70. Propellanes

Part LXXX

Baeyer-Villiger Oxidation of [4.3.3]Propellane-8,11-dione[1])

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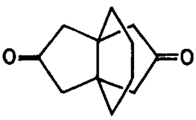
Oxidation of the title compound with *m*-chloroperbenzoic acid affords a keto-lactone, two bis-lactones and a bis-spirolactone, in varying amounts depending upon the reaction conditions. The structures were established by means of X-ray diffraction, ^{1}H- and ^{13}C-NMR spectroscopy.

Various propellanes ([6.3.2], [5.3.2], [4.3.2], [3.3.2]), all of which contain a cyclopentanone ring, have been subjected to *Baeyer-Villiger* oxidation. This ring is enlarged to a δ-lactone ring [2]. Since we have large quantities of [4.3.3]propellane-8,11-dione (**1**), we studied its behavior under similar reaction conditions. In principle one may expect, for reasons of symmetry, one monolactone **2** and two isomeric bis-lactones, the head-to-tail isomer **3** and the head-to-head isomer **4**.



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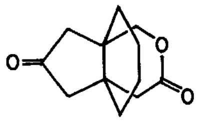

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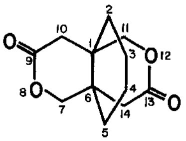

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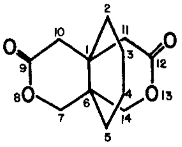

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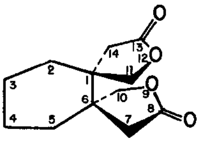

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We have indeed obtained these three products but although these were obtained in different amounts depending upon the reaction conditions, a third bis-isomer was always present in the reaction mixture. This exhibited absorption in the IR spectrum at 1779 cm^{-1} and turned out to be the dispiro-isomer **5** containing γ- rather than δ-lactone functions.

In a separate experiment it was shown that **3** under acidic conditions is converted by ring-opening and recyclization into **5** which is evidently thermodynamically more stable.

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Treatment of **1** with *m*-chloroperbenzoic acid (*m*-CPBA) in the presence of $NaHCO_3$ gave a mixture of the four products: **2** (12%), **3** (26%), **4** (20%), and **5** (11%). When TsOH was present with the *m*-CPBA, **4** and **5** were isolated in 35% and 46% yield, respectively.

It was possible to determine the X-ray structures of **4** and **5** which afforded crystals suitable for such analysis. Although symmetry therefore dictates by ironclad logic the structure of the isomer **3**, it is nevertheless fortunate that the corresponding structures may also be directly assigned from the ^{1}H- and ^{13}C-NMR spectra.

ORTEP representations of the structures **4** and **5** are shown in *Fig. 1* and *2*, respectively.

NMR Spectral Data. The structures of the lactones **3**–**5** are supported and confirmed by their ^{1}H- and ^{13}C-NMR spectra, measured in $CDCl_3$ solution at 400 and 100 MHz, respectively. The ^{1}H-NMR spectra exhibit typical resonance ranges for the CH_2O, $COCH_2$ and $C-CH_2$ groups and thus indicate the structural elements, whereas the ^{13}C-NMR spectra permit a clear differentiation between the dispiro-bis-δ-lactone **5** and the bis-δ-lactones **3** and **4**, as well as an assignment of the C_s (**4**) and C_2 (**3**) bis-δ-lactone structures.

The dispiro-lactone **5** gives two *AB* quartets and a rather narrow absorption at 1.6 ppm for the 8 CH_2 protons of the bridge. The high-frequency *AB* system ($\delta(A) = 4.190$, $\delta(B) = 4.129$ ppm; $J(AB) = 9.60$ Hz) must be assigned to the two homotopic CH_2O

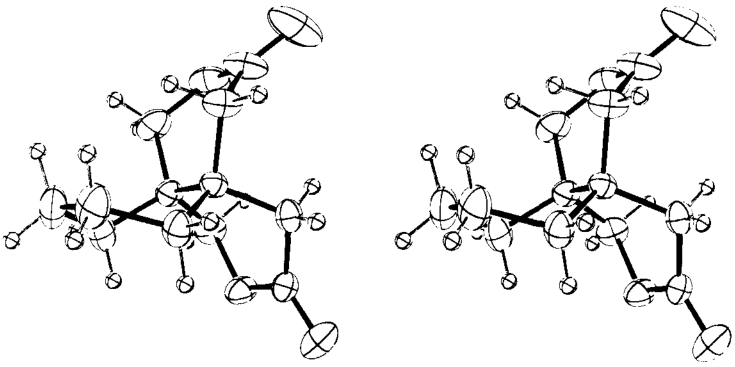

Fig. 1. *ORTEP representation of* **4**

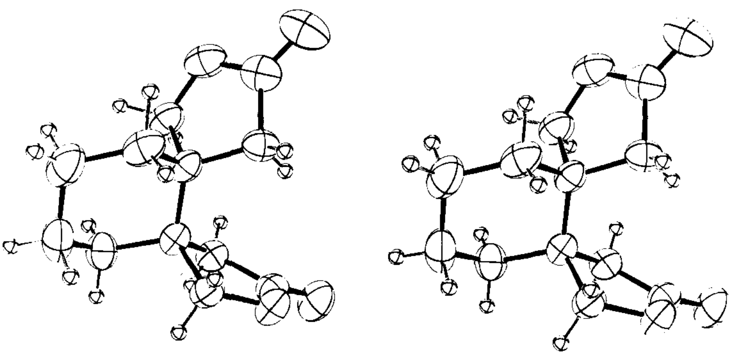

Fig. 2. *ORTEP representation of* **5**

groups, and the low-frequency *AB* system ($\delta(A) = 2.482$, $\delta(B) = 2.396$ ppm; $J(AB) = 17.8$ Hz) to the homotopic $COCH_2$ groups. The observed geminal H,H coupling constants are characteristic, the large value for the $COCH_2$ protons supporting the γ-lactone structure [4]. The two bis-δ-lactones exhibit the expected number of proton signals for C_2 and C_s structures, *i.e.* two *AB* systems each for the pairs of equivalent CH_2O and $COCH_2$ groups, respectively. The C_s structure **4** shows a high-frequency CH_2O *AB* system with $\delta(A) = 4.153$, $\delta(B) = 4.125$ ppm and $J(AB) = 12.3$ Hz, a low-frequency $COCH_2$ *AB* system with $\delta(A) = 2.573$, $\delta(B) = 2.372$ ppm and $J(AB) = 15.8$ Hz, and 3 multiplets for the bridging CH_2 protons centered at 1.7 ppm (4H), 1.6 ppm (2H) and 1.5 ppm (2H). The corresponding signals of the C_2 isomer **3** are found at 4.133 ppm ($\delta(A)$), 4.003 ppm ($\delta(B)$) with $J(AB) = 12.0$ Hz (CH_2O); 2.554 ppm ($\delta(A)$), 2.450 ppm ($\delta(B)$) with $J(AB) = 16.4$ Hz ($COCH_2$) together with multiplets at ~ 1.7 ppm (6H) and ~ 1.45 ppm (2H) for the bridging CH_2 groups.

The signal pattern of the 8 cyclohexane protons is clearly different in the spectra of the C_s and C_2 isomers, the larger chemical shift dispersion being observed in the C_s structure with 4 non-equivalent CH_2 groups, whereby the 4H of the central CH_2 groups form an apparent first-order quintet pattern at 1.68 ppm. Double irradiation at the frequency of this signal results in singlets for the 2 terminal CH_2 groups at 1.5 and 1.6 ppm. The unambiguous assignment of the two δ-lactone structures, however, is achieved on the basis of the ^{13}C-NMR spectra.

The ^{13}C-NMR spectra *(Table)* confirm the structures of the three lactones. First, the two δ-lactones **3** and **4** show very similar resonance positions for the carbonyl C-atoms, 170.48 and 170.51 ppm, respectively, whereas the corresponding signal of the γ-lactone **5** is shifted to higher frequency (174.89 ppm) [5]. Second, the C_s and C_2 structures can be differentiated by the number of ^{13}C resonances observed. The spectrum of **4** (C_s isomer) shows two signals at 35.29 and 36.15 ppm for the non-equivalent quaternary C-atoms and 4 signals for the CH_2 groups of the cyclohexane ring. In contrast, **3** (C_2 isomer) exhibits a single line for the quaternary C-atoms (35.70 ppm) and only 2 signals for the 4 cyclohexane CH_2 C-atoms. Since a complete assignment of all ^{13}C signals of **3** has been achieved *(Table)*, the C_2 structure of this isomer is clearly proven by the NMR data notwithstanding the unavailability of suitable crystals of **3** for an X-ray structure analysis. A comparison of the chemical shifts of certain C-atoms in the C_2 isomer **3** with the average chemical shifts of the corresponding pair of C-atoms in the C_s isomer **4** yields a

Table. *^{13}C Chemical Shifts of* **3**–**5** (Numbering of the atoms in the formulae **3**–**5** is arbitrary)

3		**4**		**5**	
δ [ppm]	C-atom	δ [ppm]	C-atom	δ [ppm]	C-atom
35.70	C(1)	35.29[a]	C(1)	44.27	C(1)
28.71	C(2)	25.55[c]	C(2)	33.70	C(2)
16.98	C(3)	16.51[b]	C(3)	21.29	C(3)
16.98	C(4)	16.85[b]	C(4)	21.29	C(4)
28.71	C(5)	31.93[c]	C(5)	33.70	C(5)
35.70	C(6)	36.15[a]	C(6)	44.27	C(6)
73.62	C(7), C(11)	71.23	C(7), C(14)	73.89	C(10), C(11)
170.48	C(9), C(13)	170.51	C(9), C(12)	174.89	C(8), C(13)
36.13	C(10), C(14)	39.60	C(10), C(11)	36.27	C(7), C(14)

[a] [b] [c] The assignments of the respective data pairs may be reversed.

further confirmation for the symmetry of the two isomers. Thus, the resonance position of the quaternary C-atoms in **3** (35.70 ppm) agrees with the average chemical shift (35.72 ppm) of the non-equivalent quaternary C-atoms in **4** and similarly, the chemical shift of the CH_2 group of the cyclohexane ring (28.71 ppm) corresponds to the average of the values of the 2 non-equivalent CH_2 groups in **4** (28.74 ppm), as expected for additivity of the shielding effects.

Experimental Part

IR spectra were measured using a *Perkin-Elmer 257* or *237* spectrometer, NMR spectra in the experimental section on a *Varian T-60* instrument and MS on a *MAT-711* (100 eV) instrument. M.p.'s are uncorrected. The more informative ^{1}H-NMR spectra were measured at 400.13 MHz and 23° in $CDCl_3$ soln. (0.07M, 5 mm sample diameter) on a *Bruker AM-400-w.b.* spectrometer, chemical shifts referred to TMS as internal standard. The ^{13}C-NMR spectra were obtained in the same solvent and in similar concentration with 10 mm sample tubes at 100.61 MHz and 30° under proton-noise-decoupling conditions. Assignments of ^{13}C resonances were supported, when necessary, by selective ^{13}C-{^{1}H}-decoupling experiments.

Oxidations of [4.3.3]Propellane-8,11-dione (**1**). *a*) A mixture of **1** (1.94 g), TsOH (1.9 g), *m*-CPBA (10 g) in CH_2Cl_2 (500 ml) was stirred at r.t. for 7 days, *m*-CPBA (5 g) was added and stirred at r.t. for 7 days followed by a repetition (65 g) for another 11 days at r.t. (25 days total time). After washing with aq. $NaHCO_3$ and H_2O, and evaporation of solvent the residual solid (2.36 g) was purified by flash chromatography using AcOEt/hexane 6:1: *3,9-dioxa[4.4.4]propellane-4,8-dione* (**4**; 710 mg; 35%), had m.p. 270–272° (benzene/hexane). IR ($CHCl_3$): 1755. ^{1}H-NMR ($CDCl_3$): 4.15 (*s*, 2 CH_2O); 2.47 (*AB*, 2 CH_2O); 1.8–1.5 (*m*, 4 CH_2). MS: 224 (12, M^+), 194 (11), 182 (47), 166 (7), 153 (11), 152 (100), 136 (13), 124 (34), 123 (7), 108 (82). M.W.: calc. 224.1048, found 224.1057.

Dispiro[tetrahydrofuran-3,1'-cyclohexane-2',3''-tetrahydrofuran]-5,5''-dione (**5**; 960 mg; 46.4%), had m.p. 252–254° (benzene/hexane). IR ($CHCl_3$): 1779. ^{1}H-NMR ($CDCl_3$): 4.2 (*s*, 2 CH_2O); 2.5 (*s*, 2 CH_2O); 1.65 (*s*, 4 CH_2). MS: 224 (4, M^+); 194 (14); 182 (29); 166 (10); 153 (6); 152 (11); 136 (19); 124 (8); 123 (18); 108 (100). M.W.: found 224.1065.

b) A mixture of **1** (1.94 g), $NaHCO_3$ (16.8 g), *m*-CPBA (10 g) in CH_2Cl_2 (500 ml) was stirred at r.t. for 7 days. *m*-CPBA (5 g) was added twice as described in *a*. After 25 days and workup as in *a* a precipitate (2.1 g) was obtained in benzene/hexane. Flash chromatography as in *a* carried out 8 consecutive times afforded **2** (260 mg; 11.6%), **5** (250 mg; 11.4%); 4 (447 mg; 19.9%), and **3** (539 mg; 25.7%).

3-Oxa[4.4.3]propellane-4,12-dione (**2**). M.p. 212–214° (CH_2Cl_2/hexane). IR ($CHCl_3$): 1775, 1745. ^{1}H-NMR (60 MHz; $CDCl_3$): 4.2 (*AB*, CH_2O); 2.7–2.15 (*m*, 3 CH_2O); 1.6 (*m*, 4 CH_2). ^{1}H-NMR (400 MHz, $CDCl_3$): 4.21, 4.19 (*AB*, J_{AB} = 12.2, CH_2O); 2.67, 2.52 (*AB*, J_{AB} = 18.6, $COCH_2$); 2.41, 2.36 (*AB*, J_{AB} = 18.7, $COCH_2$); 2.48, 2.14 (*AB*, J_{AB} = 19, $COCH_2$); 1.4, 1.8 (*m*, 4 CH_2). MS: 208 (33, M^+), 166 (41), 152 (3), 136 (38), 124 (4), 123 (3), 108 (100). M.W.: calc. 208.1099, found 208.1094.

3,8-Dioxa[4.4.4]propellane-4,9-dione (**3**). M.p. 272–274° (benzene/hexane). IR ($CHCl_3$): 1755. ^{1}H-NMR ($CDCl_3$): 4.0 (*AB*, 2 CH_2O); 2.5 (*s*, 2 CH_2O); 1.6 (*m*, 4 CH_2). MS: 224 (20, M^+), 194 (35), 182 (10), 166 (13), 153 (11), 152 (100), 136 (9), 124 (2), 123 (8), 108 (44). M.W.: found 224.1036.

Conversion of **3** *into* **5**. A mixture of **3** (24 mg), TsOH (24 mg) in benzene (10 ml) was stirred for 7 days at r.t. After workup as in *a* the product was shown by TLC, IR, and NMR to be **5**. When **4** was treated exactly in the same way it was recovered unchanged.

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