Table 2 .- Crystal data and some details of the struture determinations

	3v	3v'	3l	4
molecular formula	$C_{18}H_{27}N_3O_2S$	$C_{18}H_{25}N_3O_3S$	$C_{19}H_{29}N_3O_2S$	$C_{31}H_{43}N_5O_2S_2$
formula weight	349.9	363.47	363.52	581.82
crystal system	orthorhombic	monoclinic	orthorombic	trigonal
space group	$P2_12_12_1$	$P2_1$	$P2_12_12_1$	$P3_2$
a (A)	7.096(1)	7.203(1)	7.332(1)	11.521(2)
b (A)	14.290(2)	14.732(2)	14.203(2)	11.521(2)
c (A)	19.363(3)	9.453(1)	21.038(3)	21.758(4)
α (°)	90	90	90	90
β (°)	90	98.39(1)	90	90
γ (°)	90	90	90	120
V (A^3)	1963.4(5)	992.4(2)	2190.8(5)	2501.1(8)
Z	4	2	4	3
diffraction density (gcm^{-3})	1.182	1.216	1.102	1.159
crystal description	colourless plates	colourless plates	colourless prisms	yellow prisms
crystal size (mm)	0.40x0.35x0.20	0.57x0.38x0.27	0.42x0.21x0.15	0.40x0.15x0.15
2θ range (°)	3 - 60	3 - 66	3-56	3 - 56
unique reflections	5718	7473	5307	8051
observed reflections ($>2\sigma_I$)	2022	3054	1021	1426
Flack parameter	-0.01(12)	-0.08(10)	0.03(20)	0.30(13)
R1 for observed reflections	0.0527	0.0556	0.0620	0.0679
wR2 for unique reflections	0.1518	0.1960	0.1412	0.1140
$\Delta\rho_{max}/\Delta\rho_{min}$ ($e\AA^{-3}$)	0.27/-0.19	0.73/-0.28	0.17/-0.24	0.21/-0.22

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Solvent Effect in Pericyclic Reactions. X.[1] The Cheletropic Reaction.

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Abstract. The effect of the solvent on the cheletropic reaction of 3,4-dimethyl-2,5-dihydrothiophen-1,1-dioxide was kinetically investigated in 14 solvents. The rate constants of the forward reaction as well as those of the reverse process and the corresponding equilibrium constants were found to be linearly correlated with the $E_T(30)$ solvent polarity parameter. The solvent effect can be interpreted in terms of change of polarity during the activation process. The different response of the forward and reverse process to the increase of solvent polarity pointed out a clear difference between pericyclic reactions characterized by non-specific solvent effects and those whose medium effect is determined by the specific interaction between the FMO of solute and solvent. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

In the previous paper of this series,[1] it was investigated the solvent effect on the ene reactions, and the observed results closely parallel those found for the Diels-Alder (DA) reaction.[2] Both reactions, with the exceptions of very few examples whose small solvent effect correlates with the Hildebrand's parameter, are indeed characterized by significant solvent effects due to specific solute-solvent interactions, with rate increasing with the increase of the solvent acidity[3] or decreasing with the increase of the solvent basicity.[3] DA and ene reactions can be considered as a class of pericyclic processes whose solvent effects are not negligible and they are governed by the specific interaction between the frontier orbitals of solute and solvent.

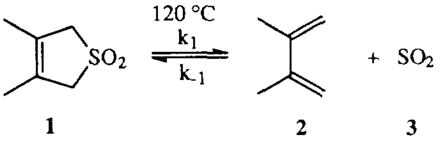
A second class of pericyclic processes concerns the reactions with the solvent effect depending on the polarity of the medium. The 1,3-dipolar cycloadditions, whose solvent effect was extensively investigated by Huisgen,[4] the Claisen,[5,6] diaza-Claisen,[7] and retro-Claisen rearrangements,[8] belong to this important class. In all these reactions, the usually small solvent effect is a linear function of the $E_T(30)$ parameter[9] with either positive or negative slope.

The next step of our investigation inferred the influence of the solvent on the cheletropic reaction, a process that was investigated in detail from both experimental[10-15] and theoretical[16,17] point of view, in order to test the presence of specific interactions between solvent and sulphur dioxide (a potential acceptor).

RESULTS

To avoid complications due to the competition between cheletropic and hetero-DA reaction[15,17,18] the thermal decomposition of 3,4-dimethyl-2,5-dihydrothiophen-1,1-dioxide (**1**) was chosen as reaction model to investigate the solvent effect (Scheme 1). The cheletropic reaction on mono- and disubstitued 2,5-dihydrothiphen-1,1-dioxide was studied by Isaacs and co-workers[10-12] and found to occur by an essentially neutral concerted mechanism little influenced by the electronic effects of substituents. The effect of 8 solvents, most of them rather unusual, on the thermolysis of 3-methyl-2,5-dihydrothiophen-1,1-dioxide was determined,[10] and the overall variation from benzophenone to *N*-acetylbenzylamine was found to be 1.82, a very small solvent effect.

Scheme1



The kinetic determinations at 120 °C were studied by ^{1}H-Nmr spectroscopic analysis of the reaction mixture: the relative concentration of **1** at the time *t* was determined by integration of the methyl signals of **1** and **2**. The first order rate constants, average of at least three independent kinetic runs, are reported in Table 1.

The rate was found to decrease by a factor of 4.5 in going from cyclohexane to methanol, and this change is in accordance with the small value reported in the literature.[10] When the kinetic data in Table 1 were plotted *vs* the $E_T(30)$ solvent parameter,[9] the graph reported in Figure 1 was obtained. Obviously this assumes that the $E_T(30)$ values reported in Table 1 do not differ significantly from those of the corresponding deuterated solvent. The good linear relationship (r = 0,908) is characterized by a negative value of the slope (ρ = -0.022), and the rate slightly decreases with the increase of the solvent polarity.

Table 1. Rate constants at 120 °C of the cheletropic reaction of **1** in differing deuterated solvents with corresponding $E_T(30)$ values.

Solvent	$E_T(30)$	$10^5 \times k_1$ (sec^{-1})
Cyclohexane	31.2	7.57 ± 0.37
Benzene	34.5	4.55 ± 0.05
1,4-Dioxane	36.0	3.70 ± 0.15
THF	37.4	4.67 ± 0.08
Chlorofom	39.1	3.30 ± 0.10
Pyridine	40.5	3.60 ± 0.07
Nitrobenzene	42.0	2.75 ± 0.01
Acetone	42.2	3.52 ± 0.03
DMF	43.0	3.85 ± 0.10
DMSO	45.0	3.34 ± 0.05
Acetonitrile	46.0	2.93 ± 0.15
Nitromethane	46.3	2.18 ± 0.14
Acetic acid	51.2	2.13 ± 0.07
Methanol	55.5	1.7 ± 0.2

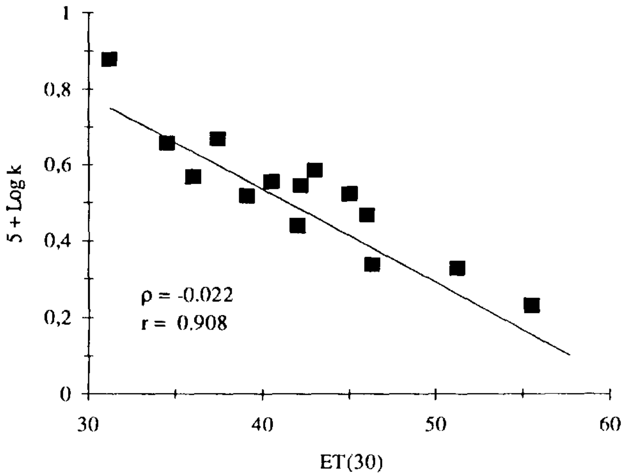


Figure 1. Rate constants at 120 °C of the cheletropic reaction of **1** (Table 1) *vs* $E_T(30)$ solvent parameters.

The rate constants reported in Table 1 are calculated from the initial part of the graph log $[A°]/[A_t]$ *vs* the time *t*. The range of linearity strongly depends on the polarity of the solvent: for cyclohexane the linearity is observed up to 98% of the reaction completion, while in the case of methanol an early deviation is evidenced, and in Figure 2 are reported the trends of these graphs. From the data corresponding to the plateau observed for prolonged reaction time it can be determined the concentrations of reagent and products at the equilibrium and hence the equilibrium constant for each solvent.

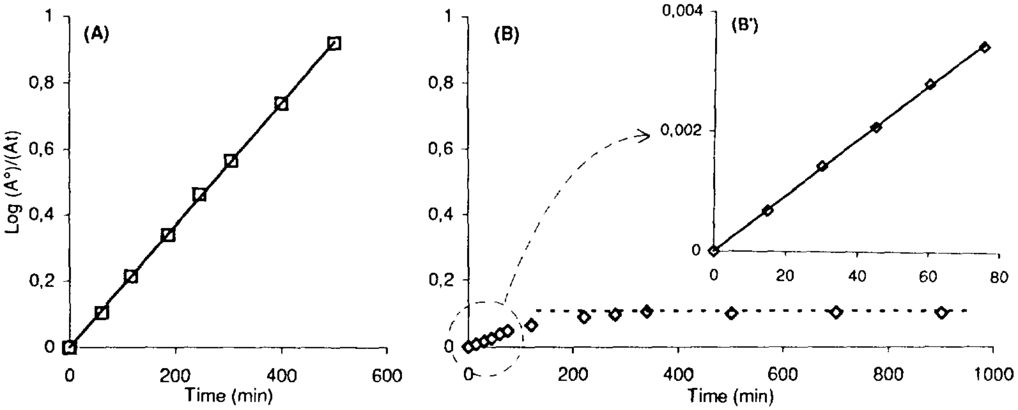


Figure 2. Plot of log $[A°]/[A_t]$ *vs* t for cyclohexane (graph A) and methanol (graph B) at 120 °C. The dotted line in graph B was used to calculate K_{eq}, the full line in the expanded B' part to calculate k_1.

From the K_{eq} values determined by prolonged heating of the reaction mixture and from the k_1 data reported in Table 1, the rate constant of the [4+1] cycloaddition of **2** and **3** (k_{-1}) can be calculated for each solvent. In Table 2 are collected both K_{eq} and k_{-1} values.

From the data reported in Table 2 it is evident an effect of the solvent on K_{eq} and k_{-1} larger than that on k_1: the equilibrium was found to decrease by a factor of 140 in going from benzene to methanol, and k_{-1} increased by a factor of 53.

When the equilibrium constants and the kinetic data in Table 2 were plotted *vs* $E_T(30)$, the graphs reported in Figure 3 and 4 were obtained. In both cases a good linear relationship (r = 0,908 and 0.905 respectively) is observed, but the regressions are characterized by opposite slopes (ρ = -0.10 and 0.08 respectively): the equilibrium constant decreases with the increase of the solvent polarity, but k_{-1} increases with the increase of the $E_T(30)$ parameter.

Table 2. Rate constants of the cycloaddition **2** + **3** to **1** and the corresponding equilibrium constants in differing deuterated solvents at 120 °C.

Solvent	$E_T(30)$	K_{eq} (M^{-1})	$10^5 \times k_{-1}$ (M^{-1} sec^{-1})
Cyclohexane	31.2	> 48	< 0.16
Benzene	34.5	4.90 ± 0.50	0.93 ± 0.09
1,4-Dioxane	36.0	0.88 ± 0.07	4.20 ± 0.25
THF	37.4	1.45 ± 0.40	3.2 ± 0.9
Chlorofom	39.1	2.07 ± 0.03	1.60 ± 0.03
Pyridine	40.5	0.90 ± 0.07	4.0 ± 0.2
Nitrobenzene	42.0	0.6 ± 0.2	4.6 ± 1.7
Acetone	42.2	0.71 ± 0.08	5.0 ± 0.5
DMF	43.0	0.70 ± 0.05	5.5 ± 0.3
DMSO	45.0	0.30 ± 0.01	11.1 ± 0.2
Acetonitrile	46.0	0.12 ± 0.01	24.4 ± 0.7
Nitromethane	46.3	0.05 ± 0.01	44.9 ± 1.4
Acetic acid	51.2	0.05 ± 0.01	43 ± 7
Methanol	55.5	0.035 ± 0.005	49 ± 2

DISCUSSION AND CONCLUSION

The small solvent effect evidenced by the data reported in Table 1 can be rationalized in terms of non-specific solute-solvent interactions. The only study of solvent effect on the cheletropic reaction reported in the literature[10] explained the small solvent effect in terms of donor properties of the solvent with rate increasing with the increase of the solvent basicity. This seems not to be the case since a fully scattered plot was obtained when the kinetic data reported in Table 1 were plotted *vs* the Donor Number of the solvent.

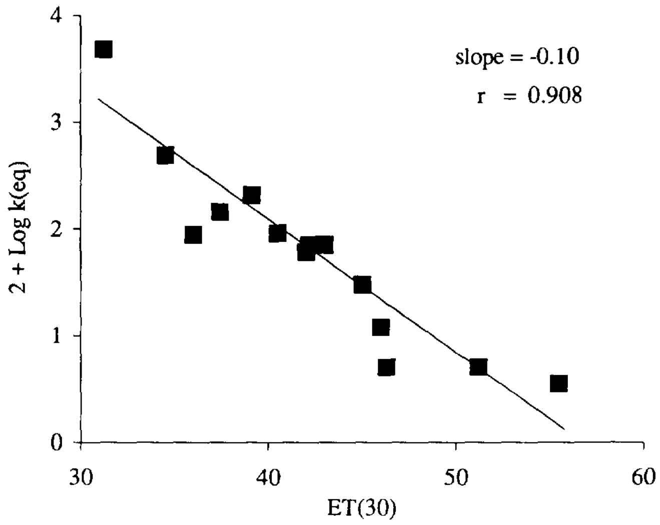


Figure 3. Equilibrium constants at 120 °C of the cheletropic reaction of **1** (Table 2) *vs* $E_T(30)$ solvent parameters.

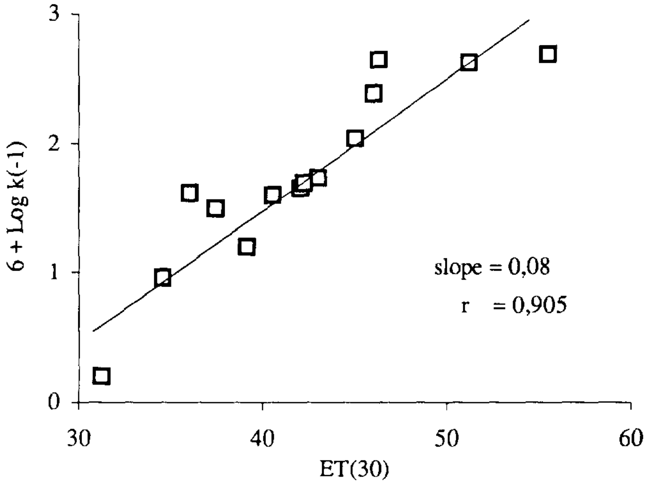


Figure 4. Rate constants at 120 °C of the cheletropic reaction of **2** + **3** (Table 2) *vs* $E_T(30)$ solvent parameters.

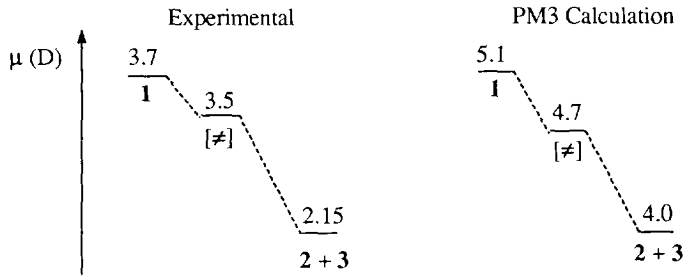
The correlations between between both kinetic and equilibrium data with the solvent polarity suggest a change of the polarity during the activation process.

The negative slope of the graph in Figure 3 requires a decrease of the dipole moment (μ) in going from reactant to products. The dipole moment of **1** can be taken as ~ 3.7 D,[19] while the μ of **2** and **3** are 0.52[20] and 1.63 D[21] respectively. Hence the $\Delta\mu$ is of 1.55 D, and this is in accordance with the equilibrium shifted toward the more polar derivative (**1**) with the increase of the solvent polarity.

To explain the influence on the reaction rate, the μ of the transition state ($\mu^{\neq}$) is required. This can be calculated with the Kirkwood-Laidler-Eyring equation,[22] following the procedure described by Huisgen.[4]

From the comparison of the slopes of the graphs in Figures 1 and 4, and taking into account the volumes[12] and the dipole moments of **1-3**, a $\mu^{\neq}$ of 3.5 D can be determined. A support to this result is obtained by calculating (PM3 method) the μ of reactant (5.1 D), products (0.4 and 3.6 D for **2** and **3** respectively), and t.s. of the reaction. This last value ($\mu^{\neq}$ = 4.7 D) was obtained by a PM3 single point calculation on the reported optimized t.s. geometry.[16] All these results are summarized in Scheme 2.

Scheme 2



From the reported results, the cheletropic reaction seems to be insensitive to both the solvent acidity and basicity, being only influenced by the polarity of the solvent. Both the experimental results and the PM3 calculations give a satisfactory explanation of the observed solvent effect and the following behaviours are expected. The change of the solvent polarity will influence the rate less than the equilibrium. The rate constants will be characterized by opposite effect of the polarity: k_1 will slightly decrease with the increase of $E_T(30)$, k_{-1} will increase under the same conditions. Since $\Delta\mu^{\neq}$ (**1**→≠) is -0.2/-0.4 D and $\Delta\mu^{\neq}$ (**2** + **3**→≠) is +1.35/+0.7 D, the effect on k_{-1} will be larger than that on k_1.

An other important conclusion can be obtained by the comparison of the rate constants of the forward and the reverse process.

In reactions showing solvent effects depending on the specific interactions between the FMO of solute and solvent, the DA and ene reactions, the rate constants of *both the forward and the reverse reaction* are increased by the solvent acidity or decreased by the solvent basicity.[23] When the solvent effect depends, as in the present case, on the polarity of the medium, *the forward and the reverse reaction are influenced by the solvent in an opposite way.*