## Note

The thermal decomposition of some 1,2,4-trioxanes

Charles W. Jefford, Amer Jaber, John Boukouvalas and Paul Tissot

Department of Organic Chemistry and Department of Applied Chemistry, University of Geneva, CH-1211 Geneva 4 (Switzerland)

(Received 22 January 1991)

Chemists generally believe that the O–O bond of the peroxide function is inherently unstable. In fact, many peroxides readily decompose on heating [1]. By analogy, 1,2,4-trioxanes which are cyclic peroxides, would also be expected to be equally thermally unstable. Consequently, it comes as a surprise to discover that the naturally occurring 1,2,4-trioxane, arteannuin, of some renown on account of its anti-malarial activity, survives heating for 2.5 min at 200°C, some 50°C above its melting point [2,3]. Other less exotic trioxanes also require heating at equally high temperatures to bring about their decomposition [4–9]. In order to complement earlier observations, we decided to undertake a thermogravimetric study of the thermal decomposition of a series of cis-fused bicyclic 1,2,4-trioxanes (**1–8**):
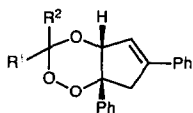
1 $R^1 = R^2 = H$	**5** $R^1 = H, R^2 = Me$
2 $R^1 = R^2 = Me$	**6** $R^1 = H, R^2 = n\text{-Pr}$
3 $R^1 = Me, R^2 = n\text{-Pr}$	**7** $R^1 = Me, R^2 = CH_2Ph$
4 $R^1, R^2 = \text{-}CH_2CMe_2CH_2CMe_2CH_2\text{-}$	**8** $R^1 = R^2 = n\text{-Pr}$

EXPERIMENTAL

The trioxanes chosen (**1–8**) were prepared using recently developed synthetic procedures [10–12]. Four are solids (**1–4**) and four are liquids (**5–8**) at 20°C. All the trioxane samples were analysed thermogravimetrically (TG) using a Mettler thermal gravimeter Model TA1, aluminium crucible, nitrogen atmosphere (5 l h^{-1}) and a rate of heating of 2°C min^{-1} for sample weights 5.7–13.3 mg. The variation of their weights with the rate of heating was recorded (Fig. 1). Differential scanning calorimetry (DSC) was performed on a Mettler calorimeter Model TA 2000 (aluminium crucible, nitrogen atmosphere (1 l h^{-1}) with a heating rate of 2°C min^{-1} and sample
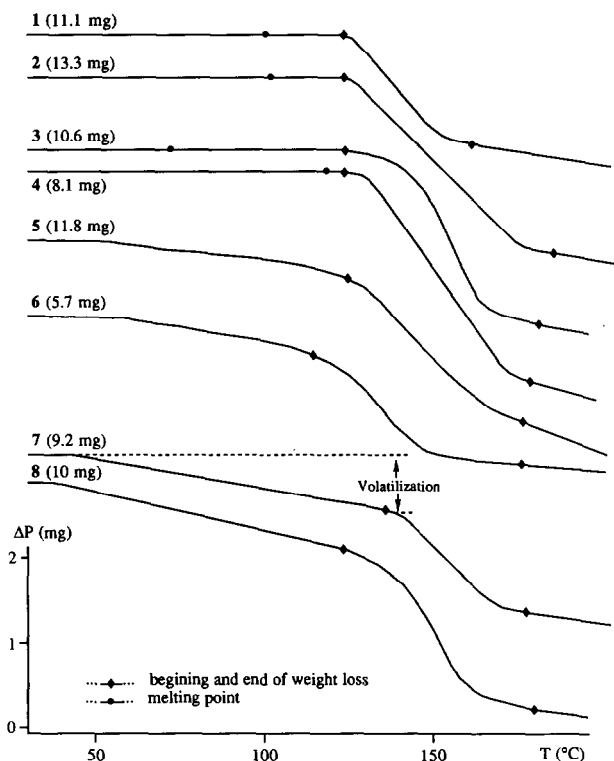
Fig. 1. Variation in the weight of some 1,2,4-trioxanes (1–8) with temperature.

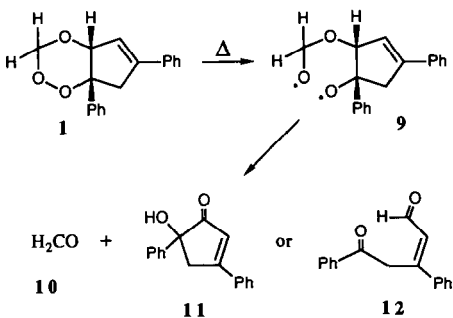weights of 3–4 mg) to determine the temperatures and enthalpies of melting of the solid samples (1–4) (Table 1). Flash thermolysis of trioxane 2 was carried out as follows. The sample was first placed in a round-bottomed flask connected by a liquid-N_2-cooled trap to the vacuum line. The whole apparatus was flushed with argon several times, after which the vacuum was established. The flask was plunged into an oil bath maintained at 80°C. The temperature of the bath was raised progressively to 130°C over 5 min and kept at 130°C for 15 min. The volatile decomposition product (acetone) was collected in the trap.

RESULTS AND DISCUSSION

The progressive loss of weight with rising temperature is remarkably similar for all eight compounds (Fig. 1). Moreover, the onset of decomposition occurs at more or less the same temperature. The four solids start to decompose at 114–132°C regardless of their melting points which range from 78 to 116°C. In all cases, decomposition is complete at 178 ± 3°C, except for 1 which finishes at 143 ± 3°C. It is also worth noting that the four solid trioxanes conserve their initial weight beyond their melting points

339

TABLE 1

Thermolysis of some cis-fused diphenylbicylic 1,2,4-trioxanes (1–8)

Cpd. No.	C-3 substituents	Mol. wt.	M.p. (°C)	ΔH fusion (kJ mol^{-1})	Temp. range of decomposition (°C)	Wt. loss on decomposition (%)	Wt. loss calc. for R^1R^2CO (%)	Δ (actual − calc. wt.) loss (%)
1	H,H	280.34	98	21.7	114–146	13	10.7	2.3
2	Me,Me	308.40	96	22.1	124–180	23	18.8	4.2
3	Me,Pr	336.37	78	16.6	120–172	26	25.6	0.4
4	$CMe_2CH_2CMe_2$ $CH_2 \quad CH_2$	404.59	116	15.0	132–178	36	38.1	−2.1
5	H,Me	294.37	liq	–	120–172	19	15.0	4.0
6	H,Pr	322.43	liq	–	120–172	20	22.4	−2.4
7	Me,CH$_2$Ph	384.50	liq	–	127–168	20	34.9	−14.9
8	Pr,Pr	364.42	liq	–	120–172	29	31.3	−2.3

Scheme 1.

until they start to decompose. The weight loss between 25 and 120°C is slight being 0.15%. In contrast, the liquid samples begin to lose weight from 50°C onwards, probably by evaporation. Consequently, it is difficult to determine with precision the point of decomposition and the concomitant weight loss. Therefore, the experimental weight losses observed on decomposition are estimated values, taking into account the preceding volatilisation (Table 1). The similarity of the thermogravimetric curves indicates that the mechanism of decomposition is the same for all compounds. The weight loss in each case closely corresponds to the excision of the carbonyl component from the trioxane ring. The agreement between the theoretical and experimental loss in weight is good; the discrepancy being usually less than 3% (Table 1). The only significant anomaly ($\Delta = -14.9\%$) is shown by 7 which probably decomposes by another pathway as a smaller fragment is eliminated. Proof for the proposed cleavage of trioxanes 1–6 and 8 was obtained by carrying out flash thermolysis of 2 which yielded acetone as the only volatile product.

It should be mentioned that all the compounds are racemates and compounds 5, 6 and 7 are also diastereomeric mixtures. Compound 3 exists as a single isomer. The heats of fusion are roughly the same for trioxanes 1–4, which is to be expected as all are cis-fused and will have similar conformations and crystal lattices. Less energy for reorganisation is required
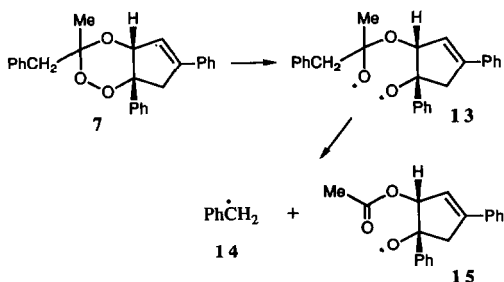
Scheme 2.

for **3** and **4**, probably because of their more sterically encumbered C-3 substituents. In keeping with previous interpretations [4,6,8], it appears that the first event on thermolysis is the homolytic rupture of the O–O bond to give a diradical which subsequently undergoes cleavage. With the exception of **7**, all the trioxanes (**1–6** and **8**) exhibited a similar decomposition pattern. The initial diradical, exemplified by **9**, would lose the carbonyl entity **10**, accompanied either by the acyloin, **11**, or the aldehydic ketone, **12**, (Scheme 1). Unfortunately, the reaction mixture was too complex to permit a distinction between these possibilities. In any event, the weight losses on decomposition of **1–6**, and **8** agree well with the excision of the carbonyl element (Table 1). Lastly, the benzyl trioxane, **7**, because its weight loss was less than that calculated, probably decomposes by another route. The initial diradical **13** could undergo easy scission to the benzyl and oxy radicals, **14** and **15**, which could then evolve further to toluene and other products (Scheme 2).

CONCLUSIONS

In conclusion, the present results confirm that solid 1,2,4-trioxanes are stable up to their melting points, and that liquids and solids both decompose at temperatures between 114 and 180°C. A similar behaviour has been observed for 1,2,4,5-tetroxanes [13].

ACKNOWLEDGEMENT

REFERENCES

1 A.G. Davies, Organic Peroxides, Butterworths, London, 1961, p. 195.
2 A.J. Lin, D.L. Klayman, J.M. Hoch, J. Silverton and C.F. George, J. Org. Chem., 50 (1985) 4504.
3 X. Luo, H.J.C. Yeh and A. Brossi, Heterocycles, 23 (1985) 881.
4 G.B. Schuster and L.A. Bryant, J. Org. Chem., 43 (1978) 521.
5 A. Padwa and T. Brookhart, J. Org. Chem., 44 (1979) 4021.
6 H. Yamamoto, M. Akutagawa, H. Aoyama and Y. Omoto, J. Chem. Soc., Perkin Trans. 1 (1980) 2300.
7 B. Kerr and K.J. McCullough, J. Chem. Soc., Chem. Commun., (1985) 590.
8 T. Fujisaka, M. Miura, M. Nojima and S. Kusabayashi, J. Chem. Soc., Perkin Trans. 1, (1989) 1031.
9 R.M. Wilson, S.W. Wunderly, T.F. Walsh, A.K. Musser, R. Outcalt, F. Geiser, S.K. Gee, W. Brabender, L. Yerino, Jr., T.T. Conrad and G.A. Tharp, J. Am. Chem. Soc., 104 (1982) 4429.
10 C.W. Jefford, D. Jaggi, J. Boukouvalas and S. Kohmoto, J. Am. Chem. Soc., 105 (1983) 6497.

11 C.W. Jefford, J. Boukouvalas and S. Kohmoto, J. Chem, Soc., Chem. Commun., (1984) 523.
12 C.W. Jefford, J. Boukouvalas, D. Jaggi, S. Kohmoto and G. Bernardinelli, Helv. Chim. Acta, 69 (1986) 941.
13 L.F.R. Cafferata, G.N. Eyler, E.L. Svartman, A.I. Cañizo and E.J. Borkowski, J. Org. Chem., 55 (1990) 1058.