Articles

Solvent Effect in the Thermal Decomposition Reaction of *trans*-3,3-Dimethyl-5,6-tetramethylene-1,2,4-trioxacyclohexane

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The kinetic data of the thermal decomposition reaction of *trans*-3,3-dimethyl-5,6-tetramethylene-1,2,4-trioxacyclohexane has been measured in different solvents (benzene, toluene, 2-propanol, 2-methoxyethanol, and *p*-dioxane) at 0.02 mol kg^{-1} initial concentration and in the temperature range of 135.0−165.0 °C. The enthalpy and entropy of activation of the unimolecular reaction of this trioxane in several organic solvents have been correlated through "isokinetic relationships" to validate the existence of a genuine solvent effect on that reaction.

Introduction

Cyclic peroxides of the substituted 1,2,4-trioxanes type are structurally related to the six-membered ring 1,2,4,5-tetroxanes and 1,2,4,5-trioxazines. Many derivatives of a 1,2,4-trioxane are now available for study thanks to new synthetic methods[1] in an effort to obtain these cyclic peroxides in good yields and to know in deep their reactions. It is interesting to mention that the antimalarial activity of the plant extract qinghaosu is associated with the presence of the 1,2,4-trioxane ring in molecules of compounds (Artemisinin) found in its composition.[1]

The 1,2,4,5-tetroxanes conformational aspects and kinetic data of the thermolysis reaction in solution[2−5] have been extensively investigated, and comparative analysis[3] of the reactivities of cyclic peroxides of the substituted 1,2,4,5-trioxazines families of compounds was also performed considering their reaction products and available kinetic data in several media.

On the other hand, it has been reported a further effect of solvent polarity on the thermal decomposition rate of acyclic peroxides[6,7] and cyclic diperoxides[4,8] (1,2,4,5-tetroxanes). In particular, that effect was observed on the activation parameter values. All the cases previously cited constitute a common "reaction series"[9] where the rate-determining step is the O−O bond rupture in each molecule.

Table 1. Pseudo-First-Order Rate Constant Values for the Thermal Decomposition Reaction of *trans*-3,3-Dimethyl-5,6-tetramethylene-1,2,4-trioxacyclohexane (0.02 mol kg^{-1} Initial Concentration)

reaction solvent	T (°C)	$k_{\mathrm{exp}} \times 10^5$ (s^{-1})	r[a]
2-propanol	145.0	2.12	0.986
	160.0	5.53	
	175.0	27.6	
2-methoxyethanol	135.0	1.96	0.987
	140.0	2.22	
	150.0	6.63	
	165.0	14.9	
benzene	145.0	0.51	0.986
	154.5	2.24	
	162.0	2.54	
	175.5	12.5	
toluene	135.0	0.11	0.999
	140.0	0.204	
	147.0	0.40	
	156.0	1.02	
	165.4	2.39	
	171.2	4.15	
p-dioxane	135.0	1.98	0.988
	143.0	4.11	
	143.0	3.19	
	150.0	7.07	
	150.0	7.20	
	165.5	15.8[b]	

[a] Correlation coeficient according to the Arrhenius equation (eqs 1−5). [b] k_{exp}value obtained up to 43% **1** decomposition, because at higher conversions the first-order law is not obeyed.

Here, available kinetic data on the thermal decomposition reaction of *trans*-3,3-dimethyl-5,6-tetramethylene-

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Table 2. Activation Parameters for the Unimolecular Thermal Decomposition Reaction at 160 °C of *trans*-3,3-Dimethyl-5,6-tetramethylene-1,2,4-trioxacyclohexane (1) in Solution

solvent	Δt (°C)	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (cal mol^{-1} K^{-1})	$\Delta G^{\ddagger}$ (kcal mol^{-1})	ref
2-propanol	30.0	30.7 ± 2.0	-5.4 ± 4.6	33.0 ± 2.0	this work
2-methoxyethanol	30.0	24.6 ± 1.8	-18.3 ± 4.3	32.6 ± 1.8	this work
benzene	30.0	37.6 ± 1.1	8.6 ± 2.6	33.8 ± 1.1	this work
toluene	36.2	34.9 ± 1.0	1.1 ± 1.0	34.4 ± 1.0	this work
p-dioxane	30.5	24.0 ± 1.1	-19.8 ± 2.6	32.6 ± 1.1	this work
n-octane	27.9	39.2 ± 0.2	12.2 ± 0.5	33.9 ± 0.2	10

1,2,4-trioxacyclohexane (**1**) in *n*-octane[10] solution were compared with those obtained in toluene, 2-propanol, benzene, *p*-dioxane, and 2-methoxyethanol to learn about the solvent effect on the thermolysis of this trioxane.

Results and Discussion

Rate measurements on the thermal decomposition reaction of *trans*-3,3-dimethyl-5,6-tetramethylene-1,2,4-trioxacyclohexane (**1**) in all the solvents at 0.02 mol kg^{-1} initial concentration in the temperature range of 135.0−165.0 °C (Table 1) show a first-order kinetic law behavior up to ca. 60% trioxane conversions.

The temperature effect on the experimental rate constant values (k_{exp}) in the solvents investigated can be represented by the following Arrhenius equations (1−5) where the errors shown are standard deviation from a least-mean-squares data treatment[11] and the activation energy is expressed in kcal mol^{-1}.

$$\ln k_{\mathrm{exp}}\text{2-propanol } (\mathrm{s}^{-1}) = (27.1 \pm 4.6) - (31\,570 \pm 2\,004)/RT \quad (1)$$

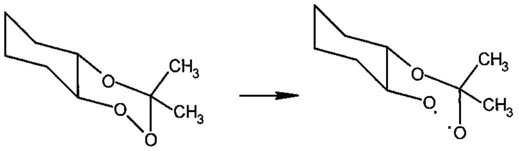
$$\ln k_{\mathrm{exp}}\text{2-methoxyethanol } (\mathrm{s}^{-1}) = (20.6 \pm 4.3) - (25\,510 \pm 1813)/RT \quad (2)$$

$$\ln k_{\mathrm{exp}}\text{benzene } (\mathrm{s}^{-1}) = (34.2 \pm 2.6) - (38\,415 \pm 1135)/RT \quad (3)$$

$$\ln k_{\mathrm{exp}}\text{toluene } (\mathrm{s}^{-1}) = (35.0 \pm 1.0) - (35753 \pm 1012)/RT \quad (4)$$

$$\ln k_{\mathrm{exp}}p\text{-dioxane } (\mathrm{s}^{-1}) = (19.9 \pm 2.6) - (24900 \pm 1107)/RT \quad (5)$$

The linearity of those Arrhenius equations (Table 1) over relatively large temperature ranges suggests that the calculated activation parameters values for the **1** thermal decomposition reaction (Table 2) belong to a single process, which could be its unimolecular thermal cleavage of the O−O bond as the initial bond breaking step (eq 6).



(6)

Schuster and Bryant[10] have postulated several reactions paths to open to the diradical formed from this bond cleavage in *n*-octane solution (hydrogen atom abstraction, α-cleavage, and *β*-cleavage). They observed that upon thermolysis the trioxane **1** undergoes unimolecular cleavage to form acetone and adipaldehyde (≅95%) and reported that the diradical formed from homolysis of the O−O bond must rearrange rapidly (most probably) by an α-cleavage reaction.

The reaction products analysis for **1** thermolysis in benzene solution in the initial concentrations range where induced decomposition is absent indicates adipaldehyde as the main product, acetone in low yield, and traces of *trans*-1,2-cyclohexanediol. In toluene solvent,[12] the benzaldehyde derived from solvent oxidation is the main product, while acetone, adipaldehyde, and *trans*-1,2-cyclohexanediol are minor products. In this case, bibenzyl and benzyl alcohol were found in low yields. In *p*-dioxane, the molar yield of acetone is ca. 30%. In 2-methoxyethanol, the yields of acetone, *trans*-1,2-cyclohexanediol, and methane were qualitatively determined. In 2-propanol, the main products derived from the **1** thermal decomposition are adipaldehyde and methane. In this case, the molar yield of acetone is higher than 1 mol per mol of **1** decomposed, probably, because of the oxidation of the solvent, as it was found in the thermal decomposition reaction of acetone cyclic diperoxide in 2-propanol.[13]

The activation enthalpy and entropy values corresponding to the unimolecular thermal decomposition reaction (eq 6) can be compared with already reported data for analogous homolysis of **1** in *n*-octane[10] solution (Table 2). Those values indicate a marked solvent effect on the unimolecular decomposition reaction of **1** in going from *n*-octane to *p*-dioxane as solvent.

Benzoyl peroxide,[6] di-*tert*-butyl peroxide,[7] and cyclic diperoxides derived from acetone[4] and cyclohexanone[8] show solvent effect on the rate of decomposition reaction in solution. As an example, we report the rate constant values of acetone cyclic diperoxide in differents solvents (Table 3), where the least activation enthalphy and entropy were found in protic solvent (2-propanol and acetic acid) because of the hydrogen bonding formed between them and the O−O bond of the cyclic diperoxide.

Nevertheless, **1** shows the least activation enthalpy and entropy in *p*-dioxane, but this solvent and the O−O bond cannot form hydrogen bonding, so it is possible to assume that the actual interaction process is more complex.

A linear relationship between the activation enthalpies and entropies ($\Delta H^{\ddagger} = \Delta H^{\circ} + \beta\Delta S^{\ddagger}$, $r = 0.996$) of the unimolecular thermolysis reactions of the trioxane **1** can

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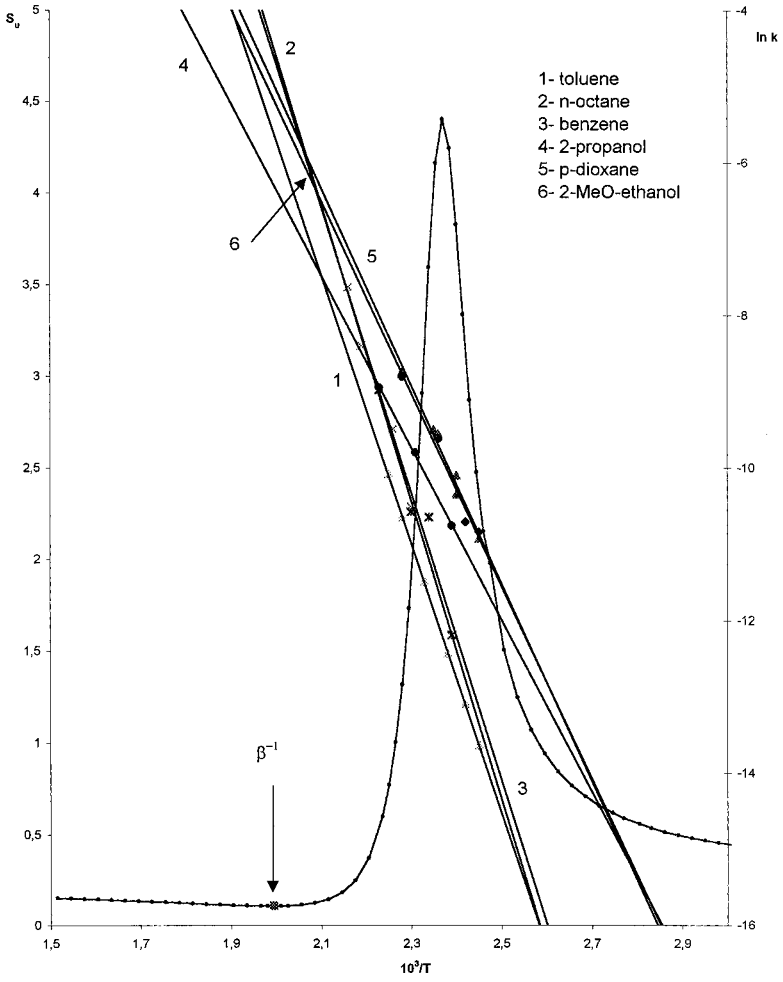

Figure 2. Dependence of the residual sum of squares S_u on the supposed isokinetic temperature β for the **1** unimolecular thermolysis in different solvents.

Table 3. First-Order Rate Constant Values for the Unimolecular Thermolysis of Acetone Cyclic Diperoxide

solvent	T (°C)	$k_{exp} \times 10^5$ (s^{-1})	ref
benzene	150.5	0.283	2
toluene	147.7	0.344	2
acetonitrile	150.0	0.600	2
n-octane	145.0	0.076	2
acetophenone	150.0	1.14	2
2-propanol	148.0	7.90	13, 14
acetic acid	150.0	9.96	14

be found according to Leffler's treatment[15] (Figure 1). It should be noted that the "isokinetic temperature" ($\beta \cong$ 211 °C) is far from the experimental temperatures where the kinetic measurements were performed (135.0−171.2 °C), and the ranges of the $\Delta H^‡$ and $\Delta S^‡$ values ($\Delta\Delta H^‡$= 15.2 kcal mol^{-1} and $\Delta\Delta S^‡$= 32.0 eu) are large compared to the probable errors of those parameters.

Later, Exner[16,17] suggested that the single point of intersection of lines in the Arrhenius plane could be used for a sound statistical test since ln k and T are statistically independent; this is the basis of the isokinetic relationship. The expected correlation would be not valid if that intersection point is not found. To estimate the isokinetic temperature (β) value, the residual sums of squares (S_u) are given and β is then defined by the minimum of the S_u when varying the abscissa of the intersection point along the 1/T axis[17,18] (Figure 2). Accordingly, with this mathematical treatment the corresponding isokinetic temperature value for **1** thermolysis is ca. 228 °C, which is in reasonable agreement with the β value obtained according to Leffler treatment. Without any doubt, an important solvent effect is operative on the rate of thermal decomposition of **1**.

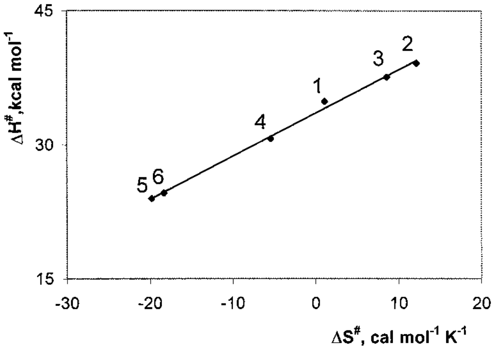

Figure 1. "Isokinetic relationship" according to Leffler for the thermal decomposition reaction of *trans*-3,3-dimethyl-5,6-tetramethylene-1,2,4-trioxacyclohexane: 1, tolueno; 2, *n*-octane; 3, benzene; 4, 2-propanol; 5, *p*-dioxane; 6, 2-methoxyethanol.

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Experimental Section

Materials. *trans*-3,3-Dimethyl-5,6-tetramethylene-1,2,4-trioxacyclohexane was prepared according to the method described elsewhere.[19] The solvents employed in the reactions were purified by standard techniques,[20] except the 2-propanol, which was distilled from ethylenediaminetetraacetic acid disodium salt dihydrate to remove traces of metallic ions,[21] and their purity, suitable for kinetic studies, was checked by GC analysis.

Kinetic Methods. Pyrex glass tubes (6 cm long × 4 mm o.d.), half filled with the appropriate **1** solution were thoroughly degassed under vaccum at −196 °C and sealed with a flame torch. To perform the runs, the ampules were immersed in a thermostatic silicone oil bath (±0.1 °C) and withdrawn after selected times, stopping the reaction by cooling at 0 °C. The trioxane **1** remaining in the solution was determined by quantitative GC analysis (internal standard method, *n*-octane in *p*-dioxane, and biphenyl in the other solvents) using a methyl silicone gum rubber packed column at 70 °C for 5 min, followed by a temperature increase of 10°/min up to 150 °C for 15 min, injector temperature at 150 and 250 °C FID temperature, with nitrogen as the carrier gas. Under these conditions, the retention time of **1** was ca. 23 min. The corresponding first-order rate constant values were obtained by least-means-squares treatment of the GC data plotting the values of ln [concentration of **1**] vs time. The reaction products were identified by GC and GC−MS analyses. Acetone was identified by HPLC when 2-propanol was the reaction solvent. The activation parameters were calculated according to the Eyring equation, and the errors were worked out by the Arrhenius equation method using a least-means-square data treatment.[11]

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