214. Propellanes

Part LXXXII[1])

Preparation and Labelling of [20.3.3]Propellane-24,27-dione

by **Pnina Ashkenazi, Jürgen Kettenring, Shmuel Migdal, Arie L. Gutman,** and **David Ginsburg***

Department of Chemistry, Israel Institute of Technology, Haifa, Israel

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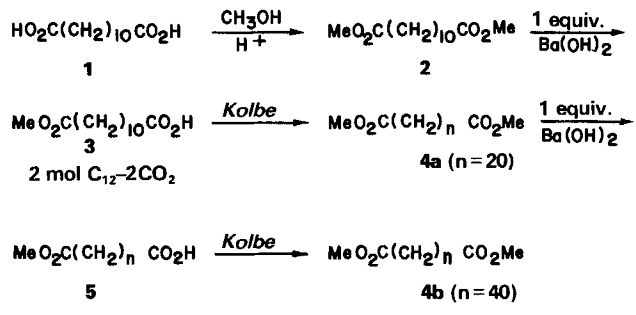
The title diketone has been prepared by a synthetic sequence beginning with decane-1,10-dicarboxylic acid.

Introduction. – We wanted to obtain the diketone **8a** mentioned in the title in order to attempt the threading of the 22-membered ring in a derivative thereof with an aliphatic chain [2]. The size of the large ring was dictated by the price of the starting material, decane-1,10-dicarboxylic acid **1** [3]. We believed that the ring size sufficed for our purpose since its CPK model could be assembled.

Synthesis. – The starting material **1** was esterified by the classic *Fischer* method to afford the corresponding dimethyl ester **2** *(Scheme 1)*. Another old method [4a] was used to convert this into the half-ester **3**. *Kolbe* condensation using the standard method [5] gave the C_{22} dimethyl ester **4a**, whose corresponding half-ester **5** was also submitted to the *Kolbe* reaction to afford the C_{42} dimethyl ester **4b**. (The latter, when converted into a [40.3.3]propellane would certainly have a large ring capable of being threaded should this not succeed in the [20.3.3]propellane derivative.)

Acyloin condensation of **4a** in the presence of Me_3SiCl afforded the cyclic C_{22} acyloin **6a** [6] *(Scheme 2)*. Its oxidation [7] gave the corresponding C_{22} diketone **7a**. When the

Scheme 1



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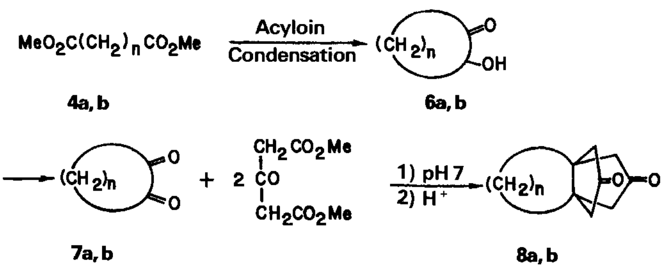
[1]) Part LXXXI [1].

Scheme 2



latter was submitted to the slightly modified conditions of the *Weiss* reaction [8], a high yield of [20.3.3]propellane-24,27-dione (**8a**) was obtained along with some easily separable dimethyl 3-oxoglutarate used in the *Weiss* reaction, which decomposes into acetone during workup.

For further work in connection with attempted threading of the *syn,syn*-diol reduction product of the title deketone, we wished to do a double labelling experiment involving both ^{3}H and ^{14}C. We report here deuteration of the diketone as a model reaction and its tritiation. We shall report in another connection the deuteration of [4.3.3]propellane-8,11-dione.

We have also prepared the C_{42} diester **4b** by using the half-ester **5** in a *Kolbe* reaction. Its acyloin condensation afforded **6b**, whose oxidation gave the cyclic C_{42} diketone, **7b**. At this point, we were given a gift of the lower homolog, the C_{40} diester, *i.e.* **4**, with n = 38[2]). We, therefore, did not continue with the preparation of [40.3.3]propellane-42,45-dione (**8b**). We are interested not in a specific compound but in a property, a large hole within a large ring. We shall, therefore, turn to the preparation of [38.3.3]propellane-40,43-dione in order to conduct threading experiments of chains through the large ring.

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Experimental Part

General. M.p. are uncorrected. IR spectra were recorded on a *Perkin-Elmer 237* spectrometer, ^{1}H-NMR spectra on a *Varian T-60* spectrometer and mass spectra on a *Varian MAT-711 spectrometer.*

Kolbe Reaction. a) Dimethyl 1,12-dodecanedicarboxylate was prepared and saponified to the half-ester **3** according to the procedure of *Signer* and *Sprecher* [4a], yield 80%, m.p. 52°. [4a]: yield 85%, m.p. 52°. IR (KBr): 3150, 2920, 2850, 1740, 1705. ^{1}H-NMR ($CDCl_3$): 11.50 (br. *s*, 1 CO_2H); 3.70 (*s*, 3 CH_3); 2.64–2.24 (*m*, 4 CH_2CO); 1.90–1.20 (*m*, 32 CH_2).

The *Kolbe* reaction was then carried out according to *Swann* and *Garrison* [5] on the C_{12} half-ester **3** (80 g) using KOH (5 g) and dry MeOH (700–800 ml) during 5 days (2 amp). After the usual workup, the waxy C_{22} diester **4a** (57–64% yield) was recrystallized from hexane, m.p. 68–70°.

b) The corresponding homolog **4b** was prepared by a *Kolbe* reaction of **5** [5] as above. The crude diester, **4b** (7 g) was stirred with hexane (100 ml) and the undissolved solid (6 g) was dissolved in benzene (200 ml) and carefully washed (avoid heavy shaking to prevent emulsion formation) with aq. $NaHCO_3$ (5%; 150 ml) and with H_2O (100 ml). Drying of the benzene layer ($CaCl_2$) and removal of solvent at the water pump gave an oil. Adding

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[2]) Through the kindness of Dr. *R. Rienäcker, Max-Planck*-Institut für Kohlenforschung, Mülheim/Ruhr. To be published.

hexane afforded **4b** as a colorless waxy solid (4 g), m.p. 60–65°. IR (KBr): 2940, 2870, 1705. ^{1}H-NMR (C_6D_6): 3.52 (*s*, 6 CH_3); 2.40 (*m*, 4 CH_2CO); 1.98–1.84 (*m*, 76 CH_2).

Acyloin Condensation. – 'Method A' was used [6], employing a *Hershberg* stirrer and an Ar atmosphere.

a) C_{22} *Acyloin* **6a**. The crude bis(trimethylsilyl)product (25 g; 90%) was obtained from the C_{22} dimethyl ester **4a** (17 g). Hydrolysis in THF (150 ml) of this product (18.3 g) with aq. HCl (1N; 30 ml) was effected by heating under reflux for 3 h under N_2. After cooling the soln. was treated with $CaCO_3$ (20 g), the solid removed by filtration, and the solvent was evaporated from the mother liquor. The residue was taken up in $CHCl_3$, dried ($MgSO_4$) and the solvent was removed, to afford the waxy crude acyloin **6a** (11.4 g; 89%). IR($CHCl_3$): 3500, 2930, 2860, 1708. ^{1}H-NMR ($CDCl_3$): 2.2 (*m*, 3 COCH); 1.2 (br. *s*, 36 CH_2); OH unobserved. M.W.: calc. 338.3184, found 338.3168.

b) C_{42} *Acyloin* **6b**. Acyloin condensation of the C_{42} dimethyl ester **4b** (5 g) was conducted as above by adding it in dry toluene (200 ml) with Me_3SiCl (50 ml), to Na (2 g) in dry toluene (400 ml). The crude acyloin **6b** (4 g; 88%) was a waxy solid. IR ($CHCl_3$): 3700, 3610, 2930, 2860, 1710. ^{1}H-NMR($CDCl_3$): 1.23 (br. *s*). It was used to prepare **7b** without further purification.

Oxidation of the Acyloins. a) To the crude acyloin **6a** (3.89 g) in AcOH (100 ml) was added Bi_2O_3 (6.43 g). The whole was stirred at 100–110° for 45 min. Precipitation of Bi begins after 5 min. The hot soln. was filtered without vacuum through paper and the precipitate was washed with benzene (100 ml). H_2O was added to the filtrate and the org. phase was washed with H_2O (3 × 20 ml), dried ($MgSO_4$) and evaporated to one quarter of its volume. (If an emulsion develops it is broken by filtration at the water pump.) The bright yellow soln. was filtered through alumina (5 g, basic II). Removal of solvent gave a crude residue (2.98 g; 77%) of the yellow oily diketone **7a**. Purification (overall yield 51%) could be effected on a silica column using hexane/benzene 4:1 as eluent. IR ($CHCl_3$): 1775, 1465. ^{1}H-NMR ($CDCl_3$): 2.5–2.1 (*m*, 4 CH_2CO); 1.7–1.25 (*s*, *m*, 36 H_2). MS: 336 (100, M^+), 320(23), 304(32). M.W.: calc. 336.3028, found 336.3046.

b) Oxidation of **6a** with cupric acetate gave the crude diketone **7a** in 51% yield.

c) The acyloin **6b** (0.7 g), Bi_2O_3 (0.6 g) in AcOH were heated to 150° for 2.5 h. Bi begins to precipitate after 1 h. After filtration as above, the precipitate was washed with $CHCl_3$ (150 ml). H_2O was added to the filtrate and the org. phase washed with H_2O (3 × 80 ml). It was dried ($MgSO_4$), evaporated to one-third of the original volume and filtered through alumina (1 g, basic, grade II). Evaporation gave **7b** (0.44 g; 63%) as a yellow wax. IR ($CHCl_3$): 2940, 2870, 1715. ^{1}H-NMR ($CDCl_3$): 1.25 (br. *s*). MS: 588 (32, M^+), 575 (13), 574 (32), 560 (25). M.W.: calc. 588.5844, found 588.5826.

[20.3.3]Propellane-24,27-dione (**8a**). To a soln. of the C_{22} diketone **7a** (1.79 g) in dry benzene (10 ml) was added under N_2 dimethyl β-oxoglutarate (1.85 g; 2 equiv.) and a soln. of KOH (0.6 g; 2 equiv.) in dry MeOH (18 ml). The whole was stirred for 10 days at r.t. Removal of solvent followed by extraction with hexane (100 ml) and removal of solvent gave a residue (0.6 g) containing a mixture (NMR) of the dione/glutarate 2:1. To the hexane-insoluble residue (the tetraester diketone), HCl (6N; 12 ml) was added and the whole was heated at a bath temp. of 100° for 24 h. After cooling, addition of $NaHCO_3$ to neutral pH and extraction with AcOEt the crude propellanedione **8a** (1.65 g) was obtained. Purification on a silica column using benzene/$CHCl_3$ 85:15, afforded the pure product (1.43 g; 83.3%). IR ($CHCl_3$): 1740, 1460, 1410. ^{1}H-NMR ($CDCl_3$): 2.35 (*s*, 8 CH_2CO); 1.35 (*s*, 40 CH_2). MS: 416 (95, M^+), 375(36), 373(94), 358(100).

The tetramethylester reaction intermediate en route to the diketone had m.p. 125–127° (see above). IR ($CHCl_3$): 3620, 1745, 1680, 1450. ^{1}H-NMR ($CDCl_3$): 5.9–5.5 (*m*, 12 CO_2Me, 4 CHCO); 1.2 (*s*, 40 CH_2).

Labelling of **8a**. *a*) *Deuteration.* The diketone **8a** (30 mg) was dissolved in dry THF (1 ml; distilled from K) and placed in a 10-ml ampoule. D_2O (0.2 ml) and conc. HCl (0.02 ml) were added. After evacuations of air (0.1 mm Hg), the ampoule was sealed and heated in an autoclave for 1 h at 120°. After cooling the soln. was washed out with benzene (10 ml), dried (Na_2SO_4) and evaporated to dryness. TLC showed identity of the colorless oily residue (30 mg) with the starting material. The ^{1}H-NMR spectrum indicated that > 90% of the CH_2CO atoms were replaced by D. The MS indicated the presence of a mixture containing D_4, D_5, D_6, D_7, and D_8 molecules.

b) *Tritiation.* To the diketon **8a** (110 mg) in THF (1 ml) as above was added tritiated H_2O (0.2 ml; 120 mCi, *Amersham*) and conc. HCl (0.02 ml). After treatment as above and opening of the ampoule, its contents were transferred to a round-bottom flask (25 ml) and the solvent (containing most of the unreacted HTO) was vacuum-transferred to another ampoule. The residue was dissolved in benzene (20 ml), and dried (Na_2SO_4) to remove any remaining HTO by evaporation of solvent. The second benzene distillate contained virtually no radioactivity. The residue (105 mg) contained > 7 mCi (6% ^{3}H-incorporation based upon the activity of the tritiated water).

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