ON THE DECOMPOSITION OF 1,2,4-TRIOXAN-5-ONES

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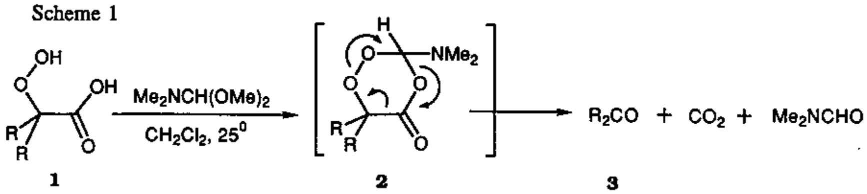
Abstract - The thermal and chemical properties of six 3,6-substituted 1,2,4-trioxan-5-ones were studied by flash-vacuum thermolysis (FVT) and by treatment with electron-transfer agents. The 1,2,4-trioxan-5-ones exhibited unusual stability both chemically and thermally, but eventually underwent decomposition with loss of carbon dioxide yielding the carbonyl components.

Chemists have believed that the 1,2,4-trioxan-5-one ring is intrinsically unstable and that it would decompose spontaneously to carbon dioxide and its carbonyl constituents. Typically, the decarboxylation of α-hydroperoxy carboxylic acids (**1**) in the presence of the acetal of dimethylformamide[1] to give aldehydes and ketones (**3**) was thought to proceed through the intermediacy of a frangible 1,2,4-trioxan-5-one (**2**) (Scheme 1). Similarly, the photo-oxygenation[2] of α-pyrones (**4**) gave the bridged bicyclic trioxanones (**5**) which, however, lost carbon dioxide almost immediately at room temperature to give the 1,2-diacylethylenes (**6**) (Scheme 2). Besides these examples, few 1,2,4-trioxan-5-ones have been reported.[3] However, as part of a program for discovering 1,2,4-trioxanes of anti-malarial potential,[4] we recently devised an operationally simple method for preparing 3,3,6,6-tetra-substituted 1,2,4-trioxan-5-ones[5] and were surprised to find that they were sufficiently stable to be characterized by X-ray.[6] Consequently, we now present our findings on some of their chemical and physical properties, in particular on the behavior of representative members (**7**-**12**) towards heat and electron transfer agents (Scheme 3).

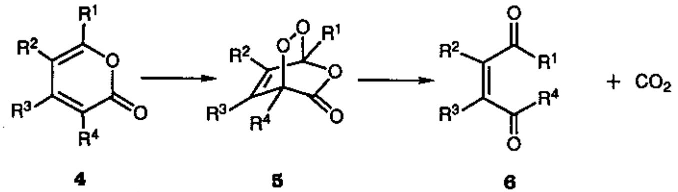
Submission of all of them to a first qualitative thermal test showed them to be more stable than expected. Injection onto a capillary column in a gas chromatograph at a temperature of less than 180 °C simply revealed the chromatogram characteristic of each particular trioxanone.[7] However, raising the temperature to 210 °C resulted in decomposition to give the corresponding carbonyl products, *e.g.* cyclohexanone, 2-adamantanone, pivalaldehyde, or 1-adamantylcarboxaldehyde.

In a further experiment, heating **7**-**10** in boiling decalin (bp 189 °C) under a gentle stream of argon led to complete decomposition in 2-3 h, whereas **11** and **12** under the same conditions required 3-5 h. Passage of the ef-

Scheme 1

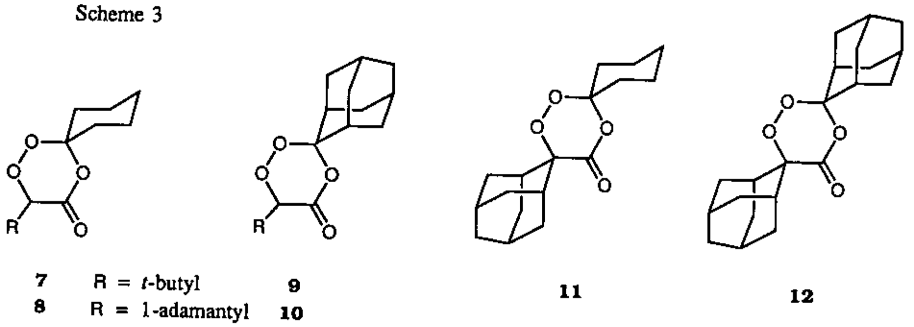


Scheme 2

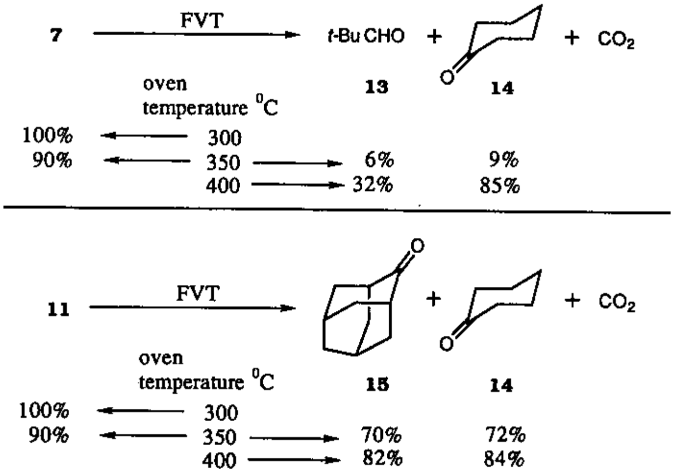


$R^1 = R^2 = R^3 = R^4 =$ H or Ph
$R^1 = R^3 = R^4 =$ H, $R^2 = CO_2H$ or CO_2Me

Scheme 3



Scheme 4



fluent gas through an aqueous solution of barium hydroxide caused precipitation of barium carbonate in amounts indicative of yields of 80-100% of carbon dioxide.[8] Flash-vacuum thermolysis (FVT)[9] confirmed the thermal stability. The *t*-butyl and the spirocyclic adamantane derivatives (**7**) and (**11**) survived temperatures of 300 °C, but progressively fragmented into carbon dioxide, pivalaldehyde (**13**), cyclohexanone (**14**) and 2-adamantanone (**15**) at temperatures of 350-400 °C (Scheme 4).[10] Trioxanones (**8-10**) showed similar FVT behavior, whereas **12** volatilized only difficultly owing to its high melting point (216 °C).

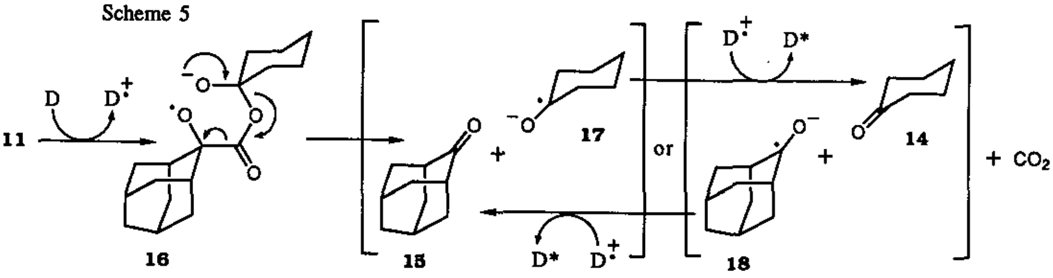
Next, the stability of the trioxanones (**7-12**) towards electron transfer agents was assayed.[11] It is well known that the peroxide bond is susceptible to scission, especially by electron donors.[12] Unexpectedly, trioxanones (**7-12**) were found to be quite resistant to the action of sodium azide, sodium iodide or triethylamine in diethyl ketone at 25 °C. In the boiling solvent (bp 103 °C), trioxanones (**7-10**) decomposed in 1 h, whereas when a higher boiling solvent, tetrachloroethylene (bp 122 °C), was used, decomposition was over in 10-20 min. In contrast, trioxanones (**11**) and (**12**) displayed greater stability to the aforementioned electron transfer agents and required 24-31 h in boiling diethyl ketone or tetrachloroethylene to undergo complete fragmentation. In the absence of the agents, exposure to the boiling solvents for more than 48 h was necessary for complete fragmentation.

Metal salts and complexes known to have an affinity for the peroxide bond, such as $Fe(ClO_4)_2$, $Fe(p\text{-}TsO)_2$,[13] $Pd(PPh_3)_4$,[14] Co(II)*m*-TPP,[15] and Zn(II)*m*-TPP[16] at concentrations of 5-6% molar equivalent in either tetrachloroethylene, THF (bp 66 °C) or acetonitrile (bp 82 °C) had a similar effect on **7-12**. Reaction times for complete decomposition were usually 1-14 h.

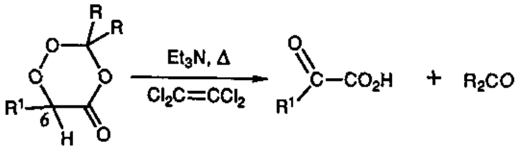
The aforementioned agents (D) initiated fragmentation by a mechanism that is best explained by electron exchange (Scheme 5).[17] Taking trioxanone (**11**) as an illustration, the electron donor, D, gives an electron to the oxygen-oxygen σ^*-bond to afford the radical anion (**16**). Subsequently, cleavage can occur giving either the adamanto- or cyclohexano-ketyl radicals (**17**) or (**18**). Restitution of the electron by **17** or **18** to the donor radical cation ($D^{.+}$) creates an excited donor (D*) and liberates adamantanone (**15**) and cyclohexanone (**14**) respectively. No luminescence was visible to the naked eye. However, heating the trioxanone alone in 1-phenyldecane as solvent (bp 294 °C) above 200 °C resulted in light emission as detected by a photo-multiplier tube.[18]

Although triethylamine decomposes **11** and **12** by electron exchange, a different mechanism was followed by trioxanones (**7-10**). In boiling tetrachloroethylene after 50 min. they were effectively deprotonated at the C6

Scheme 5



Scheme 6



7,9 R^1 = *t*-butyl **19** R,R, = >adamantane

8,10 R^1 = 1-adamantyl **20** R,R = $(CH_2)_5$

position with excision of adamantanone or cyclohexanone[19] to produce the corresponding α-keto carboxylic acids (**19**, **20**) in 100% yield (Scheme 6).

The conclusion is that 1,2,4-trioxanones (**7**-**12**) are unusually thermally stable. Their decomposition is facilitated by electron transfer agents but high temperatures (100-120 °C) are required. These trioxanones stand in contrast to the bridged bicyclic analogues (**5**) which probably owe their inherent fragility to the endocyclic double bond. Experiments on the chemistry and physical properties of **7**-**12** are under way and the results will be reported in due course.

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7. Analytical glc was performed on a Hewlett Packard model 5880 A instrument equipped with a flame ionization detector and a Hewlett Packard Ultra 1 capillary column (stationary phase: cross-linked PhMe silicone, length x internal diameter x film thickness = 25 m x 0.22 mm x 0.11 μm), carrier gas: N_2.

8. The yields of carbon dioxide obtained were calculated from the amount of barium carbonate recovered.

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10. The products were identified by both gc and ^{1}H-nmr. The yields were determined on the basis of the ^{1}H-nmr spectra by using an internal standard (1,3,5-tribromobenzene). Low yields of pivalaldehyde were probably due to rearrangement, alternative reaction pathways, or loss at the high temperatures and low pressures used in these experiments.

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