271. Propellanes

Part LXIX

Preparation of Lactones from the Three Isomeric [4.3.3]Propellane-8,11-diols[1])

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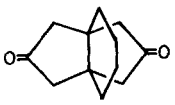
Summary

Each of the three isomeric[4.3.3]propellane-8,11-diols was lactonized by using 1,ω-diacids of different chain lengths. The minimal chain length required to bridge the *syn-syn* diol is $-CO(CH_2)_{11}CO-$.

[4.3.3]Propellane-8,11-dione (**1**) is readily prepared in a one-pot reaction from cyclohexane-1,2-dione and dimethyl 3-ketoglutarate [2]. We reduced **1** with $LiAlH_4$ and obtained a mixture of the three diols **2, 3, 4** whose formation is dictated by the C_{2v}-symmetry of the diketone. The cyclohexane ring in these propellanes is used as the frame of reference; **2, 3** and **4** are formed in a ratio of 1 : 2.5 : 2. While this work was done *Askani et al.* described $LiAlH_4$-reduction of **1**, in which **2, 3**, and **4** were obtained in a ratio of 1 : 2.3 : 1.8 [3]. $NaBH_4$-reduction of **1** gave **2, 3**, and **4** in a ratio of 1.8 : 1.6 : 1. Thus, employing either of these reducing agents the relative yields may be varied as desired.



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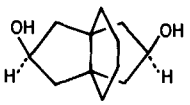

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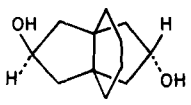
(*syn-syn*)



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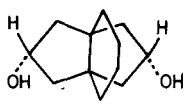
(*syn-anti*)

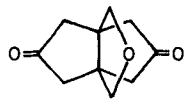


4
(*anti-anti*)

We wanted to treat diols with 1,ω-diacids under conditions leading to lactonization ($TsOH/C_6H_6$) and to determine the minimal chain length required to bridge both hydroxy groups. Reduction of **5** also affords three diols, the ratio of the products *syn-syn* : *syn-anti* : *anti-anti* being 5 : 9 : 1 (unpublished work in this laboratory). In that case the *anti-anti* product afforded a cyclic carbonate **6**. A single C-atom sufficed to bridge two *anti*-hydroxy groups in such a propellane [4].

[1]) Part LXVIII: [1].

In the present case, however, the *anti-anti*-diol **4** did not give the corresponding cyclic carbonate. Since we had no particular motive for forcing the issue we were satisfied with obtaining dilactones of type **7** in which $n = 0 - 9$.



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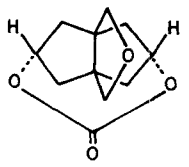

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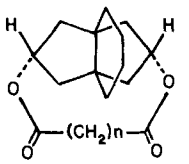

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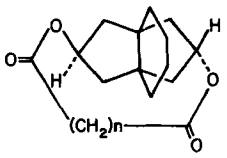
Using **3** we found that the *syn*- and *anti*-hydroxy groups may be bridged by chains in which $n \geqq 9$, leading to products of type **8**. It is obvious from models that a larger chain than that resulting from the C_{11}-diacid ($n = 9$) would be required to bridge the *syn-syn* hydroxy groups in **2**. Indeed the shortest bridge in this case could be obtained from the C_{13}-diacid, leading to a product of type **9**.



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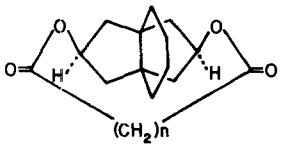

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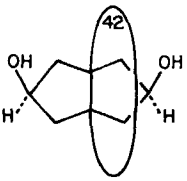
The motivation for conducting this work is not merely the preparation of propellane diols and lactones therefrom. Having used the [4.3.3]propellane skeleton as a model system we can now turn to the preparation of an [n. 3.3]propellanedione in which n is large. *Wasserman* has shown that a 1,34-diester could give not only an acyloin but that the ring thus formed could be penetrated to some extent by as yet uncyclized aliphatic diester. When the latter was then cyclized a catenane resulted [5]. We are hoping to prepare [40.3.3]propellane-44,47-dione and to reduce it to the three [40.3.3]diols analogous to **2, 3,** and **4** and to treat the *syn-syn*-diol analogue **10** with a chain too short to bridge the two hydroxy groups to form a compound of type **9**. In this *syn-syn*-diol we want to learn whether we may be able to 'thread' the large ring with just one C-chain to afford **11**.



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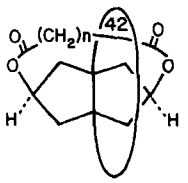

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In principle this has a better chance of success than the preparation of *Wasserman*'s catenane. If we succeed we shall also use compounds having the skeletal structure of **10** as solid anchors (they ought to be solid owing to their symmetry and high molecular weight)

for the formation of catenanes. If a 1,34-diester can give a catenane then [40.3.3]propellane (no oxygen) ought to be penetrated by long-chain ω-diesters and afford catenanes in an acyloin condensation. We shall report on this prospect in due course.

We thank the *Lady Davis Fellowship Trust* for a postdoctoral fellowship to *S.B.*

Experimental. – *General.* M.p. are uncorrected. IR spectra (cm^{-1}) were measured on a *Perkin-Elmer 237* spectrometer. ^{1}H-NMR, spectra were measured on a *T-60* or a *Bruker WP-60* instrument and high-resolution and routine mass spectra on a *Varian MAT-711* spectrometer.

Reduction of [4.3.3]propellane-8,11-dione (**1**). *a)* To a solution of the diketone **1** (1 g) in dry MeOH (100 ml) was added portionwise with stirring under N_2 $NaBH_4$ (1.05 g) during 40 min. The whole was then stirred magnetically for 48 h. After the usual workup the residue was extracted with CH_2Cl_2 (3 × 25 ml). Drying (Na_2SO_4) and removal of solvent gave the diol mixture (0.9 g). It was crystallized from Et_2O (0.87 g; 84%).

b) To $LiAlH_4$ (1.2 g) in dry Et_2O (100 ml) under N_2 was added dropwise during 30 min a solution of **1** (2.3 g) in dry Et_2O (50 ml). After heating under reflux for 2 h and usual workup with dilute (5%) H_2SO_4 the diol mixture was obtained (1.9 g; 82%). This reduction has already been reported [3].

The diols were separated on basic alumina (grade II), the *syn-syn-* and *syn-anti*-diols being eluted using $CHCl_3$, followed by the *anti-anti*-isomer (MeOH/$CHCl_3$, 1:19), in the ratio of 33:29:18 for *a* and 15:37:30 for *b* (isolated yields).

syn-syn-*Diol.* M.p. 164° (Et_2O) ([3]: 163–164°). IR ($CHCl_3$): 3800, 3700–3400. ^{1}H-NMR ($CDCl_3$): 4.5–4.2 (br. *m*, 2CHOH); 1.9–1.6 (*m*, 8CH_2CHOH); 1.6–1.5 (*m*, 8CH_2).

syn-anti-*Diol.* M.p. 140° (Et_2O) ([3]: 137–139°). IR ($CHCl_3$): 3600, 3500–3200. ^{1}H-NMR ($CDCl_3$): 4.5–4.1 (br. *m*, 2CHOH); 2.0–1.5 (*m*, 8CH_2CHOH); 1.5–1.4 (*m*, 8CH_2).

anti-anti-*Diol.* M.p. 122–123° (Et_2O) ([3]: 120–122°). IR ($CHCl_3$): 3595, 3500–3200. ^{1}H-NMR ($CDCl_3$): 4.5–4.2 (br. *m*, 2CHOH); 2.2–1.8 (*m*, 8CH_2CHOH); 1.3 (*s*, 8CH_2).

General Procedure for Preparation of Dilactones. A mixture of the diol (1 equiv.), the diacid (0.98 equiv.), and TsOH (0.25 equiv.) was heated under reflux in dry benzene (20 ml) using an azeotropic separator for 24 h (*anti-anti*) or 48 h (other isomers). The mixture was cooled, the solvent was removed and the residue was basified with aq. $NaHCO_3$ (10%) and extracted with $CHCl_3$ (2 × 25 ml) and with EtOAc (2 × 25 ml.). The combined org. phases were dried (Na_2SO_4) and the solvent removed. The residue was purified on prep. SiO_2 plates using benzene/$CHCl_3$ 2:1 (*anti-anti* and *syn-syn*) or $CHCl_3$ (*syn-anti*). The pertinent data, is summarized below.

Diol	$HO_2C(CH_2)_nCO_2H$ n	Yield of dilactone	M.p. [°C] (MeOH)
anti-anti	0	66	295
	1	22	225–226
	2	40	167–170
	4	50	174–175
	9	70	oil
syn-anti	9	8	oil
	11	12	oil
syn-syn	11	7	oil

Dilactones from anti-anti-*Diol. a)* n = 0. IR ($CHCl_3$): 1730, 1720, 1270, 1170. ^{1}H-NMR ($CDCl_3$): 5.4–5.0 (br. *m*, 2CHOCO); 2.45–2.15 (*m*, 8CH_2); 1.4 (*s*, 8CH_2). MS: 206 (6, M^+-CO_2); 161 (95), 160 (100), 132 (49).

$C_{14}H_{18}O_4 \cdot$ ½ CH_3OH Calc. C 65.39 H 7.57% Found C 64.91 H 7.50%

b) n = 1. IR ($CHCl_3$): 1730, 1720, 1270, 1170. ^{1}H-NMR ($CDCl_3$): 5.6–5.2 (br. *m*, 2CHOCO); 3.45–3.3 (*s*, 2$COCH_2$CO); 2.5–2.0 (br. *m*) + 1.2 (br. *s*, 16CH_2). MS: 264.1305 (10), 161 (76), 160 (100), 132 (88), 120 (44).

$C_{15}H_{20}O_4 \cdot$ ½ CH_3OH Calc. C 64.84 H 8.16% Found C 64.55 H 7.44%

c) n = 2. IR ($CHCl_3$): 1720, 1270, 1170. ^{1}H-NMR ($CDCl_3$): 5.4–5.0 (br. *m*, 2CHOCO); 2.45–1.45 (br. *m*) + 1.4–1.2 (br. *m*, 20CH_2). MS: 278.1499 (18), 161 (91), 160 (100), 133 (36), 132 (89), 120 (60).

$C_{16}H_{22}O_4 \cdot \frac{1}{2}\ CH_3OH$ Calc. C 67.32 H 8.22% Found C 67.90 H 8.57%

d) n = 4. IR ($CHCl_3$): 1710, 1270, 1180. ^{1}H-NMR ($CDCl_3$): 5.45–5.0 (br. *m*, 2CHOCO); 2.5–1.3 (*m*, $22CH_2$).

$C_{18}H_{26}O_4 \cdot \frac{1}{2}\ CH_3OH$ Calc. C 68.91 H 8.75% Found C 69.19 H 8.45%

e) n = 9. IR ($CHCl_3$): 1700, 1250, 1200. ^{1}H-NMR ($CDCl_3$): 5.4–5.0 (br. *m*, 2CHOCO); 2.5–1.7 (*m*) + 1.5–1.3 (br. *s*, $34CH_2$). MS: 376.2592 (4), 199 (19), 161 (26), 160 (100), 132 (97), 120 (59).

$C_{23}H_{36}O_4$ Calc. C 73.36 H 9.64% Found C 72.82 H 10.20%

Dilactones from syn-anti-*Diol. a*) n = 9. IR ($CHCl_3$): 1710, 1270, 1170. ^{1}H-NMR ($CDCl_3$): 5.5–5.0 (br. *m*, 2CHOCO); 2.6–1.2 (*m*, $34CH_2$). MS: 376 (5), 217 (15), 178 (11), 161 (33), 160 (100), 133 (19), 132 (90), 131 (21), 120 (46), 118 (41). M.W.: Calc. 376.2612, Found 376.2669.

b) n = 11. IR ($CHCl_3$): 1710, 1270, 1170. ^{1}H-NMR ($CDCl_3$): 5.45–5.0 (br. *m*, 2CHOCO); 2.4–1.2 (*m*, $38CH_2$). MS: 404 (12), 161 (89), 160 (100), 132 (70), 131 (30), 120 (100). M.W.: Calc. 404.2926, Found 404.2929.

Dilactone from syn-syn-*Diol. a*) n = 11. IR ($CHCl_3$): 1710, 1270, 1170. ^{1}H-NMR ($CDCl_3$): 5.5–5.0 (br. *m*, 2CHOCO); 2.4–1.2 (*m*, $38CH_2$). MS: 404 (3), 227 (28), 161 (46), 160 (100), 133 (28), 132 (41), 131 (33), 128 (16), 121 (20), 120 (100), 119 (53). M.W.: Calc. 404.2926, Found 404.2930.

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