	1	1′	-6.29	62.1	-2.89	28.5
	4	2′	-2.26	84.7	-1.13	42.2
	3	3′	-2.46	29.8	-1.13	13.7
2	1	2′	-4.17	61.8	-1.42	21.0
	4	1′	-3.53	80.4	0.77	17.6
	2	3′	-3.95	66.3	-0.50	8.4

atoms involved in secondary Woodward–Hoffmann interactions.

(c) The interactions between the terminal atoms indicate an asymmetric bond formation. In the *endo*-configuration **1** (Fig. 1) the bond 1–1′ should be formed faster than the 4–2′ bond. This asymmetry in bond formation is diminished by the 3–3′ interaction.

(d) The interactions between the terminal atoms are determined by the interacting frontier orbitals. However, for the secondary interactions, the frontier orbitals predominate only in the *endo*-configuration leading to the unobserved isomer **2**.

(e) The charge transferred from the diene to the dienophile is mainly due to the interacting frontier orbitals.

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