120. An Efficient Synthesis of 2,3,5,6-Tetramethylidene-7-oxanorbornane[1])

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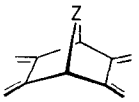
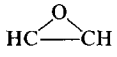
Summary

Palladium-catalyzed double carbomethoxylation of the *Diels-Alder* adduct of furan and maleic anhydride yielded the methyl all-*exo*-7-oxanorbornane-2,3,5,6-tetracarboxylate (**7**) which was transformed in three steps into 2,3,5,6-tetramethylidene-7-oxanorbornane (**1**), a useful synthon. Six isomeric methyl 7-oxanorbornane-2,3,5,6-tetracarboxylates (**7**–**12**) have been isolated and their ^{1}H- and ^{13}C-NMR. data are compared.

Introduction. – The 2,3,5,6-tetramethylidene-bicyclo[2.2.n]alkanes **1**–**5** have interesting properties. Evidence for transannular interactions between the homoconjugated s-*cis*-butadiene functions were found in the UV. [1–4] and photoelectron spectra [5][3]). The first equivalent of a strong dienophile adds more rapidly than the second equivalent. Thus **1**–**5** are very attractive starting materials for the preparation of polycyclic, polyfunctional systems by two successive *Diels-Alder* additions with different dienophiles. The ether-tetraene **1** can be used to prepare various anthracycline derivatives [8] [9]. Until now, **1** was prepared in six steps from methyl furan-3,4-dicarboxylate and methyl acetylenedicarboxylate [1], very expensive starting materials. This fact made our doubly convergent synthesis of anthracyclinones [8] [9] prohibitive for practical use. We report now a more efficient synthesis of **1** starting with the inexpensive *Diels-Alder* adduct of furan and maleic anhydride **6** [10].



Z=O	CH_2	CH_2–CH_2	CH=CH	
1 [1]	**2** [2]	**3** [3]	**4** [3]	**5** [4]

Results and discussion. – *Stille et al.* [11] have reported the reaction of cyclic olefins with carbon monoxide in methanol to form 1,2- and 1,3-diesters in the presence of catalytic amounts of $PdCl_2$ and stoichiometric amounts of $CuCl_2$.

[1]) Preliminary report: [1].

[2]) Author to whom correspondence should be addressed.

[3]) For other systems containing two non-conjugated exocyclic s-*cis*-butadiene groups, see [6]; for 2,3,5,6,7,8-hexamethylidene-bicyclo[2.2.2]octane (or [2.2.2]hericene), see [7].

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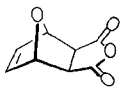
Under the usual conditions (3–4 atm. CO, 0.02 mol-equiv. $PdCl_2$, 2 mol-equiv. $CuCl_2$, abs. MeOH, 20–25°, 24 h) the oxanorbornene derivative **6** was bis-carbomethoxylated and esterified to the methyl all-*exo*-7-oxanorbornane-2,3,5,6-tetracarboxylate (**7**) in 55–56% yield. In the presence of 4 mol-equiv. of $CuCl_2$, **7** was obtained in 90–92% yield. The excess of the oxidant was necessary because of the following competitive reaction [11] that consumes the water formed by esterification of **6**:

$$Pd^{++} + H_2O + 2CO + MeOH \rightarrow HCOOCH_3 + Pd^0 + 2H^+ + CO_2$$
$$Pd^0 + 2H^+ \xrightarrow{2CuCl_2} PdCl_2 + 2CuCl$$

The structure of **7** was deduced from its ^1H- and ^{13}C-NMR. spectra (C_{2v}-species) and by comparison with those of other isomeric tetraesters **8–12** (see *Tables 1* and *2*). The all-*exo* configuration was indicated by the vicinal coupling constants $^3J_{H-C(1),H-C(2)} = {}^3J_{H-C(1),H-C(6)} \simeq 0$ Hz [12].



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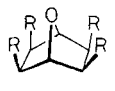
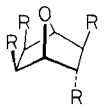


R = $COOCH_3$ **7**
R = CH_2OH **15**
R = CH_2Cl **16**



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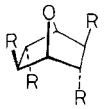
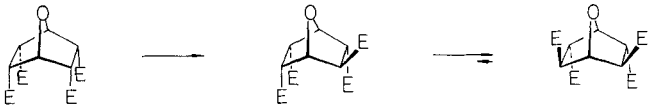


9
13
14

Substantial amounts of the catalyst were lost during the reaction by precipitation of metallic Pd. We found that *$PdCl_2$ can be replaced advantageously by 10% Pd/C* (0.004–0.008 equiv. of Pd) which was more active (faster carbonylation) and more efficient (larger turnover number)[4]).

Former studies on the sequence tetraester → tetrol → tetratoluenesulfonate, tetramethanesulfonate or tetrachloride → tetraene [1–4] suggested that an all-*trans* tetraester was necessary to ensure good yields, *cis*-bis(hydroxymethyl)-derivatives giving tetrahydrofurans competitively [13]. When treated with K_2CO_3/MeOH, **7** gave first the mono-*endo*-tris-*exo* tetraester **8** which isomerized into a thermodynamic mixture of methyl 7-oxanorbornane-2,3,5,6-tetracarboxylates, the all-*trans* isomer **9** being the major compound (~80%). A minor constituent was the isomer **10** (~20%) (C_s-symmetry). The tetraesters **8**, **9**, **10** were isolated by controlled isomerization and fractional crystallization. Their spectroscopic data are compared in *Tables 1* and *2* with those of the isomeric esters **11** and **12**. The all-*endo* tetraester **12** was obtained by catalytical hydrogenation (Pd/C, MeOH) of methyl 7-oxanorborna-2,5-diene-2,3,5,6-tetracarboxylate. In acidic conditions (MeOH or acetone +0.15% $HClO_4$, Pd/C, *cf.* [14]), a mixture of **12** (*ca.* 75%) and the mono-*exo* isomer



12 E = $COOCH_3$ **11** ⟶ **9** ⟵ **10**

4) For other oxidations with Pd^{++}, *cf.* [20].

11 (*ca.* 25%) was obtained[5]). Ester **11** was prepared by isomerization of **12** in the presence of K_2CO_3 in abs. methanol (the **12** → **11** isomerization was *ca.* 10 times as fast as that of **11** → **9** + **10**, 25°). The ^{1}H- and ^{13}C-NMR. data of **7**–**12**, their relative stabilities, as well as their mode of formation allowed unambiguous determination of their structures.

After purification by crystallization, **9** (61%) was reduced to the tetrol **13** ($LiAlH_4$/THF, 80%). Reaction with $SOCl_2$/pyridine yielded the tetrachloride **14** (90%) which eliminated four equivalents of HCl in excess *t*-BuOK/THF yielding the tetraene **1** in 95% yield (38% from **6**). The low yield step of this synthesis is the ester isomerization **7** → **9**. This was due in part to the presence of *ca.* 20% of **10** and to competitive polymerization (yields were lower using MeONa/MeOH or CsF/DMF [15]).

The isomerization step **7** → **9** could be avoided if the reduction and the reaction with $SOCl_2$/pyridine were carried out under strict control of concentration and temperature (see experimental part). Reduction of the all-*exo* tetraester **7** furnished the tetrol **15** (83%) which led to the tetrachloride **16** in 85% yield. Quadruple elimination of HCl yielded **1** (98%, or 64% from **6**).

Conclusion. – The 2,3,5,6-tetramethylidene-7-oxanorbornane (**1**) is a building block readily available from inexpensive furan and maleic anhydride. The sequence tetraester → tetrol → tetrachloride → tetraene is a useful approach to generate four exocyclic double bonds at the same time. Moreover, the heterogeneous catalyst Pd/C can advantageously replace $PdCl_2$ in carbonylation reactions using $CuCl_2$ as oxidizing agent.

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Experimental Part

General Remarks. Melting points (m.p.), *Tottoli* apparatus (not corrected). IR. spectra (ν [cm^{-1}]), *Beckman* IR-20A and *Beckman* IR-4230 spectrometers. UV. spectra, *Pye Unicam* SP 1800 instrument (λ_{max} [nm] (ε)). Mass spectra (MS.) in electron ionization mode, CEC 21-490 *Bell-Howell & Hewlett Packard* HP 5980A (*m/z* [amu] (% base peak)). ^{1}H-NMR. spectra, *Bruker* WP 80 CW spectrometer (δ [ppm], apparent coupling constants *J* [Hz], number of protons, tentative attribution); *s* singlet, *d* doublet, *t* triplet, *qa* quadruplet, *qi* quintuplet, *m* multiplet, $\delta_{TMS} = 0.0$ ppm, br. broad. ^{13}C-NMR. spectra, *Bruker* WP 60 spectrometer (15.08 MHz, spectrum width: 3750 Hz, 4096 points, FT Mode): δ [ppm], apparent coupling constants $^1J_{CH}$ [Hz], tentative attribution. Elementary analyses were performed by the microanalytical laboratory of the University of Geneva (Dr. *K. Eder*). Abbreviations: *i.V. in vacuo*, RT. room temperature, sh. shoulder, THF tetrahydrofuran, anh. anhydrous, sat. saturated, aq. aqueous, TLC. thin layer chromatography on SiO_2.

Methyl all-exo-*7-oxanorbornane-2,3,5,6-tetracarboxylate* (**7**). The furan-maleic anhydride adduct [10] (65 g, 0.39 mol), anh. $CuCl_2$ (210 g, 1.56 mol), 10% Pd/C (3 g, 2.8 mmol) and anh. methanol (600 ml) were placed in a 2 l Pyrex flask (*Parr* apparatus). After careful degassing, the mixture was pressurized with CO (4 atm.) and stirred for 3–4 h at RT.; the CO pressure was maintained at 3–4 atm. After removal of the solvent *i.V.*, water (500 ml) and $CHCl_3$ (500 ml) were added. The solid was filtered off (Celite). The organic layer was washed with sat. aq. $NaHCO_3$-solution (3 to 5×, 200 ml)

[5]) The tetraesters **7**–**12** were stable under these acidic conditions.

until absence of the blue colour. After evaporation to dryness, the yellowish residue was stirred energetically with methanol/ether 2:1 (150 ml) and the suspension was collected by filtration. Yield: 118.5 g (92%); white powder, m.p. 156–157° (MeOH). – IR. ($CHCl_3$): 2880, 1750, 1440, 1285, 1240, 1170, 1015, 950. – ^{1}H-NMR., see *Table 1.* – ^{13}C-NMR., see *Table 2.* – MS. (70 eV): 299 ($M^+ - 31$, 5), 267 (3), 293 (2), 212 (4), 185 (10), 153 (6), 145 (4), 113 (16), 95 (6), 69 (100).

$C_{14}H_{18}O_9$ (330.28) Calc. C 50.91 H 5.49% Found C 51.07 H 5.58%

All-exo-*2,3,5,6-tetrakis(hydroxymethyl)-7-oxanorbornane* (**15**). To a vigorously stirred suspension of $LiAlH_4$ (*Fluka*, purum[6]), 17 g, 0.44 mol) in anh. THF (500 ml) maintained at 0°, a suspension of **7** (53 g, 0.16 mol) in anh. THF (500 ml) was added portionwise (1–1.5 h). The mixture was allowed to reach RT. and was then heated under reflux for 4 h. After cooling to RT., water (100 ml) was added dropwise (30 min) and the mixture was heated under reflux for 1 min and immediately filtered through silica gel (300 g). The solid (SiO_2 + aluminium salts) was extracted with boiling methanol (3 × 500 ml). The filtrates were combined; the precipitate formed at RT. was filtered off (inorganic salts). The solution was concentrated *i.V.* to 45–50 ml and allowed to stand overnight at 0°. Yield: 29 g (83%); colourless crystals, m.p. 208–209° (EtOH). – IR. (KBr): 3260–3220, 2880, 2850, 1480, 1380, 1200, 1025, 920, 870, 840. – ^{1}H-NMR. (D_2O): 4.9 (*s*, 4 OH + DHO); 4.45 (*s*, H–C(1,4)); 3.65 (*m*, 8 H, 4 H_2COH); 2.3 (*m*, H–C(2,3,5,6)). – ^{13}C-NMR. (dioxane): 82.55 (*d* × *m*, 162); 47.94 (*d*, 132, C(2,3,5,6)); 60.7 (*t*, 140, CH_2OH). – MS. (70 eV): 182 ($M^+ - 36$, 19), 169 (100), 151 (52), 129 (63), 127 (48), 111 (83), 95 (58), 81 (73), 69 (73), 55 (56), 41 (54).

$C_{10}H_{18}O_5$ (218.25) Calc. C 55.03 H 8.31% Found C 55.15 H 8.37%

All-exo-*2,3,5,6-tetrakis(chloromethyl)-7-oxanorbornane* (**16**). To a stirred mixture of anh. pyridine (24.5 g, 0.31 mol) and $SOCl_2$ (46 g, 0.386 mol), **15** (17 g, 78 mmol) was added portionwise, *without cooling*. More $SOCl_2$ (70 g, 0.59 mol) was added and the mixture was heated to 60–70° for 2 h (the temperature should never exceed 70°!). After cooling to RT., CH_2Cl_2 (600 ml) was added. The excess of $SOCl_2$ was destroyed slowly by dropwise addition of water (50 ml) under external cooling and reflux. The organic layer was washed with water (3 × 300 ml) and dried ($MgSO_4$). After removal of the solvent *i.V.*, 19.4 g (85%) of **16** was obtained as a yellowish-white powder, pure enough for the next step, m.p. 149° (EtOH). – IR. (KBr): 2880, 1450, 1350, 1290, 1200, 1105, 1020, 990, 970, 930, 910, 900, 825, 810, 610. – ^{1}H-NMR. ($CDCl_3$): 5.15 (*s*, H–C(1,4)); 4.15 (*m*, 8 H, 4 H_2CCl); 2.5 (*m*, 4 H). – ^{13}C-NMR. ($CDCl_3$): 83.4 (*d*, 156, C(1,4)); 49.1 (*d*, 135, C(2,3,5,6)); 42.3 (*t*, 148, CH_2Cl). – MS. (70 eV): 296 (4), 294 (19), 292 (48), 290 (26) [M^+], 259 (26), 257 (52), 255 (70), 243 (93), 241 (100), 205 (15), 203 (37), 201 (41), 91 (67).

$C_{10}H_{14}Cl_4O$ (292.05) Calc. C 41.23 H 4.84 Cl 48.68% Found C 41.25 H 4.76 Cl 48.51%

2,3,5,6-Tetramethylidene-7-oxanorbornane (**1**). Solid *t*-BuOK (*Fluka*, pract., 18 g, 0.16 mol) was added in small portions (*ca.* 30 min) to a stirred solution of **16** (5 g, 0.0171 mol) in anh. THF (100 ml) cooled to 0°. The mixture was stirred at RT. for 12 h. The end of the elimination was checked by TLC. (CH_2Cl_2/CCl_4 3:2, revelation by phosphomolybdic acid/ethanol). Water (50 ml) was added portionwise until complete dissolution of KCl. The brownish mixture was extracted with pentane (3 × 100 ml). The organic extracts were combined and washed with water (6 × 100 ml). After drying ($MgSO_4$ + active charcoal), the solution was evaporated to dryness in the dark. Yield: 2.45 g (98%) (a 90% yield was obtained when starting with 40 g of **16**); colourless needles, m.p. 35–37°. – UV. (isooctane): 263 (1900), 248 (sh., 5200), 238 (sh., 6900), 228 (12,900), 221 (12,400). – IR. ($CHCl_3$): 3080, 3000, 2920, 2860, 1650, 1425, 895. – ^{1}H-NMR. ($CDCl_3$): 5.15 (br. *s*, 4 H, H(*E*) of 4 methylidene); 4.95 (br. *s*, 4 H, H(*Z*) of 4 methylidene); 4.85 (br. *s*, 2 H, H–C(1,4)). – ^{13}C-NMR. *cf.* [16]. – MS. (70 eV): 146 (63), 145 (18), 131 (8), 119 (13), 118 (90), 117 (100), 115 (78), 103 (25), 91 (87), 78 (18). – Photoelectron spectrum, see [5].

$C_{10}H_{10}O$ (146.23) Calc. C 82.16 H 6.89% Found C 81.97 H 6.95%

When using the all-*trans*-tetrakis(chloromethyl)derivative **14** (see below), the quadruple elimination of HCl was terminated in 1 h under the same conditions as above, yielding 95% of **1**.

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[6]) Good quality $LiAlH_4$ is essential for a high yield.

Table 1. *^{1}H-NMR. data of methyl 7-oxanorbornane-2,3,5,6-tetracarboxylates* **7**–**12** (δ_H ppm in $CDCl_3$, values in parenthesis: δ_H in C_6D_6; internal ref. TMS; attributions confirmed by selective double irradiation experiments)

		 **7**	 **8**	 **9**	 **10**	 **11**	 **12** E=$COOCH_3$
δ_H	H–C(1)[a]	5.17 (5.17)	5.04 (5.05)	5.05 (5.15)	5.11 (5.28)	4.87 (4.80)	4.97 (4.65)
	H–C(2)[b]	3.01 (2.39)	3.07 (3.12)	3.16 (3.45)	3.21 (3.25)	3.89 (4.27)	3.43 (3.12)
	H–C(3)[b]	3.01 (2.39)	3.07 (2.85)	3.60 (3.80)	3.56 (3.73)	3.60 (3.81)	3.43 (3.12)
	H–C(4)[a]	5.17 (5.17)	5.15 (5.33)	5.05 (5.15)	5.04 (4.93)	5.02 (4.83)	4.97 (4.65)
	H–C(5)[b]	3.01 (2.39)	3.04 (2.94)	3.16 (3.45)	3.56 (3.73)	3.56 (3.20)	3.43 (3.12)
	H–C(6)[b]	3.01 (2.39)	3.55 (3.66)	3.60 (3.80)	3.21 (3.25)	3.21 (2.80)	3.43 (3.12)
	CH_3	3.64 (3.32)	3.68 (3.33)	3.74 (3.27)	3.63 (3.27)	3.61 (3.35)	3.62 (3.44)
			3.68 (3.26)	3.77 (3.24)	3.71 (3.21)	3.61 (3.32)	
			3.72 (3.20)			3.65 (3.32)	
			3.75 (3.14)			3.78 (3.27)	
$^3J_{1,2}$ [Hz]		~0.0	~0.0	~0.0	~0.0	~0.0	2.6[c]
$^3J_{2,3}$[d][e]		–	9.4[d]	5.4[e]	5.8[e]	7.4[e]	–
$^3J_{3,4}$		–	0.0	5.7	5.0	4.9	2.6
$^3J_{4,5}$		–	0.0	~0.0	5.0	5.1	2.6
$^3J_{5,6}$		–	5.0	5.4	5.8	11.9[d]	–
$^3J_{1,6}$		–	5.5	5.7	~0.0	4.4	2.6
$^4J_{1,3}$							2.5

[a]) Somewhat larger δ_H are observed for bridgehead H-atoms when the vicinal ester substituents are *exo* rather than *endo*, **11** being an exception.

[b]) Larger δ_H are found for H*exo* than for H*endo* (anisotropy of the oxygen bridge?).

[c]) Typical (J = 4.5–5.5 Hz) are observed between bridgehead H-atoms and vicinal H*exo*-atoms; **12** is an exception (J = 2.6 Hz), probably because of steric repulsions between the four *endo* ester substituents that lead to a distorted oxanorbornane skeleton.

[d]) As expected, the vicinal coupling constants are larger for *cis*- than for *trans*-H-atoms. The *cis-exo*-$^3J_{5,6}$ in **11** (11.9 Hz) is larger than the *cis-endo*-$^3J_{2,3}$ in **8** (9.4 Hz).

[e]) The *trans*-$^3J_{2,3}$ in **11** is somewhat larger than the *trans*-$^3J_{2,3}$ or *trans*-$^3J_{5,6}$ in **8**–**10** (5–5.8 Hz). This can be attributed to skeletal distortion due to repulsions between the three *endo* ester groups in **11**.

Table 2. *^{13}C-NMR. data of methyl 7-oxanorbornane-2,3,5,6-tetracarboxylate* **7**–**12** (δ_C ppm ($^1J_{CH} \pm 1$ Hz) in $CDCl_3$, internal ref. TMS; attributions confirmed by 'off-resonance' proton decoupling experiments [18])

	7	**8**	**9**	**10**	**11**	**12**[a])
C(1)	80.2 (166)	81.9 (167)	81.3 (166)	83.9 (167)	81.9 (165)	80.9 (166)
$^3J_{C,H-C(4)}$	11.0	10.0[b])	~9.0	10.5	~10.0	~9.0
C(2)	51.4 (136)	50.7 (137)[c])	46.4 (136.5)[f])	49.8 (136.5)[e])	44.2 (138)[h])	46.4 (134)[i])
C(3)	51.4 (136)	50.1 (139)[e])	50.1 (135.5)	50.3 (136.5)[e])	50.6 (131)	46.4 (134)[i])
C(4)	80.2 (166)	79.4 (167)	81.3 (166)	78.9 (166)	79.1 (166)	80.9 (166)
$^3J_{C,H-C(1)}$	11.0	10.0[d])	9.0	10.0	~10.0	~9.0
C(5)	51.4 (136)	47.4 (137)[e])	46.4 (136.5)	50.3 (136.5)[e])	45.9 (143)	46.4 (134)[i])
C(6)	51.4 (136)	49.7 (139)	50.1 (135.5)	49.8 (136.5)[e])	48.9 (134)	46.4 (134)[i])
CH_3	50.9 (147)	52.3 (147.4)	52.6 (148)	52.5 (147.7)	55.6 (147.4)	51.0 (147)
		52.3 (147.4)		51.9 (147.7)	51.6 (147.4)	
		51.9 (147.4)			51.2 (147.4)	
		51.9 (147.4)			51.2 (147.4)	
CO	170.0	171.1	171.7 (*exo*)[g])	171.3 (*exo*)[g])	172.6	167.9
		170.7	170.0 (*endo*)	169.9 (*endo*)	170.6	
		170.3			169.4	
		170.3			169.4 (*exo*)[g])	

a) Same numerotation of the carbon atoms as in *Table 1.*

b) $^nJ_{CH} = 1.8$ (*d*).

c) $^3J_{C,H-C(6)} = 4.6$ (*d*).

d) $^nJ_{C,H} = 4.1$ (*d*).

e) Attributions could be interchanged.

f) $^3J_{C,H-C(6)} \cong 6$.

g) Configuration attribution based on $^3J_{C,H-C(1 \text{ or } 4)}$ [15] [19].

h) $^nJ_{C,H} = 11.4$ and 5.5.

Bis-adduct of tetracyanoethylene to **1**. The tetraene **1** (60 mg, 0.41 mmol) in CH_3CN (0.3 ml) was added to a solution of tetracyanoethylene (111.5 mg, 0.9 mmol) in CH_3CN (2 ml). After heating to 90° for 24 h, the mixture was evaporated to dryness. The residue was recrystallized from CH_3CN. Yield: 100 mg (60%); colourless powder, m.p. 320–321°. – UV. (EtOH, 96%): 240 (sh., 3930), 210 (7150). – IR. (KBr): 2980, 2940, 2280, 1450, 1280, 1240, 1070, 860. – ^{1}H-NMR. ($CDCl_3$): 5.45 (*s*, 2 H); 3.55 (*s*, 8 H).

$C_{22}H_{10}N_8O$ (402.38) Calc. C 65.66 H 2.50 N 27.85% Found C 65.24 H 2.74 N 27.72%

Methyl 7-oxanorborna-2,5-diene-2,3,5,6-tetracarboxylate. Methyl furan-3,4-dicarboxylate (18.4 g, 0.1 mol) and methyl acetylenedicarboxylate (14.2 g, 0.1 mol) were heated together at 120° for 15 h (or at 80° for 4 days) in a sealed Pyrex tube, thoroughly degassed *i.V.* After cooling to RT., the Pyrex tube was opened and the crude adduct was recrystallized from methanol. Yield: 27.8 g (85%); m.p. 113–114° ([17]: 108–109°).

*Methyl 7-oxanorborn-2-ene-2,3,5*endo,*6*endo-*tetracarboxylate.* Methyl 7-oxanorborna-2,5-diene-2,3,5,6-tetracarboxylate (326 mg, 1 mmol) was partially hydrogenated (25 ml H_2, 100 mg 10% Pd/C) in methanol or acetone. The catalyst was filtered off and the solution evaporated to dryness *i.V.* Recrystallization from methanol yielded 300 mg (91%) of colourless crystals, m.p. 108–109°. – UV. (EtOH, 96%): end abs. ε_{220}: 5100. – IR. (KBr): 2980, 1740, 1650, 1070, 1000. – ^{1}H-NMR. ($CDCl_3$): 5.38 (*d*×*d*, *J*=3 and 2.5, H–C(1,4)); 3.8 (*s*, 6 H); 3.6 (*s*, 6 H); 3.53 (*d*×*d*, *J*=3 and 2.5, H_{exo}–C(5,6)). – ^{13}C-NMR. ($CDCl_3$): 169.3 (*s*); 161.8 (*s*); 143.0 (*s*); 81.9 (*d*, 173); 51.6 (*qa*, 148); 47.3 (*d*, 142). – MS. (70 eV): 296 (5), 269 (4), 268 (5), 264 (29), 237 (10), 209 (3), 184 (27), 153 (100), 123 (18), 113 (58), 59 (13).

$C_{14}H_{16}O_9$ (328.28) Calc. C 51.22 H 4.91% Found C 51.48 H 4.87%

*Methyl all-*endo-*7-oxanorbornane-2,3,5,6-tetracarboxylate* (**12**). Methyl 7-oxanorborna-2,5-diene-2,3,5,6-tetracarboxylate (1.65 g, 5 mmol) was hydrogenated in the presence of 10% Pd/C (200 mg) in acetone (*ca.* 24 h, until end of H_2 absorption). The catalyst was filtered off and the solution evaporated *i.V.* to dryness. Recrystallization from methanol yielded 1.65 g (99%); colourless crystals, m.p. 131–132°. – UV. (EtOH, 96%): end abs., ε_{220}=240. – IR. (KBr): 3008, 2960, 2920, 2850, 1770, 1750. – ^{1}H-NMR., *cf. Table 1.* – ^{13}C-NMR., *cf. Table 2.* – MS. (70 eV): 330 (7), 298 (92), 270 (25), 266 (27), 265 (46), 168 (100), 157 (25), 151 (24).

$C_{14}H_{18}O_9$ (330.28) Calc. C 50.91 H 5.49% Found C 51.12 H 5.56%

*Methyl 7-oxanorbornane-2*exo,*3*endo,*5*exo,*6*endo-*tetracarboxylate* (**9**). The all-*exo* tetraester **7** (20 g, 60.5 mmol) and 0.5 g anh. K_2CO_3 in 320 ml anh. methanol (*Fluka*, heated under reflux with Mg and I_2 and freshly distilled) were stirred at RT. for 48 h. The precipitate was filtered off and the solution evaporated *i.V.* to dryness. The oily residue was taken up with $CHCl_3$ (200 ml) and was washed with water (3×50 ml). After drying ($MgSO_4$) and solvent removal *i.V.*, the yellowish oil was crystallized from methanol. The crude tetraester **9** was recrystallized twice from ether. Yield: 12.2 g (61%); white crystals, m.p. 81–82°. The residue from the evaporated mother liquors could be recycled with another isomerization of **7**→**9**. – UV. (EtOH, 96%): end abs. ε_{230}=250. – IR. (KBr): 3030, 3000, 2950, 2850, 1740, 1720. – ^{1}H-NMR., *cf. Table 1.* – ^{13}C-NMR., *cf. Table 2.* – MS. (70 eV): 330 (1), 298 (25), 281 (3), 267 (25), 238 (59), 220 (73), 211 (93), 185 (100), 179 (96), 127 (86).

$C_{14}H_{18}O_9$ (330.28) Calc. C 50.91 H 5.49% Found C 51.15 H 5.69%

2exo,*3*endo,*5*exo,*6*endo-*Tetrakis(hydroxymethyl)-7-oxanorbornane* (**13**). A solution of the all-*trans* tetraester **9** (4 g, 12.1 mmol) in dry THF (*Fluka puriss.*, p.a., freshly distilled over $LiAlH_4$) was added dropwise (20–30 min) under N_2 to a stirred 1.8 M solution of $LiAlH_4$ in anh. THF (20.2 ml, 36.4 mmol) cooled to 0°. After the end of the addition, the mixture was heated under reflux for 15 h and then cooled to 0°. A sat. aq. solution of Na_2SO_4 (10 ml) was added dropwise under vigorous stirring. The precipitate was filtered off and extracted successively with boiling EtOH (20 ml, 2 h) and boiling 20% aq. KOH-solution (2 h). These operations were repeated twice. The combined filtrates were evaporated *i.V.* to dryness. The crude tetrol **13** was recrystallized from ethanol. Yield: 2 g (76%);

colourless crystals, m.p. 160–161°. – IR. (KBr): 3300, 2920, 2860, 1110, 1080, 1000, 930, 910. – ^{1}H-NMR. (D_2O): 4.75 (OH); 4.45 (*d*, J=4, H–C(1,4)); 3.63 (*m*, 8 H, 4 CH_2OH); 1.88 (*m*, 4 H, H–C(2,3,5,6)). – ^{13}C-NMR. (D_2O): 89.9 (*d*, 160), 62.4 (*t*, 144), 59.2 (*t*, 144), 46.4 (*d*, 131), 40.5 (*d*, 132).

$C_{10}H_{18}O_5$ (218.25) Calc. C 55.03 H 8.31% Found C 54.79 H 8.25%

2exo,3endo,5exo,6endo-Tetrakis(acetoxymethyl)-7-oxanorbornane. The tetrol **13** (100 mg, 0.46 mmol) in anh. pyridine (3 ml) and acetic anhydride (1 ml) was allowed to react at RT. for 48 h. The mixture was evaporated *i.V.* to dryness and crystallized from $CHCl_3/CCl_4$ 1:1. Yield: 120 mg (68%); colourless crystals, m.p. 47–48°. – UV. (EtOH, 96%): end abs. ε_{220}=455. – IR. (KBr): 2960, 2900, 1740, 1370, 1250, 1080, 1040, 960, 920. – ^{1}H-NMR. (CCl_4): 4.45–3.75 (*m*, 10 H); 2.35–1.7 (br. *s*+*m*, 16 H). – MS. (70 eV): 386 (4), 327 (11), 336 (46), 295 (24), 271 (31), 267 (29), 266 (63), 253 (20), 207 (34), 206 (100), 193 (20), 164 (43), 163 (20), 153 (31), 146 (100), 133 (47), 119 (43).

$C_{18}H_{26}O_9$ (386.4) Calc. C 55.95 H 6.78% Found C 56.05 H 6.73%

2exo,3endo,5exo,6endo-Tetrakis(chloromethyl)-7-oxanorbornane (**14**). To a cooled (0°) solution of the tetrol **13** (1 g, 4.58 mmol) in anh. pyridine (15 ml), $SOCl_2$ (*Fluka, puriss.* p.a., 4.36 g, 36.6 mmol) was added dropwise under N_2. The mixture was heated to 70° for 2 h. The dark mixture was cooled to 0°, hydrolyzed slowly (50 ml H_2O) and extracted with ether (3×20 ml). After drying ($MgSO_4$), the ethereal extract was evaporated *i.V.* to dryness. The yellowish solid obtained was recrystallized from $CHCl_3$/pentane 2:1. Yield: 1.2 g (90%); m.p. 110–111°. – UV. (EtOH, 96%): end abs. ε_{210}=200. – IR. (KBr): 3010, 2980, 2940, 2920, 2880, 1450, 1440, 1320, 1290, 1120, 1095, 1040, 1000, 960, 930, 870, 850, 730, 700. – ^{1}H-NMR. ($CDCl_3$): 4.46 (*d*, J=5, H–C(1,4)); 4.0–3.15 (*m*, 8 H, 4 CH_2Cl); 2.5–1.7 (*m*, 4 H, H–C(2,3,5,6)). – MS. (70 eV): 257 (1), 256 (1.5), 255 (2.5), 254 (5), 253 (3), 252 (5), 242 (6), 240 (23), 238 (24), 221 (5), 220 (5), 219 (30), 218 (42), 217 (12), 205 (48), 203 (76), 181 (22), 179 (5), 177 (8), 167 (52), 163 (37), 161 (100), 141 (25), 139 (25).

$C_{10}H_{14}Cl_4O$ (292.05) Calc. C 41.13 H 4.83% Found C 41.24 H 4.97%

Methyl 7-oxanorbornane-2exo,3endo,5endo,6endo-tetracarboxylate (**11**). A sat. solution of anh. K_2CO_3 in anh. methanol (10 ml) was added to a solution of the all-*endo* tetraester **12** (2 g, 6.06 mmol) in anh. methanol (100 ml) cooled to −10°. The mixture was stirred at −10° for 15 min. After addition of water (100 ml), the mixture was extracted at −10° with $CHCl_3$ (2×100 ml). The extracts were combined and washed with ice/water (2×100 ml) and dried ($MgSO_4$). After evaporation *i.V.* to dryness, the crude tetraester **11** was recrystallized from ether at −10°. Yield: 1.3 g (65%); colourless crystals, m.p. 95–96°. – UV. (EtOH, 96%): end abs. ε_{210}=280. – IR. (KBr): 3000, 2960, 2840, 1750, 1740, 1730, 1440, 1370, 1290, 1180, 950. – ^{1}H-NMR., *cf. Table 1.* – ^{13}C-NMR., *cf. Table 2.* – MS. (70 eV): 330 (<0.1), 329 (<0.1), 300 (10), 299 (56), 298 (26), 281 (7), 271 (17), 267 (18), 239 (32), 238 (48), 211 (48), 185 (48), 179 (47), 169 (67), 145 (50), 128 (40), 113 (100), 95 (30).

$C_{14}H_{18}O_9$ (330.28) Calc. C 50.91 H 5.49% Found C 51.05 H 5.56%

Methyl 7-oxanorbornane-2exo,3endo,5endo,6exo-tetracarboxylate (**10**). A sat. solution of anh. K_2CO_3 in anh. methanol (10 ml) was added at RT. to a solution of the all-*endo* tetraester **12** (4 g, 12.1 mmol) in anh. methanol (150 ml). The mixture was cooled to −10° (selective crystallization of **10**). After 4 h at −10°, the precipitate was collected and washed with methanol. Yield: 1.8 g (45%); colourless crystals, m.p. 130–131°. – IR. ($CHCl_3$): 3040, 3010, 2965, 2915, 2860, 1735, 1440, 1370, 1340, 1300, 1225, 1180, 1090, 1050, 1000, 980, 945, 900, 860, 830. – ^{1}H-NMR., *cf. Table 1.* – ^{13}C-NMR., *cf. Table 2.* – MS. (70 eV): 330 (<0.1), 299 (5), 298 (3), 281 (2), 267 (6), 266 (5), 249 (4), 238 (15), 221 (16), 211 (26), 185 (35), 179 (67), 169 (40), 153 (50), 151 (54), 145 (53), 127 (100), 126 (57), 113 (82), 95 (67), 59 (27).

$C_{14}H_{18}O_9$ (330.28) Calc. C 50.91 H 5.49% Found C 51.01 H 5.53%

Methyl 7-oxanorbornane-2exo,3exo,5exo,6endo-tetracarboxylate (**8**). A mixture of the all-*exo* tetraester **7** (1 g, 3 mmol), anh. K_2CO_3 (0.3 g) and anh. methanol (150 ml) was stirred at 25° for 2 h. After addition of water (100 ml), the mixture was extracted with $CHCl_3$ (2×100 ml). The extracts were combined and washed with water (2×100 ml), dried ($MgSO_4$) and evaporated *i.V.* to dryness. The

oily residue was separated by column chromatography (silica gel, 40 g, ether). The crude tetraester **8** was recrystallized from ether/pentane 2:1. Yield: 0.65 g (65%), colourless crystals, m.p. 65–66°. – IR. ($CHCl_3$): 3040, 3005, 2960, 2855, 1740, 1440, 1365, 1340, 1300, 1280, 1170, 1030, 1000, 940, 905. – ^{1}H-NMR., *cf. Table 1.* – ^{13}C-NMR., *cf. Table 2.* – MS. (70 eV): 330 (<0.1), 300 (5), 299 (20), 298 (5), 267 (25), 266 (22), 239 (32), 238 (46), 221 (29), 211 (67), 207 (29), 185 (100), 179 (65), 169 (44), 153 (58), 151 (45), 145 (42), 127 (36), 113 (58), 95 (42), 59 (94).

$C_{14}H_{18}O_9$ (330.28) Calc. C 50.91 H 5.49% Found C 51.03 H 5.56%

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