Dispiro-1,2,4-Trioxanes as Precursors of Medium Ring Lactones: Thermolysis of Indan-2-spiro-3′-(1′,2′,4′-trioxane)-6′-spiro-1″-cyclohexane

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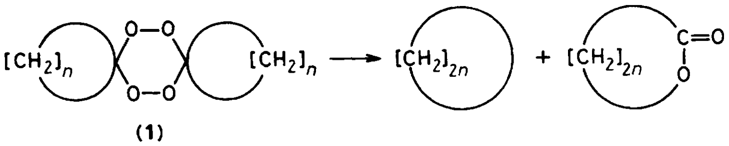
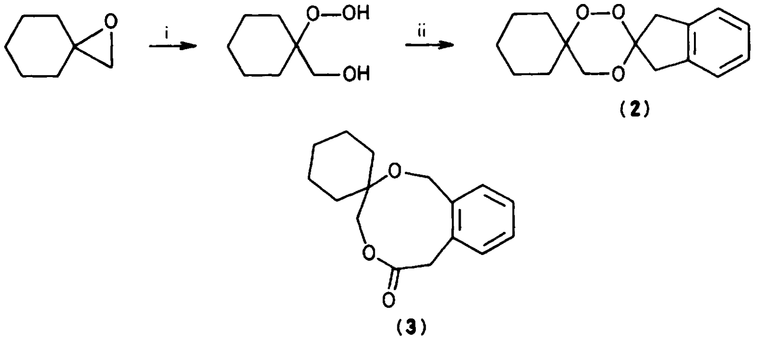
Thermolysis of the dispiro-trioxane (**2**) in decane at 190 °C afforded a novel nine-membered ring lactone whose structure has been determined by *X*-ray crystallography.

Although there exist a variety of synthetic approaches to 1,2,4-trioxanes,[1—5] little has been reported on the chemistry of these compounds in comparison to other six-membered ring endoperoxides such as 1,2-dioxanes[6] and the 1,2,4,5-tetraoxanes.[7,8] The latter attracted considerable interest since Story and coworkers found that the dispiro-derivatives (**1**), on thermolysis, afforded macrocyclic hydrocarbons and lactones [reaction (1)] in acceptable yield[8] *via* a complex, radical rearrangement.[9] In contrast, thermolysis of trioxanes is reported to produce only the corresponding carbonyl compounds arising from extensive fragmentation of the central trioxane ring.[3,10] In this work, the dispiro-trioxane (**2**) was prepared and its thermal rearrangement examined.

The trioxane (**2**) was prepared in 10—15% yield from



(1)



(2)

Reagents and conditions: i, H_2O_2, Et_2O, H^+, 0 °C; ii, indan-2-one, H^+, Et_2O, 0 °C.

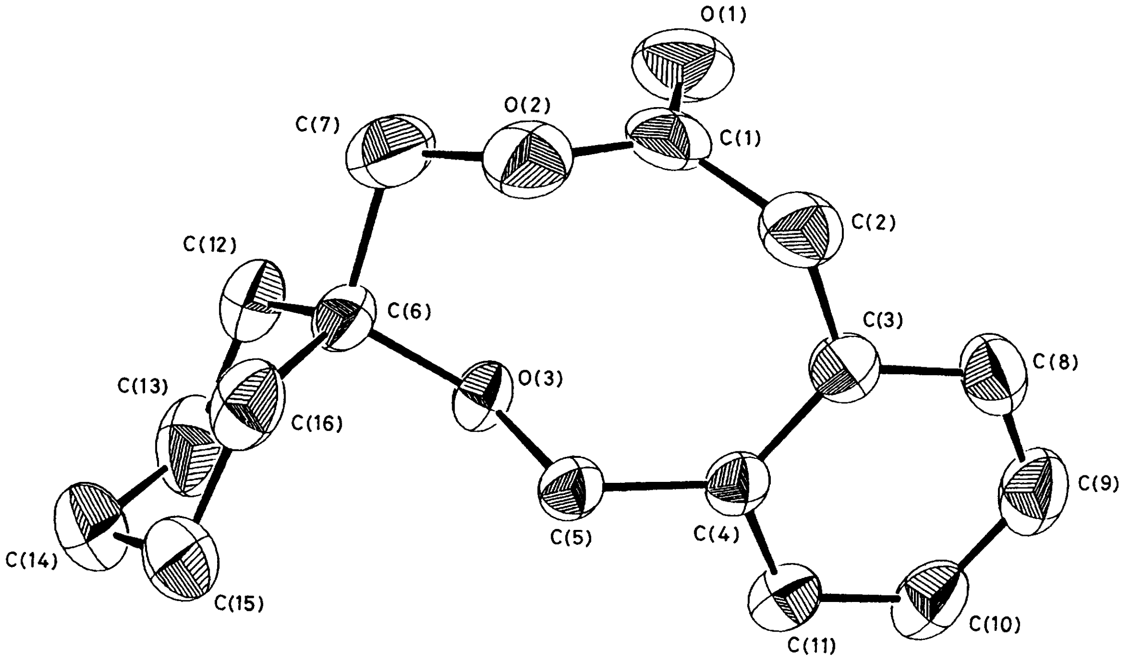
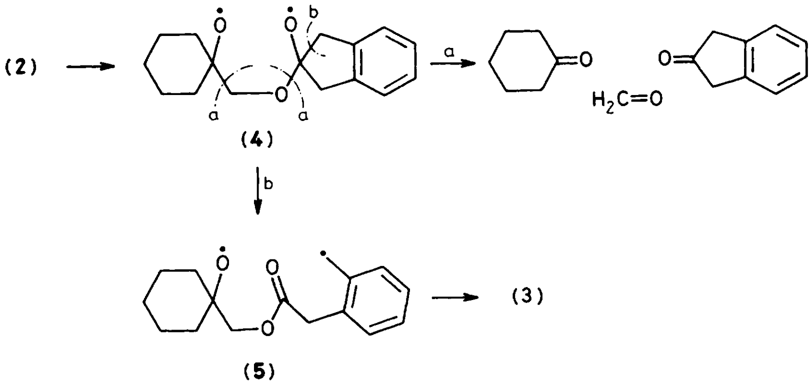


Figure 1. *X*-Ray crystal structure of the lactone (**3**) showing the crystallographic numbering scheme. Hydrogen atoms have been omitted for clarity.



Scheme 1

methylenecyclohexane oxide [reaction (2)].† Thermolysis of (**2**) (2% w/v in degassed decane, N_2, 190 °C, 6—8 h) gave three isolable products, two of which were readily identified as cyclohexanone and indan-2-one. Although the spectroscopic and analytical data‡ for the third product (50—53%) indicated that it had most likely been formed from (**2**) without fragmentation, the structure of this compound could only be resolved by an *X*-ray crystal structure determination.§

Thus the rearrangement product was unambiguously identified as the structurally novel lactone (**3**) (Figure 1) containing an uncommon nine-membered heterocyclic ring with a spirocyclohexane substituent. In the rearrangement of (**2**) to (**3**), a partial ring expansion involving only the trioxane and indan rings has occurred leaving the cyclohexane ring intact. A plausible mechanism for the thermolysis of (**2**) based on radical scission pathways is outlined in Scheme 1.

The thermolysis conditions required for (**2**) are consistent with an initial O–O bond homolysis to give the oxybiradical (**4**).[10] Subsequent collapse of (**4**) *via* pathway a would yield the indicated carbonyl fragments.¶ Alternatively a selective β C–C bond scission in the indan ring of (**4**) would generate the heterobiradical precursor (**5**) of the observed product (**3**) (pathway b). The extent of formation of (**3**) is unexpected since 1-alkyl cycloalkoxyl radicals analogous to the moiety in (**5**) normally undergo rapid ring opening to give carbon-centred radicals.[11] Since the cyclisation of (**5**) to (**2**) necessarily occurs within the lifetime of the oxyl radical, then the solvent cage must constrain the radical centres in (**5**) to be in close proximity hence favouring radical coupling.

In addition to mechanistic aspects, the more general synthetic utility of spiro-1,2,4-trioxanes as precursors of medium ring lactones is currently under investigation.

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† The method was similar to that outlined in ref. 1. Satisfactory microanalytical data have been obtained. Compound (**2**), from CH_2Cl_2–MeOH, m.p. 96—97 °C; δ_H (200 MHz, CD_2Cl_2, Me_4Si, −10.5 °C) 1.2—1.8 (9H, m), 2.3—2.5 (1H, m), 3.04 (1H, d, *J* 17.5 Hz), 3.16 (1H, d, *J* 17.5 Hz), 3.28 (1H, d, *J* 16.7 Hz), 3.65 (1H, d, *J* 11.6 Hz), 3.72 (1H, d, *J* 11.6 Hz), 3.77 (1H, d, *J* 16.7 Hz), and 7.1—7.3 (4H, m); *m*/*z* 260 (M^+).

‡ Crystalline solid, from CH_2Cl_2–Et_2O, m.p. 161—163 °C (decomp.); $\nu_{max.}$ ($CHCl_3$) 1745br. (CO stretch) cm^{-1}; δ_H (200 MHz, $CDCl_3$, Me_4Si) 1.2—1.7 (8H, m), 1.85—2.0 (2H, m), 3.76 (2H, s), 4.34 (2H, s), 4.76 (2H, s), and 7.2—7.6 (4H, m); *m*/*z* 260 (M^+).

§ *Crystal Data:* compound (**3**), $C_{16}H_{20}O_3$, $M = 260.3$. Monoclinic, $a = 10.426(3)$, $b = 10.792(4)$, $c = 12.605(4)$ Å, $\beta = 107.59(2)°$, $U = 1352.0$ Å^3, space group $P2_1/n$ (alt. $P2_1c$, No. 14), $Z = 4$, $D_c = 1.279$ g cm^{-3}, $\mu(\text{Mo-}K_{\bar{\alpha}}) = 0.81$ cm^{-1}, $F(000) = 560.0$. The intensity data were collected on CAD-4 diffractometer (Mo-K_α radiation, ω—2θ scanning) and corrected for Lorentz and polarisation effects. Of 2375 unique data measured, 1523 had $I > 2.5\sigma(I)$. The structure was solved by direct methods (SHELX84) and refined (SHELX76) by full-matrix least-squares methods (all non-hydrogen atoms anisotropic). The hydrogen atoms were all located on difference-Fourier maps and included at idealised positions with isotropic group temperature factors in the final stages of refinement. At convergence the final *R* factor was 0.048. The bond distances and angles were within expected ranges. The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

¶ Formaldehyde was not observed, and was presumably lost during the reaction. The isolated yields of indan-2-one (25—30%) and cyclohexanone (5%) are lower than theoretical yield owing to losses on work-up.