Additions of Cyclopentadiene to a Dissymmetric Maleic Anhydride: Semiempirical Calculations of Their Thermodynamics and Kinetics

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Z. Naturforsch. **51a**, 1134–1138 (1996); received July 23 1996

There are four conceivable products of the title addition, however only two of them have been prepared. MNDO, AM1, and PM3 quantum-chemical computations have been used in order to rationalize the observation. Activated complexes have been computed for the four possible additions and it was found that one C-C bond rather than two is created on the path from the reactants to the activated complex (the C-C bond varies between 1.70 and 1.87 Å). Only one activated complex has been localized on each reaction path. The two types of products observed in experiment are computed to be both thermodynamically more stable and kinetically more feasible, and hence the computations agree with the observations.

1. Introduction

In a recent study [1] dealing with Diels-Alder addition of cyclopentadiene to a facially dissymmetric tetracyclo-fused maleic anhydride only two products were observed, namely *syn-exo* and *syn-endo* isomers (see Figure 1). However, there are also two other isomers possible, *anti-exo* and *anti-endo*, as shown in Figure 1. The selectivity must be due to some thermodynamic and/or kinetic reasons. This paper performs a systematic quantum-chemical semiempirical analysis of the problem.

2. Computations

Computations have been performed with the standard version of the MNDO method [2] and checked with more recent AM1 [3] and PM3 [4] methods. The bulk of the computations was done with the implementation of the methods in the SPARTAN program package [5], though some computations were also carried out with their implementations in the GAUSSIAN program package [6].

The complete geometry optimizations were performed for the reactants and products at the MNDO level. The geometry optimizations were carried out in Cartesian coordinates with analytically constructed energy gradient. The optimizations were followed by vibrational analysis based on the force-constant matrix constructed by a numerical differentiation of the analytical energy gradient. This treatment allows for a reliable check of the stationary-point nature (no imaginary vibrational frequency in local energy minima, just one imaginary frequency in the activated complexes), and also for evaluations of thermodynamic and activation terms.

While the geometry optimizations are well established procedures for local energy minima, they still require a special care in the case of activated complexes. The reason comes from a different nature of the local energy minima and activated complexes. In a minimum all curvatures are positive. However, in an activated complex, the curvature in one direction, i.e. the path between reactants and products, is negative. For this particular direction a path of steepest descent cannot be followed, and just opposite, an uphill direction leads towards the activated complex. This special optimization requirement is met [7] by a procedure different from a simple geometry optimization. It is more sensitive to the quality of the starting point and needs the force-constant matrix constructed numerically from the analytical gradient. Moreover, it can frequently fail, and consequently search for activated complexes is still a quite demanding task. The optimizations of the activated complexes were performed at the MNDO, AM1, and PM3 level. Once the activated-complex structure optimization is finished, the vibrational analysis must be performed in order to check the presence of just one imaginary frequency and its physical significance.

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0932-0784 / 96 / 1000-1134 $ 06.00 © – Verlag der Zeitschrift für Naturforschung, D-72072 Tübingen

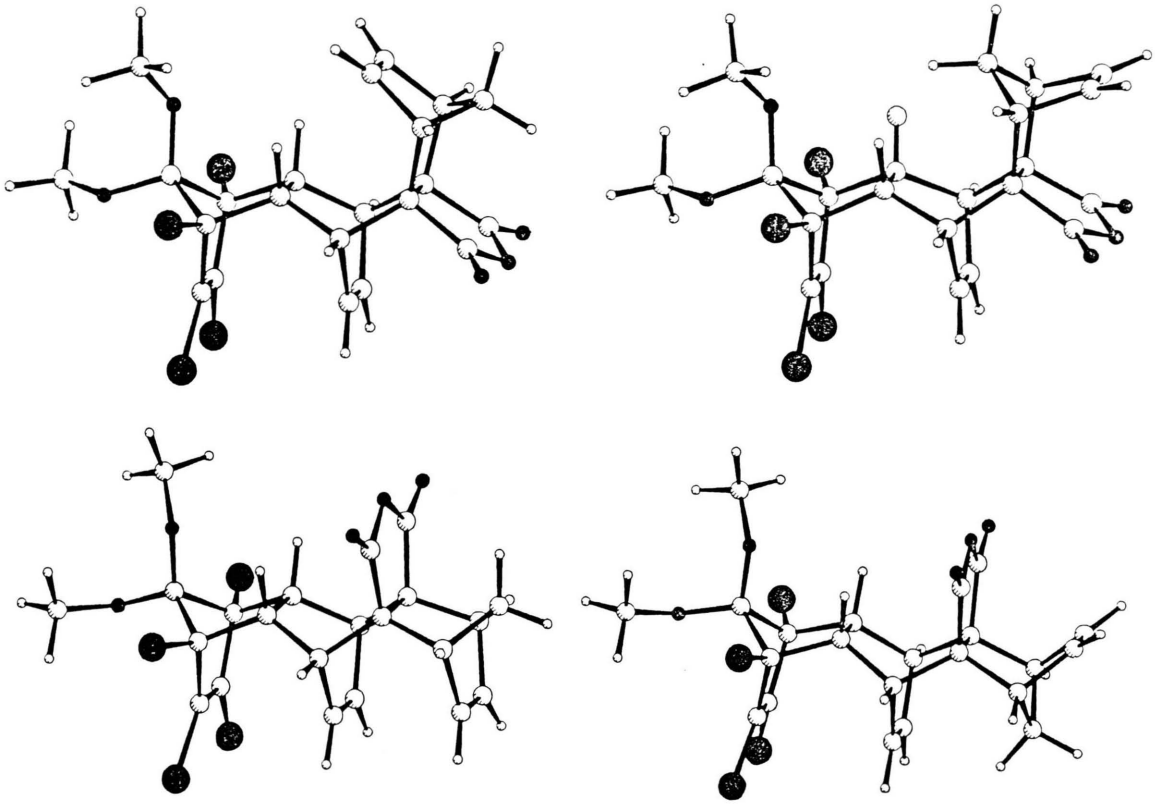

Fig. 1. The MNDO optimized structures of the products: *anti-exo* – top left; *anti-endo* – top right; *syn-exo* – bottom left; *syn-endo* – bottom right. C – larger, H – smaller, Cl – larger black, O – smaller black circles.

3. Results and Discussion

The study started with the MNDO geometry optimizations of the four possible isomers of the Diels-Alder adduct of cyclopentadiene and dissymmetric tetracyclo-fused maleic anhydride (Figure 1). Semiempirical quantum-chemical methods primarily yield heats of formation at room temperature. Although this is basically enough for a discussion of thermodynamic stability, a more accurate approach also requires addition of the entropy term. Moreover, both terms should be computed [8] not at room temperature but at a temperature relevant for experiment (353 K in our case). For our purpose it is enough to deal with the relative stabilities (i.e., the stabilities related to one selected reference species). The thermodynamic stabilities were evaluated in terms of the relative heats of formation ΔH^0_{298} and the relative standard Gibbs functions ΔG^0_{353} at the experimental temperature of 353 K. Table 1 shows that the relative ΔH^0_{298} and ΔG^0_{353} terms are quite similar. The two isomers lowest in both energy scales, *syn-exo* and *syn-endo*, are identical with the species observed in experiment [1]. Let us note that the *syn-exo* and *syn-endo* isomers are computed almost isoenergetic, with the

Table 1. The MNDO computed relative reaction (^{0}) and activation ($^{\neq}$) enthalpies (H) and Gibbs functions (G) (kJ/mol) and the activated-complex structural characteristics.

Approach	$R^{\neq}_{CC}$ [a] (Å)	$\omega^{\neq}$ [b] (cm^{-1})	ΔH^0_{298}	ΔG^0_{353}	$\Delta H^{\neq}_{298}$	$\Delta G^{\neq}_{353}$
anti-exo	1.859	566*i*	14.5	14.7	23.7	22.5
anti-endo	1.861	591*i*	6.9	7.1	15.6	16.7
syn-exo	1.865	576*i*	2.7	2.9	3.0	3.3
syn-endo	1.847	575*i*	0.0	0.0	0.0	0.0

[a] The CC bond created in the activation process.
[b] The solitary imaginary frequency of the activated complex ($i=\sqrt{-1}$).

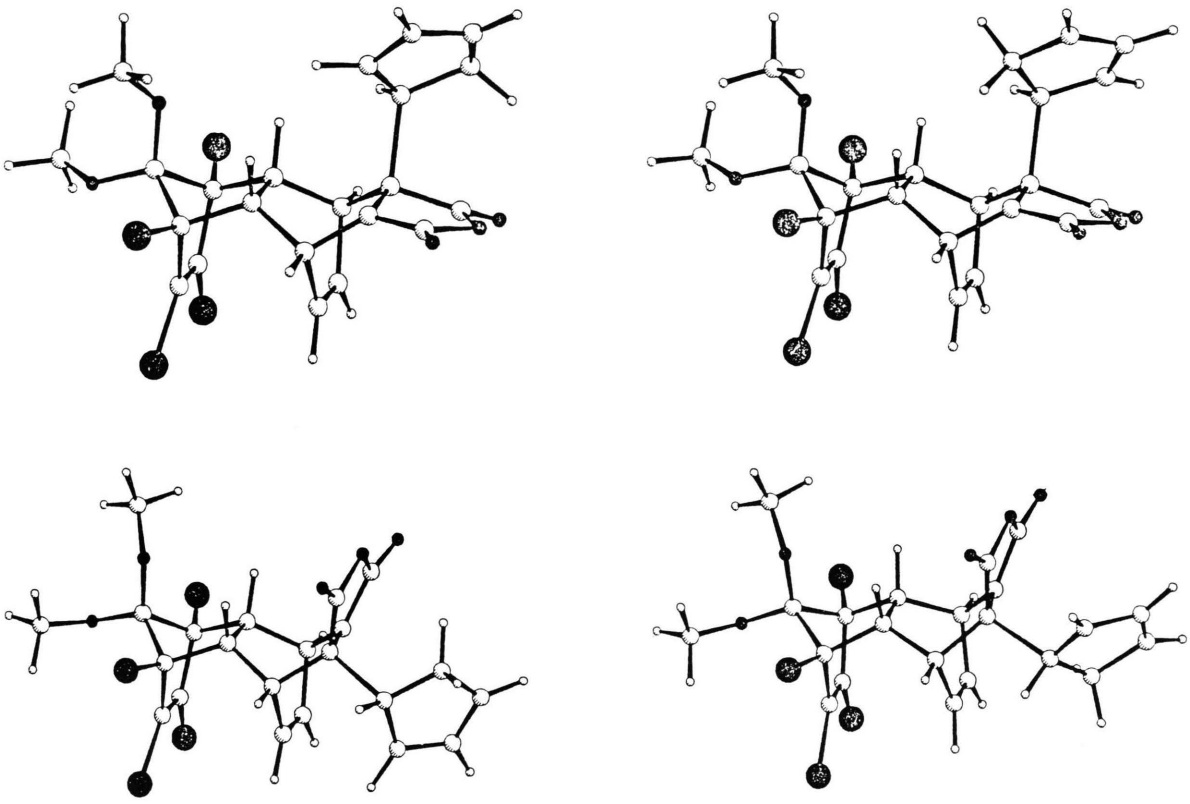

Fig. 2. The MNDO optimized structures of the activated complexes: *anti-exo* – top left; *anti-endo* – top right; *syn-exo* – bottom left; *syn-endo* – bottom right. C – larger, H – smaller, Cl – larger black, O – smaller black circles.

latter structure being slightly lower in energy. However, experimentally the isomeric ratio was 2:1 (if we neglect entropy, it places the *syn-exo* about 2 kJ/mol below the *syn-endo* species). We would need a change in the computed separation energy of about 5 kJ/mol. Truly speaking, we cannot expect such high precision from any of the available semiempirical methods for relatively large molecules [9–11].

More importantly, we cannot be sure that the conditions of thermodynamic equilibrium were achieved in the experiment, and therefore computations of thermodynamic stability are only a pre-requisite. We have to check the rates of production, i.e. activation parameters, too. While experiment can supply structures of reactants and products, it cannot directly yield geometries of activated complexes. Therefore, we tried to compute activated complexes either with only one C-C bond formed or with already two C-C bonds as in the products. Moreover, we *a priori* did not rule out that there might be more than one activated complex on the path from the reactants to products (i.e., a mechanism called non-concerted by Dewar [12]). Although we tried various starting configurations, at the MINDO level we always ended with activated complexes with only one C-C bond and not with two C-C bonds (Figure 2). The C-C bond is predicted by the MNDO method in a narrow interval 1.85–1.87 Å (Table 1). Similarly, the solitary imaginary frequency is quite similar for the four different activated complexes ($566i-591\,i\,cm^{-1}$).

The relative kinetic stabilities have been treated in the relative activation terms ($\Delta H^{\neq}_{298}$, $\Delta G^{\neq}_{353}$), however only forward, no backward reactions have been considered. Table 1 reports the relative activation terms from the MNDO calculations. The relative activation terms actually yield the same conclusions as extracted from the standard thermodynamic terms. Hence, the $\Delta H^{\neq}_{298}$ and $\Delta G^{\neq}_{353}$ terms are rather similar, and the

syn-exo and *syn-endo* isomers are formed with the highest (and almost equal) forward rate. The *anti-exo* and *anti-endo* isomers are more disfavoured kinetically than they were thermodynamically. For example, the relative Gibbs activation function of the *anti-endo* isomer (16.7 kJ/mol) in fact means an about 300 times slower rate of the forward reaction compared to the *syn-endo* species. Still, we have a problem that the *syn-endo* isomer is kinetically also slightly preferred at the MNDO level (as it is thermodynamically).

Once an activated complex is located, we can apply a more sophisticated approach, viz. the intrinsic reaction coordinate treatment [13–15] which examines the reaction path down from the activated complex (in both directions), however only with a selected step. We used this option [6] to search further for a second activated complex but did not succeed. It is however true that for a very flat potential hypersurface the search is very difficult. Hence, there still might be an activated complex hidden at very long separations. However, it would be a kind of van der Waals complex with a very limited significance for the overall kinetics. Hence, the MNDO treatment suggests that the kinetics is realized through only one activated complex, and the activated complex contains only one C-C bond. The formation of the second bond does not already require a barrier crossing. Traditionally, HOMO-LUMO gaps have been used as a quick test of stabilities, though it is only a useful approximation (after all, the terms are temperature independent while relative stabilities can change with temperature). The MINDO computed HOMO-LUMO gaps are 9.54, 9.57, 9.28, and 9.56 eV for the *anti-exo*, *anti-endo*, *syn-exo*, and *syn-endo*, respectively. Hence, the quotient is not well correlated with the thermodynamic or kinetic stability (its discriminatory power is not very impressive either, as three of the values are too close). Finally, let us mention that as long as we deal with the relative activation terms there is no need to address specifically the symmetry numbers of the activated complexes [16, 17], as their contribution exactly cancels out.

Activated complexes frequently exhibit some long bonds, and we indeed observed this feature (Table 1). In fact, the AM1 and PM3 methods were introduced in order to correct failures of the MNDO procedure (hydrogen bonds, small rings, energies at van der Waals distances). Hence, it is useful to check the MNDO results for activated complexes with the more advanced AM1 and PM3 methods, and we indeed repeated the kinetic treatment (Table 2). The most important change concerns the *syn-exo* activated complex, as this reaction path exhibits the highest forward rate, i.e., both AM1 and PM3 predictions agree with the observation. Of course, the forward process is decisive only for relatively short times; for long times it competes with the backward kinetics (and eventually the thermodynamic equilibrium results from the competition).

Table 2. The AM1 and PM3 computed relative activation enthalpies (H) and Gibbs functions (G) (kJ/mol).

Approach	$R_{CC}^{\neq}$ [a] (Å)	$\Delta H_{298}^{\neq}$	$\Delta G_{353}^{\neq}$
AM1			
anti-exo	1.793	23.3	24.5
anti-endo	1.802	12.3	15.5
syn-exo	1.834	−5.8	−3.9
syn-endo	1.808	0.0	0.0
PM3			
anti-exo	2.254; 2.263	−10.2	5.4
anti-endo	1.704	2.8	6.0
syn-exo	1.765	−1.6	−1.6
syn-endo	1.728	0.0	0.0

[a] The CC bond(s) created in the activation process.

The relative $\Delta H_{298}^{\neq}$ and $\Delta G_{353}^{\neq}$ terms possess similar proportions in the AM1 computations but not in the PM3 treatment. In the latter case we actually encounter an interesting overcompensation by the entropy term. The Gibbs function is a rigorous measure of stability; enthalpy is only an approximation of the G term. The approximation is good if the entropy part is not significant. From a purely physical point of view we should discuss only the Gibbs function, but this is still rarely done as its evaluation is more demanding. The PM3 *anti-exo* activated complex is an exceptional case. Only in this situation we could find an activated complex with two C-C bonds (though quite long Table 2). Those two C-C bonds produce a higher rigidity of the complex, which is sensed by the entropy term. As the entropy term is lowered, the Gibbs function is increased (which is enhanced by a relatively high temperature of 353 K). We cannot say for sure if this activated complex with two C-C bonds is a physical reality or rather a computational artifact. This could only be decided at a correlated *ab initio* level, the treatment being practically impossible for our system, at least at present. However, it is not critically important as the *anti-exo* path is not important in experiment. There is still another question: should we

prefer the AM1 or PM3 predictions? The semiempirical methods are primarily tested on stable molecules as there are precise thermochemical data available for the species. For example, in a set of halogen-atom containing molecules [11] the AM1 method had a better performance: the mean signed error in calculated heats of formation was 0.53 and 3.01 kcal/mol for the AM1 and PM3 method, respectively. However, a similar comparison for activation terms is rare [18] – the computations are more demanding and experimental data less common and probably less precise. Hence, we cannot really decide yet which of the two methods should be given preference.

4. Conclusion

The semiempirical quantum-chemical methods MNDO, AM1, PM3 in a mutual agreement confirm the experimental finding of only two adducts out of four conceivable products in the additions of cyclopentadiene to the facially dissymmetric tetracyclofused maleic anhydride. The selectivity is the same, regardless if we consider thermodynamic or kinetic control. The activation process should happen within only one activated complex, and only one C-C bond should be created in the first part of the activation process. The computations were performed in terms of the Gibbs function, i.e. in rigorous thermodynamic and kinetic terms. Finally, a correlated *ab initio* check of all the semiempirical findings would be highly desirable though practically impossible at present.

Acknowledgements

The research was supported by the National Science Council, Taiwan, Republic of China, and the National Chung-Cheng University. The authors also thank the National Center for High-Performance Computing in Hsinchu for computer time on the Convex C3840 and Convex-SPP machines.

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