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SOLVENT EFFECT AS THE RESULT OF FRONTIER MOLECULAR ORBITAL INTERACTION—1

THE DIELS–ALDER REACTION BETWEEN 1,4-NAPHTHOQUINONE AND 2,3-DIMETHYLBUTADIENE

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Abstract—A kinetic investigation of the solvent effect in the Diels–Alder reaction of 2,3-dimethylbutadiene and 1,4-naphthoquinone was undertaken and a hyperbolic correlation was obtained with the Acceptor Numbers (AN) of the solvent. Since ANs corrrelate with the LUMO of the solvent, the results can be rationalized in terms of an interaction between the LUMO of the solvent and the HOMO of the quinone which determines the MO energy of the solvated quinone. This rationalization seems useful when reactants, products and transition state are weakly polar.

Polar solvents increase the rates of reactions proceeding through dipolar transition states even if reactants and products are weakly polar.[1]

In the field of cycloaddition reactions, where the solvent effect is a useful tool in inferring the reaction mechanism,[2] this becomes evident in [2 + 2] cycloadditions of electron-rich with electron-deficient ethylene derivatives; e. g. the reaction between TCNE and ethyl isobutenyl ether exhibits a 4900 fold rate increase in changing the medium from carbon tetrachloride to acetonitrile.[2]

Conversely 1,3-dipolar cycloadditions and Diels–Alder reactions exhibit a significantly lower change; e.g. the reactions of N-methyl-C-phenylnitrone with ethyl acrylate[3] and anthracene with TCNE[4] exhibit a rate variation of 2.6 and 5.7 folds resp. in changing from benzene to acetonitrile.

This was correctly interpreted by Huisgen[2] as strong evidence in favour of a zwitterionic intermediate in these [2 + 2] cycloadditions and of a concerted mechanism involving a reactant-like structure of the transition state in 1,3-dipolar and Diels–Alder cycloadditions.

The mechanism by which the solvent acts on these reactions is clear from the linear relationship obtained if log k_2 is plotted vs the empirical solvent parameter E_T[5] which is an excellent measure of the polarity of the solvent.

This is true for the above mentioned [2 + 2] cycloadditions thus indicating a strong solvating effect along the reaction coordinate (solvation of the zwitterion) which lowers the activation barrier.

This is true for 1,3-dipolar cycloadditions even though examples are known where the linear relationships have both positive and negative signs for the slope. Thus, the rate constants of ethyl acrylate and phenyldiazomethane increase by a factor of 3.4 on going from benzene to methanol[6] whereas those of N-methyl-C-phenylnitrone to the same dipolarophile decrease by a factor of 4.9.[3]

The different polar character of the reagent 1,3-dipoles rationalizes these results. 1,3-dipolar cycloadditions lie in a border region where the reagents may be more or less polar than the transition states Thus, the free enthalpies of activation may be raised or lowered by an increase of the polarity of the solvent. It is not surprising that some cycloadditions (e.g. the reaction of phenyldiazomethane with norbornene[6]) are nearly insensitive to change of solvent.

Now, by which mechanism does the solvent act on a Diels–Alder reaction which occurs between weakly polar reactants going to weakly polar products through weakly polar transition states?

These problems clearly emerge from several experimental observations. The activation parameters of the reaction between anthracene and TCNE[4] do not correlate with the dielectric constant of the solvent (D-1/2D + 1). Furthermore, the reactions of maleic anhydride with butadiene[7] and isoprene[8] as well as the reaction of acrylonitrile and isoprene[7] gave poor correlations with the δ (or δ^2) parameters,[9] based on the cohesive energy density of the solvent, and with E_T parameters.

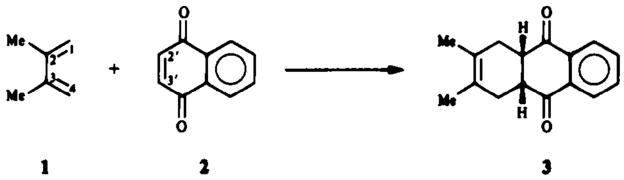
The kinetic data of the reactions of bicycloheptadiene with TCNE,[10] 9,10-dimethylanthracene with TCNE[10] and fumaronitrile[11] correlate neither with δ^2 nor with E_T or Ω parameters of the solvent (the latter scale being derived[12] from endo/exo product ratios in Diels–Alder reaction).

Up to now the solvent effect in Diels–Alder reactions seems rationalized only if a strictly homogeneous series of solvents is considered (CH_2Cl_2, $CHCl_3$, CCl_4).[13]

RESULTS

We have investigated the solvent effect on the kinetics of the Diels–Alder reaction between 2,3-dimethylbutadiene (**1**) and 1,4-naphthoquinone (**2**), which are known to give quantitatively 2,3-dimethyl-1,4,4a,10a-tetrahydroanthraquinone (**3**)[14] (Scheme 1).

The kinetic runs were studied at 80° and followed to 60–80% completion by spectroscopic analysis of the disappearing quinone **2** in the UV-visible region. The details of the method are reported in the experi-



Scheme 1.

mental part. It is necessary to avoid the use of glass vials in the kinetic runs since the results are irreproducible. Good kinetic results are obtained only if quartz vials are used.

The reaction follows second order kinetics, first order with respect to each reagent, as shown by experiments performed in acetic acid (Table 2). A 50–200 fold molar excess of butadiene gave pseudo-first-order rate constants, using a wide range of solvents (Table 1).

The reaction is faster in strongly polar solvents and the second order rate constants decrease by a factor of 31 changing from the highly polar acetic acid to the least polar cyclohexane. This is not a dramatic change but sufficient to be considered as the result of specific effects.

Every attempt to correlate the kinetic data with the previously mentioned solvent parameters failed; scatter plots were obtained using (D-1/2D + 1), E_T, Ω,[15] log k_{ion},[16] or Z[17] parameters.

Since approaches in terms of exclusive solvation of reagents or transition state failed, a completely different effect of the solvent was considered.

An approach, developed by Mulliken,[18] considers the solvent molecule as electron-acceptor and/or electron-donor and the solvent/solute interaction as as a donor/acceptor interaction.

The donor-acceptor properties of the solvent are expressed by two series of parameters developed by Gutmann and coworkers[19] and defined as Donor Numbers (DN) and Acceptor Numbers (AN) respectively. This would remain just one of several series of solvent parameters, if Paoloni and coworkers[20] had not given a quantum chemical interpretation for them. They found that DNs correlate with the energy of the HOMO and ANs with the energy of the LUMO of the solvent.

When the log k_2 values of our Diels–Alder reaction were plotted vs. AN (Table 1), a good hyperbolic relationship was obtained (Figure 1).

Thus a relation has to be found between the kinetic data and the LUMO energy of the solvent acting as acceptor, obviously the donor being one of the reactants.

It is well known that electrophiles coordinate at the unshared electron pairs of α,β-unsaturated carbonyl compounds or nitriles, thus lowering the energy of the π orbitals. Houk[21] showed that protonation of

Table 1. Rate constants for the reaction of 2,3-dimethylbutadiene with 1,4-naphthoquinone at 80°C in different solvents, and Acceptor numbers (AN) of the solvents

N°	Solvent	AN	$10^4 \times k$ ($l\,mol^{-1}s^{-1}$)
1	Cyclohexane	~ 0	0.84 ± 0.03
2	n.Hexane	0	0.86 ± 0.03
3	Ethyl acetate	9.3	1.40 ± 0.11
4	Benzene	8.2	1.54 ± 0.07
5	Diethyl ether	3.9	1.72 ± 0.18
6	Acetone	12.5	2.63 ± 0.25
7	Diglyme	10.2	3.43 ± 0.11
8	Dioxane	10.8	3.99 ± 0.23
9	Acetonitrile	18.9	4.14 ± 0.12
10	Dimethylformamide	16.0	4.46 ± 0.20
11	Chloroform	23.1	4.95 ± 0.29
12	Dimethylsulphoxide	19.3	8.3 ± 0.53
13	t.Butanol	27.1	10.1 ± 0.29
14	Isopropanol	33.8	12.1 ± 0.21
15	Ethanol	37.9	12.5 ± 0.31
16	Methanol	41.3	14.6 ± 0.39
17	Acetic acid	52.9	26 ± 1.1

Table 2. Rate constants for the reaction of 1 (initial concentration C_B) with 2 (initial concentration C_N) at 80°C in acetic acid

Run	$10^3 \times C_B$	$10^3 \times C_N$	C_B/C_N	$10^4 \times k$ (l mol^{-1}s^{-1})[a]
1	21.95	2.53	8.68	27.6[b]
2	32.08	2.79	11.50	24.5[b]
3	44.91	3.47	12.94	24.8[b]
4	118.55	2.84	41.74	26.6[c]
5	140.72	3.24	43.43	24.9[c]
6	153.17	2.48	61.76	25.7[c]
7	195.31	2.57	76.00	25.6[c]
8	232.27	2.30	100.99	27.8[c]

a) The average of 5 runs measured under pseudo-first-order conditions was reported in Table 1: with all 8 runs considered, a mean value of $(25.9 \pm 1.3) \times 10^4$ is obtained.

b) Second order conditions. c) Pseudo-first order conditions.

acrolein decreases the LUMO and π-HOMO energies by about 9.5 and 9 eV, respectively. In the same way acceptor solvents should coordinate quinone 2 at the oxygen functions lowering its LUMO as well as its HOMO.

This simple consideration suffices to rationalize qualitatively the effect of the solvent on the rate.

There is no doubt that the reaction of dimethylbutadiene and naphthoquinone is $\text{HOMO}_{\text{diene}}$–$\text{LUMO}_{\text{dienophile}}$ controlled.[22] Correlation of FMOs of reagents can be derived by taking into account their HOMOs and LUMOs. The first IP of 2,3-dimethylbutadiene is 8.26 eV[23] and its LUMO can be assumed to be in the range 0.7/0.9 eV since EA of butadiene and 1,3-cyclohexadiene are −0.62 and −0.80 eV, respectively.[24] 1,4-Benzoquinone has the π-HOMO at 9.67 eV[25] and the LUMO at 1.75 eV[26] as determined from charge-transfer spectra. The latter value seems consistent with Houk's MO calculations[27] of benzo- and naphthoquinone. Thus the dominant interaction occurs between HOMO of dimethylbutadiene and LUMO of naphthoquinone.

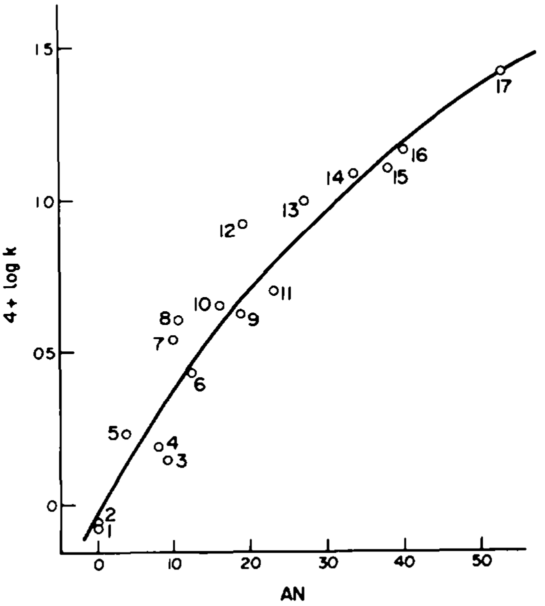


Fig. 1. Rate constants of the Diels–Alder reaction of 2,3-dimethylbutadiene and 1,4-naphthoquinone at 80°C in different solvents, plotted vs. the solvent AN (numbers refer to Table 1).

The more strongly naphthoquinone is coordinated by the solvent, the lower the quinone LUMO becomes; the increasing FMO interaction results in rate acceleration.

To rationalize the solvent effect quantitatively, the hyperbolic shape of the function in Fig. 1 has to be reproduced. The interaction of $\text{HOMO}_{\text{butadiene}}$ and $\text{LUMO}_{\text{quinone}}$ gives rise to a stabilization energy represented in eq. 1 with the coefficients figures referring to those in Scheme 1

$$\Delta E = \frac{[c^1_{\text{HO}} \cdot c^{2'}_{\text{LU}} + c^4_{\text{HO}} \cdot c^{3'}_{\text{LU}}]^2 \beta^2}{E^{\text{butadiene}}_{\text{HO}} - E^{\text{solvated quinone}}_{\text{LU}}}. \tag{1}$$

Since the coefficients are probably not significantly altered with the solvent, Sustmann's approximation[22] is adopted: the coefficients in the numerator and energy of the HOMO of 2,3-dimethylbutadiene are assumed to be constant. Thus ΔE becomes a function of the LUMO energy of the solvated quinone only, with A and B being constants (eqn 2)

$$\Delta E = \frac{A}{B - E^{\text{solvated quinone}}_{\text{LUMO}}}. \tag{2}$$

To evaluate the effect of an electrophilic solvent on the energy of quinone let us remember that two orbitals ψ_i^R and ψ_j^S of energies E_i and E_j (with $E_i > E_j$) will mix in perturbation theory to give new orbitals, the energy of the lower being derived, to second order, from eqn (3).

$$E_j'' = \frac{(H_{ij}')^2}{E_j - E_i}. \qquad (3)$$

If, as a first approximation, the numerator of eqn (3) is taken as a constant (as well as the energy of the LUMO of the unsolvated quinone), the energy of the LUMO of the solvated quinone becomes a function of the LUMO energy of the solvent, with C and D being constants (eqn 4).

$$E_{\mathrm{LUMO}}^{\mathrm{solvated\ quinone}} = \frac{C}{D - E_{\mathrm{LUMO}}^{\mathrm{solvent}}}. \qquad (4)$$

Under the assumption that the LUMO energy of the solvent, in accordance to Paoloni,[20] is a linear function of its Acceptor Numbers, eqn (5) is obtained with a, b, c and d being new constants.

$$E = \frac{a - bAN}{c - dAN}. \qquad (5)$$

This is the equation of an hyperbola and if ΔE is a linear function of log k, a hyperbolic shape results if log k is plotted vs AN. To fullfil this, two further points must be cleared.

To compare ΔE and log k, since $\log k = -\Delta G/RT$, means to assume a direct proportionality between the FMO stabilization energy and the free energy. This is true if the entropy is reasonably constant since the enthalpy only is affected by MO interactions.

Therefore we have determined the Eyring parameters in benzene and acetic acid, the extremes of the series of solvents tested. $\Delta S^{\neq}$ values[28] are −41 and −38 e.u. respectively, reason enough to assume the variation of $\Delta S^{\neq}$ is small in the whole series.

Finally, the hyperbolic shape of Fig. 1 could derive, not from eqn (5), but from eqn (2) with the LUMO energy of the solvated quinone being a linear function of AN. However, when 1/log k was plotted vs AN, no linear relationship but a further hyperbola was obtained.

Table 3. Rate constants and thermodynamic parameters for the reaction of **1** and **2** in benzene and acetic acid

Temp. (°C)	$10^4 \times k$ ($l\ mol^{-1} s^{-1}$)	
	Benzene	Acetic acid
22	--	0.94 ± 0.04
38.2	--	2.83 ± 0.03
60	0.51 ± 0.02	9.2 ± 0.3
70	0.93 ± 0.06	--
80	1.54 ± 0.07	26.2 ± 1.1
90	2.62 ± 0.11	--
$\Delta E^{\neq}$ (Kcal/mol)	13.0 ± 0.4	11.7 ± 0.3
$\Delta S^{\neq}$ (e.u.)	-41 ± 1.0	-38 ± 0.8

Therefore the solvent acts as acceptor on a donor reactant, thus determining the variation of the rate constants.

This approach is suitable for reactions between weakly polar reagents going to weakly polar products through weakly polar transition states.

Two points require further research: the rationalization of the solvent effect on the Diels–Alder reaction with "inverse" electron demand[22] and the effect of the redistribution of the orbital electron densities, induced by solvent, on the regiochemistry of the reaction. But these will be the topic of future researches.

EXPERIMENTAL

Materials. 1,4-Naphthoquinone and 2,3-dimethylbutadiene were recrystallized (resp. redistilled) Fluka pure reagents. Solvents for the kinetic runs were freshly distilled reagent grade. To avoid any trace of acid, acetonitrile was purified by calcium hydroxide treatment.

Kinetics. The overall reaction rates were measured by following the disappearance of **2** at 334.5 nm on a Beckman DU-2 spectrophotometer; solutions were measured in 1.00 cm OS Hellma cells of 3 ml capacity.

A sample of 1,4-naphthoquinone (**2**) (concentration range 0.0003–0.005 M) was accurately weighed into a 50 ml volumetric flask and dissolved in the minimum amount of the required solvent. 2,3-Dimethylbutadiene (**1**) was weighed into a thin sealed glass tube, the reactants were mixed and solvent added up to 50 ml. Immediately 0.50 ml portions of the homogeneous solution were removed with a microsyringe and placed into quartz tubes which were rapidly sealed. About 8–10 samples were prepared for each run. At time zero the samples were placed into ultrathermostat at the required temperature and a 0.50 ml portion of the solution was diluted to 3.00 ml with spectrograde ethanol (benzene for kinetics performed in this solvent) and the absorbance determined. At appropriate time intervals (from 3 min for acetic acid at 80° to 90 min for the slower reactions) the residual absorbance was measured after dilution to 3.00 ml with ethanol (or benzene).

Experiments at 80° with variation of the diene concentration in acetic acid (Table 2) gave results fitting the second order rate equation. Using large initial concentrations of dimethylbutadiene (0.05–0.3 M) the results fit a pseudo-first-order equation from which second order rate constants can be obtained. Good agreement was found between second order rate constants obtained under both conditions (Table 2). Thus pseudo-first-order conditions were followed to determine the rate constants listed in Tables 1 and 3 (see later). These data are average values of 5–7 kinetic runs using different initial concentrations of quinone and butadiene for each run.

To measure the activation parameters of the reaction in benzene and acetic acid, kinetic determinations at four different temperatures were performed (Table 3). The kinetic determinations in acetic acid at 22^c and 38.2° were obtained by placing the sample, diluted to 3.00 ml, in the thermostatted cell of the spectrophotometer. At appropriate time intervals the absorbance was determined and the reaction followed to 60–80% completion.

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