INTRAMOLECULAR DIELS-ALDER REACTION OF BICYCLO[6.4.0]DODECA-4,9,11-TRIENE

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<u>Abstract</u>: cis-Bicyclo[6.4.0]dodeca-4,9,11-triene (5) has been synthesized and the kinetics of its intramolecular Diels-Alder reaction have been measured from 50-75°C

Intramolecular Diels-Alder reactions find a growing application in modern organic synthesis because they are highly stereospecific and sufficiently exothermic to allow the construction of strained systems. Kinetic measurements of these reactions, however, are scarce and were performed on substrates, which for synthetic reasons were heavily substituted¹⁾. We report on the intramolecular Diels-Alder reaction of cis-bicyclo[6.4.0]dodeca-4,9,11-triene (5) which is not affected by substituents and for which intermolecular models are well documented.

Earlier attempts to synthesize **5** or its 9,10,11,12-tetrachloro derivative remained without success, as the compounds cyclize already at room temperature²⁾. Therefore, our strategy called for the introduction of the dienophilic double bond at low temperature in the last step of the synthetic sequence (s.Scheme 1): The adduct 1^{2a} of 7,7-dimethoxy-tetrachlorocyclopentadiene to cycloocta-1,5-diene was reduced with sodium in liquid ammonia after which chlorine was added to the less shielded double bond by means of iodobenzene dichloride. The mixture of diastereomeric dichloroketals 2 was hydrolyzed with 80% aqueous acetic acid to give the ketones 3, which were decarbonylated by flash vacuum pyrolysis at 350°C. The resulting diastereomeric dichlorides 4^{3} could be separated by column chromatography on silica gel with pentane. The crucial elimination of chlorine from the mixture of cis- and trans-4 was achieved in 59% yield with disodium phenanthrene in THF (0.5 M) at 0°C.



cis-Bicyclo[6.4.0]dodeca4,9,11-triene $(5)^{4)}$ cyclizes slowly at room temperature to tetracyclo[6.4.0.0^{4,12}.0^{5,9}]dodecene-10 $(6)^{2a,5)}$. This intramolecular cycloaddition is faster than the intermolecular addition of maleic anhydride (2.5 M in CDCl₃) and only the highly reactive 4-ethyl-1,2,4-triazoline-3,5-dione (ETAD) yields a Diels-Alder adduct. The rate of the intramolecular Diels-Alder reaction of 5 was measured in n-dodecane solution (10^{-4} M) by monitoring continuously the decrease of the extinction of the educt at 285 nm. The first order rate constants (50.3°C, 0.71E-04 sec⁻¹), (55.2, 1.06E-04), (59.9, 1.68E-04), (65,0, 2.85E-04), (70.2, 4.76E-04) and (75.0, 7.70E-04) follow the Arrhenius equation:

 $log(k) = (10.58 \pm 0.34) - (21850 \pm 520)/2.303 * RT$



At the average temperature of 62.6°C the kinetic parameters are $\Delta H^{\#} =$ 21.18 \pm 0.52 kcal/mol and $\Delta S^{\#}$ = -12.34 \pm 1.53 eu which may be compared with the respective values⁶⁾ for the <u>intermolecular</u> cycloaddition of propene to cyclohexa-1,3-diene to give exo-5-methyl-bicyclo[2.2.2]octene-2 (7), i.e. $\Delta H^{\#} = 26.7$ kcal/mol and $\Delta S^{\#} = -34.7$ eu at 283°C. It becomes clear that the large acceleration of the intramolecular reaction is mainly due to an increase of $\Delta S^{\#}$ by 22 units. The remaining activation entropy of -12 eu is in the same order of magnitude which is needed for the freezing of eight or nine membered rings in the transition states of 1,5-hydrogen shifts⁷⁾ or 6e electrocyclic ring closures⁸⁾. It has to be noted, however, that a decrease of the activation enthalpy also accelerates the intramolecular cycloaddition. The amount of 4.8 kcal/mol vs.the intermolecular model reaction may be too large due to the differences in temperature and phase of the measurements but the trend should be right. This is surprising from the thermodynamic point of view, since - because of the steric strain in the cage product $\mathbf{6}$ - the cyclisation of $\mathbf{5}$ is less exothermic by 17 kcal/mol than the intermolecular model reaction⁹⁹. However, a calculation of the steric strain in the transition states of both reactions for synchronous bond formation at a distance of 2.2 Å between the reacting centers shows that the transition state of the model reaction retains the strain of the educts whereas that of the intramolecular cycloaddition looses 1.2 kcal /mol of strain. The calculation thus explains the experimental result by indicating that the transition state of an intramolecular Diels-Alder reaction may be attained with release of strain whereas the considerable strain of the product is built up in a later stage of the reaction.

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References and Notes

 H. G. Gschwend, A. O. Lee, H.-P. Meier, J. Org. Chem. 1973, 38, 2169.
a) J. A. Akhtar, G. J. Fray, J. M. Yarrow, J. Chem. Soc. C, 1968, 812; b) M. S. Raasch, J. Org. Chem. 1980, 45, 856.

3) trans-4: ¹H-NMR (300 MHz, C_6D_6): $\delta = 5.74$ (2H), 5.42 (1H), 5.27 (1H), 3.99 (2H), 2.29 (1H), 2.07 (2H), 1.8-1.1 (7H); ¹³C-NMR (75.5 MHz, C_6D_6): $\delta =$ 131.27, 131.15, 123.63, 123.53, 66.90, 66.67, 36.24, 35.50, 31.81, 31.33, 24.95, 23.97; DA adduct with N-phenylmaleimide: mp 245°C (from benzene). cis-4: mp 55°C; 1H-NMR (90 MHz, C_6D_6): $\delta = 5.62$ (AA'BB',4H), 4.10 (2H), 2.5-0.9 (10H); DA adduct with N-phenylmaleimide: mp 261°C (from benzene).

4) 5: ¹H-NMR (300 MHz, C_6D_6): $\delta = 5.89$ (H10,11), 5.58 (H9,12), 5.50 (H4,5), 2.57 (H1,8), 2.45 (2H), 2.01 (2H), 1.87 (2H), 1.28 (2H); ¹³C-NMR (75.5 MHz, C_6D_6): $\delta = 132.43$, 128.80, 123.83, 36.59, 28.66, 27.99; UV (cyclohexane): $\lambda_{max} = 240$ nm ($\varepsilon = 2190$), 250 (3490), 257 (3950), 260 (3840), 264 (3530) 270 (2830), 280 (1300); DA adduct with ETAD: mp 153°C; Anal.Calcd for $C_{16}H_{21}N_3O_2$: C,66.88; H,7.37; N,14.62. Found: C,66.60; H,7.04; N,14.51.

5) **6**: mp 84°C; ¹H-NMR (300 MHz, C_6D_6): $\delta = 6.27$ (2H), 2.07 (2H), 1.69 (4H), 1.61 (4H), 1.33 (4H); ¹³C-NMR (75.5 MHz, C_6D_6): $\delta = 131.30$ (C10,11), 43.10 (C9,12), 40.53 (C1,4,5,8), 26.10 (C2,3,6,7).

6) G. Huybrechts, H. Poppelsdorf, L. Maesschalck, B. van Mele, Int. J. Chem. Kinet. 1984, 16, 93.

7) D. S. Glass, R. S. Boikess, S. Winstein, Tetrahedron Lett. 1966, 999.

8) E. Vogel, W. Grimme, E. Dinné, Tetrahedron Lett. 1965, 377.

9) A force field calculation (MMPM1, Serena Software, Bloomington, Ind.) gives the following standard enthalpies of formation and strain energies: 5 (ΔH°_{f} = 36.4 kcal/mol, SE = 18.2 kcal/mol), 6 (22.5, 40.6), 7 (-0.8, 15.3).



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