ISSN 1070-3632, Russian Journal of General Chemistry, 2008, Vol. 78, No. 6, pp. 1273–1276. © Pleiades Publishing, Ltd., 2008.

Catalytic Effect of Cuprous Ions on the Thermal Decomposition of 3,3,6,6-Tetramethyl-1,2,4,5-tetraoxane in Methanol Solution[1]

L. I. Giménez[a], **J. M. Romero**[a], **S. Bustillo**[a], **N. L. Jorge**[a],
M. E. Gómez Vara[a], and **E. A. Castro**[b]

[a] *Cátedra de Química Física Ic, Facultad de Ciencias Exactas y Naturales y Agrimensura,*
Universidad Nacional del Nordeste, Av. Libertad 5460, (3400) Corrientes, Argentina
phone/fax: (03783) 457996; e-mail: lidianj@exa.unne.edu.ar

[b] *Theoretical Chemistry Division, INIFTA, Suc. 4, C.C. 16, La Plata 19900, Buenos Aires, Argentina*
e-mail: eacast@gmail.com; castro@quimica.unlp.edu.ar

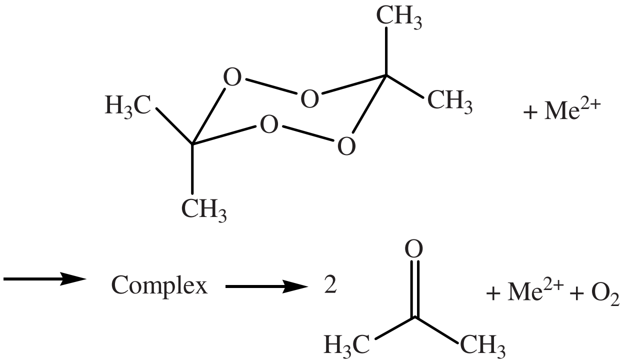
Received December 13, 2007

Abstract—Thermal decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane was examined in methanol solution (1.69×10^{-2} M) containing cuprous ions (5.05×10^{-7} M) in the temperature range from 130 to 166°C using UV spectroscopy as analytical method. The ion-catalyzed reaction follows first-order kinetics with respect to the peroxide and added cuprous ions. The temperature effect on the rate of thermal decomposition of the title compound was described by the corresponding Arrhenius equations, and its stability in solution was estimated on a quantitative level. The activation parameters of the initial step of decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane were determined ($\Delta H^{\neq} = 14.7\pm0.8$ kcal mol^{-1}; $\Delta S^{\neq} = -38.9\pm1.4$ cal mol^{-1} K^{-1}; $\Delta G^{\neq} = 31.0\pm0.8$ kcal mol^{-1}). Electron-transfer mechanism was proposed for the reaction under study.

DOI: 10.1134/S1070363208060303

Some 1,2,4,5-tetraoxanes and 1,2,4-trioxanes attract great interest due to their potential as antimalarial agents [1, 2]. Such compounds are prone to undergo decomposition in the presence of catalytic amounts of transition metal ions through initial complex formation at the peroxide bond [3]. Previous studies have shown that the unusually high rate of decomposition of tetramethyl-1,2-dioxetane in methanol is due to catalysis by metallic impurities present in the solvent. [4]. The addition of cuprous chloride considerably accelerates decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane (TMT) in propan-2-ol. It was found that cuprous salts hardly affect the thermal decomposition in acetic acid solution, for cupric ions exert no catalytic effect on peroxide compounds [5]. We recently demonstrated that cupric ions have catalytic effect on peroxides [6]. Three mechanistic possibilities can be considered for the observed catalysis [2, 3] (Scheme 1): (1) coordination or Lewis acid, (2) insertion, and (3) electron transfer.

Scheme 1.



In this work we examined thermal decomposition of a cyclic peroxide, 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane, in methanol in the presence of copper(I) ions to estimate the catalytic effect of the latter in homogeneous medium. UV spectrophotometry was used as analytical method.

The thermal decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane was studied in methanol solution with an initial concentration of 1.69×10^{-2} M in the temperature range from 130 to 166ºC in the presence of copper(I) chloride (5.05×10^{-7} M); the reaction was found to follow first-order kinetic laws until ~60%

---

[1] The text was submitted by the authors in English.

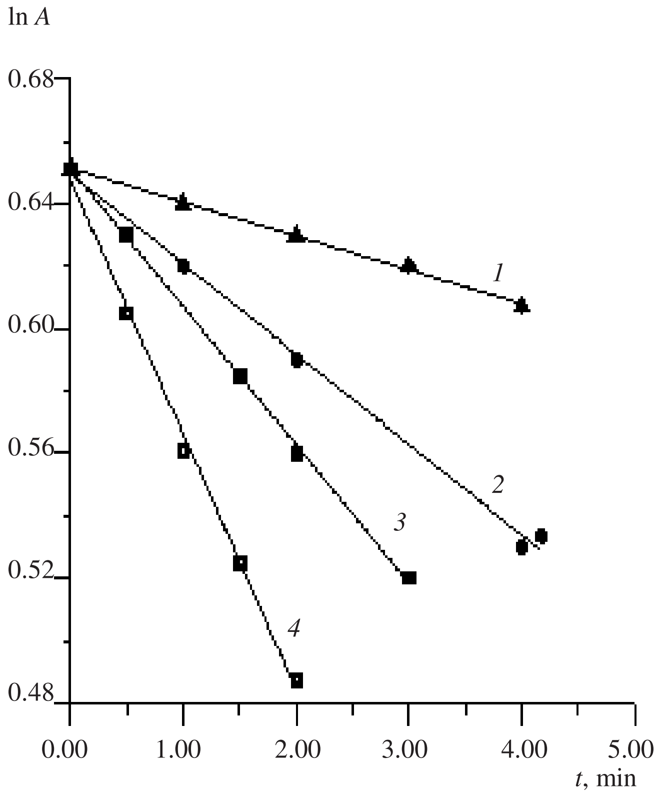


Fig 1. First-order kinetic plots for the thermal decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane in methanol in the presence of CuCl at (*1*) 130, (*2*) 140, (*3*) 150, and (*4*) 166°C.

conversion of the substrate (Fig. 1). The apparent rate constants (k_{exp}) for the decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane in methanol in the presence of CuCl were much greater than those obtained using commercial methanol as solvent [7] (Table 1). Thus the Cu(I)-catalyzed decomposition is much more effective than the decomposition catalyzed by copper(II) ions [6].

Table 1. First-order rate constants for the decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane in methanol containing CuCl[a]

Temperature, °C	[TMT]×10^2, M	$k_0\times10^5$, s^{-1}	$k_{\mathrm{ap}}\times10^5$, s^{-1}
130	1.69	0.40	27.19
140	1.69	1.00	49.44
150	1.69	2.44	73.64
166	1.69	6.59	136.61

[a] k_0 is the experimental rate constant for the decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane in methanol at an initial concentration of 1.69×10^{-2} M; k_{ap} is the apparent rate constant for the decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane in methanol ($c_{\mathrm{TMT}} = 2.34\times10^{-2}$ M) in the presence of CuCl ($c_{\mathrm{CuCl}} = 5.05\times10^{-7}$ M).

The catalytic effect was verified as a marked increase of k_{exp} and low activation energy. Complexation of 3,3,6,6-tetramethyl-1,2,4,5-tetra-oxane by a metal ion should favor decomposition by removing orbital symmetry restrictions or by lending positive character to one or both peroxide oxygen atoms, thus destabilizing the peroxide bond and facilitating ring cleavage. Copper(I) chloride in methanol undergoes dissociation to give solvated ion $Cu^+(MeOH)_x$. Two necessary conditions for catalysis are dissociation of the metal salt and fast exchange of ligands around the metal ion.

Temperature effect on the rate constant (k_{exp}) for unimolecular reaction can be represented by the Arrhenius equation where the errors are standard deviations determined by the least-squares treatment of the kinetic data [8, 9].

$$\ln k\ (\mathrm{s}^{-1}) = (11.22\pm0.8) - (15518.39\pm1000)/T[\mathrm{CuCl}] = 5.05\times10^{-7}\ \mathrm{M}.$$

The corresponding plot is almost linear ($r = 0.993$) within a relatively large temperature range ($\Delta T \approx 36$°C). This suggests that the calculated activation parameters for the decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane in methanol solution belong to a single process. The low activation barrier, about 15.5 kcal, confirms the catalytic effect.

The second-order rate constants k_2 for the catalytic decomposition were calculated by the following equation:

$$k_2 = \frac{k_{\mathrm{ap}} - k_0}{[\text{metal salt}]} = \frac{k_{\mathrm{cat}}}{[\text{metal salt}]},$$

where k_0 is the rate constant for the uncatalyzed decomposition, and k_{ap} is the apparent rate constant for the catalyzed decomposition. The second-order rate constants k_2 for the catalytic decomposition and experimental conditions are summarized in Table 2.

No counterion effect [3] was observed in the reaction catalyzed by cuprous ions (Table 3). The data in Table 3 indicate that stronger complexation of the metal ion makes the catalysis less efficient and that the presence of uncomplexed metal ions is necessary to achieve strong catalytic effect. The latter increases in parallel with the concentration of cuprous ions.

Table 2. Second-order rate constant k_2 for the catalyzed decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane in methanol in the presence of metal salt at different temperatures

Temperature, °C	[TMT]×10^2, M	k_2, M^{-1} s^{-1}
130	1.69	530.5
140	1.69	959.2
150	1.69	1409.9
166	1.69	2574.6

Table 3. Cuprous ion-catalyzed decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane in treated methanol

Anion or salt	[Anion]/[Cu^+]	$K_{cat}\times10^5$, s^{-1}
None	–	49.44
Na_2EDTA	1.2	49.74

Table 4. Activation parameters for the thermal decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane in different solvents

Solvent	$\Delta H^{\neq}$, kcal mol^{-1}	$\Delta S^{\neq}$, cal× mol^{-1} K^{-1}	Reference
Methanol	25.8±0.3	–17.9±0.6	[10]
Methanol/Cu(I)	14.7±0.8	–38.9±1.4	This paper
Propan-2-ol	19.4±1.3	–31.4±3.5	[5]
Acetic acid	13.3±4.4	–43.7±10.5	[4]

Insertion mechanism requires formal two-electron oxidation of the metal ion, while electron-transfer mechanism involves one-electron oxidation (transfer of an electron to the lowest antibonding orbital of the peroxide oxygen, followed by cleavage of the O–O bond). Coordination mechanism where the metal ion acts as a Lewis acid is completely consistent with the counterion effect and the linear free energy relationship. Complexation of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane by a metal ion might facilitate decomposition by removing positive character to one or both oxygen atoms destabilizing the peroxy bond and allowing for more facile ring cleavage [3].

The activation parameters for the unimolecular reaction under study (enthalpy variation $\Delta H^{\neq}$ and activation entropy variation, $\Delta S^{\neq}$) were determined using the Eyring equation (Table 4, Fig. 2). The error limits were calculated using an appropriate literature method [10].

The negative value of entropy variation implicates diminution of the degree of freedom of the reactive molecules in passing to a rigid transition state, assuming that the thermolysis in methanol involves rupture of the peroxide bond in the 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane molecule, which is assisted by the solvent and metal ion forming a complex with the solvent and the diperoxide (Table 4). The kinetic parameters given in Table 4 show that the behavior in methanol in the presence of metal ions is similar to the behavior observed in acetic acid.

The following conclusions can be drawn. The thermal decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane in methanol in the presence of copper(I) ions follows first-order kinetics. Analysis of the products and activation parameters led us to postulate a thermolysis mechanism typical of tetraoxanes. The process begins with homolytic dissociation of the peroxide bond to give intermediate diradical and subsequent cleavage of the C–O bond to produce acetone and oxygen as final products.

An increased catalytic effect was observed at a metal ion concentration that is only ten times larger than its concentration in commercial reagent. Thermal decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane is strongly accelerated by addition of traces of single-electron reducing agents such as copper(I) salts. The reaction involves electron transfer to the lowest

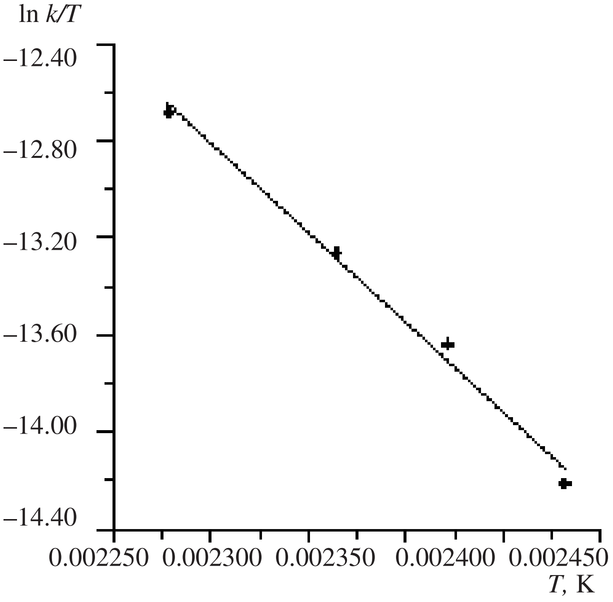


Fig. 2. Eyring equation plot for the thermal decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane in methanol containing CuCl (c_{CuCl} = 5.05×10^{-7} M).

antibonding orbital of the peroxide oxygen, followed by cleavage to the O–O bond.

At present, research is in progress to determine whether the complexation involves one or both oxygen atoms of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane. Our further study will be aimed at analyzing the effect of larger concentrations of copper(I) salts on the decomposition of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane in methanol solution.

EXPERIMENTAL

3,3,6,6-Tetramethyl-1,2,4,5-tetraoxane was prepared according to the procedure described in [9], and its purity was checked by GLC. Methanol was commercial reagent (Merck) of analytical grade; it was purified by standard techniques [11].

Pyrex glass tubes (70 mm×4 mm o.d.) filled with 2 ml of a solution of 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane in methanol containing cuprous chloride were thoroughly degassed under vacuum line at –196°C and then sealed with a flame torch. The ampoules were immersed into a thermostated silicone oil bath (±0.1°C) and withdrawn after definite time, the reaction being stopped by cooling to 0°C. The concentrations of unreacted 3,3,6,6-tetramethyl-1,2,4,5-tetraoxane and its decomposition products in the reaction mixture were determined by quantitative UV-visible analysis using a CampSpec M330 spectrophotometer. The absorbance was measured at λ 209 nm.

The corresponding first-order rate constant values were calculated from the slope of the plot of $\ln A$ (where A is the absorbance, Fig. 1) versus reaction time. In all cases, the progress of the reaction was followed for at least one half-conversion period. The activation parameters were calculated using the Eyring equation, and the errors were determined by the least-squares procedure [12, 13].

REFERENCES

1. *Free Radicals in Biology*, Pryor, W.A., Ed., New York: Academic, 1976–1984, vols. 1–6.
2. Wen-MinWu, Zhu-Jun Yao, Yu-Lin Wu, Kun Jiang, Yan-Fang Wang, Hai-Bao Chen, Feng Shan, and Ying Li, *Chem. Commun*., 1996, vol. 18, p. 2213.
3. Bartlett, P.D., Baumstark, A.L., and Landis, M.E., *J. Am. Chem. Soc*., 1974, vol. 96, p. 5557.
4. Wilson, T., Landis, M., Baumstark, A., and Bartlett, P.D., *J. Am. Chem. Soc*., 1973, vol. 95, p. 4765.
5. Moryganov, B.N., Kalinin, A.I., and Mikhotova, L.N., *Zh. Obshch. Khim*., 1962, vol. 32, p. 3414.
6. Jorge, N.L., Romero, J.M., Leiva, L.C., Castellanos, M.G., Cafferata, L.F.R., and Gómez Vara, M.E., *Afinidad*, 2003, vol. 60 (506), p. 291.
7. Leiva, L.C., Castellanos, M.G., Jorge, N.L., Cafferata, L.F., and Gómez Vara, M.E., *Rev. Soc. Quím. México*, 2002, vol. 46, no. 1, p. 1.
8. Schaleger, L.L. and Long, F.A., *Adv. Phys. Org. Chem*., 1963, vol. 1, p. 1.
9. Huyberechts, S., Halleux, A., and Kruys, P., *Bull. Soc. Chim. Belg*., 1955, vol. 64, p. 203.
10. Leiva, L.C., Castellanos, M.G., Jorge, N.L., Cafferata, L.F.R., and Gómez Vara, M.E., *Rev. Soc. Quím. México*, 1998, vol. 42, no. 5, p. 223.
11. *Organic Solvents. Physical Properties and Methods of Purification*, Riddick, J.A. and Bunger, W.B., Eds., New York: Wiley, 1970, 3rd ed.
12. Scholz, B., Butzert, H., Neumeister, J., and Nierlich, F., *Ulmann's Encyclopedia of Industrial Chemistry*, Weinheim: Wiley, 1985, vol. A16.
13. Machado, C. and Machado, V.G., *J. Chem. Educ*., 2001, vol. 78, no. 5, p. 649.