Tetrahedron Letters No. 4, pp. 131-135, 1961. Pergamon Press Ltd. Printed
in the United States of America.

SOLVENT EFFECTS ON THE STEREOSELECTIVITY OF DIELS-ALDER REACTIONS[1]

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(Received 21 February 1961)

THE Alder rule states that of the two possible stereoisomeric adducts (*endo* and *exo*) of a cyclic diene with a dienophile, that one (usually *endo*) which is formed with the "maximum accumulation of double bonds" will preponderate.[2] The physical basis for the rule has been assumed[3] to be a lower activation enthalphy for *endo*-addition.

Although many examples of violations of this rule are known,[4] it has frequently not been experimentally clear whether the preponderance of the "abnormal" *exo*-product in these cases is the result of a kinetic preference for *exo*-addition or an isomerization subsequent to formation of a kinetically favored *endo*-adduct. Even in the cases where the product mixture is suspected to be kinetically determined, it has not been established

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[1] This research was supported in part by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the donors of said fund. We are also indebted to the Alfred P. Sloan Foundation for support of part of this work.

[2] K. Alder and G. Stein, *Agnew. Chem.* **50**, 514 (1937)

[3] A. Wassermann, *J. Chem. Soc.* 828, 1511 (1935); 432 (1936); 612 (1942); *Trans. Faraday Soc.* **34**, 128 (1938); **35**, 841 (1939); R.B. Woodward and H. Baer, *J. Amer. Chem. Soc.* **66**, 645 (1944)

which of the activation parameters is responsible for the preference.

We have now investigated the effect of temperature on the kinetic ratio of stereoisomeric products in the additions of cyclopentadiene to methyl acrylate and methyl methacrylate in various solvents. Data at high temperatures were obtained with the aid of a magnetically controlled break-seal device[5] which allowed pre-heating of the addends before mixing. Control experiments showed that the product compositions were not altered by isomerization or by preferential reaction of one component with excess cyclopentadiene under the experimental conditions. Analyses were carried out by gas-liquid partition chromatography. If it is assumed that the formation of *endo-* and *exo-* products in each system follows the same rate law, the slope of the line obtained from a plot of $\log_{10}[(\text{endo}) / (\text{exo})]$ vs. $1/T$ may be identified with $(E_a^{\text{exo}} - E_a^{\text{endo}})/2.303R$, where E_a is an Arrhenius activation energy, and the intercept with $\log_{10}(A^{\text{endo}}/A^{\text{exo}})$, where A is a pre-exponential term. The results are shown in Table I. The uncertainties are estimated from the reproducibilities of replicate runs, in which the variation of the absolute value of the % of a given component was less than 0.25%.

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[4] For summaries of references, see J.A. Berson, R.D. Reynolds and W.M. Jones, *J. Amer. Chem. Soc.* **78**, 6049 (1956), and K. Alder, R. Hartmann and W. Roth, *Liebigs Ann.* **613**, 6 (1958). See also J.S. Meek and W.B. Trapp, *J. Amer. Chem. Soc.* **79**, 3909 (1957); W.R. Boehme, E. Schipper, W.G. Scharpf and J. Nichols, *J. Amer. Chem. Soc.* **80**, 5488 (1958); M. Schwarz and M. Maienthal, *J. Org. Chem.* **25**, 449 (1960).

[5] Designed by Mr. Allen Remanick of this laboratory.

TABLE I

Dienophile	Solvent	Temp. Range (°C)$^{\underline{a}}$	$\log_{10}(A^{endo}/A^{exo})$	$(E_a^{exo} - E_a^{endo})$ kcal. / mole
Methyl acrylate	decalin	-35 to + 170	+ 0.28 ± 0.02	+ 0.36 ± 0.04
Methyl acrylate	acetone	0 to + 56	+ 0.08 ± 0.08	+ 0.73 ± 0.11
Methyl acrylate	CH_3CN	0 to + 66	+ 0.13 ± 0.02	+ 0.78 ± 0.04
Methyl acrylate	MeOH	0 to + 56	- 0. 2 ± 0. 1	+ 1.48 ± 0.13
Methyl methacrylate	decalin	+56 to + 139	+ 0.20 ± 0.05	- 0.71 ± 0.03
Methyl methacrylate	acetone	0 to + 56	- 0.01 ± 0.05	- 0.34 ± 0.08
Methyl methacrylate	CH_3CN	0 to + 66	- 0.12 ± 0.05	- 0.40 ± 0.08
Methyl methacrylate	MeOH	0 to + 56	- 0. 3 ± 0.15	+ 0.08 ± 0.08

$^{\underline{a}}$ Data for methyl acrylate in decalin were obtained at five different temperatures, for all others, at three different temperatures. Plots of $\log_{10}$ [(endo)/(exo)] vs. 1/T were nicely linear in all cases.

With both dienophiles, a change to more polar solvent favors <u>endo</u>-addition in the enthalpic sense; a trend in the opposite direction obtains in the pre-exponential terms, where the preference for <u>endo</u>-addition is decreased in more polar solvent.

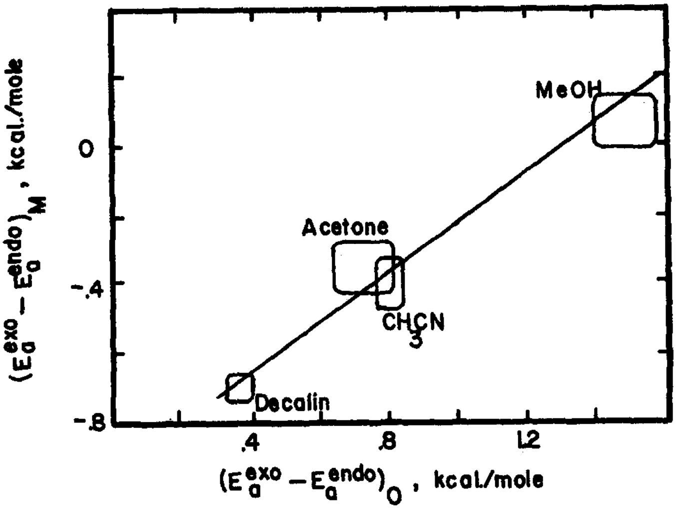

Fig. 1

Within the limited series studied, the solvent effects can be correlated approximately linearly in the enthalpy differences (Fig. 1) by an equation of the form

$$(E_a^{exo} - E_a^{endo})_M = (E_a^{exo} - E_a^{endo})_O + C$$

where M and O refer to methyl methacrylate and methyl acrylate respectively. The correlation slope, $\mu \cong 0.75$, suggests that the enthalpic stereoselectivity for methyl methacrylate is slightly less sensitive to solvent change than that for methyl acrylate. Further work is required to determine whether this kind of correlation holds for other solvents and dienophiles.

The range of enthalpic stereoselectivity produced by a change of solvent for a given dienophile is comparable in magnitude to that produced by a change of dienophile in given solvent; e.g. $(E_a^{exo} - E_a^{endo})_0$ in MeOH is greater than $(E_a^{exo} - E_a^{endo})_0$ in decalin by about 1.1 kcal /mole, while $(E_a^{exo} - E_a^{endo})_M$ in decalin differs from $(E_a^{exo} - E_a^{endo})_0$ in decalin by about 1.1 kcal /mole. It seems likely, therefore, that with some dienophiles, conformity with or violation of the Alder rule (in its enthalpic sense) will be determined by the solvent. This is already very nearly the case with methyl methacrylate. Furthermore, whatever the role of the "maximum accumulation of double bonds" in the present cases, this influence competes with those exerted by solvent and structural effects and may even be overshadowed by them.