

Ring Opening Reactions of Dispiro[5.0.5.1.]trideca- 1,5,8,12-tetraone

III.* Reactions with Formic and Acetic Acid¹

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Dispiro[5.0.5.1.]trideca-1,5,8,12-tetraone undergoes ring opening with formic and acetic acid at room temperature with formation of compounds 3, 5, and 7. The mechanism of the reaction is discussed.

Dispiro[5.0.5.1.]trideca-1,5,8,12-tetraone² (*1*) has a pronounced tendency to undergo ring opening reactions.^{3,4} The present paper deals with the reactivity of *1* towards formic and acetic acid. We have used acetic acid as a solvent in unsuccessful attempts to synthesise the homologue of *1* through oxidative coupling of methylene-bis-dimedone.²

When compound *2*, the monohydrate of *1*, was treated with acetic acid at room temperature for 24 h it gave two main products: the free tetraketone *1* and an enolic compound, C₁₅H₁₈O₆, formed by the addition of one molecule of acetic acid to *1*. The adduct gave spectra which were in complete accordance with structure 3. The UV spectrum showed the presence of two enolised 2-substituted 1,3-cyclohexanedione rings. The IR spectrum (CHCl₃) was closely related to the spectra of methylene-bis-1,3-cyclohexanedione and methylene-bis-dimedone with prominent bands at 2920 (br, OH), 1603 (s, enone system) and 1375 cm⁻¹. It also gave an ester carbonyl band at 1735 cm⁻¹.

In the NMR spectrum of 3 (CDCl₃; 60 MHz) the methylene protons of the 1,3-cyclohexanedione rings gave the typical complex resonance band in the region δ 1.7–2.8. The methylene bridge protons appeared as a singlet at δ 3.16 (2H).² The singlet at δ 2.16 (3H) was assigned to the acetoxyl-methyl group. The methine proton gave rise to a 1:1:1:1 quartet at δ 5.47 (1H) due to coupling with the adjacent nonequivalent methylene protons ($J=7$ and 9 cps).

* Nos. I and II in this series, see Refs. 3 and 4.

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A somewhat different result was obtained with formic acid. Compound 2 when treated for a few minutes with formic acid was dehydrated to give 1 as the main product. On extended reaction at room temperature two new products were detected by TLC. The major one gave the elemental composition $C_{14}H_{14}O_5$ ($1 + HCOOH - H_2O$). The UV spectrum of this compound, in both acidic and neutral ethanol, gave maxima at 228 nm (ϵ 15 000) and 302 nm (ϵ 4800). This spectrum was strikingly similar to that of the xanthene 4, derived from methylene-bis-dimedone, with maxima at 230 nm (ϵ 14 900) and 302 nm (ϵ 4700). The IR spectrum was also closely related to that of 4 except for a band at 1732 cm^{-1} assigned to an ester carbonyl group. Structures 5 or 6 would be compatible with the above data.

The NMR spectrum ($CDCl_3$) obtained with a 100 MHz instrument showed a poorly resolved band in the region δ 1.7–2.8 (10H) for the methylene protons of the cyclohexanedione rings. The formate proton produced a doublet ($J=1$ cps) at δ 8.21 (1H) due to coupling with the ring methine proton. The methylene protons of the pyran ring appeared as a quintet ($J=1.5$ cps) at δ 2.91 (compare the spectrum of 4) and the ring methine proton gave an octet (1:1:1:1:1:1:1) at δ 5.46 (1H) ($J=1, 6, \text{ and } 10$ cps), which clearly shows that the product has structure 5.

The NMR spectrum of the crude reaction mixture ($CDCl_3$; 60 MHz) indicated that the minor product, compound 7, was a lower homologue of 3. It gave the characteristic signal of methylene bridge protons² at δ 3.15 and a singlet of a formate proton at δ 8.10.

A plausible mechanism for the formation of 3, 5, and 7 is outlined in Fig. 1. Dehydration of 2 gives the free tetraketone 1. Acetic or formic acid attacks one of the spiro carbons of the protonated form of 1 to give the 2-acyloxy derivatives 8 or 9, respectively, which are in equilibrium with their enol forms 10 or 11. Acyloxy rearrangement yields 3 or 7, respectively.

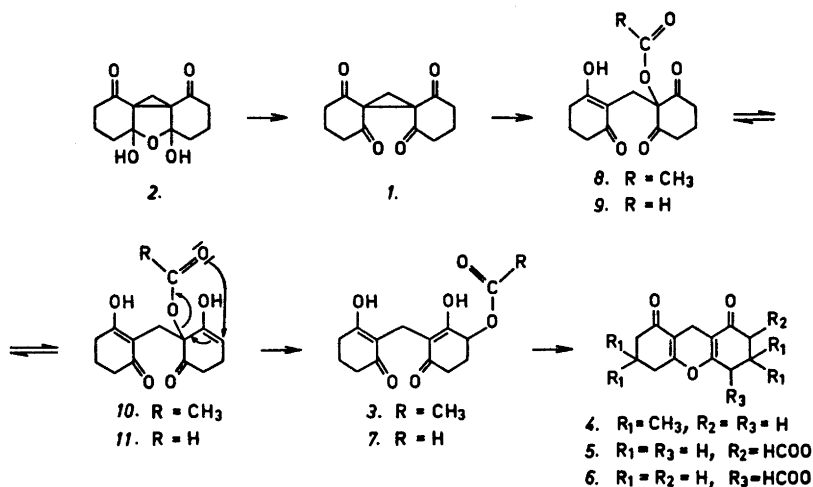


Fig. 1.

In the final step, which occurs only with formic acid, **7** is dehydrated to give the xanthene derivative **5**. The dehydrating properties of formic acid have been demonstrated earlier.⁵⁻⁷

As far as we know no analogous rearrangement of 2-acyloxy-1,3-cyclohexanediones has been reported. On the other hand, it has been shown that 2-acetoxy-dimedone is stable in acetic acid even at elevated temperatures.⁸ It is reasonable to assume that the driving force of the rearrangement is the increased stability obtained through the formation of the enolised β -diketo system. Analogous types of internal return reactions have been reported in a number of related systems,⁹⁻¹¹ e.g. in 3-chloro-5-methylcyclohexene.¹⁰ When this compound is solvolysed in acetic acid the rate of internal return is over four times the rate of solvolysis. Internal return, as expected, competes most efficiently with solvolysis in solvents that are only weakly nucleophilic.*

A route to **3**, **5**, and **7**, via 4,5,6,7-tetrahydro-spiro[benzofuran-2(3H),1'-cyclohexane]-2',4,6'-trione,² can be rejected since this compound did not react with acetic acid under the present conditions.

The results presented show that the dispiro cyclopropane derivative **1** is readily opened at room temperature by formic or acetic acid.

EXPERIMENTAL

Conditions and equipment used were those earlier described.^{2,3}

Reaction of 2 with acetic acid. The hydrate **2** (252 mg, 1 mmol) was stirred in acetic acid (5 ml) for 24 h at room temperature. The clear solution was evaporated to dryness *in vacuo*. On addition of methanol (2 ml) a crystalline residue (3, 159 mg, 54 %) was obtained, which was recrystallised from propanol, m.p. 153–160°C, λ_{max} (EtOH) in acidic solution 254 nm (ϵ 25 000), λ_{max} (EtOH) in basic solution 282 nm (ϵ 32 700). Mass spectrum: *m/e* 294 (M^+ , 12 %), 175 (16 %), 137 (11 %), 124 (13 %), 85 (14 %), 84 (12 %), 82 (18 %), 68 (11 %), 55 (31 %), 54 (11 %), 43 (CH_3CO^+ , 100 %) and 42 (34 %). (Found: C 61.4; H 6.33. $\text{C}_{15}\text{H}_{18}\text{O}_6$ (294.31) requires C 61.2; H 6.17).

The presence of compound **1**, the second major product, was demonstrated by preparative TLC and IR spectroscopy.

Dehydration of 2 with formic acid. The hydrate **2** (252 mg, 1 mmol) was dissolved in formic acid (2 ml, 97–100 %, Merck) at 30°C. The clear solution was evaporated to dryness *in vacuo* and the residue was crystallised from ethanol (99.5 %) to give pure **1** (104 mg, 45 %), m.p. 96–98°C (lit.² 97–98°C), further characterized by its IR and NMR spectra.²

Reaction of 2 with formic acid. The hydrate **2** (252 mg, 1 mmol) was stirred in formic acid (5 ml, 97–100 %) for 48 h at room temperature. The clear solution was evaporated to dryness *in vacuo*. The solid residue was crystallised from ethanol to give **5**, (99 mg, 38 %), m.p. 193–194°C. ν_{max} (CHCl_3) 2940, 1735(s), 1670(s), 1628, 1390, 1168(s) cm^{-1} . Mass spectrum: *m/e* 262 (M^+ , 98 %), 217 ($M^+ - \text{HCOO}$, 68 %), 215 (29 %), 188 (33 %), 157 (44 %), 162 (100 %), 134 (46 %), 55 (41 %) and 45 (HCOO^+ , 22 %). (Found: C 64.3; H 5.44. $\text{C}_{14}\text{H}_{14}\text{O}_5$ (262.27) requires C 64.1; H 5.38).

* *Added in proof.* Compounds **3** and **7** may be derived from **1** by an alternative route suggested by Dr. B. Åkermark.¹³ The initial step, cyclopropane ring opening of **1** with simultaneous cyclopropanone formation, is the same as previously suggested for the thermal decomposition of **1**.^{14,15} Addition of acetic and formic acid to the cyclopropane ring results in the formation of **3** and **7**, respectively.

Recent experiments¹⁶ have shown that, e.g. 2-acetoxy-2-(3-oxobutyl)-1,3-cyclohexanedione does not undergo internal return even at elevated temperatures which gives evidence against the mechanism outlined in Fig. 1.

TLC examination revealed the presence of a second compound. The NMR spectrum of the crude reaction product (CDCl_3 ; 60 MHz) when compared with that of pure **5** indicated the presence of compound **7**, a lower homologue of **3**. From the integral of the spectrum of the crude mixture, the yields of **5** and **7** were calculated to be about 85 % and 15 %, respectively.

3,4,5,6-Tetrahydro-3,3,6,6-tetramethyl-1,8(2H,7H)xanthenedione (4). Methylene-bis-dimedone (1.02 g) was stirred with polyphosphoric acid (29 g) at 150°C for 1 h. After cooling, ice water was added and the mixture was worked up as usual. The product was crystallised from ethanol:water (4:1) to yield **4** (77 %), m.p. 172–173°C (lit.¹³ m.p. 171°C). ν_{max} (CHCl_3) 2955, 1685(s), 1657(s), 1625, 1378(s), 1188, 1162(s), 1134(s) cm^{-1} . NMR: (CDCl_3) δ 1.12 (s, 12H), δ 2.30 (s, 4H), δ 2.38 (t, 4H, $J=1.6$ cps), δ 2.89 (quintet, 2H, $J=1.6$ cps).

Acknowledgements. The authors thank Dr. C. A. Wachtmeister for his interest and Dr. K.-I. Dahlqvist, Lunds Tekniska Högskola, for recording the 100 MHz spectrum. This work has been supported by *Statens Naturvetenskapliga Forskningsråd*. Thanks are due to Dr. T. A. Spencer for samples of 2-acetoxy-2-alkyl-1,3-cyclohexanedione derivatives.

REFERENCES

1. Mattsson, O. H. *Kemisk Tidskrift* **81** (1969) 38. Presented at Svenska Organikerdagarna in Uppsala, June 1969.
2. Mattsson, O. H. and Wachtmeister, C. A. *Acta Chem. Scand.* **22** (1968) 79.
3. Mattsson, O. H., Sundström, G. and Wachtmeister, C. A. *Acta Chem. Scand.* **24** (1970) 2219.
4. Mattsson, O. H. and Sundström, G. *Acta Chem. Scand.* **24** (1970) 1454.
5. Inhoffen, H. H., Logemann, W., Holweg, W. and Serini, A. *Ber.* **71** (1938) 1024.
6. Sellarby, L. and Wickberg, B. *Acta Chem. Scand.* **12** (1958) 624.
7. Mattsson, O. H. and Sundström, G. *Acta Chem. Scand.* **24** (1970) 2267.
8. Eistert, B., Elias, H., Kosch, E. and Wollheim, R. *Chem. Ber.* **92** (1959) 130.
9. Goering, H. L. and Silversmith, E. F. *J. Am. Chem. Soc.* **77** (1955) 1129.
10. Goering, H. L., Nevitt, T. D. and Silversmith, E. F. *J. Am. Chem. Soc.* **77** (1955) 5026.
11. Goering, H. L. and Silversmith, E. F. *J. Am. Chem. Soc.* **77** (1955) 6249.
12. Vorländer, D. *Z. anal. Chem.* **77** (1929) 241.
13. Åkermark, B. *Personal communication*.
14. Mattsson, O. H. *Dissertation, University of Stockholm, Stockholm* 1970, p. 9.
15. Spencer, T. A., Hall, A. L. and Fordham von Reyn, C. *J. Org. Chem.* **33** (1968) 3369.
16. Mattsson, O. H. *Unpublished results*.

Received May 5, 1970.