PMO Analysis of Cycloadditions, I

Diels-Alder Reactions of 2,3-Bis(methylene)norbornane

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A perturbational molecular orbital (PMO) treatment within the semiempirical MINDO/3 approximation is applied to the cycloadditions of 2,3-bis(methylene)norbornane (**1**) to electron-deficient olefins (**2**–**5**). Different contributions to the interaction energy deriving from steric effects, polar effects, and orbital interactions are analysed. The results, obtained by the program package PERVAL, which is developed for an IBM AT personal computer, are evaluated graphically. The origin of the reactivity sequence **2** < **3** < **4** < **5** is traced back to the $HOMO_{diene}$-$LUMO_{dienophile}$ interaction. Various possibilities to interpret the results of PMO calculations are demonstrated.

PMO-Analyse von Cycloadditionen, I. – Diels-Alder-Reaktionen von 2,3-Bis(methylen)norbornan

Eine störungstheoretische Methode (PMO) zur Berechnung der Wechselwirkung von Molekülen auf der Basis des semiempirischen MINDO/3-Verfahrens wird auf die Cycloadditionen von 2,3-Bis(methylen)norbornan (**1**) mit den elektronenarmen Olefinen **2**–**5** angewendet. Verschiedene Anteile der Wechselwirkungsenergie, von sterischen Effekten, polaren Beiträgen und Orbitalwechselwirkungen stammend, werden analysiert. Die Ergebnisse werden mit dem Programmpaket PERVAL, das für einen IBM AT Personal Computer entwickelt wurde, berechnet und graphisch ausgewertet. Die Reaktivitätssequenz **2** < **3** < **4** < **5** wird auf die dominante $HOMO_{Dien}$-$LUMO_{Dienophil}$-Wechselwirkung zurückgeführt. Es werden verschiedene Möglichkeiten der Anwendung des Programms PERVAL aufgezeigt.

An important aspect of organic chemistry is the rationalization of reactivity. This includes not only the explanation of a single experimental observation but also the attempt to place the results into the context of a more general reactivity model. The latter should provide a theoretical framework from which extrapolations and predictions are possible. In the area of pericyclic reactions perturbational molecular orbital methods, in particular in the form of frontier molecular orbital (FMO) theory, have proved to be such a valuable tool[1,2]. Rationalization of reactivity[3] and regioselectivity[4] in cycloadditions has been one of the successes of this approach. However, the approximate nature of this theory and its limitations should not be forgotten. Reactivity is explained by the FMO contributions, one or two interactions. How important they ever may be it can not be denied that there are normally many more orbitals in a molecule and that molecules also have properties which we sum up under the notions of steric demand and polarity. A more comprehensive theory of chemical reactivity, therefore, has to include other contributions than orbital interactions.

Several endeavours in this direction have been undertaken. Klopman[5] and Salem[6] devised an equation which included not only orbital interactions but also took account of closed-shell repulsions and polar effects. In the framework of semiempirical SCF theories we[7,8] and others[9] came to similar conclusions. In general one might classify these as attempts to solve the problem of reactivity by perturbation theory using configuration interaction. A more elaborate theory of reactivity, based on qualitative valence bond theory, has been advanced by Epiotis[10].

So far no detailed evaluations of the importance of other than FMO contributions to reactivity have been carried out. Klopman[11] studied the principle of hard and soft acids and bases within this framework. We have analysed ketene cycloadditions some time ago[12] and cycloadditions of diazomethane[13]. Fukui has treated the interaction of diazomethane with ethylene in detail[9]. To carry out such a program several decisions have to be made at the beginning. It seems to be meaningful to remain within the area of semiempirical MO procedures in order to keep such a treatment manageable also for larger systems. One could remain in the approximation of extended Hückel theory[6,14] or could choose a many-electron basis which leads to SCF procedures[5,8,9,12]. It is the latter approach which we decided to take earlier[7,8] and which we apply in this work. Within the ZDO approximation we derived an expression for the interaction of two molecules up to second order[7,12]. Computer programs, based on the MINDO formalism in its latest MINDO/3 version[15] were written which allow to calculate the interaction energy according to eq. (1)–(3).

The first-order energy change ($\delta E^{(1)}$) includes interactions due to δ^+ or δ^- charges of the atoms (q_k and q_l) of the interacting systems. This energy contribution is proportional to γ_{kl}, the electron repulsion integral between two electrons at atoms k and l. Depending on the relative signs of q_k and q_l this contribution may be positive (repulsive) or negative (attractive). The second part of eq. (2) will always be repulsive, being proportional to the difference between two point charge repulsions at atoms k and l ($\gamma_{N_kN_l}$) and the electron-electron repulsion integral between electrons at

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these atoms (γ_{kl}). This is multiplied by the core charges of atoms k and l (C_k and C_l) and modified by a function $f(R_{kl})$ which derives from the treatment of nuclear-nuclear repulsions in the MINDO/3 formalism. This second contribution to the first-order energy change replaces the closed-shell repulsion term in one-electron treatments where no explicit account is taken of the electron-electron, electron-nuclear, and nuclear-nuclear interactions. It is always positive and it is responsible for the existence of activation barriers in chemical reactions.

$$\Delta E = \delta E^{(1)} + \delta E^{(2)} \tag{1}$$

$$\delta E^{(1)} = \sum_{k}\sum_{l} \left(q_k q_l \gamma_{kl} + (\gamma_{NkNl} - \gamma_{kl}) C_k C_l f(R_{kl})\right) \tag{2}$$

$$\begin{aligned}\delta E^{(2)} = &-2 \sum_{u}^{occ} \sum_{p}^{unocc} \left[\sum_{\mu}\sum_{\lambda} c_{u\mu} c_{p\lambda} \beta_{\mu\lambda}\right]^2 E_u^{p-1}\\ &-2 \sum_{p}^{occ} \sum_{u}^{unocc} \left[\sum_{\lambda}\sum_{\mu} c_{p\lambda} c_{u\mu} \beta_{\lambda\mu}\right]^2 E_p^{u-1}\\ &-2 \sum_{u}^{occ} \sum_{v}^{unocc} \left[\sum_{\mu}\sum_{l} c_{u\mu} c_{v\mu} \gamma_{\mu l} q_l\right]^2 E_u^{v-1}\\ &-2 \sum_{p}^{occ} \sum_{q}^{unocc} \left[\sum_{\lambda}\sum_{k} c_{p\lambda} c_{q\lambda} \gamma_{\lambda k} q_k\right]^2 E_p^{q-1}\end{aligned} \tag{3}$$

The expression for the second-order energy change ($\delta E^{(2)}$) comprises two terms, one based on charge-transfer interactions (line 1 and 2 of eq. 3) and an interaction based on contributions from locally excited states in molecules K and L (lines 3 and 4 of eq. 3). The first two lines include the FMO interactions as two terms but also take care of the interactions of all the other occupied MOs of $K(L)$ with all unoccupied MOs of $L(K)$. $c_{u\mu}$ and $c_{p\lambda}$ are the eigenvector coefficients of MO $u(p)$ at atoms k and l, $\beta_{\mu\lambda}$ represents the resonance integral between the AOs μ and λ. E_u^{p-1} and E_p^{u-1} are the charge-transfer excitation energies. The last two lines of eq. (3) express a second-order electrostatic interaction due to contributions from locally excited states E_u^{v-1} in K and E_p^{q-1} in L. This turns out to be very small and will be omitted in the further treatment. It is listed in eq. (3) for the sake of completeness.

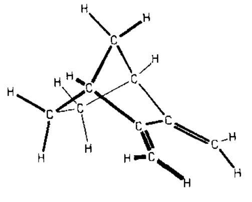
This formalism should allow, within the limitations of the validity of semiempirical SCF procedures, to analyse separately: 1. coulombic interactions between molecules due to their polar or ionic nature, 2. repulsive interactions originating in the property that the electrons and the nuclei of a molecule do not only produce attractive but also repulsive forces, 3. frontier molecular orbital interactions, and 4. covalent interactions between other than frontier molecular orbitals.

What are the limitations of such an analysis? Some approximations which involve the structure of the complex of the two molecules have to be pointed out. It seems to be logical to consider two interacting molecules in their ground state structure in order to avoid the introduction of too many degrees of freedom. However, the two molecules have to be positioned relative to each other in order to carry out the perturbation calculation. As we want to gain information on the structure and energetics of the transition state of the reaction at a point where perturbation calculations are still valid we have to remain at a position of the reaction coordinate in front of the transition state. In many cases the choice of an actual distance of the reacting molecules is facilitated by the results of elaborate ab initio calculations for transition states. In [4 + 2] cycloadditions[16] a distance of 250 – 300 pm seems to be a good choice for the perturbation calculation. The next problem concerns the symmetry of the transition state of the [4 + 2] cycloaddition. This is a controversial area[17]. At this point the intention of perturbation calculations should be remembered: to get insight in the forces which govern the interaction of two molecules and the interpretation of these results in qualitative or semiquantitative terms. Thus, if we assume a symmetrical transition state, as far as the reacting centers in the Diels-Alder addition are concerned, we may be able to recognize general features and may even make predictions that a less symmetrical approach might be more favorable. This is the point of view taken in the analysis of [4 + 2] cycloadditions of 2,3-bis(methylene)norbornane (**1**) with electron-deficient olefins.

Calculational Procedures: The structures of the individual molecules were obtained from MNDO calculations[18] with complete geometry optimisation. Either MNDO wave functions or those from MINDO/3 calculations based on the MNDO-optimised structure formed the input in the perturbation program PERVAL[19], recently developed in our laboratory. PERVAL requires as input the cartesian coordinates of the interacting molecules in the position in three-dimensional space in which the interaction is to be analysed. Furthermore eigenvalues, eigenvectors, and charges of the atoms are transferred to PERVAL. In practice we generate an input file for each molecule at the end of the SCF calculations of the individual molecules and combine these as input file for PERVAL. The perturbation calculation and for smaller molecules also the MNDO or MINDO/3 calculation are carried out on an IBM AT personal computer. For larger molecules the SCF calculation is done on the University computer and the data are sent to the personal computer by direct connection. The program PERVAL, written in FORTRAN, generates output files PERVAL.OUT and PERVAL.GRA. The former contains the numerical results, the latter forms the input file for the subprogram PERGRA. This section of the program, written in TURBO PASCAL, analyses the output data graphically and interactively on the personal computer. An option (MOLROT) allows the rotation of the molecules in the molecular complex about prechosen axes with the determination of the minimal repulsive interaction. After such a rotation the second-order energy can be recalculated and reexamined.

Results

Cycloadditions of 2,3-bis(methylene)norbornane (**1**) with the electron-deficient dienophiles **2**−**5**, represented in their MNDO-optimised structures, were examined experimentally and described in the preceding paper[20].



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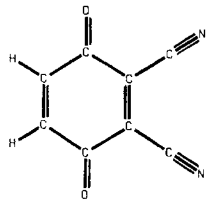

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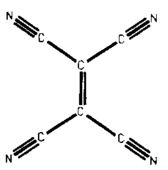

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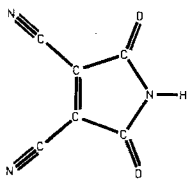

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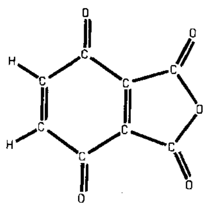

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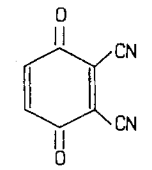
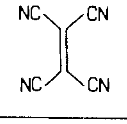
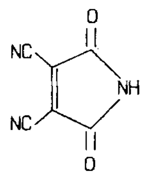
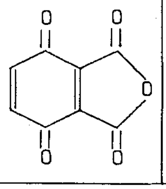
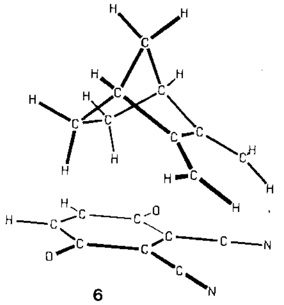
Table 1. Experimental results for the interaction of **1** with **2**−**5**

	K_{rel} (l/mol s)	$h\nu_{CT}$ (eV)	ΔE_{HO-LU} (eV)	$K_{eq.}$ (CT-complex)
2 	1	2.70-2.76	5.60	3.8
3 	81	2.90	5.67	33.5
4 	91	2.95	5.89	79.1
5 	917	2.58-2.76	5.46	---

It was observed that the dienophiles form CT complexes with **1** for which the equilibrium constants were determined in the case of olefins **2**−**4**. The reactivity sequence **2** < **3** < **4** < **5** could not be explained by the PMO-derived relationship according to which the rate of reaction should be inversely proportional to the $HOMO_{diene}$-$LUMO_{dienophile}$ gap. Neither the experimental HOMO-LUMO separation nor the CT-excitation energies reproduced the reactivity order correctly. However, the reactivity sequence followed the strengths of the CT complexes formed between **1** and **2**−**4**. Some pertinent results are collected in Table 1.

Several aspects of these cycloadditions will be examined. The failure in the reproduction of the reactivity sequence by the $HOMO_{diene}$-$LUMO_{dienophile}$ separation will be of concern. *syn/anti* and/or *endo/exo* selectivity of **2**−**5** towards **1** can occur in principle and as the experimental results proved is indeed observed. The reason for this will be analysed by calculating molecular complexes between **1** and **2**−**5**. As a starting point for the PMO analysis we choose the plane of the diene part in **1** and the molecular planes of **2**−**5** parallel to each at a separation of 250 pm. This distance was selected because the transition state of the Diels-Alder reaction is



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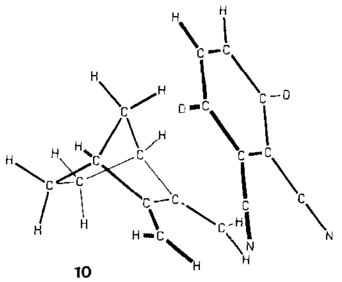

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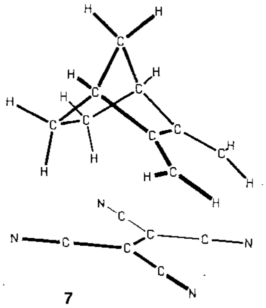

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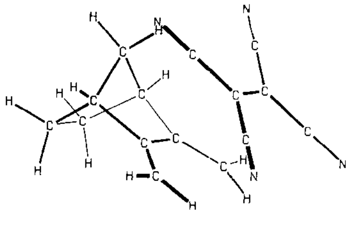

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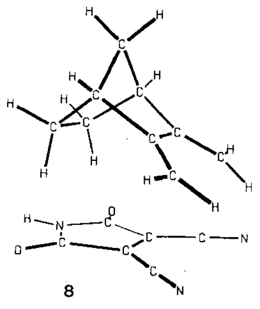

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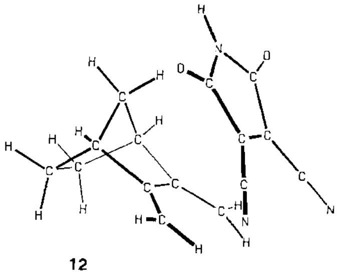

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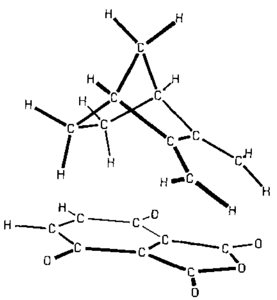

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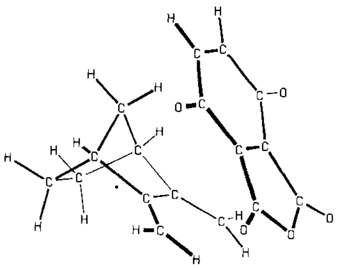

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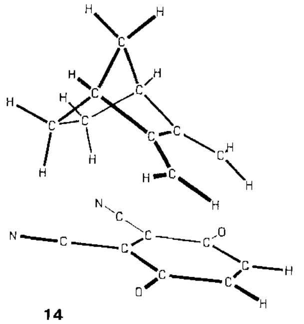
calculated[16] to have the reacting carbon atoms about 210–225 pm apart. We also assume identical intermolecular distances between the reaction centers, i. e. the approach of the two molecules occurs symmetrically. The molecular complexes between **1** and **2**–**5** are represented in **6**–**13** where *anti* (**6**–**9**) and *syn* (**10**–**13**) arrangements are considered. In addition to the *syn/anti* stereopossibility the dienophiles **2**, **4**, and **5** can approach the diene in what one might call *endo/exo* manner. For the *anti* approach this is shown in **14**–**16**. The structures of the molecular complexes are those which were obtained from minimising the repulsion between the molecules at a distance of 250 pm of the planes. For this purpose the molecules were rotated about the reacting CC-double bond (see below).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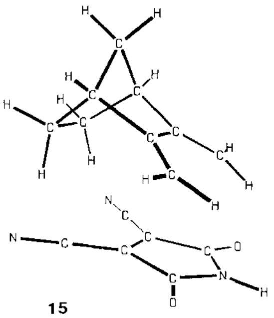
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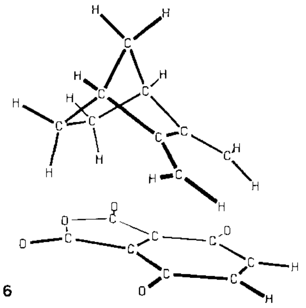
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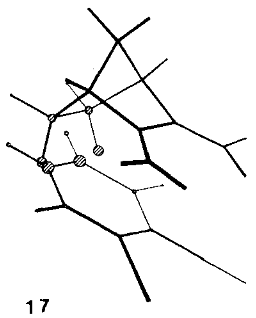
The graphical representations of the *anti* and *syn* approach permit immediately to differentiate the complexes sterically. In the *anti* mode it is the two-carbon-atom bridge together with the two hydrogen atoms pointing in the direction of the dienophile which is responsible for a steric hindrance of the reaction. This is borne out in the steric interaction energy (Table 2). Very high repulsive energies are calculated. In particular for the planar arrangements (angles 0 or 180 degrees) these seem to be extremely high. In entries 3 and 19 of Table 2, for instance, the two hydrogen atoms of the two-carbon-atom bridge are only 59 pm above two carbon atoms of 2,3-dicyano-*p*-benzoquinone, a completely unrealistic situation. The contributions of these two hydrogen atoms together with the C atoms to which they are attached and the two carbon atoms of the dienophile amount to 75% of the total steric repulsion. From this we have to conclude that it will be more realistic for the two molecules not to approach in two parallel planes. If the dienophile is allowed to rotate about the axis of the reacting carbon atoms without changing their distance from the diene part of **1** a minimal steric repulsion at a rotational angle of 31 degrees (**6**) is found, the steric hindrance decreasing by 80–90%. As we will see the covalent interactions between the reacting centers are not affected appreciably by this rotation.

As a consequence of the presence of a five-membered ring in **4** the steric repulsion is smaller if the ring is located below the two-carbon-atom bridge of (entry 13 in Table 2) **1** in complex **8**. The distance between the nitrogen atom and the two relevant hydrogen atoms is greater than between the C atoms and the corresponding hydrogen atoms in **6** and **9** (entries 3 and 19). This situation is responsible for the smaller difference in steric repulsion between *syn* and *anti* complexes of **4** than between those of **2** and **5**.

One graphical representation may illustrate the possibilities of the program PERVAL. In **17** we show the steric repulsion in **6** (planar arrangement, entry 3 of Table 2). The amount of repulsion contributed by individual atoms is indicated by the area of the circles around the atoms. The important atoms are recognized immediately. Knowing that the biggest circle corresponds to 853 kcal/mol and that the total repulsion energy is 2111 kcal/mol it can be understood that the contributions from other atoms are negligible in this orientation and that they are not visible in this scale. Rotation about the reacting CC bond reduces the unfavorable interaction and at the energetic minimum (259.2 kcal/mol) the contribution from all carbon and nitrogen atoms of the dienophile are very similar as shown in **18** (rotational angle 31°, entry 4 in Table 2).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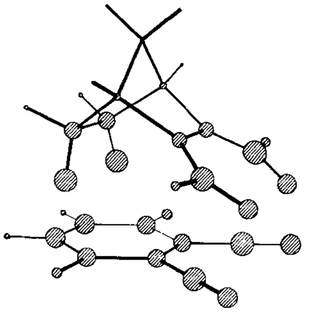
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It is interesting to note that in the set of *syn* or *anti* structures minimised with respect to the repulsion the absolute values become comparable, i.e., there should not be much differentiation between the dienophiles from this energy contribution. Sterically, however, the *syn* approach is always more favorable. An exception is made only by tetracyanoethylene which shows less repulsion in both reaction modes.

One final remark on the steric interaction concerns the differences between *endo/exo* orientation of **2**, **4**, and **5** in complexes **14**–**16** and **6**, **8**, **9**, resp., in the optimised structures. The repulsions distinguish these structures for **4** more than for **2** and **5** and therefore one might expect a different selectivity experimentally, all other factors being equal. However, because of the *syn/anti* and *endo/exo* dichotomy (see ref.[20]) it is not possible to decide between these modes of reaction. An experimental distinction is possible, for instance in the case of isodicyclopentadiene and its cycloadditions and has been studied experimentally[21] and analysed

Table 2. First- and second-order interaction energies for complexes of **1** with **2**–**5** (kcal/mol)

Dienophile	No.	Complex	*syn*/*anti*	Angle[a)]	Charge interaction	Steric interaction	Covalent interaction	Sum
2	1	–	*syn*	0	0.64	587.9	−51.1	537.5
	2	**10**	*syn*	24	0.37	163.7	−23.5	140.6
	3	–	*anti*	0	0.22	2111.2	−205.7	1905.7
	4	**6**	*anti*	31	0.06	259.2	−51.3	207.9
	5	–	*anti*	180	0.08	543.8	−96.7	447.1
	6	**14**	*anti*	153	0.04	243.9	−52.9	191.0
3	7	–	*syn*	0	0.01	137.9	−15.2	122.6
	8	**11**	*syn*	13	0.04	118.9	−13.7	105.3
	9	–	*anti*	0	0.10	494.7	−87.5	407.3
	10	**7**	*anti*	28	0.12	224.8	−37.8	187.2
4	11	–	*syn*	0	0.50	543.3	−58.9	484.8
	12	**12**	*syn*	24	0.30	162.7	−26.1	136.9
	13	–	*anti*	0	0.54	757.3	−97.6	660.3
	14	**8**	*anti*	32	0.24	249.7	−45.3	204.6
	15	–	*anti*	180	0.01	307.6	−55.7	251.9
	16	**15**	*anti*	157	0.03	210.8	−37.4	173.4
5	17	–	*syn*	0	0.63	567.3	−52.8	515.1
	18	**13**	*syn*	23	0.32	167.5	−28.7	139.2
	19	–	*anti*	0	0.16	2074.0	−203.8	1870.4
	20	**9**	*anti*	31	−0.09	266.0	−60.1	205.8
	21	–	*anti*	180	−0.13	672.9	−110.9	561.9
	22	**16**	*anti*	151	0.20	272.7	−66.5	206.4

[a)] Rotational angle between the diene plane in **1** and the plane of the dienophile.

theoretically[14,22]. It might be useful to study some of these reactions by this PMO procedure and to see how the repulsion energies influence the selectivity.

The steric interaction seems to make an unusual high contribution to the total energy and it may be asked how realistic and meaningful these values are. The evaluation according to eq. (2) is based on the MINDO approximation and, therefore, carries with it all advantages and deficiences of this semiempirical MO procedure. Supposedly intermolecular interactions are not as well represented as intramolecular ones by the function describing the nuclear-nuclear repulsion[23]. It is assumed to exaggerate these. One might be tempted to ascribe the rather high values for the steric interactions in Table 2 to this deficiency. As we are interested only in comparative studies and in the identification of the most relevant features the significance of relative energies is of more importance. A much higher degree of confidence can be attributed to this aspect and, therefore, we believe that the kind of analysis presented here is independent of possible errors in the potential function for the nuclear-nuclear repulsion.

The covalent interaction, i.e. within the perturbational model the second-order energy, is responsible for the formation of new bonds between molecules. Regardless how favorable or unfavorable a particular approach of two molecules is with respect to the steric interaction the decision about the feasibility of a chemical reaction is made on the basis of the second order energy. If this is secured then other effects may become operative and will influence the course of the reaction by their relative importance. In the FMO model the most important contribution to the formation of new bonds is ascribed to one or at most two interactions[1]. In [4 + 2] cycloadditions two new σ bonds and one π bond are formed at the expense of three π bonds. The relevant orbitals of the reacting molecules are, therefore, of π nature. It is for this reason that we concentrate on the interaction of occupied π orbitals of one molecule with unoccupied π orbitals of the other.

A discussion of the sum of the covalent interactions (Table 2) is not very meaningful. It includes the interaction of all occupied MOs of one molecule with all unoccupied MOs of the other. The analytical form of eq. (3) tells us that this interaction depends on the energetic separation of the MOs involved, the magnitude of the eigenvector coefficients and the resonance integral between atomic orbitals at different atoms. The latter is a function of the distance between the atoms. If, therefore, in a molecular complex two atoms come very close, as is the case for two hydrogen atoms and two carbon atoms in **6** and **9**, there will be a large resonance integral between the orbitals of these atoms and it may occur that occupied and unoccupied MOs in which these atoms have a major contribution, possibly of σ nature, will lead to a strong covalent interaction even though these are nonreactive contributions. This covalent stabilisation is outweighed by far by the strong steric repulsion. This feature of the calculation can be recognized in **6** and **9**. The total covalent interaction is high but the repulsion is an order of magnitude greater. This tells us that it is not wise to discuss the total covalent interaction but to single out those parts which are relevant for the formation of the new bonds.

In Table 3 we have collected the HOMO$_{\text{diene}}$-LUMO$_{\text{dienophile}}$ stabilisation energies for the complexes of Table 2, together with two other interaction energies. Column 5 corresponds to the value of the resonance integral between C-1 diene and C-1 of the dienophile multiplied with the eigenvector coefficients at these atoms in HOMO$_{\text{diene}}$ and

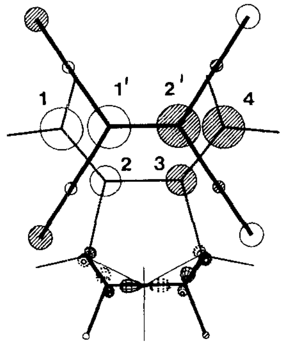
$LUMO_{dienophile}$. These values thus constitute individual elements of the sum in the numerator of eq. (3). In column 6 we represent the complete numerator for the $HOMO_{diene}$-$LUMO_{dienophile}$ interaction.

Table 3. HOMO-LUMO interactions between complexes of **1** and **2**–**5**

Dienophile	No.	Complex	α-Rot. deg.	$\Delta E^{1,1'}_{HO\text{-}LU}$ [a] kcal/mol	$\sum_{kl} \Delta E^{kl}_{HO\text{-}LU}$ kcal/mol	$\Delta E_{HO\text{-}LU}$ kcal/mol
2	1	–	0	−3.23	−10.09	−2.57
	2	**10**	24	–	–	−2.06
	3	–	0	−3.16	−11.93	−3.68
	4	**6**	31	−2.70	−10.28	−2.52
	5	–	180	−3.16	−11.74	−3.31
	6	**14**	153	−2.79	−15.57	−6.26
3	7	–	0	−4.47	−15.19	−4.49
	8	**11**	13	–	–	−4.14
	9	–	0	−4.28	−14.83	−4.32
	10	**7**	152	−3.78	−12.48	−3.06
4	11	–	0	−4.24	−15.24	−5.34
	12	**12**	24	–	–	−3.66
	13	–	0	−4.06	−14.98	−5.26
	14	**8**	32	−3.41	−11.74	−3.17
	15	–	180	−4.06	−14.27	−4.67
	16	**15**	157	−3.73	−15.24	−5.42
5	17	–	0	−3.78	−12.11	−4.66
	18	**13**	23	–	–	−4.77
	19	–	0	−3.62	−13.40	−5.86
	20	**9**	31	−3.09	−14.18	−6.16
	21	–	180	−3.62	−13.58	−5.66
	22	**16**	151	−3.16	−17.06	−9.57

[a] Calculated according to eq. (4) for C-1 of the diene and C-1 of the dienophile.

The cycloadditions of **1** with the dienophiles **2**–**5** are $HOMO_{diene}$-$LUMO_{dienophile}$ controlled, the $HOMO_{dienophile}$-$LUMO_{diene}$ contribution to the reactivity being negligible. This prediction of the FMO model is confirmed by the calculations. In every case the $HOMO_{diene}$-$LUMO_{dienophile}$ stabilisation is less than 0.001 kcal/mol. This can not only be due to the greater $HOMO_{dienophile}$-$LUMO_{diene}$ separation but it is augmented by other effects. The origin of these can be delineated from a comparison of **19** and **20** where for complex **8** the $HOMO_{diene}$-$LUMO_{dienophile}$ (**19**) and the $HOMO_{dienophile}$-$LUMO_{diene}$ (**20**) are drawn.



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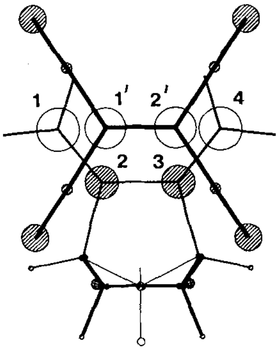


20

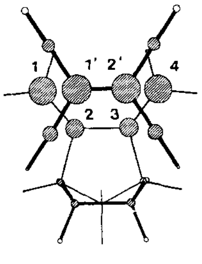
In this projection the π orbitals appear as circles. As required the phases of the two MOs in each case are such that a stabilising interaction between the reacting centers is possible. However, there is one other remarquable interaction. The phase distribution in $LUMO_{diene}$ (**20**) in combination with the distances between the reacting atoms of the dienophile and C-1 and C-2 of the diene shows that there is an antibonding interaction between the reacting dienophile C-atom and C-2 of the diene which compensates due to the spatial arrangement of the complex most of the interaction between C-1_{diene} and the bond forming atom of the dienophile. This compensation effect occurs twice and is the main reason for the small $HOMO_{dienophile}$-$LUMO_{diene}$ stabilisation. This is a general result and it must have some relevance for the classification of Diels-Alder reactions in those of normal and those of inverse electron demand. The dominant $HOMO_{diene}$-$LUMO_{dienophile}$ stabilisation (**19**) is augmented by this type of interaction as can be seen from **19**. The phases of the AOs in $HOMO_{diene}$ at C-1 and C-2 are identical leading to an increased interaction. From an analysis of the phase relationships in the Diels-Alder reaction with inverse electron demand (**20**) it was concluded some years ago that this reaction should exhibit less concert[24].

The program PERVAL offers the option to calculate and to display graphically the contributions of individual atoms to charge-transfer interactions. These are determined from the elements of a matrix with dimension R (number of atoms in *K*) times S (number of atoms in *L*) where individual elements are evaluated according to eq. (4).

$$\Delta E^{kl}_{up} = \sum_{\kappa} \sum_{\lambda} c_{u\kappa} c_{p\lambda} \beta_{\kappa\lambda} \qquad (4)$$

ΔE^{kl}_{up} corresponds to an interaction energy between atoms *k* and *l* of molecules *K* and *L* for the pair of molecular orbitals *u* (occupied) and *p* (unoccupied). The index κ(λ) runs over the atomic orbitals of atom *k*(*l*). $\beta_{\kappa\lambda}$ is the resonance integral between AOs κ and λ. These quantities may either be positive or negative, their sum enters the numerator of eq. (3). The square of this sum divided by the CT-excitation energy determines the amount of the CT interaction.

In order to analyse the composition of the sum we can choose two different graphical representations. In the first one we display the sums of the rows and the sums of the columns of the interaction matrix as circles at the position of the atoms indicating by the area of the circles the magnitude of the contribution. This value corresponds to the interaction of a particular atom in one molecule with all the atoms of the other molecule. This is done in **21** and **22** for the two aforementioned HOMO-LUMO interactions (**19** and **20**). In **21** we recognize the prominent contribution from the reacting atoms. Even C-2 and C-3 of the diene and two C atoms of the nitrile groups produce bonding, in the latter case some kind of secondary orbital interaction. This is different in **22**. C-1 and C-4 show contributions of opposite sign from those of atoms C-2 and C-3 thus compensating each other. Furthermore due to the sum character of these values the reacting C atoms of the dienophile have a lesser share in the total sum than C-1 and C-4 of the diene. In the second mode we display individual elements of a row or column of the matrix for a particular atom in *K* or *L*, this uncovers the elements of the sums in the first representation. In **23** we present one example for the $HOMO_{dienophile}$-$LUMO_{diene}$ interaction. The sum represented in **22** for one carbon atom of the CC double bond of TCNE is composed mainly of contributions from C-1 and C-2 of the diene. This underlines the compensation effect.



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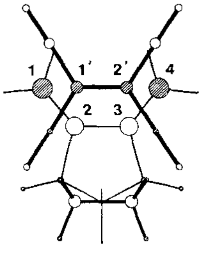

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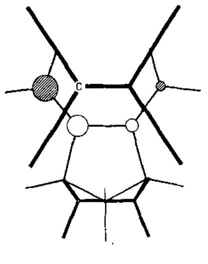

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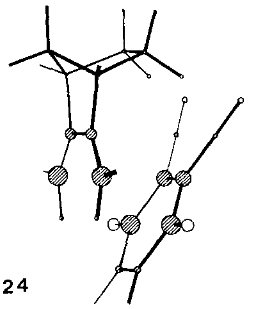
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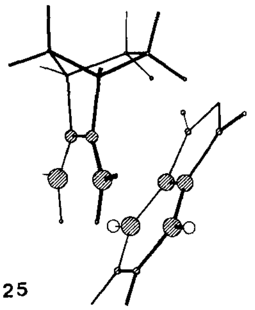
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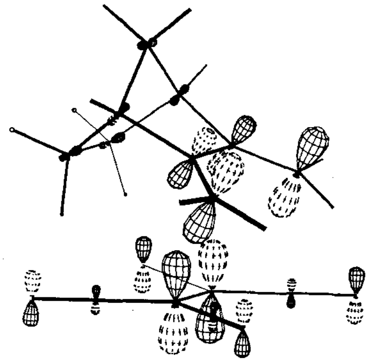
Two more HOMO-LUMO interactions merit to be mentioned. The complexes **14** and **16** display a considerable increase in this stabilisation (Table 3, entries 6 and 22) as compared to the nonrotated structures. In **24** and **25** we analyse this in terms of the elements of the numerator for the CT interaction (eq. 3). As a consequence of the rotation the carbon atoms of the carbonyl groups of the dienophile come closer to the C atoms of the diene.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This strengthens their interaction and because the LUMO of **2** and **5** contain appreciable contributions from these C atoms we observe a favorable increase in covalent bonding. However, this is the result of secondary orbital interactions. The important interaction for the bond forming process between the reacting centers is actually smaller in **14** and **16** than in the parallel arrangements. Compare $E_{HO\text{-}LU}$ for entries 6 and 22 with those for 5 and 21 in Table 3. For the actual bond forming process we have to provide as good an overlap as possible between the p orbitals at C-1 and C-1' and this is realised in the parallel approach. A pictorial view of the change in orbital overlap upon rotation is given in **26**.

Table 4. HOMO-LUMO separations, charge-transfer excitation energies, HOMO-LUMO stabilisation energies, and *RM* values for complexes of **1** with **2**−**5**

Entry in Table 2	$E_{HO}-E_{LU}$ eV	$h\nu_{CT}$ (HO-LU) eV	$\Delta E_{HO\text{-}LU}$[a] kcal/mol	*RM* eV · 10^3
3	7.35	3.35	−3.68 (3.31)[b]	11.2
9	8.43	4.42	−4.32	15.6
13	7.77	3.71	−5.26 (4.67)	16.7
19	6.70	2.66	−5.86 (5.66)	18.5

[a] $HOMO_{diene}$-$LUMO_{dienophile}$. — [b] Values in brackets are for entries 5, 15, and 21 of Table 2.

If the $HOMO_{diene}$-$LUMO_{dienophile}$ interaction is mainly responsible for the reactivity then it should also reproduce the order of reactivity of the dienophile **2**−**5** towards **1**. The comparison of the stabilisation $HOMO_{diene}$-$LUMO_{dienophile}$ (Table 4) in the planar *anti* orientation shows an increase from **2** to **5** as is required by the experimental order of reactivity. This is not changed if **2**, **4** and **5** are rotated by 180 degrees (values in brackets in Table 4), i.e. *endo* or *exo* approach in the *anti* orientation reproduces the experimental order of reactivity. As we showed in the preceding paper the experimental HOMO-LUMO separations or the measured charge-transfer excitation energies did not conform with the order of reactivity (see also Table 1). The same conclusion is derived from the calculated values even though the experimental and calculated order is not identical. However, it is noteworthy that only the full expression for the HOMO-LUMO interaction provides satisfactory results. The calculated reactivity order is not modified if the stabilisation is evaluated for the rotated structures although the absolute values are smaller. This follows from the reduced overlap between the p orbitals (see **26**). On the other hand in the *syn* complexes either optimised with respect to the steric interaction (entries 2, 8, 12, and 13 of Table 3) or not (entries 1, 7, 11, and 17) the experimental sequence does not correspond to the calculated one. The dienophile **5** shows a pronounced difference between *syn* (**13**) and *anti* (**9**) arrangement.

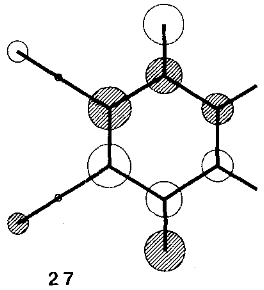
The dienophiles **2**−**5** are characterised by extended π systems. It might therefore be expected that other unoccupied orbitals than the LUMO will contribute to the stabilisation of the transition state. A survey shows that for **3** and **4** there is in fact only one CT interaction ($HOMO_{diene}$-$LUMO_{dienophile}$) which makes a sizable contribution. For **2** and **5** we could identify in each case one more orbital interaction. There exists an unoccupied molecular orbital in these dienophiles of the same symmetry as the LUMO. In the complex between **1** and **2** (entry 3 of Table 3) and between **1** and **5** (entry 19) the interaction of this additional orbital with $\text{HOMO}_{\text{diene}}$ amounts to -1.17 and -0.66 kcal/mol, respectively. If added to the HOMO-LUMO contribution the reactivity of **2** and **5** should increase. **2** then approaches **3** and **4** whereas **5** separates even more from the other olefins.

Another approximate analysis of the perturbation calculations can be carried out. The order of the $\Delta E^{1,1'}_{\text{HO-LU}}$ values in Table 3 (column 5) for comparable entries, for instance 3, 9, 13, and 19, is not in accordance with the observed reactivity sequence. **3** and **4** show a higher interaction energy than **2** and **5**. The situation is similar for the corresponding values in column 6. In calculating $\Delta E_{\text{HO-LU}}$ the sum of the $\Delta E^{kl}_{\text{HO-LU}}$ values is squared, divided by the excitation energy and multiplied by -2. In an approximate way one can use $\Delta E^{1,1'}_{\text{HO-LU}}$, take its square, multiply by -2, and divide by the excitation energy. This defines a quantity *RM* (Reactivity Measure) according to eq. (5).

$$RM = -2 \frac{[\Delta E^{1,1'}_{\text{HO-LU}}]^2}{h\nu_{\text{CT}}(\text{HO-LU})} . \qquad (5)$$

These values were calculated and can be found in column 5 of Table 4. The main effect is that the $\Delta E^{1,1'}_{\text{HO-LU}}$ values are weighed by the excitation energies. As the smallest $h\nu_{\text{CT}}$(HO-LU) is calculated for **5** its *RM* value takes the lead and the others follow in the order of the experimental relative rates. A related quantity was defined a long time ago in π electron theory by Fukui[25] and was called superdelocalisability. It has to be seen in further applications how general eq. (5) can be used.

As far as the reacting double bond is concerned the dienophiles **2** and **5** exhibit specificity. Although there are two choices only the more highly substituted double bond reacts. This had been observed in other cycloadditions of these dienophiles[24]. A simple rationale for this derives from the shapes of the LUMOs of **2** and **5** (**27** and **28**) shown in a projection from above the plane of the molecules.



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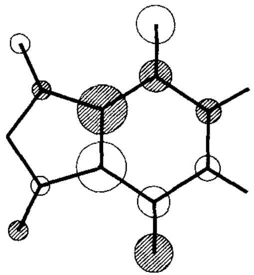

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The carbon atoms of the more substituted double bond contribute more to the LUMOs than the atoms of the other double bond. In accordance with the explanation of regioselectivity[4] we expect the reaction to take place at this double bond.

Conclusion: The graphically oriented computer program PERVAL for perturbation calculations and their analysis on an IBM AT personal computer has been applied to Diels-Alder reactions and has shown its usefulness. One of its advantages is the easy interpretation of the individual components of the perturbation by computer graphics. This allows a fast evaluation in a representation which is familiar to chemical visualisation. As it allows not only the analysis of CT interactions but includes other contributions to the interaction of molecules it seems to provide a good basis for further applications. In the future it will be valuable to test on a broader scale the importance of the repulsive term of eq. (2) and to work out its significance in relation to the covalent contribution. Also reactions in which ionic interactions will be more important have to be considered.

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