Tetrahedron Vol. 49, No. 10, pp. 2093-2100, 1993
Printed in Great Britain

0040-4020/93 $6.00+.00

Solvent Effect in Pericyclic Reactions. VIII.(1) The Retro Claisen Rearrangement

G. Desimoni*, G. Faita, S. Gatti Comini, P.P. Righetti, and G. Tacconi.

Dipartimento di Chimica Organica, Università di Pavia, V.le Taramelli 10, 27100 Pavia, Italy.

(*Received in UK* 13 *November* 1992)

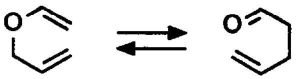
Abstract - The solvent effect on the retro Claisen rearrangement was kinetically investigated in 17 solvents. The rate constants were found to be a linear function of the Reichardt's $E_T(30)$ solvent polarity parameter. Tha rate was measured in 3 lithium perchlorate-methanol solutions, their $E_T(30)$ values determined, and the kinetic data found to lie on the previous linear relationship. Hence the solvent effect (as well as the activation parameters) of the retro Claisen rearrangement confirmed the nature of concerted reaction with a partial charge separation in the transition state, as previously demonstred for the forward process.

The investigation of the solvent effect on organic reactivity(2) is a very useful tool to understand the reaction mechanisms.

The generally accepted statement that pericyclic reactions are not sensitive to solvent effects, suggested to our group an investigation of the solvent effect in this field, and we started with the study of the Diels-Alder reaction. Our kinetic results(3), together with those taken from the literature(4), were rationalized in terms of specific solute-solvent interactions. Three different classes of solvent effects were evidenced(3): in *type a* solvent effect, the significative rate increasing was the result of the increase in the electrophilic character of the medium; in *type b* solvent effect, the significative rate decreasing was the result of the increase in the nucleophilic character of the medium; in *type c* solvent effect, the small increasing of the rate was the result of the increase of solvent internal pressure. The polarity of the medium gave contributions of secondary importance to the solvent effect in some cases only.

The above classification was verified also for the retro-Diels-Alder reaction(1): the solvent effect on a retro-cycloaddition belongs to the same class to which the solvent effect on the forward reaction belongs.

The next step of our investigation inferred the [3,3] sigmatropic rearrangements beginning with the Claisen rearrangement (C.R.) and the inverse reaction (the retro C.R.) that, even if it is not so popular as the direct process, it can occur under specific circumstances(5).



Three different studies on the solvent effect in the C.R. are reported in the literature.

White and Wolfarth(6) in 1970 reported the rate of the ortho C.R. of allyl *p*.tolyl ether in the gas phase and in 17 solvents of different polarities at 170 °C. The rate was found to increase by a factor of 100 in going from the least polar (tetradecane) to the most polar (*p*.chlorophenol) solvent studied. The kinetic data were correlated with the Kosower's empirical solvent polarity parameter (Z)(7) and a satisfactory linear relationship (r = 0.892) was obtained. This relation suggested a transition state with a dipolar character or a partial charge separation.

Seventeen years later, Gajewski and co-workers(8) published a study on the mechanism of rearrangement of chorismic acid. The solvent effect on the rearrangement of *trans,trans*-4-methyl-3-oxa-1,5,7-nonatriene was studied in 9 solvents at 75 °C. The rate was found to increase by a factor of 117 in going from the least polar (cyclohexane) to the most polar (2:1 methanol/water) solvent studied. The kinetic data were interpreted in terms of increased solvent polarity quantified by the $E_T(30)$ parameter(2).

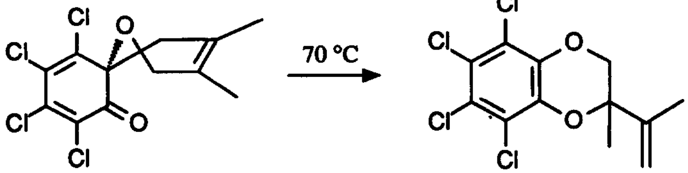
In 1989 Grieco and Gajewski(9) studied the effect of polar solvents on the C.R. of sodium- and methyl-8-vinyloxy-9-decenoate. In the case of the esther derivative, the kinetic study was performed in 8 solvents and in 4 aqueous mixtures; the rate was found to increase by a factor of 56 in going from cyclohexane to trifluoroethanol. The rate data were correlated with Y(OTs)(10) parameter obtaining a linear relationship with a slope of 0.23 (r = 0.99). This value was taken as an evidence that even in polar, hydroxylic solvents, the C.R. has substantially less polar character than solvolyses(9).

Till now no studies on the **retro C.R.** have been performed, and in this paper we wish to report our results on this topic.

Result and Discussion

During the study of the solvent effect on the Diels-Alder reaction, the cycloaddition between tetrachloro-*o*-benzoquinone and 2,3-dimethylbutadiene was investigated(3). As reported by Ansell and Leslie(11), this reaction gave (from equimolar amounts of reactants) two products: 7,8,9,10-tetrachloro-3,4-dimethyl-1-oxaspiro[5,5]undeca-3,7,9-trien-11-one (**1**) and 5,6,7,8-tetrachloro-2,3-dihydro-2-isopropenyl-2-methyl-1,4-benzodioxane (**2**) in a relative ratio about 9:1; **1**, in boiling benzene(3,11), rearranges to **2** (scheme). This reaction is the rearrangement of an substituted γ,δ-unsaturated carbonyl derivate to a substituted allyl vinylether, just the reverse of the C.R.

Scheme



1 **2**

The kinetic runs at 70 °C were studied by u.v.-vis. spectroscopic analysis of the disappearing chromophore **1** at the suitable wavelength (370-400 nm depending on the solvent), up to 70% completion. All reaction mixtures were checked by h.p.l.c. analysis in order to exclude any side-product (see Experimental for details). The first order rate constants, average of at least three kinetic runs, are reported in table 1.

Table 1. Rate constants at 70 °C of the retro-C.R. of 1 in differing solvents with corresponding $E_T(30)$.

solvent	$E_T(30)$	10^4 x k (sec^{-1})
n.hexane	30.9	1.58 ± 0.01
cyclohexane	31.2	1.41 ± 0.05
carbon tetrachloride	32.5	1.86 ± 0.03
benzene	34.5	2.4 ± 0.1
1,4-dioxane	36.0	2.96 ± 0.03
chlorobenzene	37.5	3.0 ± 0.1
ethyl acetate	38.1	3.3 ± 0.1
chloroform	39.1	3.3 ± 0.1
1,2-dichloroethane	41.9	3.6 ± 0.2
acetone	42.2	4.15 ± 0.15
t.butanol	43.9	4.4 ± 0.2
acetonitrile	46.0	5.8 ± 0.1
i.propanol	48.6	7.6 ± 0.1
acetic acid	51.2	7.1 ± 0.3
ethanol	51.9	8.4 ± 0.1
methanol	55.5	10.4 ± 0.2
trifluoroethanol	59.8	16.3 ± 0.3

The rate was found to increase by a factor of 11.5 in going from cyclohexane to trifluoroethanol: the solvent effect being significantly lower than those of the previously reported forward C.R.s. When the kinetic data in table 1 were plotted *vs* the $E_T(30)$ solvent polarity parameter(2), the graph reported in figure 1 was obtained. The excellent linear relationship ($r = 0.989$) is characterized by a positive value of the slope ($\rho = 0.034$): the rate slightly increases with the increase of the solvent polarity.

In the graph showed in figure 1, the largest part of the solvents are included in an $E_T(30)$ range between 30 and 50, while only four solvents have higher values of polarity. In order to increase the number of reaction media with high polarity values testing solutions with $E_T(30)$ values higher than 60, we took in consideration methanol solutions of lithium perchlorate (LP)(12). The $E_T(30)$ of LP-methanol solutions, up to 5.0 M, were easily calculated(2,12) from the wavelengths of the absorbance maximum (λ_{max}) of the Reichardt's betaine(13).

The rate constants in three LP-methanol solutions at 70 °C were obtained by extrapolation of the Arrhenius diagram obtained with the kinetic data at four different temperatures in the range 20-35 °C (see Experimental for details), and each reaction mixture was checked by h.p.l.c. analysis at 70 °C. The extrapolated rate constants, together with the λ_{max} of the Reichardt's betaine and the calculated $E_T(30)$ values, are reported in table 2.

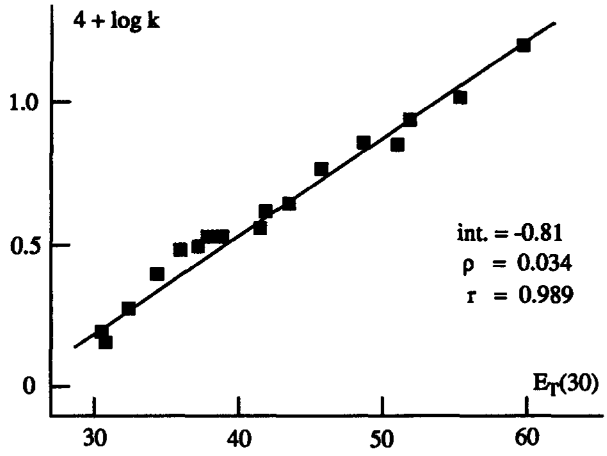


Figure 1. Rate constants of the retro-C.R. of 1 at 70 °C (Table 1) plotted vs $E_T(30)$ of the solvents.

From these data, a regular increase of the rate with the increase of the medium polarity can be observed. More interesting, when the kinetic data both in tables 1 and 2 are plotted *vs* the $E_T(30)$ parameter, an excellent linear relationship was again obtained (r = 0.993 - Figure 2) with the regression coefficients (intercept and slope) identical to those obtained for solvents only (see figure 1).

Activation parameters.

The activation parameters, determined for five selected solvents and for the three LP-methanol solutions, are reported in table 3. The activation entropy values are in the range between -4 e.u. (cyclohexane) and -12 e.u. (LP-methanol solutions). Such variations cannot be considered unusual; White and Wolfarth(6) found variations in $\Delta S^{\neq}$ in the range between -10 and -27 e.u.. The authors discussed these results in terms of possible hydrogen bonding or acid catalysis influences on the rate of the C.R., but the isokinetic correlation between $\Delta H^{\neq}$ and $\Delta S^{\neq}$ do not imply changes in the mechanism. The same reasoning can be applied to the $\Delta S^{\neq}$ values reported in table 3, and the data can be taken as an evidence of a concerted process for the retro-C.R. of 1.

Table 2. Rate constants for the retro-C.R. of 1 in methanol and LP-methanol solutions with λ_{max} and $E_T(30)$ values of the media.

solvent	λ_{max}	$E_T(30)$	10^4 x k (sec^{-1})
methanol	515.0	55.5	10.4 ± 0.2
methanol-$LiClO_4$ 1.15 M	484.2	59.0	13.4 ± 0.5
methanol-$LiClO_4$ 3.25 M	462.0	61.9	19.0 ± 1
methanol-$LiClO_4$ 5.00 M	445.2	64.2	26.5 ± 1.5

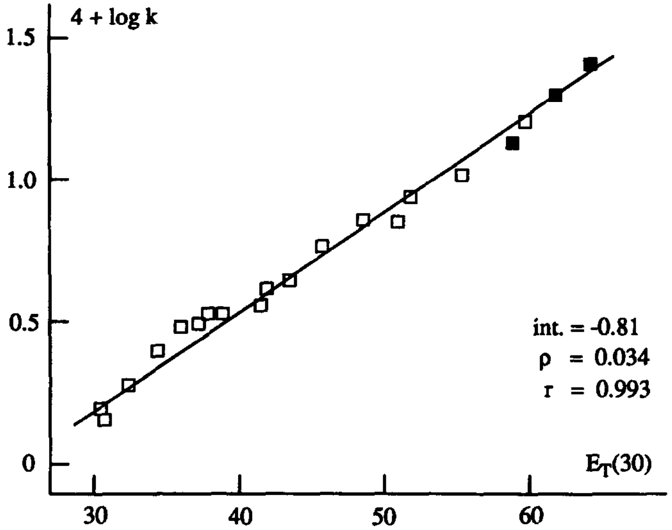


Figure 2. Rate constants of the retro-C.R. of 1 at 70 °C in differing solvents (☐) and LP-methanol solutions (■) plotted vs $E_T(30)$ parameter of the medium.

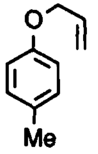
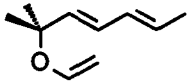
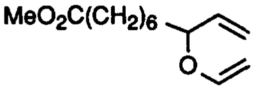
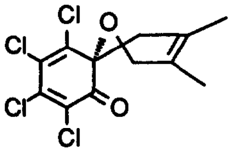
Table 3. Activation parameters for the retro-C.R. of 1 determined for five selected solvents and three LP-methanol solutions.

solvent or solution	$\Delta H^{\neq}$ (kcal mol^{-1})	$-\Delta S^{\neq}$ (cal K^{-1} mol^{-1})
cyclohexane	24.6 ± 0.6	4 ± 2
benzene	22.2 ± 0.3	10 ± 1
i.propanol	23.0 ± 0.4	6 ± 1
acetic acid	21.0 ± 0.6	11 ± 1
methanol	22.1 ± 0.3	8 ± 1
LP-methanol 1.15 M	20.7 ± 0.2	11 ± 0.5
LP-methanol 3.25 M	20.3 ± 0.4	12 ± 1
LP-methanol 5.0 M	20.0 ± 0.3	12 ± 1

Conclusions

The three examples of C.R.s discussed in the introduction were rationalized in terms of solvent polarity, each using different polarity parameters: Z, $E_T(30)$, and Y(OTs). An homogeneus treatment with $E_T(30)$ parameters give results, summarized in table 4, that enable a comparison between the solvent effects observed in forward and retro C.R.s.

Table 4. Result of the linear regression between the rates of the forward- and retro-C.R. with $E_T(30)$ parameter.

Substrate	no. of solvents	ρ	r	Ref.
	Claisen rearrangement			
	13	0.0515	0.967	6
	9	0.0677	0.968	8
	12	0.0535	0.902	9
	retro-Claisen rearrangement			
	20	0.034	0.993	(a)

(a) This paper.

All the correlations obtained for the forward C.R. have good regression coefficients and positive slopes with values in the range 0.052-0.068. These values are consistent with a charge separation much lower than that of the Menschutkin reaction between triethylamine and iodoethane (process taken as a reference) for which the linear relationship of the kinetic data with $E_T(30)$ gave a ρ value of 0.248 (r = 0.920)(14).

For the retro-C.R. the slope (0.034) is about one half of that found for the forward reaction, again indicating a partial charge separation during the transition state. The absence of any acid catalysis is confirmed by the kinetic effect of the LP-methanol solutions, since no significant accelerations - typical of cationic Lewis acid catalysis(15) - were observed.

In conclusion, if the forward-C.R. is characterized by a transition state with partial charge separation(16), the same is true for the retro rearrangement. The dipolar character of these transition states gives rise to solvent effects which are the result of non-specific solute-solvent interactions, while the specific ones, in contrast to that observed for the Diels-Alder reaction(3), seem to play a marginal role only.

EXPERIMENTAL SECTION.

7,8,9,10-tetrachloro-3,4-dimethyl-1-oxaspiro[5,5]undeca-3,7,9-trien-11 -one 1. This was prepared as reported in the literature(11) and the product had m.p. 97-98 °C from petrol ether (lit.(11), 99-100 °C).

5,6,7,8-tetrachloro-2,3-dihydro-2-isopropenyl-2-methyl-1,4-benzodioxan e 2. This was prepared as reported in the literature(11) and the product had m.p. 95-96 °C from petrol ether (lit.(11), 94-95 °C).

Kinetics. The overall reaction rates were measured by following the disappearance of the chromophore 1 on a Perkin Elmer Lambda 5 spectrophotometer provided with thermostatted cell transport assembly and an automatic multicell programmer. The solutions were measured in 1.00 cm OS Hellma couvettes with 3 cm^3 capacity. Measuraments were taken at the wavelenghts in the range 370-400 depending on the solvent.

For the determination of the rate constants at temperature higher than 35 °C, a solution of **1** in a 25 cm^3 volumetric flask was prepared, being the concentration in the range 5-7 x 10^{-4} M. Portions (*ca.* 3 cm^3) of this solution were placed into glass tubes which were sealed. Approximately 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 (1-60 min, depending on solvent and temperature) the reaction was quenched, and the residual absorbance of **1** was determined.

For the determination of the rate constants in the temperature range 20-35 °C, variable amounts (2.0-2.5 cm^3) of the LP-methanol solutions were directly thermostatted at the required temperature in the cell transport assembly of the spectrophotometer. Amounts of **1** were then added to the solution in order to obtain absorbance values in the range 0.8-1.6 A. After vigorous mixing, the kinetic determinations were initiated.

To determine the activation parameters, the rate constants at four different temperatures were measured; for pure solvents the temperature range was 45-90 °C depending on the solvent, for LP-methanol solutions between 20 and 35 °C following the procedures above described. The rate constants used for the determination of the activation parameters (Table 3) are reported in table 5.

Table 5. Rate constants of the retro-C.R. of 1 in pure solvents and LP-methanol solutions.

Solvent T (°C)	10^4 x k (sec^{-1}) cyclohexane	 benzene	 *i*.propanol	 acetic acid	 methanol
45	---	---	0.51 ± 0.01	0.60 ± 0.01	0.76 ± 0.01
50	---	---	0.82 ± 0.03	1.01 ± 0.02	1.28 ± 0.01
60	0.56 ± 0.02	1.02 ± 0.01	2.56 ± 0.04	3.03 ± 0.05	3.91 ± 0.02
70	1.41 ± 0.05	2.4 ± 0.1	7.6 ± 0.1	7.10 ± 0.3	10.4 ± 0.2
80	4.28 ± 0.05	7.63 ± 0.05	---	---	---
90	12.6 ± 0.4	16.8 ± 0.5	---	---	---

LP sol. T (°C)	10^5 x k (sec^{-1}) 1.15 M	 3.25 M	 5.0 M
20	0.65 ± 0.01	1.03 ± 0.02	1.56 ± 0.02
25	1.21 ± 0.01	1.82 ± 0.02	2.73 ± 0.02
30	1.98 ± 0.02	3.20 ± 0.03	4.80 ± 0.03
35	3.99 ± 0.04	5.93 ± 0.04	8.75 ± 0.05

H.p.l.c. analysis of reaction mixtures. These were performed on a Waters Associated ALC/CPC liquid chromatograph with a Waters mod. 490 E detector operating at 310 nm; stainless column (25 cm length x 4 mm internal diameter) pre-packed with Lichrosorb 60 (10 μm) Merck; eluant: cyclohexane - ethyl acetate 9:1; flow: 1.2 cm^3 min^{-1}; retention times: **1**, 4.0 min; **2**, 6.5 min.

Solutions of **1** (*ca.* 0.005 M) in each solvent and in LP-methanol solutions were thermostatted at 70 °C. At three different degrees of completion of the rearrangement, a portion of the reaction mixture was quenched and, in the case of LP solutions, was extracted with dichloromethane. The solvent was evaporated and the residue, dissolved in a small amount of eluant, was analyzed. Each solution was tested on two independent samples at least three times each: in any case only the starting reagent **1** and the reaction product **2** were evidenced.

Aknowledgement. The National Research Council (C.N.R.) and the M.U.R.S.T. offered financial support to this research.

REFERENCES AND NOTES

1) Part VII (as solvent effect as the result of frontier molecular orbital interaction). Desimoni, G.; Faita, G.; Pasini, D.; Righetti, P.P. *Tetrahedron* **1992**, *48*, 1667.
2) The leading reference on this topic is: Reichardt, C. *"Solvents and Solvent Effects in Organic Chemistry"*, VCH, Weinheim, 1988.
3) Desimoni, G.; Faita, G.; Righetti, P.P.; Toma, L. *Tetrahedron* **1990**, *46*, 7951.
4) Sauer, J.; Sustmann, R. *Angew. Chem. Int., Ed. Engl.* **1980**, *19*, 779.
5) Jefferson, A.; Scheinman, F. *Quarterly Rev.* **1968**, *22*, 391.
6) White, W.N.; Wolfarth, E.F. *J. Org. Chem.* **1970**, *35*, 2196.
7) Kosower, E.M. *J. Am. Chem. Soc.* **1958**, *80*, 3253, 3261, 3267.
8) Gajewski, J.J.; Yurayj, J,; Kimbrough, D.R.; Gande, M.E.; Ganem, B.; Carpenter, B.K. *J. Am. Chem. Soc.* **1987**, *109*, 1170.
9) Brandes, E.; Grieco, P.A.; Gajewski, J.J. *J. Org. Chem.* **1989**, *54*, 515.
10) Bentley, T.W.; Carter, G.E. *J. Org. Chem.* **1983**, *48*, 579.
11) Ansell, M.F.; Leslie, V.J. *J. Chem. Soc. (C)* **1971**, 1423.
12) Rezende, M.C. *Tetrahedron* **1988**, *44*, 3513.
13) Commercially available from Aldrich-Chemie.
14) Abraham, M.H.; Grllier, P.L. *J. Chem. Soc., Perkin Trans. II* **1976**, 1735.
15) Desimoni, G.; Faita, G.; Righetti, P.P.; Tacconi, G. *Tetrahedron* **1991**, *47*, 8399.
16) Coates, R.; Rogers, B.; Hobbs, B.; Peck, D. *J. Am. Chem. Soc.* **1987**, *109*, 1160. Desimoni, G.; Faita, G.; Gamba, A.; Righetti, P.P.; Tacconi, G.; Toma, L. *Tetrahedron* **1990**, *46*, 2165.