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STERIC COURSE, KINETICS AND MECHANISM OF THE 2+2 CYCLOADDITIONS OF ALKYLPHENYLKETENES TO ETHYL CIS- AND TRANS-PROPENYL ETHER

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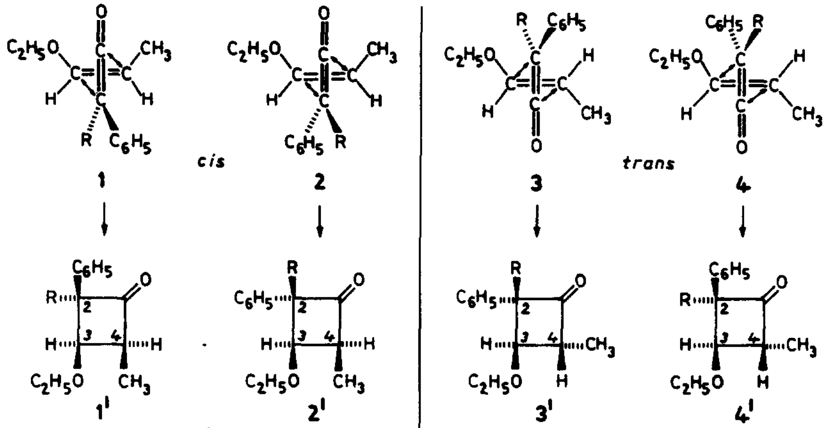
The reaction of alkylphenylketenes with the cis-trans isomeric ethyl propenyl ethers in benzonitrile at 40° quantitatively produces the cyclobutanones 1′ - 4′ with retention of ketenophile structure. The configurational elucidation by nmr[2] allows to deduce the structure of the orientation complexes 1 - 4 of the $[_{\pi}2_a + _{\pi}2_s]$ reaction (Table I). The double arrows indicate the incipient σ bonds.

In the preceding communication we have demonstrated that the orientation complex is a good model for the transition state and that trans enol ethers choose orientation complexes of type 3 and 4 in which the ketene substituent is placed between ethoxy and hydrogen.[3] In 1 and 3 the ketene alkyl is in the zone of steric pressure while it is phenyl in 2 and 4.

With increasing bulk of R the formation of cyclobutanone 2′ from ethyl cis-propenyl ether is favored over 1′, i.e., the thermodynamically less stable product is always preferred. This is attributed to the increase of van der Waals strain in 1 on varying R from methyl to t-butyl. Whereas ethylphenyl- and propylphenylketene use the pathways via 1 and 2 to a nearly equal extent, isopropylphenyl- and t-butylphenylketene react only via 2. The predilection for the sterically more crowded cyclobutanone is analogous to the behavior of cyclopentadiene[4] and other cis disubstituted ethylenes[5] towards mixed ketenes.

On the other hand, the cycloaddition to the trans enol ether furnishes predominantly the more stable product via the more favored orientation complex (3 for methyl to propyl, 4 for isopropyl and t-butyl). A meaningful interpretation of 3 : 4 rests on the assumption that the ketene substituent is located between ethoxy and hydrogen. If methyl and hydrogen of the enol ether were to interact with the ketene substituent in the orthogonal arrangement, an increase of the ratio 3′ : 4′ should accompany the branching of R in contrast to observation.

Table I. Orientation Complexes, Product Distribution, Partial Rate Constants ($10^6 k_2$, $l \cdot mol^{-1} sec^{-1}$) and Activation Free Energies for the Cycloadditions of Alkylphenylketenes to Ethyl cis- and trans-Propenyl Ether in Benzonitrile at 40°



R	% yield	k_1	$\Delta G_1^{\ddagger}$	% yield	k_2	$\Delta G_2^{\ddagger}$	% yield	k_3	$\Delta G_3^{\ddagger}$	% yield	k_4	$\Delta G_4^{\ddagger}$	$\frac{k_1}{k_3}$	$\frac{k_2}{k_4}$
CH_3	88	985	22.68	12	130	23 94	100	61	24.41	0	–	–	16	–
CH_2CH_3	54	77	24.26	46	65	24.37	90	3.5	26.19	10	0.40	27.54	22	164
$CH_2CH_2CH_3$	51	65	24.37	49	62	24.40	87	2.4	26.42	13	0.35	27 62	27	176
$CH(CH_3)_2$	–	–	> 26.80	100	26	24 94	15	0.022	29.34	85	0.13	28.24		200
$C(CH_3)_3$	–	–	–	100	5.1	25.95	0	–	–	100	0.028	29.19		183

The combination of kinetic data with the stereochemical results allows a quantitative evalution. The photometrical addition rate constants for the cis- and trans-propenyl ether are partitioned according to product composition (Table I), i.e., $k_{cis} = k_1 + k_2$, and $k_{trans} = k_3 + k_4$.

The decrease of k_2 and k_4 with growing bulk of R cannot have steric reasons because R is pointing outwards and is hence not involved in the steric interaction of ketene and ketenophile substituents in 2 and 4. Probably, two electronic factors cooperate in reducing the cycloadditions rate by lifting the ketene LUMO energy : the electron release by R (Taft's σ^*) as well as the out-of-plane twisting of phenyl increase with branching of R.

On varying the alkylphenylketene from methyl to isopropyl one observes that $\Delta G_1^{\ddagger}$ increase by 4 kcal/mol and $\Delta G_2^{\ddagger}$ only by 1.0 kcal/mol. With the same electronic deactivation in both series the additional 3 kcal/mol in $\Delta G_1^{\ddagger}$ reflect the greater steric strain in the transition state on replacing methyl by isopropyl.

Analogously, $\Delta G_3^{\ddagger}$ increases more steeply than $\Delta G_4^{\ddagger}$.

In the complexes 1 and 3 the ketene alkyl is oriented toward the interior, the region of van der Waals repulsion. The increase of k_1/k_3 from 16 for R = methyl to 27 for propyl mirrors the additional energy consumption in overcoming the interference of R with ethoxy and hydrogen in 3 compared with that of R between two hydrogens in 1.

On the other hand, the cis-trans rate ratio k_2/k_4 stays in the range of 180 ; *i.e.*, 3.2 kcal/mol are required to conquer the additional steric repulsion of phenyl between ethoxy and hydrogen in 4 *vs.* that of phenyl and two hydrogens in 2. *The ratio k_2/k_4 does no longer depend on the size of R which juts outwards and, therefore, plays no active role in the steric interaction of the substituents in the transition state.* As R ends up at the cis position to ethoxy in 2′ and at the trans location in 4′, the constancy of k_2/k_4 is only reconcilable with an early transition state.

Ethyl *cis*- and *trans*-propenyl ether having nearly equal free energies,[6] the rate ratios k_1/k_3 and k_2/k_4 reveal unique steric effects in the transition states. Though the singular preference for cis 1,2-disubstituted ethylenes as ketenophiles is a significant mechanistic criterion, it is not an unequivocal proof for the $[{}_{\pi}2_a + {}_{\pi}2_s]$ process. The findings are also consistent with a concerted pathway $[{}_{\pi}2_s + {}_{\pi}2_s + {}_{\pi}2_s]$ [7] for which a diagonal attack of the ketenophile π system on one orbital each of the CC and the CO double bond of the ketene is postulated. While the orientation complexes are still different, the two schemes are becoming virtually indistinguishable as the rehybridization proceeds.

Apparently, the cis preference does not occur in 2+2 cycloadditions *via* zwitterionic intermediates ; the cyclobutane formation from tetracyanoethylene and enol ethers may be regarded as a prototype.[8] The rate ratios of TCNE with *cis*- and *trans*-1-alkenyl alkyl ethers are close to unity.[9]

REFERENCES

1) The new cyclobutanones gave satisfactory CH analyses and were characterized by their spectra.

2) H. Mayr and R. Huisgen, *Tetrahedron Lett.*, 1349 (1975).

3) R. Huisgen and H. Mayr, *Tetrahedron Lett.*, preceding communication.

4) P.R. Brook, J.M. Harrison, and A.J. Duke, *J.C.S. Chem.Comm.*, 589 (1970) ; M. Rey, S. Roberts, A. Dieffenbacher, and A.S. Dreiding, *Helv.Chim.Acta*, **53**, 417 (1970) ; W.T. Brady and R. Roe, *J.Amer.Chem.Soc.*, **92**, 4618 (1970) ; W.T. Brady and E.T. Hoff, *J.Org.Chem.*, **35**, 3733 (1970).

5) T. Do-Minh and O.P. Strausz, *J.Amer.Chem.Soc.*, **92**, 1766 (1970) ; W.T. Brady and R. Roe, *ibid.*, **93**, 1662 (1971) ; W.T. Brady, F.H. Parry, and J.D. Stockton, *J.Org.Chem.*, **36**, 1486 (1971) ; R.C. De Selms and F. Delay, *ibid.*, **37**, 2908 (1972).

6) T. Okuyama, T. Fueno, and J. Furukawa, *Tetrahedron*, **25**, 5409 (1969).

7) R.B. Woodward, private communication to R.H., 1968 ; see R. Huisgen, L.A. Feiler, and G. Binsch, *Chem.Ber.*, **102**, 3460 (1969).

8) R. Huisgen and G. Steiner, *J.Amer.Chem.Soc.*, **95**, 5054, 5055 (1973) ; G. Steiner and R. Huisgen, *ibid.*, **95**, 5056 (1973) ; R. Huisgen, R. Schug, and G. Steiner, *Angew.Chem.*, *Int.Ed.Engl.*, **13**, 80, 81 (1974).

9) R. Huisgen and G. Steiner, *Tetrahedron Lett.*, 3763 (1973).