The Ene Reaction of Maleic Anhydride with Alkenes

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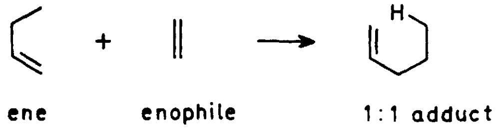
The kinetics of the ene reaction between maleic anhydride and various alkenes have been investigated. The kinetics, based on a 100% mass balance, have been determined for a number of alk-1-enes ranging from hex-1-ene to dodec-1-ene and for *cis*- and *trans*-dec-5-ene. The reaction has been found to follow second-order kinetics up to 75% conversion with no significant solvent effects. The kinetics have been determined over the range 125—224 °C and the Arrhenius parameters have been calculated. In the absence of detectable quantities of cyclobutane derivatives in the product and the negligible effect of free radical inhibitors on the rate of the ene reaction, a concerted mechanism is favoured. The *trans*-configuration of the products, alkenylsuccinic anhydrides, and the lack of variation of the reaction rate with increasing alkyl chain length of the alk-1-enes point to an *exo*-transition state. *trans*-Dec-5-ene appears to favour an *exo*-transition state whilst the greater negative entropy of activation for *cis*-dec-5-ene is attributed to steric hindrance favouring an *endo*-transition state.

THE ene reaction has been defined as the indirect substituting addition of a compound with an electron deficient double bond (enophile) to an alkene possessing an allylic hydrogen atom (ene).[1] Early reported examples of the ene reaction include the thermal Prins reaction [2] but current interest in this reaction stems from a paper by Alder *et al.*[3] A comprehensive review was published by Hoffman [1] in 1969.



The majority of the published work on the ene reaction is of a qualitative nature [4] and most of the quantitative work appears to be on relative rates of reaction,[5] or based on the disappearance of one reactant.[6]

In this paper the investigation of the quantitative aspects of the ene reaction based on a full mass balance is described.

EXPERIMENTAL

Reactants.—The reactants and solvents were obtained as the purest grade available from commercial sources (B.D.H., Koch–Light, Flurochem Ltd). The reactants and solvents were distilled under nitrogen and middle cut fractions were used in the kinetic experiments.

The 1 : 1 adducts were prepared by reaction of the alkenes and maleic anhydride. The adducts were purified by molecular evaporation and characterised by microanalysis, mass spectrometry, and i.r. and n.m.r. spectroscopy. The spectroscopic analyses indicated that the double bond in the 1 : 1 adduct had a *trans*-configuration.

Reaction System.—The reactants and solvent were weighed into thick-walled glass reaction tubes of 25 cm^3 volume, which were then sealed, warmed to 60 °C to homogenise the reactant mixture, and then placed in a thermostat bath for the required time (6 h—20 days). On removal, the contents of the tubes were diluted to 25 cm^3 with acetone. Portions of the acetone solution were used for the analysis of maleic anhydride, alkene, and 1 : 1 adduct.

Analysis.—Maleic anhydride was analysed by extracting a portion of the reaction mixture in chloroform with excess of water and titrating the aqueous solution of maleic acid with standard sodium hydroxide solution.[6] Under these conditions, maleic anhydride hydrolysed rapidly and completely whilst the 1 : 1 adduct was stable and remained in the organic phase.

The alkene and 1 : 1 adduct were quantitatively analysed by g.l.c. by reference to a suitable internal standard. 95% Confidence limits for the analyses were in the range ±1—3% over the full range of concentrations encountered (Table 1).

TABLE 1

G.l.c. analysis of alkenes and alkenylsuccinic anhydrides

Solute	Column †	T/K	Internal standard
Hexene	10% Carbowax 20M on Chromosorb	338	Benzene
Isohexene	10% Carbowax 20M on Chromosorb	338	Benzene
Octene	3% OV1 on Universal	338	n-Heptane
Dec-5-ene	3% OV17 on Universal	348	n-Nonane
Dodecene	3% OV1 on Universal	423	Diethyl adipate
HexenylSA *	3% OV17 on Universal	473	Di-n-butyl adipate
IsohexenylSA	3% OV17 on Universal	473	Di-n-butyl adipate
OctenylSA	3% OV17 on Universal	483	Octadecene
DecenylSA	3% OV17 on Universal	473	Di-n-pentyl adipate
DodecenylSA	3% OV17 on Universal	508	Di-n-pentyl adipate

Chromatograph: Pye 104 dual katharometer.

* SA = succinic anhydride. † All 2 m.

The mass balance using these analytical techniques was typically better than 98%.

RESULTS

The majority of the work was carried out with equimolal solutions of alkene and maleic anhydride. The concentration term molality (mol kg^{-1}) was used rather than molarity (mol l^{-1}) due to the inhomogeneity of the initial reaction mixture at room temperature. The use of molality eliminates the need to correct for changes in the density of the reaction mixture with temperature and time. Under the conditions of time and temperature used during the kinetic experiments, the conversion varied between 35 and 75%.

The reaction kinetics for all the alkenes studied were found to be second order overall and a limited number of runs at differing mole ratios of alkene and maleic anhydride indicated that the kinetics were first order with respect to both alkene and maleic anhydride. The majority of the runs were performed in the presence of quinol (2% with respect to alkene) which was used as a free radical inhibitor. In the absence of both quinol and air, the reaction kinetics

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[1] H. M. R. Hoffman, *Angew. Chem. Internat. Edn.*, **1969**, **8**, 556.

[2] H. J. Prins, *Chem. Weekblad*, **1919**, **16**, 1510.

[3] K. Alder, F. Pascher, and A. Schmitz, *Ber.*, **1943**, **76**, 27.

[4] A. M. Lautzenheiser and P. W. LeQuesne, *Tetrahedron Letters*, **1969**, 207.

[5] C. Agami, M. Andrac-Taussig, and C. Prevost, *Bull. Soc. chim. France*, **1966**, 173.

[6] C. S. Rondestvedt and B. H. Wark, *J. Org. Chem.*, **1955**, **20**, 368.

were identical to those with quinol and the limited quantity of air sealed in the tubes. In the absence of quinol and in the presence of air, a side reaction leading to the formation of a maleic anhydride–alkene copolymer occurred. An almost quantitative yield of copolymer was formed in the presence of benzoyl peroxide.

The reaction rate constants for a number of alkenes at various temperatures were calculated from plots of reciprocal molality *versus* time, for both reactants (maleic anhydride and alkene) and for the product (1 : 1 adduct), using the method of least squares. These values are shown in Table 2. Typically, values of the correlation coefficients were close to 0.99 and the range represented by the 95% confidence limits was *ca.* 10% of the mean value of the rate constants.

TABLE 2

Alkene	T/K	Rate constant (10^7k/kg^{-1} s^{-1})		
		From maleic anhydride	From alkene	From product
Hex-1-ene	398	3.721	4.051	4.140
	448	91.30	97.21	90.73
Isohexene	398	4.146	3.995	3.964
Oct-1-ene	398	3.746	4.023	3.399
	421	21.80	21.92	22.18
	448	96.41	93.92	90.15
Dodec-1-ene	398	4.140	4.300	4.019
	448	101.3	93.06	80.61
	477	364.9	407.8	287.3
	497	831.7	954.9	753.8
cis-Dec-5-ene	411	6.786	6.053	6.628
	433	18.04	18.24	17.99
	455	53.08	56.88	57.25
trans-Dec-5-ene	411	18.11	17.35	18.13
	433	49.46	54.61	50.95
	455	162.4	151.8	169.3

The solvent used for these runs was 1,2-dichlorobenzene, but kinetic runs were also performed in 1,4-dichlorobenzene, nitrobenzene, and oct-2-enylsuccinic anhydride without any significant change in the rate of the ene reaction. However, in nitrobenzene a side reaction occurred leading to loss of maleic anhydride.

As the rates of reaction of the alk-1-enes were found to be identical within experimental error, the values of all the rate constants were combined in a single Arrhenius plot. A similar Arrhenius plot for *cis*- and *trans*-dec-5-ene gave the energies and entropies of activation shown in Table 3. The least squares lines for *cis*- and *trans*-dec-5-ene were compared statistically at the 5% level of significance. The difference between the slopes of the lines was not significant at this level, but the difference between the intercepts was significant. Thus the lines were taken to be parallel but not coincident and hence an average value for the energy of activation for the dec-5-enes was calculated.

TABLE 3

Alkenes	Kinetic parameters [a]	
	Energy of activation (E/kJ mol^{-1})	Entropy of activation ($\Delta S^{\ddagger}$/J mol^{-1} K^{-1})
Alk-1-enes	90.0 ± 3.0	-152 ± 4.4
cis-Dec-5-ene	75.5 ± 6.4	-191 ± 14.8
trans-Dec-5-ene	77.1 ± 6.4	-178 ± 14.8
cis–trans-Dec-5-ene (joint value)	76.4	

[a] Experimental errors are shown as 95% confidence limits, and activation entropies refer to a standard state of 1 mol kg^{-1}.

DISCUSSION

Free Radical Effects.—The presence of a free radical inhibitor (quinol) had no effect on the rate of disappearance of reactants or appearance of products in the ene reaction of maleic anhydride and acyclic alkenes. Thus it appears that a free radical chain reaction is inoperative.

Solvent Effects.—The negligible effect of change of solvents on the rate of the ene reaction does not favour a mechanism involving the formation of discrete ionic intermediates. This does not however rule out the possibility of some charge-transfer in the transition state leading to a short lived zwitterion.

*Effect of Alkyl Chain Length in Alk-*1*-enes.*—It was expected that increasing alkyl chain length would lead to increasing steric hindrance and thus would decrease the rate of reaction. This was found not be be the case; no effect of alkyl chain length was found on passing from n-propyl to n-nonyl. This suggests that the alkyl group is orientated in such a way as to be unaffected by the incoming maleic anhydride. This suggestion is further strengthened by the observation that the alkene bond in the product appears to be in the *trans*-configuration. This latter observation is in agreement with the results published by Agami *et al.*[7] for the reaction of maleic anhydride and hex-1-ene, and Simmons [8] for the reaction of oct-1-ene with benzyne.

Relative Rates of 1,2-*Disubstituted Alkylalkenes.*—The relative rates for *cis*-, *trans*-, and alk-1-enes within the temperature range studied was *trans* > alk-1-enes > *cis*. This agrees with the results of Agami *et al.*[7] for the reaction of maleic anhydride with alkenes at 190 °C but the order of activities is directly opposite to that suggested by Hoffman [1] on the basis of chemical intuition.

The energies of activation were in the order *trans* ≈ *cis* < alk-1-enes. As the reaction requires electron-rich enes, this lowering of activation energy can be assigned in the first instance to the increased electron density of the disubstituted alkene bond. The difference in activation energies for alk-1-enes and *cis*- and *trans*-dec-5-enes leads to the existence of two isokinetic temperatures and illustrates the dangers of basing a discussion of relative rates of reaction on data pertaining to only one reaction temperature.

From the data in Table 2, approximate values for the isokinetic temperatures may be obtained by short extrapolation. Thus below 371 K, the predicted reaction rates are in the order alk-1-enes < *cis* < *trans*; between 371 and 481 K the order is *cis* < alk-1-enes < *trans*; above 481 K the order is *cis* < *trans* < alk-1-enes. The highly negative entropies of activation point to a highly ordered transition state, and the values obtained, -150 to -190 J K^{-1} mol^{-1}, are comparable with those for the 'concerted' Diels–Alder addition which has a typical value of -130 J K^{-1} mol^{-1}.

The relative order of the entropies of activation, alk-1-enes ⩾ *trans* > *cis*, can be rationalised by the

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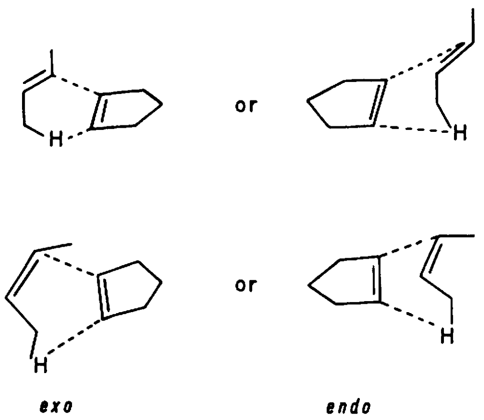
[7] C. Agami, M. Andrac-Taussig, C. Justin, and C. Prevost, *Bull. Soc. chim. France*, **1966**, **54**, 119.

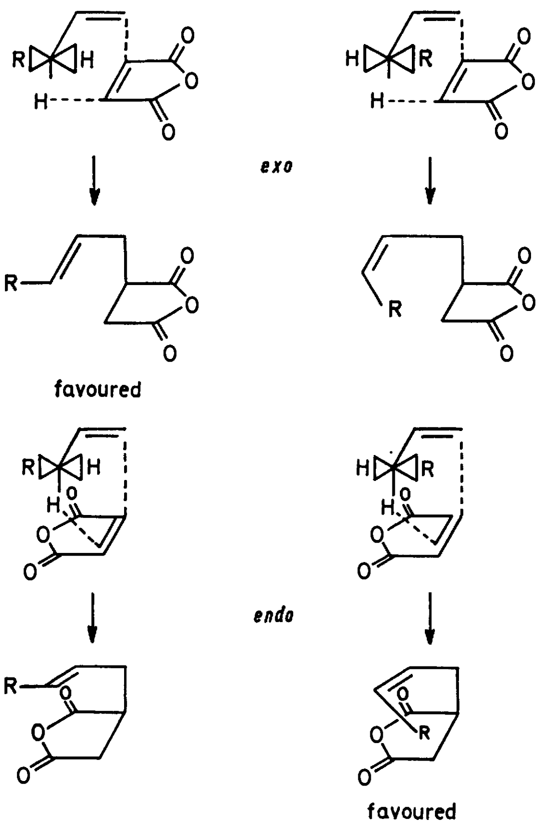
[8] H. E. Simmons, *J. Amer. Chem. Soc.*, 1961, **83**, 1657.

increased loss of degrees of freedom in the transition state associated with the extra alkyl group in the disubstituted alkenes relative to monosubstituted alkenes.

endo *versus* exo *Addition*.—Berson *et al.*[9] have concluded from the reaction of maleic anhydride and *cis*- and *trans*-but-2-ene that *endo*-addition is favoured in the ene reaction.



The present results for α-olefins and dec-5-ene are, however, better explained by *exo*-addition. Examination of models shows that *exo*-addition should lead to a *trans*-product and should be sterically favoured over *endo*-addition which would in turn favour a *cis*-bonded adduct as shown in the Scheme for α-olefins.



Scheme

In the case of *trans*-dec-5-ene, models suggest that the non-reacting alkyl group should not interact with the incoming enophile and as in the case of alk-1-enes an *exo*-transition state leading to a *trans*-double-bonded product would be expected; this agrees with the result that the product contained a large amount of the *trans*-double-bonded adduct.

In the case of *cis*-dec-5-ene, the high steric hindrance in the *exo*- should favour an *endo*-transition state. The i.r. spectra of the product was consistent with a *trans*-double-bonded adduct (band at 975 cm^{-1} and absence of bands at 1 662—1 626 and 730—665 cm^{-1}) although on the previous argument a *cis*-product would be expected from an *endo*-approach. This contradiction can be explained by the high steric hindrance afforded by the non-reacting alkyl group to the configuration required for a *cis*-product.

Thus the *cis*-dec-5-ene could react either *via* a sterically hindered *exo*-approach or *via* an *endo*-approach leading to a *trans*-product. In either case greater steric hindrance should be encountered relative to the reaction of the *trans*-dec-5-ene and this is reflected in the lower entropy of activation of the former. Further work on the reaction of symmetrical olefins of varying chain length would give further insight into this facet of the ene reaction.

Conclusions.—This paper shows that the ene reaction of maleic anhydride and acyclic alkenes does not occur *via* a free radical chain mechanism and further, due to negligible solvent effects on the reaction rate, a mechanism involving charge transfer and the resultant generation of ionic intermediates is unlikely. This work cannot differentiate between a diradical and concerted mechanism but in the absence of detectable quantities of cyclobutane derivatives a concerted mechanism is favoured.

The susceptibility of the ene reaction to steric effects has been demonstrated in the cases of alk-1-enes and *cis*- and *trans*-dec-5-ene with the result that the *exo*-transition state is sterically more favourable than the *endo* for alk-1-enes and *trans*-dec-5-ene. In the case of *cis*-dec-5-ene, where *exo*-approach is sterically hindered and *endo*-approach is favoured, the result is a decrease in the activation entropy relative to *trans*-dec-5-ene.

Further work is required to investigate quantitatively the electronic requirements of the ene and enophile, and the rates of reaction of a range of symmetrical internal alkenes.

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[5/2228 *Received, 17th November,* 1975]

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[9] J. A. Berson, R. G. Wahl, and H. D. Perlmutter, *J. Amer. Chem. Soc.*, 1964, **88**, 187.