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CYCLOADDITION REACTION OF TROPONOIDS WITH MALEIC ANHYDRIDE, MECHANISTIC STUDY

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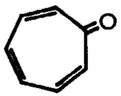
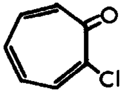
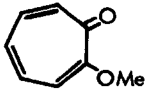
Diels-Alder reaction is kinetically characterized by the large negative entropy of activation ($\Delta S^{\ddagger}$ $\sim$-35 eu) and small frequency factor (log A~6), which indicate highly ordered transition state and synchronous formation of new σ-bonds (1, 2).

Ionic two-step mechanism was once suggested (3) for cycloaddition reaction of troponoids with maleic anhydride (MA) mainly from the fact that, while 2-methoxytropone yielded endo product stereospecifically, tropolone afforded both endo and exo products in nearly equal ratio. However, the tight transition state was later revealed for the cycloaddition reaction with acrylonitrile on the basis of the isotopically labeled experiment (4). Consequently, kinetic study of the former reactions was undertaken, using tropone (I), 2-chlorotropone (II), 2-methoxytropone (III) and tropolone (IV), in the solvents with different polarity in order to establish the nature of the transition state by observing the extents of substitution effect and solvent dependency of the reaction.

The reaction was carried out at four different temperatures in p-cymene and in adiponitrile under pseudo-1st order condition (5) and followed by the decrease in the intensity of the UV maxima of troponoids. The resulted reaction rates and activation parameters are listed in TABLES I and II, except for IV which is discussed later.

The activation parameters shown in TABLE II are in good agreement with the general values found for the typical Diels-Alder reaction (1, 2). Further, the rate constant k shown in TABLE I decreases in the order of MeO > H > Cl in each solvent, the reversed order from that for the reactions of troponoids and cyclopentadiene (F > Cl > H > OMe) (6) and the relative rates $k_{H/Cl}(=k_{I/II})$ and $k_{MeO/Cl}(=k_{III/II})$

TABLE I. The Rates for Cycloaddition Reaction of Troponoids with Maleic Anhydride

			 I				 II				 III		
Reaction rates* ($\times 10^5$/sec)	k_A		k_B			k_A	k_B		k_A		k_B		
Relative ratios		k_A I/II		k_B I/II	$k_{B/A}$			$k_{B/A}$		k_A III/II		k_B III/II	$k_{B/A}$
at 120°C	3.78	(5.3)	2.02	(3.0)	0.53	0.718	0.678	0.94	5.83	(8.1)	4.82	(7.1)	0.83
130	6.03	(4.6)	3.60	(3.0)	0.60	1.30	1.21	0.93	10.1	(7.8)	7.38	(6.1)	0.73
140	8.95	(2.9)	7.52	(3.5)	0.84	3.05	2.12	0.70	17.7	(5.8)	14.9	(7.0)	0.84
150	19.7	(4.1)	13,7	(3.8)	0.70	4.78	3.60	0.75	31.5	(6.6)	22.0	(6.1)	0.70

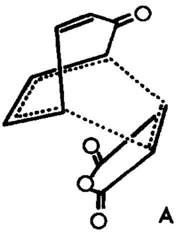
* A=in p-cymene, B=in adiponitrile

TABLE II. Activation Parameters for Cycloaddition Reaction of Troponoids with Maleic Anhydride

Troponoids	I		II		III	
Solvents*	A	B	A	B	A	B
E_a(kcal/mole)	14.5	22.1	14.3	18.5	18.9	19.1
A (/sec)	4.10×10^3	3.75×10^7	8.92×10^2	1.42×10^5	1.72×10^6	1.83×10^6
$\Delta S^{\ddagger}$ (eu)	-42.6	-24.5	-45.6	-35.3	-30.6	-30.5
$\Delta H^{\ddagger}$ (kcal/mole)	13.6	21.3	13.5	17.7	18.0	18.3
$\Delta G^{\ddagger}$ (kcal/mole)	30.8	31.2	31.9	32.0	30.4	30.5

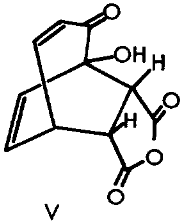
* A=p-cymene, B=adiponitrile

are much smaller than the normal ionic reaction but close to the value found in the cycloaddition of anthracene derivatives and MA (7). These values strongly indicate that the reactions proceed as the normal cycloaddition reactions through the highly oriented compact transition states in all the three cases. However, the reactions in adiponitrile are definitely slower than in p-cymene ($k_{B/A}$ in TABLE I). This observation, meaning that the stabilization by solvation of polar solvent occurs more in the starting systems than in transition states due to the dipolar character of troponoids, can be attributed to the less polar transition state such as A. Thus, all of the data provide strong collaborative evidence to the four-centered concerted mechanism for the present cycloaddition reactions. The less negative $\Delta S^{\ddagger}$ values in adiponitrile compared with those in p-cymene are consistent with the above conclusion.

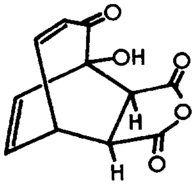


A

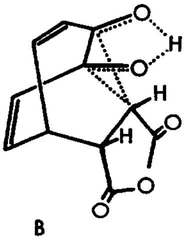
As is mentioned before, tropolone (IV) gives the exo adduct (VI) as well as the normal endo adduct (V) (3a), only exception in the mode of reactions between simple troponoids and MA. Our kinetic study provided no reliable quantitative result because V and VI form concurrently and the intensity change of the UV maximum of IV stops at early stages under the conditions used for the above reactions. However, at the lower temperatures (up to 100°), the predominant formation of V over VI was observed in the NMR spectrum of the reaction mixture. Furthermore, the mutual isomerizations between V and VI were able to be traced at 80-100° by the same technique and the reaction rate $k_{V \rightarrow VI}$ was found to be ca 1.6 times larger than $k_{VI \rightarrow V}$. Intramolecular nature of the isomerizations was verified by the reaction in the presence of tropolone-3,5,7-d_3 (IV-d_3) (8); No IV-d_3 was incorporated in the reaction products at the earlier stage of the reaction (9). Therefore, the major course of the cycloaddition reaction can be visualized by the initial formation of V as in the other cases, followed by the intramolecular isomerization to VI possibly via transition state B, although the direct formation of VI can not be ignored (10).



V



VI



B

Information about the shape of the transition state in the cycloaddition was obtained from the investigation of the cycloreversions. Activation parameters, Ea ~34 kcal/mol, A ~4×10^{13}/sec. and $\Delta S^{\ddagger}$~+3.5 eu. were found for both reactions, V→IV + MA and VI→IV + MA, the values comparable for the general cycloreversions (11). Furthermore, secondary isotope effect k_H/k_D determined using V-d_3 and VI-d_3, was found to be 1.03 and 1.09 for V and VI, respectively. These values are again in good agreement with those found in the similar cycloreversions (12). From these pieces of evidence, the transition state in the reactions IV→V is also highly oriented as in the other cases described before.

References and Footnotes

1) For example, A. Wassermann, "Diels-Alder Reactions", Elsevier, New York (1965).

2) J. Sauer, Angew. chem. internat. Edit., **6**, 16 (1967) and the literatures cited therein.

3) a. S. Itô, H. Takeshita, Y. Shoji, Y. Toyooka and T. Nozoe, Tetrahedron Letters, 3215 (1968), b. Y. Toyooka, Ph.D. Thesis, Tohoku University (1960).

4) S. Itô, H. Takeshita and Y. Shoji, Tetrahedron Letters, 1815 (1969).

5) The molar ratio, maleic anhydride/troponoids, was fixed to 20. The reaction rates were practically unchanged at the ratio of 40.

6) K. Sakan, unpublished results.

7) J. Sauer, D. Lang and A. Mieler, Angew. chem., **74**, 352 (1962).

8) S. Itô, J. Tsunetsugu, T. Kanno, H. Sugiyama and H. Takeshita, Tetrahedron Letters, 3659 (1965).

9) At the later stage of the reaction, a considerable amount of IV was formed.

10) The direct formation of VI was implied from the fact that the exo-endo ratio obtained under the same reaction condition is larger for the cycloaddition reaction than for the isomerization.

11) A. Wassermann, Trans. Faraday Soc., **34**, 128 (1938).

12) P. Brown and R.C. Cookson, Tetrahedron, **21**, 1993 (1965), S. Seltzer, J. Am. Chem. Soc., **87**, 1534 (1965), **85**, 1360 (1963), Tetrahedron Letters, 457 (1962).