Solvent Effect in Pericyclic Reactions, XI[+]
The Electrocyclic Reactions

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Keywords: Cyclizations / Electrocyclic reactions / Solvent effects / Salt effect

The rate constants of the electrocyclic ring closure of (1*Z*,3*Z*,5*E*)-1,2,6-triphenylhexa-1,3,5-triene (**1**) and of the ring opening of dimethyl 3,4-dimethyl-1,2-diphenylcyclobutene-*cis*-3,4-dicarboxylate (**3**) were determined in 15 and 16 solvents, respectively. The ring closure of **1** shows, in spite of theoretical predictions, neither solvent nor salt effects. For the ring opening of **3**, small solvent and salt effects were found, suggesting the possibility of observing small acceleration due to specific solute–solvent or salt interactions.

Introduction

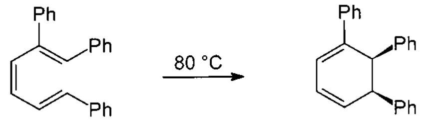
Reactions involving activation complexes isopolar with the reagents, such as pericyclic processes, are usually expected, on the basis of the Hughes−Ingold model, to exhibit negligible solvent effects.[1] Nevertheless, it has been found that significant solvent dependencies can be observed when specific solute−solvent interactions are involved. In particular, Diels−Alder (DA) cycloadditions[2][3] and ene reactions[4] are usually characterized by specific solvent effects and the reaction rates increase (or decrease) with the increase in the solvent acidity (or basicity). 1,3-Dipolar cycloadditions,[5] Claisen,[6][7] retro Claisen,[8] diaza Claisen rearrangements,[9] as well as cheletropic reactions[10] belong to a second group of pericyclic processes characterised by generally small solvent effects which are functions of solvent polarity.

Even though electrocyclic reactions are important both from a theoretical[11] and a synthetic point of view,[12] there have been few detailed investigations of the influence of the solvent on reactivity; only two studies on the effect of a limited number of solvents on two different pericyclic processes have been reported in the literature. The conrotatory cyclization of *all-cis*-2,4,6,8-tetraene to *trans*-7,8-dimethylcycloocta-1,3,5-triene has been investigated in five solvents of different polarity and a negligible increase of the rate was observed ($k_{\mathrm{rel}} \approx 1.2$).[13] The effect of the solvent on the ring opening of 2-methyl-4,4-diphenylcyclobutenone has also been determined in seven different solvents, and again it was found to be small ($k_{\mathrm{rel}} \approx 3.0$).[14]

Since the experimental investigation of small solvent effects in pericyclic reactions would provide an interesting comparison with results derived from ab initio calculations,[10][15] the rate of a six-electron−six-atom ring closure and of a four-electron−four-atom ring opening was determined for a large set of solvents.

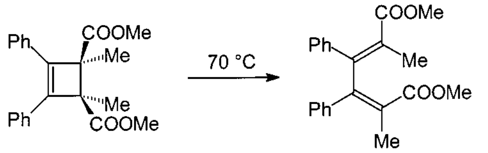
Results

Two different reactions were chosen as models of the above processes. The first was the 1,6-electrocyclization of (1*Z*,3*Z*,5*E*)-1,2,6-triphenylhexa-1,3,5-triene (**1**) to *cis*-1,5,6-triphenylcyclohexa-1,3-diene (**2**)[16] (Equation 1). The second reaction was the ring opening of dimethyl 3,4-dimethyl-1,2-diphenylcyclobutene-*cis*-3,4-dicarboxylate (**3**) to dimethyl (2*E*,4*Z*)-2,5-dimethyl-3,4-diphenylmuconate (**4**) (Equation 2).[17] The former electrocyclic process involves a totally aliphatic system, the latter a substrate characterised by the presence of carbonyl substituents able to show polar and/or specific interactions in determing the solvent effect.



1 **2**

(1)



3 **4**

(2)

The kinetic determinations, run at 80°C in 15 solvents, were performed by UV/Vis-spectroscopic analysis of the disappearing chromophore or by ^{1}H-NMR analysis of the reaction mixture. The reactions were monitored to 90−95% completion (see Experimental Section for details). The first-order rate constants, expressed as the average of at least three independent kinetic runs, are reported in Table 1.

Both electrocyclic processes are influenced very little by the solvent, but a significant difference between the two reactions was observed. The correlation of the kinetic data of the ring closure of **1** with different solvent parameters gave very poor results,[18] and, in our opinion, when a reaction run in 15 solvents has a k_1 average of 1.27 s^{-1} with a standard deviation of ±0.24, any attempt to find relationships

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1434−193X/99/0808−1921 $ 17.50+.50/0

Table 1. Rate constants of the electrocyclic ring closure of **1** at 80°C and of the electrocyclic ring opening of **3** at 70°C in different solvents

Solvent	$10^4 \times k_1(\mathbf{1})$ [s^{-1}]	$10^6 \times k_1(\mathbf{3})$ [s^{-1}]
Cyclohexane	1.44 ± 0.14	3.57 ± 0.04
Carbon tetrachloride	1.09 ± 0.05	3.50 ± 0.20
Benzene	1.27 ± 0.07	3.78 ± 0.05
1,4-Dioxane	1.58 ± 0.05	3.80 ± 0.05
Chlorobenzene	1.07 ± 0.07	–
Chlorofom	0.88 ± 0.02	4.97 ± 0.04
Pyridine	–	3.76 ± 0.08
1,2-Dichloroethane	0.95 ± 0.13	3.20 ± 0.05
Nitrobenzene	–	3.42 ± 0.04
Acetone	1.20 ± 0.20	3.20 ± 0.08
DMF	1.17 ± 0.07	3.30 ± 0.05
tert-Butyl alcohol	1.42 ± 0.12	–
DMSO	1.08 ± 0.08	3.51 ± 0.08
Acetonitrile	1.58 ± 0.08	3.60 ± 0.15
2-Propanol	1.40 ± 0.10	6.20 ± 0.05
Acetic acid	–	7.70 ± 0.08
Ethanol	1.26 ± 0.09	5.90 ± 0.10
Methanol	1.69 ± 0.06	6.30 ± 0.10

with solvent parameters is meaningless and *the reaction can only be classified as one with no solvent effect*.

The reaction of **3** was also very little influenced by the solvent, but some statistically significant correlations with solvent parameters were observed. Although a specific solute−solvent interaction shows only a small solvent effect, the Hydrogen Bond Donor (HBD) ability of a solvent may be observed to have a clear influence, since faster reactions occur in alcohols and acetic acid. When the kinetic data of the electrocyclic ring opening of **3** are plotted versus a typical HBD parameter as α,[19] the linear regression in Figure 1 is obtained.

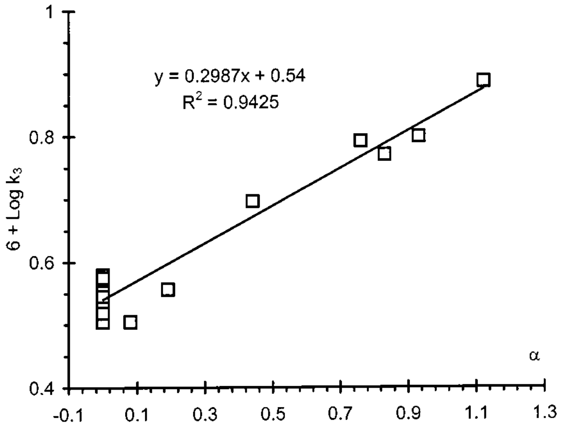

Figure 1. Rate constants of the electocyclic ring opening of **3** at 70°C plotted against the α parameter of the solvent

Activation Parameters

The activation parameters of the electrocyclic reactions of **1** and **3** were determined in acetone, benzene, DMSO, and methanol by running the reaction at four different temperatures; the results are collected in Table 2. The activation parameters of the electrocyclization of **1** are nearly constant within the solvent, while the ring opening of **3** shows the lowest activation enthalpy in methanol, the solvent with the highest HBD ability. In both cases, the values of $\Delta H^{\neq}$ and $\Delta S^{\neq}$ are in substantial agreement with the values reported in the literature for hexatriene cyclizations and cyclobutene ring opening.[20]

Discussion and Conclusion

The very small solvent effect for the electrocyclic ring closure of **1** and the absence of any significant correlation between kinetic data and solvent polarity, suggested no change of the polarity during the activation process for the reaction of **1**. This was confirmed by the computation (AM1 method) of the dipole moments of **1** and **2**. The calculated values of μ_1 and μ_2 are 0.18 and 0.12 D, respectively, and therefore the resulting $\Delta\mu(\mathbf{1}\rightarrow\mathbf{2})$, −0.06 D, is very close to zero.

In a recent paper[21] large accelerating effects by cationic lithium, sodium, and magnesium catalysis were predicted by computation for the cyclization of 1,3,5-hexatriene, with the cation strongly interacting with the π-electron cloud in the transition state. The electrocyclic conversion of **1** to **2** is therefore the appropriate model for an experimental test of calculations, even if the absence of correlation between rate constants and acidic character of the solvent do not support the expectation of a large cationic catalysis.[22−25]

On the other hand, the small solvent effect observed in the ring opening of **3** which is dependent on the HBD solvent character, suggested testing the rate-increasing properties of inorganic cations on this reaction, too.

The rate constants of the reactions of **1** and **3** were determined at 70°C in 0.5 M acetonic solutions of lithium (LP) and magnesium perchlorate (MP); the results are collected in Table 3. Taking the rates in acetone as the references, no increase of the rate was observed when the reaction was performed in the presence of inorganic perchlorates. The lithium and magnesium cations do not, therefore, have a catalytic effect.

The use of 1 equiv. of MP in noncoordinating solvents such as dichloromethane has recently been found to give higher accelerations than those observed in MP/acetone or LP/acetone solutions,[26] even if, given the intrinsic insolubility of the inorganic salt in dichloromethane, the reacting substrates must behave as a ligand to obtain homogeneous solutions. Since substrate **1** does not dissolve MP, the effect of one equiv. of MP was tested in dichloromethane in the presence of 15 equiv. of dimethyl carbonate (DMC) as auxiliary ligand. Whereas the data reported in Table 3 do not support the theoretical predictions since the ring closure of **1** is not catalyzed by MP, the rate of the ring opening of **3** was increased by a factor of 4, a value that is about two times higher than the solvent effect.

In conclusion the electrocyclic reactions investigated in this paper can be regarded as pericyclic processes with no solvent and no cationic catalysis effect in the case of totally aliphatic substrates. However, in the presence of polar

Table 2. Activation parameters of the electrocyclic reactions of **1** and **3** in different solvents

	1 → **2**		**3** → **4**	
Solvent	$\Delta H^{\neq}$ [kcal mol^{-1}]	$\Delta S^{\neq}$ [cal K^{-1} mol^{-1}]	$\Delta H^{\neq}$ [kcal mol^{-1}]	$\Delta S^{\neq}$ [cal K^{-1} mol^{-1}]
Benzene	22.7 ± 0.5	−12.1 ± 1.4	27.4 ± 0.2	−3.5 ± 0.5
Acetone	22.0 ± 1.0	−15.0 ± 1.5	28.1 ± 0.5	−1.8 ± 1
DMSO	22.0 ± 1.0	−15.0 ± 1.5	27.5 ± 0.3	−3.5 ± 0.8
Methanol	22.0 ± 1.0	−14.0 ± 2.0	26.8 ± 0.3	−4.4 ± 0.8

Table 3. Rate constants of the reaction of **1** [k(**1**)] and **3** [k(**3**)] at 70°C in acetone, in acetonic solution of lithium perchlorate (LPAC) and magnesium perchlorate (MPAC) (0.5 M), and in dichloromethane/diemethyl carbonate (DMC) solutions

Solvent	$10^5 \times k$ (**1**) [s^{-1}]	k_{rel}	$10^6 \times k$ (**3**) [s^{-1}]	k_{rel}
Acetone	4.8	1	3.2	1
LPAC 0.5 M	5.2	1.08	3.8	1.19
MPAC 0.5 M	5.0	1.04	3.5	1.09
MP (1 equiv.)/ CH_2Cl_2	2.8	0.53[a]	19.0	3.96[b]

[a] Calculated by taking as reference the rate in pure dichloromethane at 70°C (5.3×10^{-5} s^{-1}). – [b] Calculated by taking as reference the rate in pure dichloromethane at 70°C (4.8×10^{-6} s^{-1}).

methoxycarbonyl substituents with donor properties small, but nevertheless significant, contributions both from the acidic solvent character and the inorganic cations acting as Lewis acid are observed.

Experimental Section

Materials: (1*Z*,3*Z*,5*E*)-1,2,6-Triphenylhexa-1,3,5-triene (**1**) was prepared as described in the literature; m.p. 81–82°C (ref.[16] 78–80°C). Dimethyl 3,4-dimethyl-1,2-diphenylcyclobutene-*cis*-3,4-dicarboxylate (**3**) was prepared as described in the literature; m.p. 136–137°C (ref.[17] 136–138°C). The solvents for the kinetic runs were deuterated grade (% D ⩾ 99%) reagents (for the ^{1}H-NMR kinetic determinations) or distilled anhydrous UV/Vis-spectroscopic grade reagents. The metal perchlorates were A. C. S. grade reagents; lithium perchlorate (LP) was dried under vacuum at 140°C for 8 h. ***Caution:*** All perchlorates are potential explosives and must be handled with care.[27]

^{1}H-NMR Kinetic Determinations: The overall reaction rates were measured by monitoring the change of the ^{1}H-NMR spectrum of the reaction mixture recorded with a Bruker AC 300 spectrometer. About 10 mg of **3**, dissolved in the required deuterated solvent (about 0.5 mL), was heated in a sealed NMR tube in an oil ultrathermostat at 70.0 ± 0.1°C. At appropriate time intervals (from 400 to 800 min) the tube was cooled at room temperature and the ^{1}H-NMR spectrum was recorded. The relative concentrations of **3** and **4** were determined from the integral ratios of their respective methyl and methoxy signals.

UV/Vis Kinetic Determinations: The overall reaction rates were measured by monitoring the disappearance of the chromophore **1** or **3** with a Perkin–Elmer Lambda 16 spectrophotometer provided with a thermostated cell transport assembly and an automatic multicell programmer. The solutions were measured in 1.00-cm OS Hellma couvettes with 3 mL capacity. To a half-filled 25 mL volumetric flask was added about 8 mg of **1** or 30 mg of **3**, and the flask was then filled with the solvent. Seven samples were prepared for each run. At $t = 0$, the samples were placed in a thermostat at the required temperature, and the initial absorbance of the solution was determined on a further sample. At appropriate time intervals the reaction was quenched and the residual absorbance of the chromophore at 360–380 nm (for **1**) or 310–330 nm (for **3**) was determined. The activation parameters reported in Table 2 were obtained from the rate constants reported in Tables 4 and 5.

Table 4. Rates and activation parameters of the electrocyclic reaction of **1** in different solvents

T [°C]	$10^5 \times k$ [s^{-1}] Benzene	Acetone	DMSO	Methanol
60	2.03 ± 0.06	1.8 ± 0.1	2.3 ± 0.1	2.9 ± 0.3
70	5.04 ± 0.12	4.8 ± 0.1	6.1 ± 0.1	6.6 ± 0.4
80	12.7 ± 0.7	12.0 ± 0.2	10.8 ± 0.8	16.9 ± 0.6
90	39.7 ± 0.3	30.8 ± 0.2	40.1 ± 0.6	49.4 ± 0.2

Table 5. Rates and activation parameters of the electrocyclic reaction of **3** in different solvents

T [°C]	$10^6 \times k$ [s^{-1}] Benzene	Acetone	DMSO	Methanol
60	1.15 ± 0.01	0.99 ± 0.02	1.06 ± 0.01	2.02 ± 0.06
70	3.78 ± 0.05	3.20 ± 0.08	3.51 ± 0.08	6.3 ± 0.1
80	12.8 ± 0.1	11.5 ± 0.1	11.5 ± 0.2	20.8 ± 0.2
90	37.9 ± 0.2	35.6 ± 0.7	35.7 ± 0.3	61.4 ± 0.3

Acknowledgments

Thanks are due to Prof. Rolf Huisgen for helpful discussions and suggestions. Financial support for this work was provided by the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST), by the Consiglio Nazionale delle Ricerche (CNR) "Progetto Strategico Tecnologie Chimiche Innovative", and by the University of Pavia.

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[1] C. Reichardt, *Solvents and Solvent Effects in Organic Chemistry*, VCH, Weinheim, **1988**.

[2] C. Cativiela, J. I. Garcia, J. A. Mayoral, L. Salvatella, *Chem. Soc. Rev.* **1996**, *25*, 209.

[3] [3a] G. Desimoni, G. Faita, P. P. Righetti, L. Toma, *Tetrahedron* **1990**, *46*, 7951. – [3b] G. Desimoni, G. Faita, D. Pasini, P. P. Righetti, *Tetrahedron* **1992**, *48*, 1667.

[4] G. Desimoni, G. Faita, P. P. Righetti, A.Sfulcini, D. Tsyganov, *Tetrahedron* **1994**, *50*, 1821.

[5] R. Huisgen, *Pure Appl. Chem.* **1980**, *52*, 2283.

[6] W. N. White, E. F. Wolfarth, *J. Org. Chem.* **1970**, *35*, 2196

[7] J. J. Gajewski, J. Yurayj, D. R. Kimbrough, B. Gande, B. K. Carpenter, *J. Am. Chem. Soc.* **1987**, *109*, 1170.

[8] G. Desimoni, G. Faita, S. Gatti Comini, P. P. Righetti, G. Tacconi, *Tetrahedron* **1993**, *49*, 2093.

[9] T. Mitsushashi, *J. Am. Chem. Soc.* **1986**, *108*, 2400.

[10] G. Desimoni, G. Faita, S. Garau, P. P. Righetti, *Tetrahedron* **1996**, *52*, 6241.

[11] R. B. Woodward, R. Hoffmann, *The Conservation of Orbital Symmetry*, Verlag Chemie, Weinheim, **1970**.

[12] G. Desimoni, G. Tacconi, A. Barco, G. P. Pollini, *Natural Products Synthesis Through Pericyclic Reactions*, ACS Monograph 180, American Chemical Society, Washington, D.C., **1983**.

[13] R. Huisgen, A. Dahmen, H. Huber, *Tetrahedron Lett.* **1969**, 1461.

[14] H. Mayr, R. Huisgen, *J. Chem. Soc., Chem. Commun.* **1976**, 57.

[15] T. Fernandez, J. A. Sordo, F. Monnat, B. Deguin, P. Vogel, *J. Am. Chem. Soc.* **1998**, *120*, 13276.

[16] A. Padwa, L. Brodshy, S. Clough, *J. Am. Chem. Soc.* **1972**, *94*, 6767.

[17] R. Mündnich, H. Plieninger, *Tetrahedron* **1978**, *34*, 887.

[18] A regression analysis of log k against a function of the refractive index of the solvent $[(n^2 - 1)/(n^2 + 1)]$ shows a roughly linear relationship ($r = 0.622$).

[19] M. J. Kamlet, J. L. Abboud, R. W. Taft, M. H. Abraham, *J. Org. Chem.* **1983**, *43*, 2877.

[20] E. N. Marvell, *Thermal Electrocyclic Reactions*, Academic Press, London, **1980**.

[21] J. Haijun, P. von Ragué Schleyer, *J. Am. Chem. Soc.* **1995**, *117*, 11529.

[22] G. Desimoni, G. Faita, P. P. Righetti, G. Tacconi, *Tetrahedron* **1991**, *47*, 8399.

[23] A. Casaschi, G. Desimoni, G. Faita, A. Gamba Invernizzi, S. Lanati, P. P. Righetti, *J. Am. Chem. Soc.* **1993**, *115*, 8002.

[24] G. Faita, P. P. Righetti, *Tetrahedron* **1995**, *51*, 9091.

[25] J. I. Garcia, V. Martinez-Merino, J. A. Mayoral, L. Salvatella, *J. Am. Chem. Soc.* **1998**, *120*, 2415.

[26] G. Desimoni, G. Faita, M. Mella, M. Ricci, P. P. Righetti, *Tetrahedron* **1997**, *53*, 13495.

[27] J. C. Schumacher, *Perchlorates − Their Properties, Manufacture, and Uses*, ACS Monograph Series; Reinhold, New York, **1960**.

Received February 2, 1999
[O99048]