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Formation of 1,1-Bis(2,6-dioxo-4,4-dimethylcyclohexyl)-2-propanone from 1,3-Dichloroacetone and its Oxidative Cyclisation with Iron(III) Hexacyanoferrate(III)

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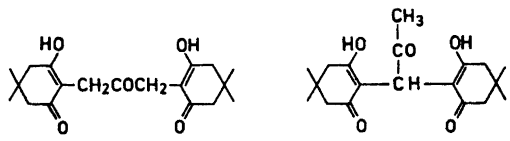
1,3-Dichloroacetone and the potassium salt of dimedone react under solvolytic conditions to form the dimedone derivative of pyruvaldehyde (*2*). The mechanism of the reaction is discussed. On treatment with iron(III) hexacyanoferrate(III) *2* undergoes intramolecular oxidative coupling with the formation of a spiro dihydrofuran (*7*) and a dispiro cyclopropane derivative (*9*).

In connection with studies on oxidative cyclisation reactions of suitable 1,3-cyclohexanedione derivatives with iron(III) hexacyanoferrate(III) [1-3] attempts were made to prepare the symmetrical *C*-alkylation product (*1*) from 1,3-dichloroacetone and two moles of dimedone (potassium salt). The reaction proceeded smoothly in aqueous methanol solution. The main product which crystallised from the reaction mixture had ultraviolet and infrared spectra and an elemental analysis in accordance with the desired compound. Its NMR and mass [4] spectra, however, could only be reconciled with the isomeric dimedone derivative of pyruvaldehyde [5] (*2*). The NMR spectrum



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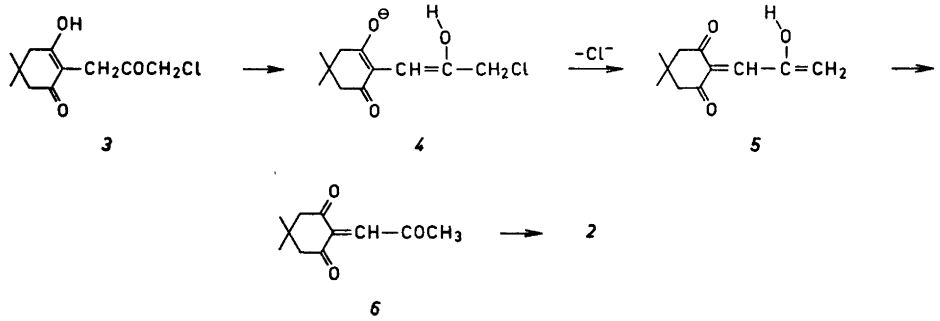
gives signals due to the dimedone methyl (δ 1.13, 12 H, s) and methylene protons (δ 2.38, 8 H, s), respectively. A three-proton signal (δ 2.12, s) is ascribed to an acetyl methyl group. Finally the signal at δ 4.63 (1 H, s) is interpreted as due to the proton on the bridge carbon atom of *2*. The mass spectrum shows fragments typical for dimedone derivatives of aldehydes,[4,6] *e.g.*, *m/e* 140 and *m/e* 194 and in addition intense peaks at *m/e* 43 (CH_3CO^+) and *m/e* 291 (M − 43).

The structure *2* of the reaction product was definitely confirmed by comparison with an authentic sample.[5]

The formation of *2* from 1,3-dichloroacetone involves an unusual type of rearrangement. Analogous rearrangement reactions have been reported, *e.g.* under solvolytic conditions in acetic acid with 1-chloro-3-(2′-methoxyphenoxy-)2-propanone [7] and 1-chloro-3-phenylthio-2-propanone.[8,9] Recently, similarly rearranged products were reported from reactions of 1,3-dichloroacetone with certain phenols in acetone in the presence of potassium carbonate and potassium iodide.[10] The reactions were interpreted in terms of an allylic type rearrangement involving participation of the lone electron pairs of oxygen and sulphur atoms, respectively.

In the present case the ionised enol form *4* of a primary reaction product *3* could undergo a concerted elimination of chloride ion with formation of an intermediate *5*, rapidly rearranged to *6*. A subsequent Michael addition of a dimedone anion would furnish *2*.

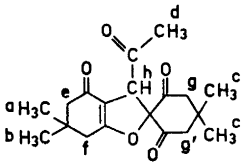


On treatment of compound *2* with an aqueous methanol solution containing equimolar amounts of iron(III) chloride and potassium hexacyanoferrate(III), it underwent intramolecular carbon-oxygen and carbon-carbon coupling by analogy with 2,2′-methylene-bis-1,3-cyclohexanedione.[1,2] Three compounds were isolated from the reaction mixture. The main component *7* (41 %) gave spectra closely similar to those of the spiro dihydrofuran derivative *8* described earlier.[1,2] In the NMR spectrum of *7* (Table 1), the presence of an acetyl group is revealed by a three-proton signal at δ 2.23. An AB-pattern with absorption positions for protons A and B at δ 2.49 and δ 3.11, respectively, ($J_{AB} = 14$ cps) is ascribed to a methylene group of the 1,3-cyclohexanedione part of the molecule. As is evident from an inspection of the Dreiding

Table 1. Proton chemical shifts of *7*.

Proton	Number of H	δ ppm	Coupling
a(b)	3	0.93	s
c	6	1.14	s
b(a)	3	1.20	s
d	3	2.23	s
e	2	2.28	s
f	2	2.59	doublet, $J=1.5$ cps
g	2	2.72	s
g′	1(A)	2.49	AB-spectrum $J_{AB}=14$ cps
g′	(1B)	3.11	AB-spectrum $J_{AB}=14$ cps
h	1	4.25	triplet, $J=1.5$ cps

model, one methylene group will contain non-equivalent protons due to the proximity of the exocyclic carbonyl group.



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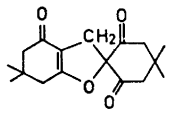

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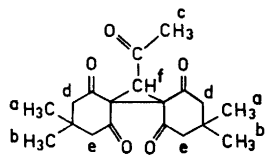

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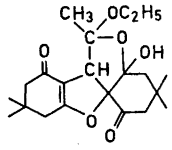
A second isomeric compound (23 %) gave ultraviolet, infrared, and NMR spectra in accordance with a dispiro cyclopropane structure *9*. The infrared spectrum, *inter alia*, showed a sharp band at 3082 cm^{-1} (KBr), assigned to the cyclopropane proton.[11,12] In the NMR spectrum (Table 2) a signal is

Table 2. Proton chemical shifts of *9*.

Proton	Number of H	δ ppm
a(b)	6	1.04
b(a)	6	1.12
c	3	1.70
d(e)	4	2.13
e(d)	4	2.40
f	1	4.19

observed at δ 4.19 (1 H, s), in reasonable agreement with chemical shifts reported for similarly substituted cyclopropane rings.[13] Further support for the proposed structures *7* and *9* is given by the fragmentation pattern of the two compounds on electron impact as discussed elsewhere.[4]

A third compound (13 %) crystallised from the ethanol mother liquors, obtained during the isolation of compound *9*. It had the composition $C_{21}H_{30}O_6$, corresponding to a hemiketal of *7* with ethanol and decomposed, at least under certain conditions, with the formation of *7*. It could, however, be sublimed unchanged in a high vacuum. A possible structure would be *10* but the detailed structure has not been further investigated.



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Experimental. The melting points were determined on a Kofler micro hot stage. The UV-spectra were determined with a Beckman DK 2 spectrophotometer, and the IR-spectra with a Perkin-Elmer 221 instrument. The NMR spectra were obtained on a Varian A-60 instrument using $CDCl_3$-solutions with tetramethylsilane as an internal standard.

1,1-Bis(2,6-dioxo-4,4-dimethylcyclohexyl)-2-propanone (2). Dimedone (14.0 g, 0.1 mole) and potassium hydroxide (5.6 g, 0.1 mole) were dissolved in a mixture of methanol (24 ml) and water (18 ml). The solution was rapidly added to 1,3-dichloro-2-propanone (6.4 g, 0.05 mole; m.p. 39–41°, Schuchardt) with stirring. After 1.5 h the crystalline reaction product was collected and washed with water (8.7 g; 52 %). It was crystallised from ethanol-water to give needles, (*2*), m.p. 161–163°, undepressed on admixture with an authentic sample,[5] m.p. 163–164°. (Found: C 68.0; H 7.68. $C_{19}H_{26}O_5$ (334.42) requires C 68.2; H 7.84).

UV-spectrum in acidified ethanol: λ_{max} 259 nm (ε=17 800); in alkaline ethanol, λ_{max} 284.5 nm (ε=31 300). IR-spectrum: ν_{max} (KBr) 3300–2500 (broad), 1712, 1600, 1575, 1387 cm^{-1}.

Intramolecular oxidative coupling of 2. To a solution of *2* (6.0 g, 18 mmol) in methanol (900 ml) and water (450 ml) was added with stirring a freshly made aqueous solution (450 ml) containing $FeCl_3$ (6.8 g, 54 mmol) and $K_3Fe(CN)_6$ (17.1 g, 54 mmol). Stirring was continued for 3 h after which the reaction mixture was extracted with ether (4 × 500 ml). The combined ether extracts were dried ($MgSO_4$), filtered and evaporated to dryness. The oily reaction product (4.4 g) was analysed by TLC on Silica gel HF_{254} using ethyl acetate-isopropyl ether (1:1) as solvent. It contained only traces of starting material. Two spots (R_F=0.4 due to compound *7* and R_F=0.5 probably due to the methyl hemiketal corresponding to *10*) were dark in UV-light and gave yellow colours on spraying with a solution of 2,4-dinitrophenyl hydrazine (0.25 M) in 85 % phosphoric acid-ethanol (3:2). A third spot, (R_F=0.6 due to *9*), visible on spraying with the carbonyl reagent, showed no absorption in UV-light.

Crystallisation of the crude reaction product from ethanol gave a fraction which on repeated crystallisation from isopropyl ether and from light petroleum (b.p. 80–110°) gave compound *7*, m.p. 146.5–147.5°. (Found: C 68.4; H 7.21; O 24.2. $C_{13}H_{24}O_5$ (332.40) requires C 68.7; H 7.28; O 24.1). UV-spectrum: λ_{max} (EtOH) 267 nm (ε=11 700). IR-spectrum: ν_{max} ($CHCl_3$): 2930, 2874, 1742, 1715, 1640, 1391 cm^{-1}.

Dispiro[5.0.5.1.]-13-acetyl-trideca-1,5,8,12-tetraone (*9*). The combined mother liquors from the isolation of *7* were evaporated to dryness *in vacuo*. Crystallisation from ethanol gave compound *9*, m.p. 137–139°. (Found: C 68.4; H 7.21; O 24.1. $C_{19}H_{24}O_5$ requires C 68.7; H 7.21; O 24.1.)

UV-spectrum: λ_{max} (EtOH) 213 nm (ε=35 700); 270 nm (ε=105). IR-spectrum: ν_{max} (KBr) 3082, 2965, 2878, 1720 cm^{-1}.

Hemiketal of 7. The ethanol mother liquors from the isolation of compound *9* on prolonged standing gave a third crystalline compound, *10* (hemiketal of *7*; structure

uncertain). Crystallisation from isopropyl ether gave *10* as needles, m.p. 155–156°. (Found: C 66.9; H 7.91; O 25.2. $C_{21}H_{30}O_6$ (378.47) requires C 66.6; H 7.99; O 25.4.)

UV-spectrum: λ_{max} (EtOH) 226 nm (ε=4270); 265 nm (ε=12 000). IR-spectrum: ν_{max} (KBr) 3380 (broad), 1725, 1640, 1620 cm^{-1}. NMR-spectrum: δ 0.92 (3 H, s), 1.15 (6 H, s), 1.18 (3 H, s), 1.22 (3 H, tr, J=7), 2.20 (2 H, s), 2.26 (2 H, s), 2.35–3.15 (7 H, m), 3.71 (2 H, quart., J=7) and 4.23 ppm (1 H, tr, J=1.5).

On heating for a short time to 160° at 15 mm Hg, compound *10* decomposed with loss of weight corresponding to one mole of ethanol. The main reaction product was identified as *7* by comparison with an authentic sample (m.p., NMR).

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