Tetrahedron Letters No. 34, pp 2965 - 2968, 1975. Pergamon Press. Printed in Great Britian.

KINETICS OF 2+2 CYCLOADDITIONS OF DIPHENYLKETENE TO ENOL ETHERS; THE STRUCTURE OF THE ORIENTATION COMPLEXES

Rolf Huisgen * and Herbert Mayr

Institut für Organische Chemie der Universität, 8 München 2, Karlstr. 23 (Germany)

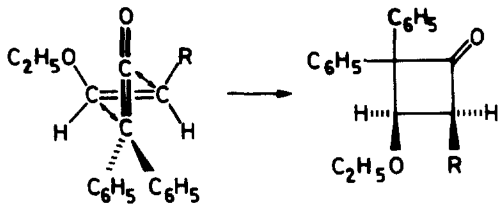
(Received in UK 23 June 1975; accepted for publication 10 July 1975)

Diphenylketene combines stereospecifically with cis- and trans-propenyl propyl ether to produce 4-methyl-2,2-diphenyl-3-propoxy-cyclobutanones; the cis enol ether reacts 170 times faster than the trans isomer.[1] This impressive cis preference was later observed in further ketene cycloadditions,[2-5] but appears to be unknown in other areas of olefinic reactivity.

The $[_{\pi}2_a + _{\pi}2_s]$ mechanism of Woodward and Hoffmann[6] offers a clue to the phenomenon. The ketene and a cis disubstituted ethylene can form an orientation complex (e.g., 1) with the orthogonal arrangement of the bond systems, in which the ketene substituent enters into van der Waals repulsion only with olefinic hydrogen. The position of the double-headed arrows for the incipient σ bonds is determined by the regioselectivity of these cycloadditions which give 3-alkoxycyclobutanones. In the addition to the trans olefin, however, one ketene substituent must squeeze into the gap between one vinyl-H and one substituent (as in 3 or 5). This steric strain is increased during the subsequent twisting motion within the $[_{\pi}2_a + _{\pi}2_s]$ mechanism and appears to be responsible for the lower reactivity of trans olefins.

The orientation complex of the reactants is suggested as an appropriate model for the transition state to correlate substituent effects and rates: 1. Cyclobutanone formation from ketenes and olefins is exothermic; 2. The reaction of ethyl cis-propenyl ether with diphenylketene in benzonitrile shows $\Delta H^{\ddagger} = 7.0$ kcal/mol and $\Delta S^{\ddagger} = -45$ eu, i.e., the entropy term makes up for 67% of the activation free energy at 40°. Therefore, bond making cannot be progressed very far in the transition state. With the formation of the orientation complex of the reactants the entropy price has been paid.

The photometric rate constants[7] of Table I confirm the result of the earlier competition experiment:[1] trans-alkenyl ethers react with diphenylketene ~10^2 faster than cis-alkenyl ethers. In the variation of β-alkyl



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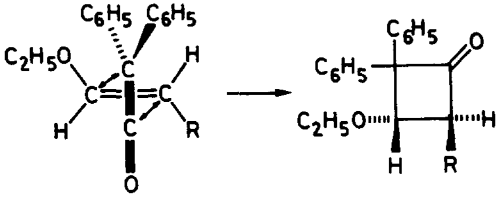

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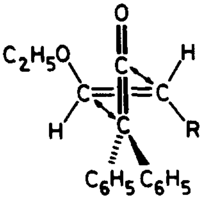

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from methyl to *t*-butyl steric strain counteracts the accelerating electron release by R. The nature of the β-alkyl has only a minor influence on k_{cis}/k_{trans} indicating that the *relative* steric hindrance in the reactions of *cis*- and *trans*-alkenyl ethers remains constant, in accordance with orientation complexes **1** and **3**. How can one exclude complex **5** as a reasonable alternative ?

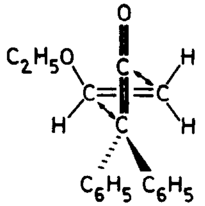
Table I. Cycloaddition Rate Constants of Diphenylketene to cis-trans Isomeric 1-Alkenyl Ethyl Ethers ; 10^4k_2 (l · mol^{-1}sec^{-1}) in Benzonitrile at 40°

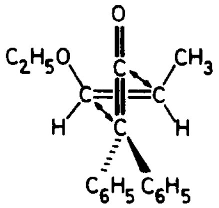
R	Formation of **2** (cis)	Formation of **4** (trans)	k_{cis}/k_{trans}
CH_3	109	1.29	84
C_2H_5	128	1.20	107
$CH(CH_3)_2$	117	0.742	158
$C(CH_3)_3$	~ 3.65	0.054	~ 68

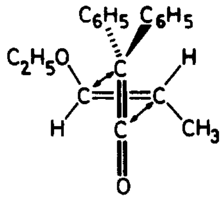
A PMO treatment reveals that ketene cycloadditions proceed the faster the lower the orbital energy of the ketenes LU(C=C) and LU(C=O) and the higher that of the HO(ketenophile) are.[8,9] The successive replacement of the β-hydrogens of ethyl vinyl ether by methyl increases the HO energy - the ionisation potential decreases by ~0.45 eV for each methyl (Table II)[10] - and should accelerate the cycloaddition.

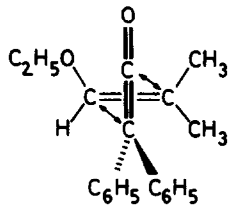
However, only the step from vinyl to *cis*-propenyl ethyl ether (complex 7) is accompanied by a 2.4fold increase of the rate constant. The *trans*-propenyl ether (complex 8) reacts 84 times slower than the cis isomer corresponding to a difference in activation free energy of 2.7 kcal/mol. The *steric* nature of the decelerating effect is emphasized by the virtually equal free energy content of *cis*- and *trans*-propenyl ethyl ether (58% cis + 42% trans at 25°).[11]

Table II. Rate Constants for Cycloadditions of Diphenylketene to Vinyl Ethyl Ether and its C-Methyl Derivatives in Benzonitrile at 40°









	6	7	8	9
$10^4 k_2$ ($l \cdot mol^{-1} sec^{-1}$)	45	109	1.29	~ 0.0015
$\Delta\Delta G^{\ddagger}$ ($kcal \cdot mol^{-1}$)	≡ 0	− 0.55	+ 2.20	+ 6.4
IP (eV)	8.95	8.48	8.47	8.04

Despite its higher HO energy, isobutenyl ethyl ether shows a dramatic reduction of cycloaddition rate. In the conceivable orientation complexes the ketene phenyl has here only the choice between bad and worse van der Waals strain. On comparing the less crowded orientation complex 9 of the isobutenyl ether with the corresponding complex 7, one observes a 70 000fold rate decrease ; $\Delta\Delta G^{\ddagger} \sim 7$ kcal/mol reveals an impressively large interaction between phenyl and β-methyl in the transition state.

The activation free energy of the diphenylketene cycloadditions to *trans*-propenyl and isobutenyl ether differ by 4.2 kcal/mol. If the *trans*-propenyl ether were to react *via* the complex 5, R = CH_3, the 860fold decrease of the addition constant after introduction of the second β-methyl would be unintelligible.

The comparison of the rates *via* complexes 6 and 7 even suggests that the additional methyl group should increase the rate constant in going from 5, R = CH_3, to 9. Thus, we must conclude that the *trans*-propenyl ether reacts via 8, i.e., the ketene phenyl prefers to cram into the gap between ethoxy and hydrogen.

The smaller hindrance by alkoxy compared with β-alkyl may be due to the s-trans conformation of the enol ether. Furthermore, substituents in the β position hinder the twisting motions in the transition state more than in α position, according to molecular models.

What is the reason for the regioselectivity leading to 3-alkoxycyclobutanones exclusively ? In the transition state the σ bond between the α carbon of the ketene and the β carbon of the enol ether is somewhat more developed than the second σ bond. That places a partial anionic charge on the ketene oxygen while a partial positive one resides on the enol ether moiety. In the language of perturbation theory the large atomic orbital coefficients on the α carbon of LU(ketene) and on the β carbon of HO(enol ether) guarantee a more efficient interaction. The predominance of the interaction LU(ketene) - HO(enol ether) causes a net flow of negative charge from enol ether to ketene in the transition state.

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