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SOLVENT EFFECT AS THE RESULT OF FRONTIER MOLECULAR ORBITAL INTERACTION. V(1). DIELS-ALDER WITH HETERODIENOPHILES: A UNIFIED APPROACH TO THE SOLVENT EFFECT OF THE DIELS-ALDER REACTIONS.

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Abstract - The solvent effect of Diels-Alder (D.A.) reactions with heterodienophiles was measured in several solvents.
The rate of the reaction between 2,3-dimethylbutadiene (DMB) and diethylazodicarboxylate increases with the increases in the Acceptor Number of the solvent which behaves as an electrophile.
The rate of the reaction between DMB and *p*.bromonitrosobenzene shows a small solvent effect which correlates with the cohesive pressure (δ_H^2) of the solvent.
The rate of the reactions between DMB and tetrachloro- or tetrabromo-*o*.benzoquinones give an inverse linear relationship with D_π basicity parameters, thus rate decreases with increases in the nucleophilic character of the solvent.
These monoparametric correlations (alternatively obtained with electrophilic, nucleophilic or cohesive pressure parameters of the solvent) rationalize the solvent effect of D.A. reactions reported in the literature, which fit one of the above reported three classes.
The same result is obtained if the Kamlet-Taft multiparametric equation is applied to the same set of reactions. The main contribution remains that outlined with the monoparametric approach and some secondary effects or some borderline cases are usefully focussed.

Previous papers of this series(1-4) investigated the solvent effect of Diels-Alder (D.A.) and Hetero-D.A. (H.D.A.) reactions with α,β-unsaturated carbonyl compounds as heterodienes. The hyperbolic correlation found between kinetic data and the Acceptor Numbers (AN)(5) of the solvent (equation 1) was interpreted in terms of coordination of the solvent acting as electrophile, either with the dienophile or with the heterodiene, always with the oxygen atom of the carbonyl group.

$$\log k = \frac{a - b \times AN}{c - d \times AN} \qquad (1)$$

This correlation results in a stabilization of the LUMO of the α,β-unsaturated carbonyl system and in a lower energy separation between FMOs of the D.A. reagents. Hence rate increases with the increase of the interaction between solvent and the solvatable reagent.

The obvious extension of this research was the investigation of the solvent effect in D.A. reactions with heterodienophiles.

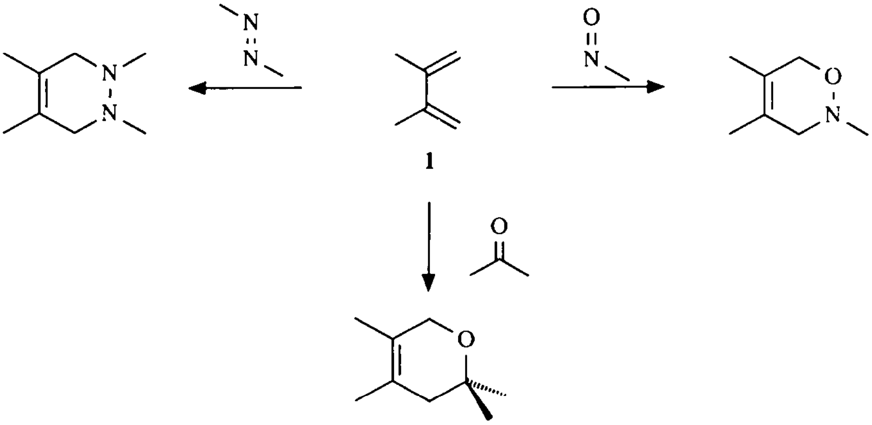
Tha data available from the literature concern the following reactions: 4-phenyl-1,2,4-triazolindione with anthracene and diphenylbutadiene (studied in 10 and 7 solvents respectively),(6) 4-ethoxy- and 4-chloronitrosobenzene with DMB (in 7 solvents)(7) and adamantanethione with acrolein (in 8 solvents).(8)

No specific relationship was derived between kinetic data and solvent parameters.(9) Only the very small solvent effect of the reaction between DMB and nitroso-arenes (a factor of about 2) was shown by Authors(7) to give a satisfactory linear correlation with the Kirkwood function, and by Reichardt(10) with the solvent polarity parameter E_T.

For the search of reactions suitable for the kinetic study of the solvent effect, a valuable help was offered by the extensive review of Boger and Weinreb(11) on H.D.A. reactions.

In view of a possible homogeneous treatment of the data, selected examples of reactions between DMB (**1**) and N=N, N=O or C=O heterodienophiles (Scheme 1) were studied.

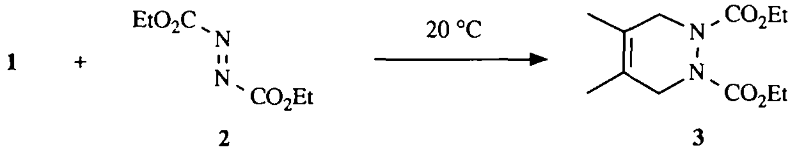
Scheme 1



Reaction of 2,3-dimethylbutadiene (1) with diethylazodicarboxylate (2).

This reaction (12) (Scheme 2) was found to be a clean second order reaction in several solvents and 1,2-dicarboethoxy-4,5-dimethyl-1,2,3,6-tetrahydropyridazine (3) was always obtained in nearly quantitative yield.

Scheme 2



The kinetic runs were studied by u.v.-vis. spectroscopic analysis of the disappearing 2 at 20 °C and 410 nm, following the reaction to about 70% completion. In the presence of a 20-60 fold excess of DMB, pseudo first order rate constants were determined and the second order rate constants were calculated. The kinetic data reported in Table 1 represent the average of at least 8 kinetic runs, each with varying reagent ratios.

The significant solvent effect was 135 in the range n.hexane-benzyl alcohol.

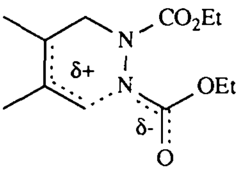
Table 1 reports both AN and E_T(13) solvent parameters and, in spite of some gaps, the rate tends to follow more the order of increase of AN than that of E_T.

Fig. 1a shows the linear correlation with E_T. To determine the best fit of the kinetic data with the hyperbolic equation 1, this was rearranged in the form of equation 2 dividing both numerator and denominator by c.

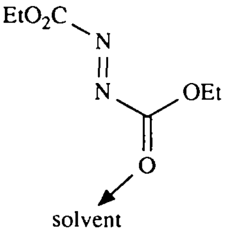
$$\log k = \frac{a/c - b/c \times AN}{1 - d/c \times AN} \qquad (2)$$

Least-squares adjustment of the parameters h = (a/c), j = (b/c) and k = (d/c) gave the hyperbolic curve of the kinetic data *vs* AN, reported in Fig1b.

These relationship involve two different assumptions: (a) a transition state having a dipolar character; (b) a coordination of the solvent, acting as an electrophile, on the carbonyl group of 2.



(a)



(b)

Table 1: Rate constants for the reaction between DMB (1) and diethylazodicarboxylate (2) at 20 °C in differing solvent with AN and E_T parameters of the solvent.

N	Solvent	AN	E_T	10^4 x k (L $mol^{-1}sec^{-1}$)
1	n.Hexane	0	31.0	0.80 ± 0.02
2	Cyclohexane	0	30.9	1.08 ± 0.03
3	THF	8.0	37.4	0.85 ± 0.04
4	Benzene	8.2	34.3	1.89 ± 0.05
5	Ethyl acetate	9.3	38.1	1.08 ± 0.03
6	1,4-Dioxan	10.8	36.0	2.14 ± 0.03
7	Aceton	12.5	42.2	1.58 ± 0.06
8	Chlorobenzene	13.0	36.8	4.38 ± 0.05
9	Nitrobenzene	14.8	41.2	8.7 ± 0.5
10	Benzonitrile	15.5	41.5	7.8 ± 0.4
11	DMF	16.0	43.8	4.0 ± 0.2
12	1,2-Dichloroethane	16.7	41.3	10.0 ± 0.2
13	PDC	18.3	46.6	15.1 ± 0.3
14	Acetonitrile	18.9	45.6	5.7 ± 0.2
15	DMSO	19.3	45.1	12.0 ± 0.4
16	Nitromethane	20.5	46.3	13.9 ± 0.4
17	Chloroform	23.1	39.1	26.5 ± 0.5
18	*ter.*Amyl alcohol	27.0	41.1	6.0 ± 0.1
19	*ter.*Butanol	27.1	43.3	6.7 ± 0.2
20	*sec.*Butanol	32.5	47.1	11.7 ± 0.2
21	*iso.*Propanol	33.8	48.4	9.1 ± 0.3
22	*n.*Propanol	37.3	50.7	17.6 ± 0.5
23	Ethanol	37.9	50.9	12.9 ± 0.4
24	Methanol	41.3	55.5	30 ± 3
25	Benzyl alcohol	50.0	50.4	108 ± 3

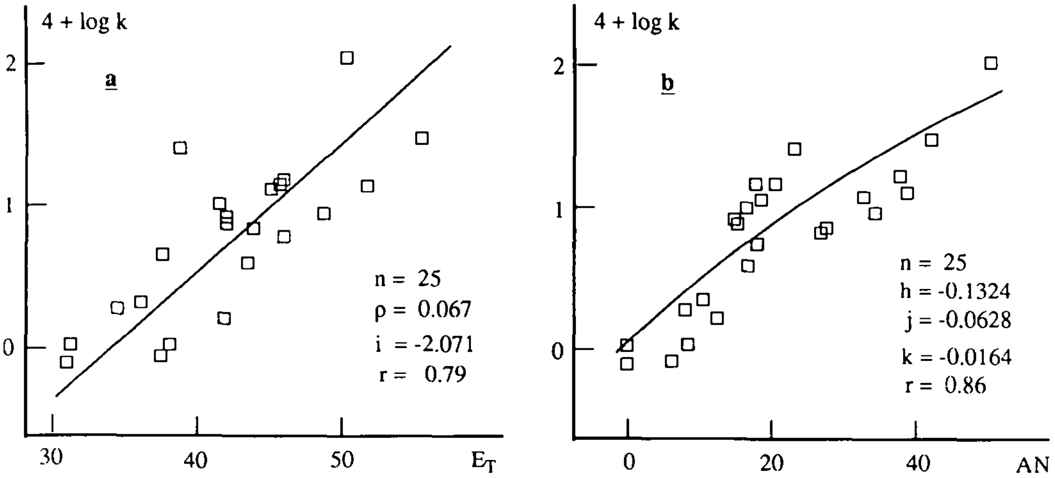


Fig. 1: Rate constants of the reaction between **1** and **2** at 20 °C in differing solvents plotted *vs* E_T (a) or *vs* AN (b) of the solvent.

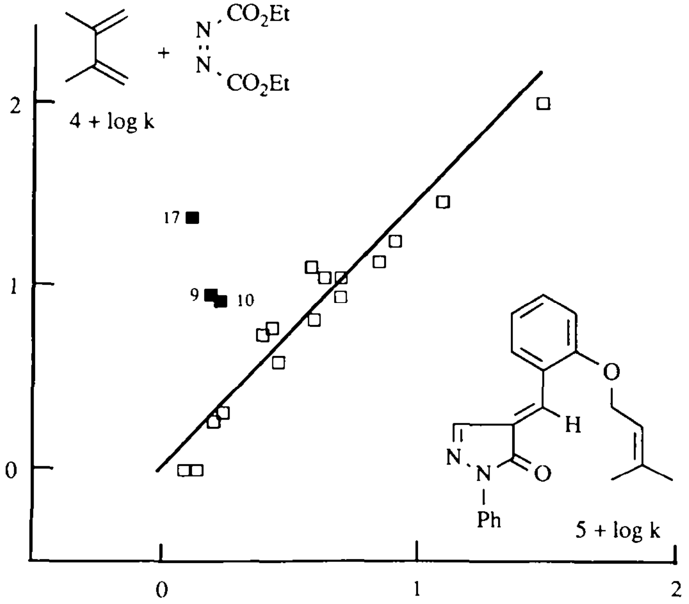


Fig. 2: Plot of the rate constants for the reaction between **1** and **2** *vs* those of the intramolecular H.D.A. reaction (ref. 1); solvents 9, 10 and 17 in Table 1 were excluded (n, 17; i, 0.0; ρ, 1.40; r, 0.97).

A better fit with AN suggests a better rationalization of the solvent effect through mechanism (b). A further support to this mechanism can be obtained. If the kinetic data in Table 1 are plotted *vs* the rate constants of the intramolecular H.D.A. reaction of 1-phenyl-4-[2(3-methyl-2-butenyloxy)benzylidene]-5-pyrazolone,(1) a reaction where solvents act as electrophiles, (with the exception of three solvents perhaps involved in some specific solvation) a nice linear correlation is obtained (Fig. 2). This obviously implies a similar mechanism of the solvent in both reactions.

Moreover, the range of the activation entropies (38-42 e.u.), measured in five selected solvents (Table 2), is in fully accordance with values reported for concerted D.A. reactions.(14)

Table 2: Rates and activation parameters of the reaction between **1** and **2** in differing solvents.

T/°C	$10^4 \times k$ (l mol^{-1} s^{-1})				
	cyclohexane	benzene	1,4-dioxan	t.butanol	methanol
20	1.08 ± 0.03	1.89 ± 0.05	2.14 ± 0.03	6.7 ± 0.2	30 ± 3
25	1.45 ± 0.05	2.38 ± 0.07	2.80 ± 0.09	8.2 ± 0.2	43 ± 1.5
30	2.06 ± 0.05	3.36 ± 0.06	3.73 ± 0.07	10.85 ± 0.25	57 ± 2
35	2.75 ± 0.08	4.47 ± 0.08	5.16 ± 0.09	14.3 ± 0.2	69 ± 1
$\Delta H^{\neq a}$	10.7 ± 0.7	9.9 ± 0.5	9.9 ± 0.5	9.5 ± 0.8	9.5 ± 1
$-\Delta S^{\neq b}$	40 ± 2	42 ± 1.5	41.5 ± 1.5	40.5 ± 1.5	38 ± 3

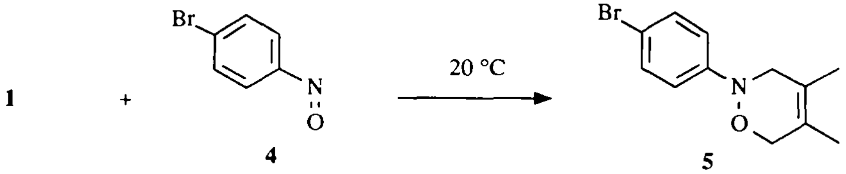
[a] kcal mol^{-1}; [b] cal K^{-1} mol^{-1}

Reaction of 2,3-dimethylbutadiene (1) with 4-bromonitrosobenzene (4).

As already mentioned in the introduction, a kinetic study of the reaction between DMB and nitroso-arenes was reported in seven solvents.(7)

Our choice as N=O heterodienophiles was 4-bromonitroso benzene (**4**), whose reaction was known to give 2-*p*.bromophenyl-4,5-dimethyl-3,6-dihydro-1,2-oxazine (**5**) (Scheme 3).

Scheme 3



The kinetic runs were studied by u.v.-vis. spectroscopic analysis of the disappearing nitrosoarene at 745 nm and 20 °C in 27 solvents. From the pseudo-first order rate constants, determined in the presence of 40-80 fold excess of DMB, the second order rate costants were calculated.

The kinetic data reported in Table 3 represent the average of at least 8 kinetic runs, each with varying reagent ratios.

Table 3: Rate constants for the reaction between DMB (1) and 4-bromonitrosobenzene (4) at 20 °C in differing solvent with E_T and δ_H parameters of the solvent.

N	Solvent	E_T	δ_H	10^3 x k (L mol^{-1}sec^{-1})
1	n.Hexane	31.0	7.27	2.14 ± 0.05
2	Cyclohexane	30.9	8.19	2.7 ± 0.1
3	Ethyl ether	34.6	7.53	1.70 ± 0.04
4	THF	37.4	9.32	2.45 ± 0.10
5	Benzene	34.3	9.16	3.4 ± 0.2
6	Ethyl acetate	38.1	8.10	2.9 ± 0.1
7	1,4-Dioxan	36.0	10.13	4.0 ± 0.2
8	Aceton	42.2	9.62	3.7 ± 0.1
9	Chlorobenzene	36.8	9.67	4.1 ± 0.2
10	Nitrobenzene	41.2	10.4	6.0 ± 0.2
11	Benzonitrile	41.5	10.7	5.9 ± 0.1
12	DMF	43.8	11.79	6.4 ± 0.3
13	1,2-Dichloroethane	41.3	9.86	5.8 ± 0.15
14	PDC	46.6	13.5	12.1 ± 0.3
15	Acetonitrile	45.6	12.11	5.5 ± 0.2
16	DMSO	45.1	13.0	14.3 ± 0.8
17	Nitromethane	46.3	12.9	7.9 ± 0.3
18	Chloroform	39.1	9.16	4.9 ± 0.1
19	*ter.*Amyl alcohol	41.1	10.5	5.7 ± 0.4
20	*ter.*Butanol	43.3	10.5	6.4 ± 0.3
21	*sec.*Butanol	47.1	11.08	5.9 ± 0.2
22	*iso.*Propanol	48.4	11.44	5.2 ± 0.2
23	*n.*Propanol	50.7	12.18	5.8 ± 0.2
24	Ethanol	51.9	12.78	4.6 ± 0.15
25	Methanol	55.4	14.5	5.4 ± 0.3
26	Benzyl alcohol	50.4	12.05	13.4 ± 0.2
27	Acetic acid	51.2	13.01	6.8 ± 0.2

The main result derived from data in Table 3 is the *unusually small solvent effect* observed in this reaction. The range from diethyl ether to dimethyl sulfoxyde is about 8 and this can give rise to correlations with uncertain statistical meaning. Certainly no correlations exists between kinetic data and AN and, dealing with a large number of solvents, the previously observed linear correlation with E_T(10) becomes less satisfactory (Fig. 3a: broken *vs* full line).

Hence, neither an electrophilic coordination of the solvent on nitrosobenzenes, nor a partial charge separation in the transition state, are the main reasons of the solvent effect.

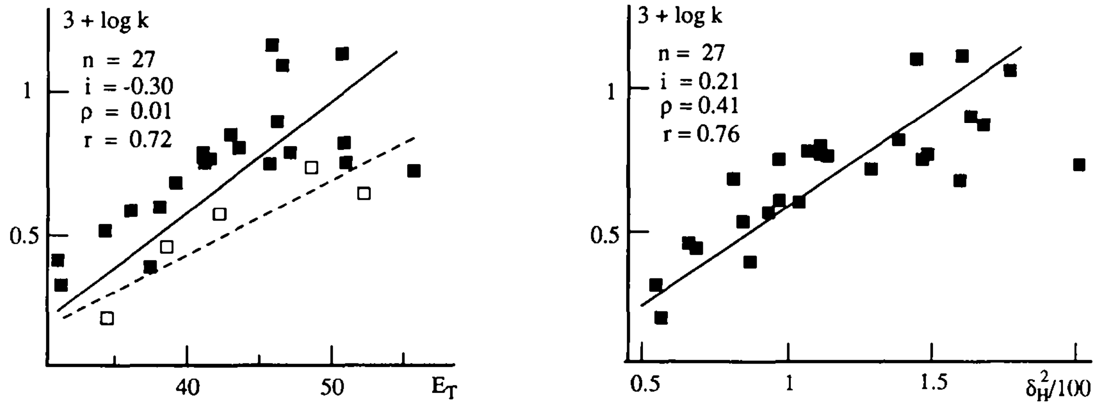


Fig. 3: Rate constants of the reaction between **1** and **4** at 20 °C in differing solvents plotted *vs* either E_T (a) or $\delta_H^2/100$ (b) of the solvent. The broken line (Fig. 3a) is the correlation derived from solvents (empty squares) investigated in ref. 7,10.

A better result is obtained if the kinetic data are plotted *vs* δ_H^2, the Hildebrand's solubility parameters(16) squared, which correspond to the cohesive pressure, characterizing the energy associated with the intermolecular solvent-solvent interactions (Fig. 3b). Thus the absence of any specific or non-specific solvent-solute interactions rationalizes the unusually small solvent effect of this reaction.

The positive ρ value has to be expected for a D.A. reaction whose activation volume is negative.(14)

The activation entropy was determined in five significant solvents and its range (31-36 e.u.) is similar to that (26-32 e.u.) determined for the reaction of DMB and 4-chloronitrosobenzene.(7)

Table 3: Rates and activation parameters of the reaction between 1 and 4 in differing solvents.

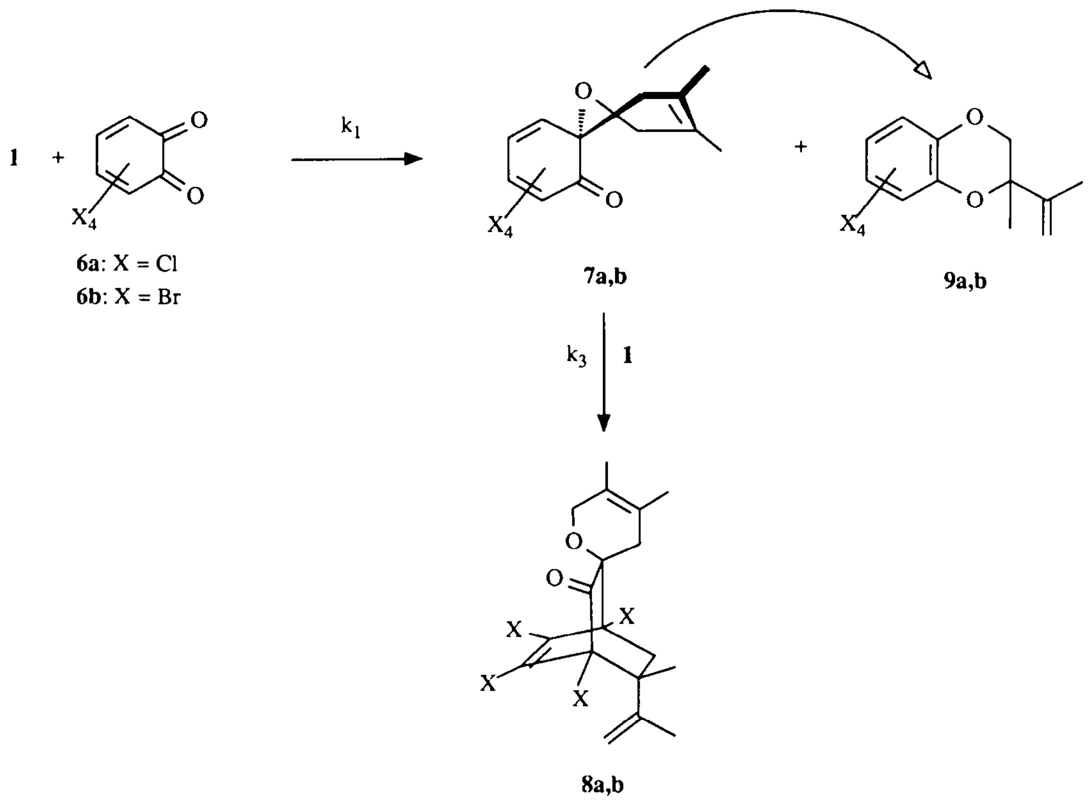
T/°C	10^3 x k (l mol^{-1} s^{-1}) cyclohexane	benzene	1,4-dioxan	t.butanol	methanol
20	2,7 ± 0,1	3,4 ± 0,1	4,0 ± 0,2	6,4 ± 0,3	5,4 ± 0,3
25	3,55 ± 0,15	4,30 ± 0,15	5,30 ± 0,25	8,1 ± 0,3	7,5 ± 0,4
30	5,2 ± 0,2	6,3 ± 0,2	7,6 ± 0,3	11,0 ± 0,5	10.5 ± 0,5
35	6,80 ± 0,25	8,0 ± 0,4	10,1 ± 0,2	15 ± 1	15,6 ± 0,8
$\Delta H^{\neq a}$	10,7 ± 0,8	10,0 ± 0,8	10,7 ± 0,8	9,7 ± 0,8	11,1 ± 0,8
$-\Delta S^{\neq b}$	34 ± 3	36 ± 2	32 ± 2	36 ± 2	31 ± 1

a) kcal mol^{-1}; b) cal K^{-1} mol^{-1}

Reaction of 2,3-dimethylbutadiene (1) with tetrachloro- and tetrabromo-o-benzoquinone (6a,b).

The reaction of a C=O group with DMB, in the absence of any catalyst, requires strong acceptor properties of the heterodienophiles. Thus a kinetic study of the reaction between **1** and tetrachloro- or tetrabromo-*o*-benzoquinone (**6a,b**) was undertaken, having the results previously obtained by Ansell and Leslie$^{(17)}$ as a model. These Authors, from the reaction of equimolecolar amounts of **1** and **6a,b** at 0 °C, in benzene or ether, isolated discrete yields of 7,8,9,10-tetrahalo-3,4-dimethyl-1-oxaspiro[5,5]undeca-3,7,9-trien-11-ones (**7a,b**). These react with DMB to give 1,4,5,6-tetrahalo-3′,6′-dihydro-endo-8-isopropenyl-4′,5′,8-trimethylspiro[bicyclo[2,2,2]oct-5-ene-2,2′-pyran]-3-ones (**8a,b**) or rearrange in boiling benzene, in accordance to a [3,3] sigmatropic shift, to 5,6,7,8-tetrahalo-2,3-dihydro-2-isopropenyl-2-methyl-1,4-benzodioxanes (**9a,b**) (Scheme 4).

Scheme 4



The kinetic runs at 30 °C were studied by u.v.-vis. spectroscopic analysis of the disappearing **6a,b** at the suitable wavelength (430-470 nm for **6a**, 450-500 nm for **6b**) depending on the solvent (see Table 11).

The reaction mixtures were found to contain all products **7-9a,b**. Hplc allowed to separated **7a** and **8a** from **9a** and, in the early stage of the reaction the ratio (**7a**) [+ eventual(**8a**)] : (**9a**) was found to be nearly constant indipendently from the nature of solvent (see experimental for the details of this measure).

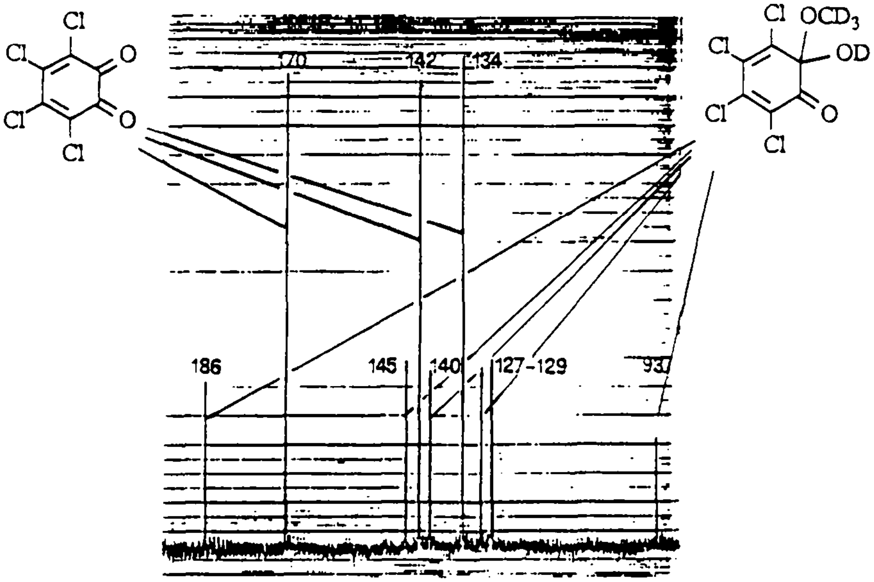


Fig. 4: ^{13}C-nmr spectrum of **6a** in CD_3OD

9a,b are primary reactions products since some preliminary experiments (see experimental) show the rate of the sigmatropic rearrangement (k_2) is not comparable with k_1. The ratio [**7a**]:[**8a**] changes with the solvent since the rate of the reaction between **7a** and DMB (k_3) is sometimes comparable with k_1. The kinetic determinations were performed under pseudo-first order conditions *in the presence of 150-700 fold excess of DMB*, hence to assume its concentration as a constant involves a variation of the calculated second-order rate constants significantly below the limit of the experimental error.

A further point had to be clarified. Even if a wide range of protic and aprotic solvents gave a clean formation of **7-9**, some unusual values of the activation parameters in methanol, ethanol and i.propanol forced us to investigate the effect of these solvent on **6a,b**. Both u.v.-vis. and i.r. spectra suggested a deep change of the reagents and the nature of this change was infererred by ^{13}C-nmr. When **6a** is dissolved in CD_3OD, the formation of a a semiacetalic adduct in equilibrium with **6a** occurs, nicely detected in the spectrum (Fig. 4) with the hemiacetalic tetrahedral carbon resonating at 93 ppm.

Since in protic solvents the disappearance of **6a,b** and the formation of **7a,b** can occur through both mechanisms outlined in scheme 4 and 5, the solvent effect was investigated in 14 aprotic solvents only.

The second-order rate constants, reported in Table 5, are the average of at least six kinetic runs, each with varying reagent ratios.

Since these kinetic data do not correlate neither with the electrophilic parameters AN, nor with the polarity-polarizability parameters E_T, nor even with the solvent cohesive pressure δ_H^2, the basicity parameters were considered. Two main classes are available in the literature:(9) the hard parameters Donor Numbers (DN), β and B whose scales, linearly interrelated, were developed by Gutman(5), Kamlet-Taft(18) and Shorter(19) respectively, and the soft parameters D_π, whose scale was developed by Oshima and Nagai.(20)

Scheme 5

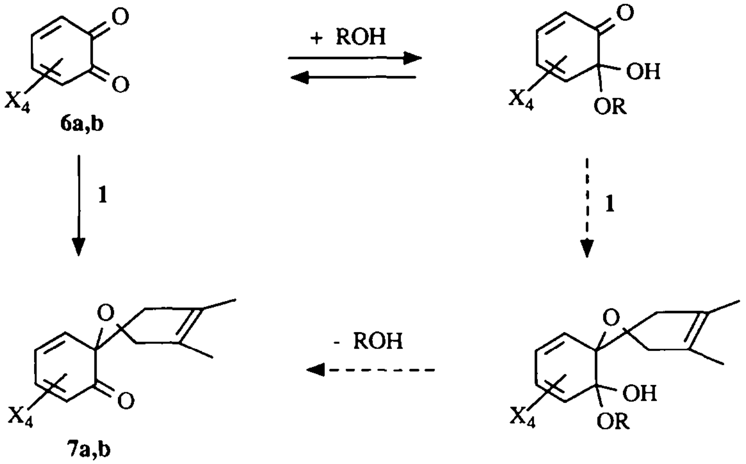


*Table 5: Rate constants for the reaction between **6a,b** and DMB at 30 °C in differing solvents with DN^N and D_π parameters of the solvent.*

N	Solvent	D_π	DN^N	$10^4 \times k$ (L $mol^{-1}s^{-1}$)	
				6a	**7a**
1	Chloroform	-1.56	--	96.5 ± 0.5	118 ± 1
2	Cyclohexane	--	--	60 ± 2	75 ± 1
3	1,2-Dichloroethane	-1.22	0	51.8 ± 0.6	61 ± 1
4	Chlorobenzene	-0.903	--	22.6 ± 0.3	26.1 ± 0.2
5	Nitromethane	-0.724	0.07	33.8 ± 0.3	30 ± 1
6	Nitrobenzene	-0.583	0.21	34.5 ± 0.5	41.6 ± 0.1
7	Acetonitrile	-0.440	0.36	11.5 ± 0.2	13.3 ± 0.3
8	Propylene carbonate	--	0.39	11.8 ± 0.2	14.2 ± 0.2
9	Benzene	0	--	10.6 ± 0.1	14.2 ± 0.1
10	Aceton	0.261	0.44	3.58 ± 0.05	4.30 ± 0.05
11	Ethyl acetate	0.289	0.44	3.87 ± 0.03	4.83 ± 0.04
12	Dimethoxymethane	0.383	--	2.33 ± 0.04	2.09 ± 0.01
13	1,4-Dioxan	0.590	0.38	1.96 ± 0.01	1.99 ± 0.05
14	THF	0.639	0.52	1.20 ± 0.01	1.23 ± 0.04

When the rate of **6a** is plotted *vs* normalized DN (DN^N) a non-linear relationship results with the rate decreasing as the donor properties of the solvent increase (Fig. 5a). Since the HOMO energy of the solvent is a linear function of its DN,(21) from the interaction between the HOMO of the solvent (acting as a donor) and the LUMO of the *o*.quinone, acting as acceptor, simple M.O. reasoning analogous to that developed in ref. 2 allows to derive equation 3.

$$\log k = -\frac{b/d - a/d \times DN^N}{1 - c/d \times DN^N} \qquad (3)$$

For **6a**, when the parameters (b/d), (a/d) and (c/d) are optimized the hyperbolic curve reported in Fig. 5a is obtained.

The origin of D_π parameters,(20) deriving from the kinetic data of a pericyclic reaction under frontier control, reduces to first-order the relation between rate and solvent donor properties. Thus, a good linear correlation is obtained when the kinetic data of **6a** are plotted *vs* D_π and the negative value of ρ (-0.82) is the result of the inverse relationship mentioned above.

The solvent effect of the reaction between **1** and **6b** is strictly similar to that of **6a**. Figure 5b reports as a broken line the result of the correlation between kinetic data and D_π, which parallels that of **6a** (ρ=-0.83).

The reason of the behaviour of solvents as nucleophiles and the inverse dependence between degree of basicity and rate is the MO energy levels of **6a,b**. These heterodienophiles are characterized by low-lying LUMOs [-2.60 and 2.65 eV respectively(22)], therefore the dominant interaction with the MOs of the solvent is $LUMO_{o.quinone}$ - $HOMO_{solvent}$, with solvent thus behaving as a donor. The stronger this interaction, the largest results the destabilization of the LUMO of the solvated quinone.

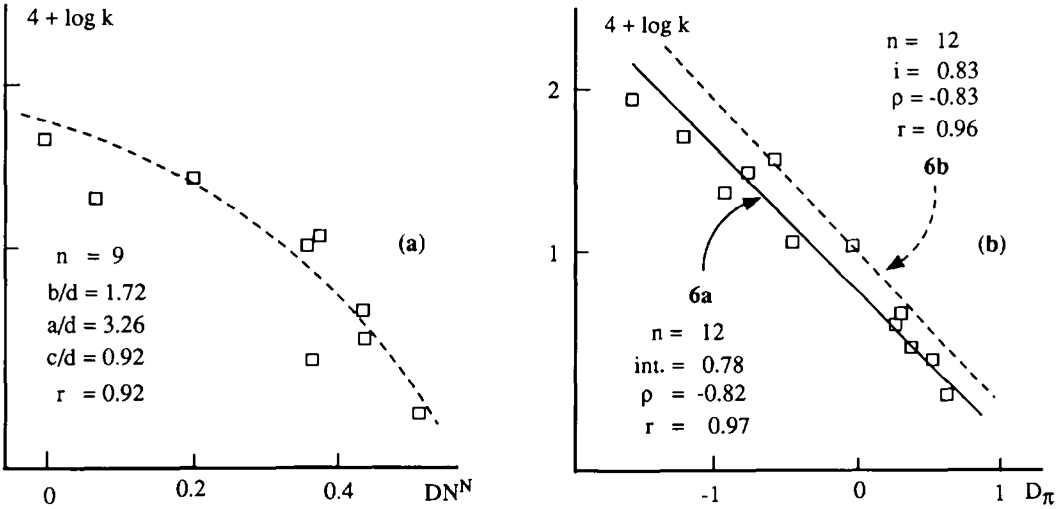


Fig. 5: Rate constants of the reaction between **6a** and **1** at 30 °C in differing solvents plotted *vs* either DN^N (a) or D_π (b) of the solvent. In fig. (b) the broken line is the result of the correlation between D_π and the rate constants of **6b**.

Since this orbital is involved in the interaction with the $\mathrm{HOMO_{DMB}}$, the stronger the interaction with the solvent, the larger the energy separation between the FMOs of the cycloaddends and the slower the cycloaddition results (Fig. 6). Obviously eq. 3 is a quantitative representation of this relationship.

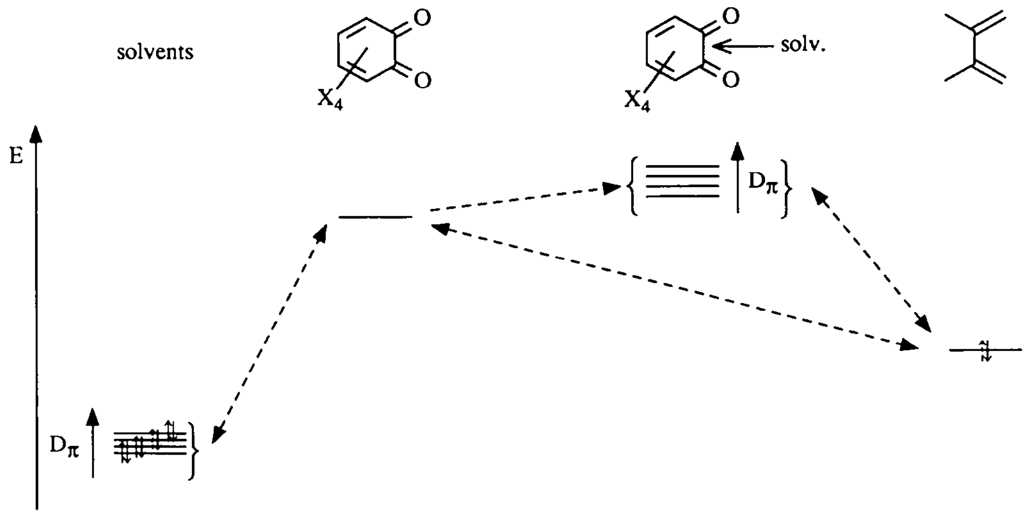


Fig. 6: Schematic representation of the effect of the FMO interactions between solvents and **6a,b**, with the results on the energy separation between $\mathrm{LUMO_{solvated\ quinone}}$ and $\mathrm{HOMO_{DMB}}$.

The activation entropies, determined in three significant solvents for both **6a,b** (Table 6) are consistent for a concerted D.A. reaction.

Table 6: Rates and activation parameters of the reaction between 1 and 6a,b in differing solvents.

T/°C		**6a**	$10^3 \times k$ (L mol^{-1}s^{-1})		**6b**	
	cyclohexane	benzene	1,4-dioxan	cyclohexane	benzene	1,4-dioxan
20	33 ± 1	5.18 ± 0.02	0.87 ± 0.01	43.8 ± 0.5	7.16 ± 0.05	0.78 ± 0.01
25	44 ± 1	7.15 ± 0.04	1.29 ± 0.01	59 ± 1	10.0 ± 0.1	1.36 ± 0.02
30	60 ± 2	10.62 ± 0.05	1.96 ± 0.01	75 ± 1	14.2 ± 0.1	1.99 ± 0.05
36	84 ± 2	16.9 ± 0.2	3.40 ± 0.03	104 ± 2	20.3 ± 0.1	2.89 ± 0.01
$\Delta H^{\neq}$ [a]	10.0 ± 0.5	12.8 ± 0.5	14.7 ± 0.5	9.6 ± 0.2	11.9 ± 0.1	15.1 ± 0.2
$-\Delta S^{\neq}$ [b]	36 ± 2	30 ± 2	27 ± 3	37 ± 1	32 ± 1	26 ± 2

[a] Kcal mol^{-1}; [b] cal K^{-1}mol^{-1}.

DISCUSSION.

The previously discussed D.A. reactions show three different types of solvent effect.

In *type A* (azodicarboxylate) the solvent acts as an electrophile, the interaction involves $\mathrm{LUMO_{solvent}}$-$\mathrm{HOMO_{solute}}$ and the rate *increases with the increase of the electrophilic character of the solvent.*

In *type B* (tetrahalo-*o*.quinone) the solvent acts as a nucleophile, the interaction involves $\mathrm{LUMO_{solute}}$-$\mathrm{HOMO_{solvent}}$ and the rate *decreases with the increase of the nucleophilic character of the solvent.*

In *type C* (*p*.bromonitrosobenzene), the small solvent effect is only the result of solvent-solvent interactions and the rate shows a *small increase with the increase of the solvent cohesive pressure.*

This behaviour suggested to investigated the solvent effect in the D.A. reactions reported in the literature, to check if these fit into types A-C. Only the examples with a significant number of solvents were considered and the results are reported in Table 7.

Examples 1A-12A are D.A. reactions with type A solvent effect and solvent behaves as an electrophile. If the D.A. has a normal electron demand(14) (1-4 and 8-12), solvent coordinates the carbonyl group of the dienophile; if the D.A. has an inverse electron demand (5-7), solvent again coordinates a carbonyl group which now belongs to the heterodiene. The kinetic data taken from examples 1A-12A give a good fit with equation 2 and hyperbolic relationships with AN were always observed.

Examples 1B-7B are D.A. reactions with type B solvent effect and solvent behaves as a nucleophile. All give good linear correlations with D_π and ρ values are always negative. All dienophiles have a low-lying LUMO (with the exception of maleic anhydride, -1.4 eV),(22) which rationalizes the preferred interaction with the HOMO of the solvent.

Examples 1C and 2C are D.A. reactions with type C solvent effect. Their main character is a very small solvent effect which give a reasonable fit with the cohesive pressure (δ_H^2) of the solvent.

This monoparametric approach emphasizes the contribution of a single effect of the solvent. Using a multiparametric approach, if the effect developed from the monoparametric relationship should again remain the main contribution, not only some minor effects could be developed, but, more important, some border-line examples could be rationalized.

To combine type A-C solvent effects, a triparametric equation involving AN, D_π and δ_H^2 (with the contribution of AN being reduced to first-order by assuming the denominator of equation 1 to be a constant) should be used.

There is no need of a further multiparametric equation in the literature. Thus it was decided to test examples in Table 7 with the Kamlet-Taft (K.T.) equation(18) (eq. 4) since, in addition to δ_H^2, α represents the acidity contribution of the solvent, β its basicity (integrated by ξ which is the co-ordinate covalency parameter), these mimic - reduced to a linear form - the contributions of AN and D_π respectively, and the equation is completed by the index of solvent dipolarity-polarizability π^* (corrected by a discontinuous polarizability term δ).

Table 7: Solvent effect of D.A. reactions: monoparametric correlations

N	Reaction(a)	N° solvents	solvent(b) parameters	Equation parameters(c)		Ref.
1A	cyclopentadiene + acrolein	15	AN	h=.9752; j=.0079; k=.0082;(d)	r=.951	(23)
2A	cyclopentadiene + methylacrylate	10	AN	h=.9624; j=.0080; k=.0027;(d)	r=.951	(23)
3A	cyclopentadiene + crotonaldehyde	10	AN	h=.8029; j=.0117; k=.0166;	r=.904	(23)
4A	cyclopentadiene + methacrolein	10	AN	h=.8695; j=-.0137; k=.0051;(d)	r=.983	(23)
5A	p.nitrobenzylidenepyrazolone + vinylether	28	AN(14)(e)	h=.5160; j=.0015; k=.0268;	r=.967	(4)
6A	o.methoxybenzylidenepirazolone + vinylether	28	AN(14)(e)	h=.4973; j=.0054; k=.0297;	r=.983	(4)
7A	4-(butenyloxybenzylidene)-5-pirazolone	21	AN	h=.1444; j=.0100; k=.0117;	r=.988	(1)
8A	DMB + naphthoquinone	17	AN	h=-.0717; j=-.0530; k=-.0182;	r=.969	(2)
9A	DMB + 5-hydroxynaphthoquinone	10	AN	h=.6369; j=-.0626; k=-.0239;	r=.961	(3)
10A	DMB + 5-methoxynaphthoquinone	10	AN	h=.2928; j=-.0431; k=-.0120;	r=.959	(3)
11A	DMB + 5-acetylnaphthoquinone	10	AN	h=.1103; j=-.0847; k=-.0343;	r=.971	(3)
12A	DMB + azodicarboxylate	25	AN	h=-.1324; j=-.0628: k=-.0164;	r=.863	(4)
1B	dimethylanthracene + maleic anhyd.	14	D_π(9)	i=1.26; ρ=-0.36;	r=.921	(24)
2B	dimethylanthracene + fumaronitrile	14	D_π(7)	i=0.84; ρ=-0.28;	r=.915	(25)
3B	diphenylbutadiene + triazolindione	7	D_π(6)	i=0.71; ρ=-0.59;	r=.987	(6)
4B	anthracene + triazolindione	10	D_π(9)	i=-0.64; ρ=-0.75;	r=.875	(6)
5B	anthracene + tetracyanoethylene	11	D_π	i=-0.27; ρ=-0.76;	r=.962	(20,26)
6B	DMB + tetrachloro-*o*-quinone	14	D_π(12)	i=0.78; ρ=-0.82;	r=.970	(f)
7B	DMB + tetrabromo-*o*-quinone	14	D_π(12)	i=0.83; ρ=-0.83;	r=.963	(f)
1C	DMB + 4-bromonitrosobenzene	27	δ_H^2	i=0.21; ρ=0.41;	r=.760	(f)
2C	cyclopentadiene dimerization	15	δ_H^2(14)	i=0.30; ρ=0.25;	r=.553	(9,27)

(a) With the exception of 3B only kinetic studies in more than 8 solvents were considered.

(b) Parameters used for the correlation (the number of solvents is added when parameters are not available for the entire set of data).

(c) For a linear correlation, intercept and slope are given; for a hyperbolic correlation h, j, and k values (see eq. 2); for both, the correlation coefficient.

(d) A good linear relationship can be obtained by plotting the kinetic data *vs* AN; this simply means that the denominator of equation (2) is about 1 since *k* value is very small.

(e) Primary and secondary alcohols excluded, see ref. 4.

(f) This paper.

Table 8: Solvent effect of D.A. reactions: multiparametric correlations with the Kamlet-Taft equation.

N	N°[a] of solvents	π^*[b]	β	α	$\delta_H^2/100$	ξ	r
1A	15	--	-0.13 (9%)	+0.99 (91%)	--	--	0.916
2A	10	--	--	+0.51 (78%)	-0.02 (22%)	--	0.944
3A	10	--	-0.54 (38%)	+0.59 (62%)	--	--	0.942
4A	10	+0.58 (20%)	--	+0.86 (80%)	--	--	0.976
5A	23	--	--	+1.50 (87%)	+0.22 (13%)	--	0.986
6A	23	--	--	+1.04 (92%)	+0.08 (8%)	--	0.923
7A	17[c]	+0.54 (25%)	--	+0.99 (75%)	--	--	0.927
8A	16	+0.75 (36%)	--	+0.90 (64%)	--	--	0.957
9A	10	+0.62 (33%)	--	+0.68 (67%)	--	--	0.947
10A	10	+0.74 (33%)	--	+0.80 (67%)	--	--	0.956
11A	10	+0.96 (37%)	--	+0.89 (63%)	--	--	0.958
12A	23	+1.29 (35%)	-0.58 (18%)	+1.33 (47%)	--	--	0.919
1B	13	--	-1.02 (80%)	--	--	-0.97 (20%)	0.845
2B	13	--	-0.56 (46%)	+0.37 (39%)	+0.13 (15%)	--	0.854
3B	6	+2.49 (31%)	-2.25 (30%)	+1.86 (39%)	--	--	0.999
4B	9	+1.59 (20%)	-2.64 (55%)	+1.64 (25%)	--	--	0.991
5B	11	+1.56 (22%)	-1.53 (47%)	--	+0.56 (31%)	--	0.922
6B	13	--	-1.89 (61%)	--	--	-3.26 (39%)	0.893
7B	13	--	-1.87 (58%)	--	--	-3.56 (42%)	0.905
1C	26	+0.38 (46%)	--	--	+0.29 (54%)	--	0.857

(a) solvents with parameters not available were excluded;

(b) in parentheses the relative weight of this and other coefficients;

(c) the chloroform point shows a large deviations and is not included in the correlation.

$$A = A_o + s \times (\pi^* + d \times \delta) + a \times \alpha + b \times \beta + h \times \delta_H^2/100 + e \times \xi \qquad (4)$$

The results are reported in Table 8. For each example the parameters showing a negligible contribution were excluded and the K.T. equation thus becomes a two-parameters-, or eventually a three-parameters-equation when a third inclusion improves significantly the correlation coefficient.

From the relative weight of each parameter clearly results that examples 1A-12A are D.A. reactions where solvent acts mainly as an electrophile. In our opinion some secondary contributions (*e.g.* β in 1A,3A or the negative contribution of δ_H^2 in 2A) are significant only from a mathematical point of view. A weight of π^* greater than 30% cannot be ignored since the contribution to the transition state of limit structures with a dipolar character [*e.g.* (a) for the reaction of **1** with **2** and the consequent relationship with E_T - Fig. 1a] could become significant.

Examples 1B-7B have their main contribution from β and ξ parameters, hence are D.A. reactions where solvent acts mainly as a nucleophile. With the exception of 1B, the weight of β (and ξ) shows a trend to increase with the order of stabilization of LUMO dienophile. Certainly the contribution from a different FMO interaction cannot be ignored, but the influence of some parameters is probably overestimated and some gaps derive from the non homogeneus range of solvents tested.

Finally 1C becomes a nice example how both correlations in Fig. 3 can reasonably be combined, and even if the solvent-solvent interactions offer the larger contribution, that of polarity-polarizability parameters$^{(10)}$ cannot certainly be ignored. The main problem of type C examples is the small change of the kinetic data within the solvent that make difficult every statistical analysis (reaction 2C) and meaningless a multiparametric approach.

In conclusion, the solvent effect of the D.A. reaction can be rationalized either through a monoparametric or a multiparametric approach. Both results develop concept largely superimposable and this topic seems now less intricate than before.

It is hoped that the solvent effect of other pericyclic reactions, not involving dipoles, can be faced with the same approach.

EXPERIMENTAL SECTION.

^{1}H and ^{13}C-nmr spectra were recorded on Brüker WP80SY spectrometer, i.r. spectra on a Perkin Elmer 983 spectrometer.

Materials - 2,3-dimethylbutadiene (**1**) and diethylazodicarboxylate (**2**) were commercial redistilled products. *p*.Bromonitrosobenzene (**3**) was prepared from *p*.bromoaniline as reported in literature$^{(28)}$ and its m.p., from aqueous ethanol was 93 °C (lit.,$^{(28)}$ 94 °C). Tetrachloro- and tetrabromo-*o*-benzoquinone (**6a,b**) were commercial recrystallized products.

Reaction of 1 and 2 - The reaction was performed as reported in the literature$^{(12)}$ and 1,2-dicarboethoxy-4,5-dimethyl-1,2,3,6-tetrahydropyridazine (**3**) was obtained in nearly quantitative yield. B.p. 102-104 °C/0.5 mm (Lit.,$^{(12)}$ 103-106 °C/0.5 mm). I.r.: ν_{CO}=1718 cm^{-1}. ^{1}H-Nmr ($CDCl_3$): 1.27 (t, 6 H, Me ester), 1.61 (s, 6 H, Me in 4 and 5), 3.93 (m, 4 H, CH_2 in 3 and 6), 4.20 (q, 4 H, -OCH_2-). The reaction, performed in each of the 25 solvents listed in Table 1, gave the same result.

Reaction of 1 and 4 - The reaction was performed as reported in the literature,(15) and 2-*p*.bromophenyl-4,5-dimethyl-3,6-dihydro-1,2-oxazine (**5**) was obtained in nearly quantitative yield. M.p. 83-84 °C from petrol ether (Lit.,(15) 81-82 °C). ^{1}H-Nmr ($CDCl_3$): 1.69 and 1.71 (s, 3 H + 3 H, Me in 4 and 5), 3.63 (broad s, 2 H, CH_2 in 3), 4.30 (broad s, 2 H, CH_2 in 6), 6.9-7.5 (4 H, aromatics). The reaction performed in each of the 27 solvents listed in Table 3, gave the same result.

Reaction of 1 and 6a,b - These reactions were performed as reported in the literature.(17) 7,8,9,10-tetrachloro-3,4-dimethyl-1-oxaspiro[5,5]undeca-3,7,9-trien-11-one (**7a**) had m.p. 97-98 °C from petrol ether (Lit.,(17) 99-100 °C). The analogous tetrabromo compound (**7b**) had m.p. 100-101 °C from petrol ether (Lit.,(17) 98-99 °C). 5,6,7,8-tetrachloro-2,3-dihydro-2-isopropenyl-2-methyl-1,4-benzodioxan (**9a**) had m.p. 95-96 °C from methanol (Lit.,(17) 94-95 °C). The analogous tetrabromo compound (**9b**) had m.p. 96-98 °C from methanol (Lit.,(17) 95-96 °C). 1,4,5,6-tetrachloro-3′,6′-dihydro-endo-8-isopropenyl-4′,5′,8-trimethyl spiro[biciclo[2,2,2]oct-5-ene-2 ,2′-pyran]-3-one (**8a**) had m.p. 127-28 °C from methanol (Lit.,(17) 128-130 °C). The analogous tetrabromo compound (**8b**) had m.p. 144-145 °C from methanol (Lit.,(17) 143-144 °C). The i.r. and ^{1}H-nmr spectra of all these compounds had data identical to those reported in the literature.(17)

Determination of the [7a + 8a]:[9a] ratios - These were performed by h.p.l.c. on a Waters Associated ALC/CPC 244 liquid chromatograph with a Beckman mod. 25 spectrophotometer operating at 255 nm as detector. The chromatographic separations were performed on a stainless column (25 cm length x 4 mm internal diameter) pre-packed with Lichrosorb Si 60 (10 μm) Merck; eluant: cyclohexane-ethyl acetate 9:1; flow 0.5 cm^3 min^{-1}; retention times (**7a** + **8a**) 6.2, (**9a**) 8.4 min.

Five solutions of known compositions of pure **7a** and **9a** were prepared with a ratio (**7a**)/(**9a**) in the range 80/20 - 97/3, each composition being tested on two indipendent samples at least four times each. A calibration curve (which is in practice a line) was obtained by fitting the composition *vs* the ratio $h_1/(h_1+h_2)$, h_1 and h_2 being the peaks height of **7a** and **9a** respectively. The unknown compositions were determined by fitting the ratio of the peaks height on the calibration curve.

Four samples of a solution of **6a** (0.01 M) and **1** (1.5 M) in the suitable solvent were heated in sealed quartz tubes at 30 °C. After a suitable time the solution was quenced, evaporated under vacuum at room temperature, and the residue dissolved in a small volume of eluant. At 10% completion of the reaction, this mixtures can be considered to be composed of **7a** and **9a** only.

The ratio (**7a**)/(**9a**) thus obtained was used to determine k_{7a} and k_{9a}, whose sum is k_1. Having determined from a sample of pure **7a** the rates k_2 and k_3 at 30 °C, Table 9 reports the rate constants in chloroform and 1,4-dioxan for the overall process illustrated in scheme 4.

Table 9: Rate constants in chloroform and 1,4-dioxan at 30 °C for the reaction of **6a** *illustrated in scheme 4.*

Solvent	$10^6 \times k$ (a)				
	k_1(b)	k_{7a}	k_{9a}	k_2	k_3
chloroform(c)	9650	9071	579	4.90	76
1,4-dioxan(c)	196	181	15	3.17	52

(a) k_1, k_{7a}, k_{9a}, and k_3 are second order rate constants (L mol^{-1} s^{-1}); k_2 is a first order rate constant (s^{-1}).

(b) $k_1 = k_{7a} + k_{9a}$

(c) The ratio (**7a**)/(**9a**), determined as described above, is [94:6] in chloroform and [92.5:7.5] in 1,4-dioxan.

From the rate constants reported in Table 9, under the assumptions of irreversible reactions, the products distribution at various degrees of completion of the reaction was computed (Table 10).

From hplc and ε values of **7a** and **8a** at 255 nm in the eluant (2620 and 1240 respectively), the products distribution was determined and these values are reported in parentheses in Table 10, with a good fit between computed and experimental data.

Since chloroform and 1,4-dioxan can be considered as extremes in the kinetic behaviour, all other solvent were simply tested at 10-15% completion of the reaction and the ratio (**7a**)/(**9a**) was found to be 93(±2):7.

Solvents - The solvents for the kinetic runs were freshly distilled reagent grade (u.v. spectroscopic grade when available).

Table 10: Computed and experimental (in parentheses) distribution of products 7a-9a from the reactions at 30 °C outlined in scheme 4, using chloroform and 1,4-dioxan as solvents.

% disappearance of **6a**	chloroform			1,4-dioxan		
	7a%	**8a**%	**9a**%	**7a**%	**8a**%	**9a**%
10	94.1	---	5.9	91.5	1.3	7.2
				(91.4)	(1.4)	(7.2)
20	94.2	0.1	5.7	89.2	2.9	7.9
30	93.9	0.2	5.9	87.5	4.4	8.1
	(93.9)	(0.1)	(6.0)	(87.8)	(4.4)	(7.8)
50	93.7	0.3	6.0	83.0	8.8	8.2
				(82.8)	(8.8)	(8.4)
70	93.5	0.5	6.0	75.6	15.6	8.8
	(93.0)	(0.5)	(6.5)	(74.4)	(15.4)	(10.2)
90	92.8	1.1	6.1	60.0	30.1	9.9
				(58.2)	(29.2)	(12.6)

Kinetics - The second-order rate constants were measured by following the disappearance of the heterodienophile on a Perkin-Elmer Lambda 5 u.v.-vis. spectrophotometer provided of thermostatted cells transport assembly and "automatic multicell programmer". The solutions were measured in 1.00 cm OS Hellma couvettes of 3 cm^3 capacity. Measuraments were made at 410 nm for **2**, at 745 nm for **4**, at the wavelengths given in Table 11 for **6a,b** in the different solvents. A solution of the suitable heterodienophile in the required solvent was prepared in a 25 cm^3 volumetric flask. The range of concentrations was 0.005-0.01 M for **2**, 0.001-0.005 M for **4**, and 0.0005-0.001 M for **6 a,b**. DMB (**1**) (*ca.* 0.5-1.0 cm^3) was added to an accurately weighed 10 cm^3 volumetric flask containing *ca.* 5 cm^3 of the required solvent. After the addition of **1**, the flask was again weighed for an accurate determination of the amount of DMB and then filled with solvent.

Six samples of the solution of the heterodienophile (2.00 cm^3 measured using a pipette) were placed in six cuvettes thermostatted at the required temperature and variable amounts (from 0.20 to 1.00 cm^2, accurately measured with a microsyringe) of the DMB solution were added. After vigorous mixing, the kinetic determinations were initiated.

Table 11: Wavelengths in nm used for the kinetic determinations of the reactions between 1 and 6a,b.

Solvent	**6a**	**6b**
Chloroform	460	480
Cyclohexane	450	460
1,2-Dichloroethane	460	470
Chlorobenzene	470	500
Nitromethane	460	460
Nitrobenzene	460	500
Acetonitrile	450	460
Propylene carbonate	450	480
Benzene	460	480
Aceton	440	460
Ethyl acetate	440	450
Dimethoxymethane	440	440
1,4-Dioxan	440	460
Tetrahydrofuran	430	460

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REFERENCES AND NOTES.

1) Part IV. Corsico Coda, A.; Desimoni, G.; Faita, G.; Righetti, P.P.; Tacconi, G. *Tetrahedron,* **1989**, *45*, 775.
2) Corsico Coda, A.; Desimoni, G.; Ferrari, E.; Righetti, P.P.; Tacconi, G. *Tetrahedron,* **1984**, *40*, 1611.
3) Desimoni, G.; Faita, G.; Righetti, P.P.; Tornaletti, N.; Visigalli, M. *J. Chem. Soc., Perkin Trans II,* **1989**, 437.
4) Burdisso, M.; Desimoni, G.; Faita, G.; Righetti, P.P.; Tacconi, G. *J. Chem. Soc., Perkin Trans II,* **1989**, 845.
5) Mayer, V.; Gutmann, V.; Berger, W. *Monatsch. Chem.,* **1975**, *106*, 1235.
6) Konovalov, A.I.; Breus, I.P.; Sharagin, I.A.; Kiselev, V.D. *Zh. Organ. Khim.*, **1979**, *15*, 361.
7) Swieton, G.; Kelm, H. *J. Chem. Soc., Perkin Trans II,* **1979**, 519.
8) Katada, T.; Eguchi, S.; Esaki, T.; Sasaki, T. *J. Chem. Soc., Perkin Trans I,* **1984**, 1869.
9) The leading reference on this topic is Reichardt, C. "Solvents and Solvent Effects in Organic Chemistry", VCH, Weinheim, 1988.
10) Reichardt, C. *Pure and Appl. Chem.*, **1982**, *54*, 1867.
11) Boger, D.L.; Weinreb, S.N. "Hetero Diels-Alder Methodology in Organic Synthesis", Academic Press, San Diego, 1987.
12) Gillis, B.T.; Beck, P.E. *J. Org. Chem.*, **1962**, *27*, 1947.
13) Ref. 9 p. 365-371 and references therein.
14) Sauer, J.; Sustmann, R. *Angew. Chem. Int., Ed. Engl.*, **1980**, *19*, 779.
15) Kojima, S. *Kogyo Kagakuzasshi*, **1956**, *59*, 951; *C.A.* **1958**, *52*, 12870.
16) Hildebrand, J.H.; Scott, R.L. "The solubility of Nonelectrolytes", 3rd ed., Dover, New York, 1964.
17) Ansell, M.F.; Leslie, V.J. *J. Chem. Soc. (C)*, **1971**, 1423.
18) Kamlet, M.J.; Abboud, J.L.; Taft, R.W.; Abraham, M.H. *J. Org. Chem.*, **1983**, *43*, 2877.
19) Burden, A.G.; Collier, G.; Shorter, J. *J. Chem. Soc., Perkin Trans II,* **1976**, 1627
20) Oshima, T.; Arikata, S.; Nagai, T. *J. Chem. Res. (S)*, **1981**, 204.
21) Sabatino, A.; La Manna, G.; Paoloni, L. *J. Phys. Chem.*, **1980**, *84*, 2641.
22) Kampars, V.; Neilands, O. *Russian Chem. Rev.*, **1977**, *46*, 508.
23) Blankenburg, B.; Fiedler, H.; Hampel, M.; Hanthal, H. G.; Just, G.; Kahlert, K.; Korn, J.; Müller, K. H.; Pritzkow, W.; Reinhold, Y.; Röllig, M.; Sauer, E.; Schnurpfeil, D.; Zimmermann, G. *J. Prakt. Chemie*, **1974**, *316*, 804.
24) Kiselev, V. D.; Konovalov, A. I. *Zh. Organ. Khim.*, **1974**, *10*, 6.
25) Sauer, J.; Wiest, H.; Mielert, A. *Chem. Ber.*, **1964**, *97*, 3183.
26) Brown, P.; Cookson, R.C. *Tetrahedron,* **1965**, *21*, 1977.
27) Cöster, G.; Pfeil, E. *Chem. Ber.*, **1968**, *101*, 4248.
28) Hamer, J.; Ahmad, M.; Holliday, E. *J. Org. Chem.*, **1963**, *28*, 3034.