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SYNTHESIS AND HYDROBORATION/OXIDATION OF TRICYCLO(5.2.1.$0^{4,10}$)DEC-8-ENE-2,5-DIONE (BIS-ACETAL): NEW SYNTHETIC ENTRY TO TRICYCLO(5.2.1.$0^{4,10}$)DECANE-2,5,8-TRIONE.

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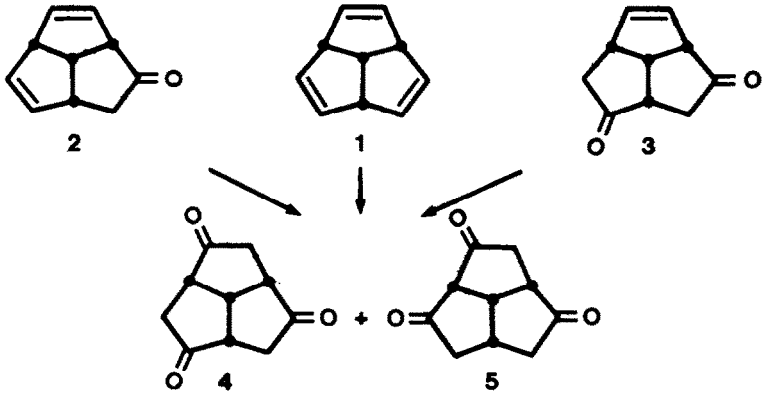
Abstract.- Tricyclo(5.2.1.$0^{4,10}$)decane-2,5,8-trione (4) has been synthesized from the corresponding bis-acetal of the unsaturated diketone 20 by a hydroboration/oxidation/deprotection sequence.

Tricyclo(5.2.1.$0^{4,10}$)decane-2,5,8-trione (4) is a chiral molecule, with a C_3 axis of symmetry, which has been especially designed as the starting material for an attempted convergent and reflexive synthesis of dodecahedrane.[1]



	Ratios of 4:5		
From	Statistical	Experimental	Ref.
2	1:3	1:4	1
1	1:3	2:3	2
3	1:1	3:2	present work

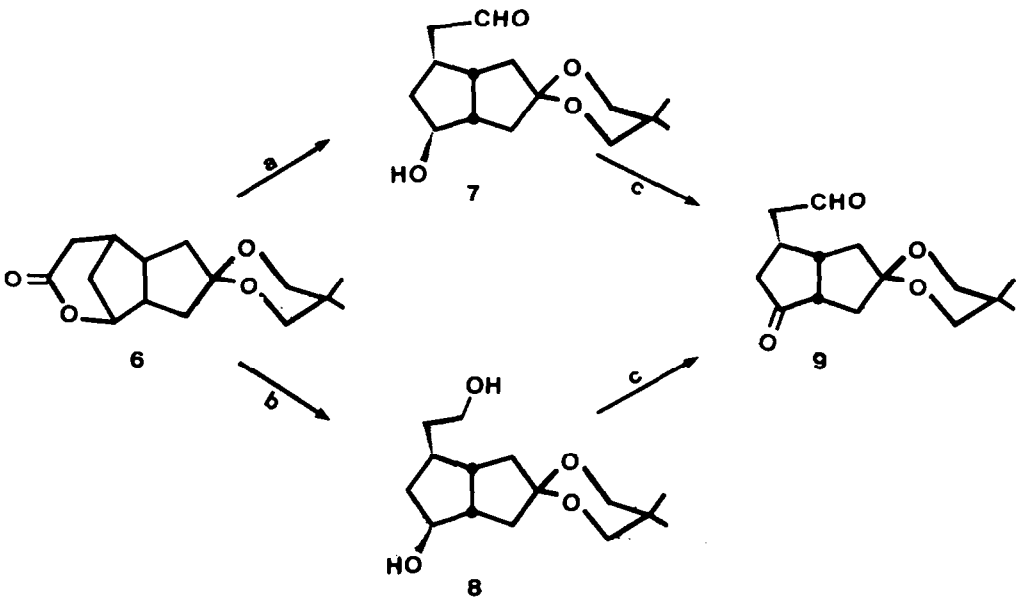
Scheme 1

Hydroboration/Oxidation of Triquinacene (1) and Mono and Diketone, 2 and 3, as the Corresponding Acetal Derivatives

One of the general strategies we devised for the synthesis of trione 4 involves the pertinent functionalization of the triquinacene skeleton, a process that requires a regioselective control in order to create the three 1,4-dissonant bifunctional relationships between the three carbonyl groups present in the molecule. According to this general strategy we have already reported the hydroboration/oxidation of either the triquinacene itself (1) or the acetal of the corresponding monoketone 2. As shown in Scheme 1, of the two possible regioisomers the wanted symmetrical triketone 4 is, in both cases, the unfavored isomer on strictly statistical basis (1:3). Although experimental conditions have been found in the case of triquinacene, in which the ratio of the symmetrical triketone 4 is higher than that (2:3),[2,3] in the case of the monoacetal of monoketone 2 a less favorable 1:4 ratio was obtained because the inductive effects of the acetal group prevail over the steric effects.[1a]

Since the yields and the statistical ratio of the regioisomers are very unfavorable in the case that two bifunctional relationships have to be created, we have prepared a substrate such as the bis-acetal of ketone 3, in which one bifunctional 1,4-dissonant relationship is already present in the molecule. In such a case, higher yields and regioselectivity must be expected because: i) it implies the functionalization of only one double bond, and ii) a 1:1 ratio of regioisomers should be expected on strictly statistical basis.

For the synthesis of diketone 3 we did follow a procedure essentially identical to that reported for monoketone 2 (Scheme 2). [1a,4]



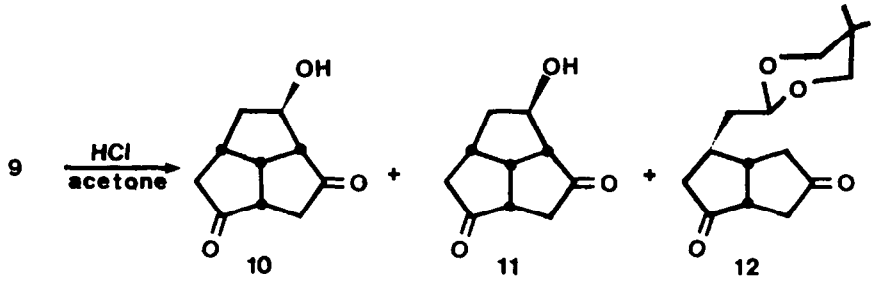
Scheme 2

a) DIBAL/benzene/ether; b) $LiAlH_4$/THF/ether; c) CCP/CH_2Cl_2

As previously reported by Deslongchamps,[5] lactone 6 could be either reduced with DIBAL or lithium aluminum hydride to afford, respectively the hydroxyaldehyde 7 or the diol 8, in quantitative yields. Oxidation of either one of these compounds with PCC afforded the ketoaldehyde 9 (58% and 73% overall yield, respectively).

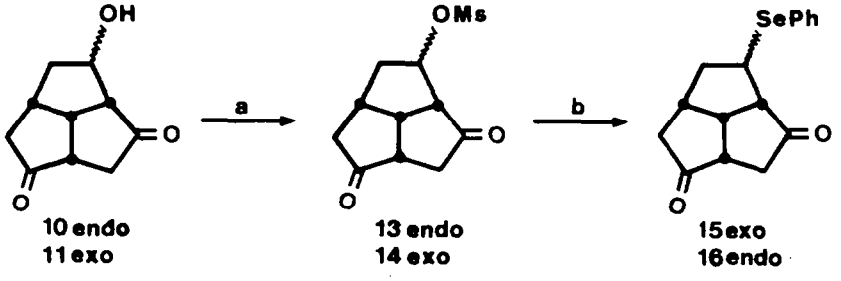
Treatment of the ketoaldehyde 9 with aqueous 2M HCl in acetone, for 3 days, leads to a 2:1 mixture of endo (10) and exo-aldol (11), together with 20% yield of acetal 12. The endo configura-

tion to the aldol 10 was assigned on the basis of X-ray analysis, as described below. The control of the reaction by ^1H NMR shows that after 2 h all the starting ketoaldehyde 9 was practically transacetalized to acetal 12, the evolution from it being extremely slow and it could be even detected after reaction times longer than 10 days (Scheme 3).



Scheme 3

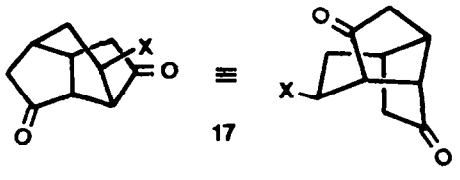
The mixture of aldols was treated with mesyl chloride, in dichloromethane solution, in the presence of either triethylamine or pyridine, to give a mixture of methanesulfonates 13 and 14 which, by a nucleophilic substitution with lithium phenylselenide,[6] led to a 9:1 mixture of selenides 15 and 16 (Scheme 4).



Scheme 4

a) MsCl/Pyr/CH_2Cl_2; b) PhSeSePh/BuLi/benzene

In one of the intramolecular aldol operations, in which the reaction mixture was allowed to react for 10 days, besides a decreasing of the yields of the corresponding aldols 10 and 11, it was observed a higher proportion of the acetal 12 and the presence of a third aldol that must be a constitutional isomer of 10 and 11 -probably formed by condensation from an activated position other than the one leading to the expected triquinacene skeleton-, to which we assigned the bridged structure 17 (X = OH).

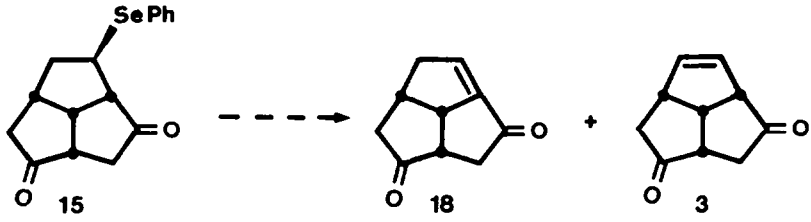


On the other hand, careful column chromatography over silica gel of the crude reaction product resulting from the mesylation of the aldols allowed the isolation of a third methanesulfonate, the ^1H and the ^{13}C NMR spectra of which strongly supports the structure 17 (X = OSO_2CH_3).

Since in all the performed aldol cyclizations the ratio of aldols 10:11 was rather constant (2:1), it was quite surprising that the mixture of the corresponding selenides was basically formed by one of the isomers. In order to obtain some insight into this fact, the two aldols 10 and 11 were separated by column chromatography and each one was separately mesylated. It was observed that although substitution on either one of two methanesulfonates 13 and 14 leads, in 60-62% yield, to the same seleno compound 15, in the crude mixture resulting from the exo isomer 14 some endo-selenide 16 was also detected by t.l.c. The analysis of the ^1H NMR spectrum allowed the assignation of the exo configuration to the seleno derivative 15, since for the exo isomer the observed values of the coupling constants for the α H to the phenylselenide group are 1.4, 1.4, and 5.6Hz, corresponding to two J_{trans} and to one J_{cis}, whereas for the endo isomer the values are 12.0, 8.4 and 6.0Hz, corresponding to two J_{cis} and one J_{trans}.

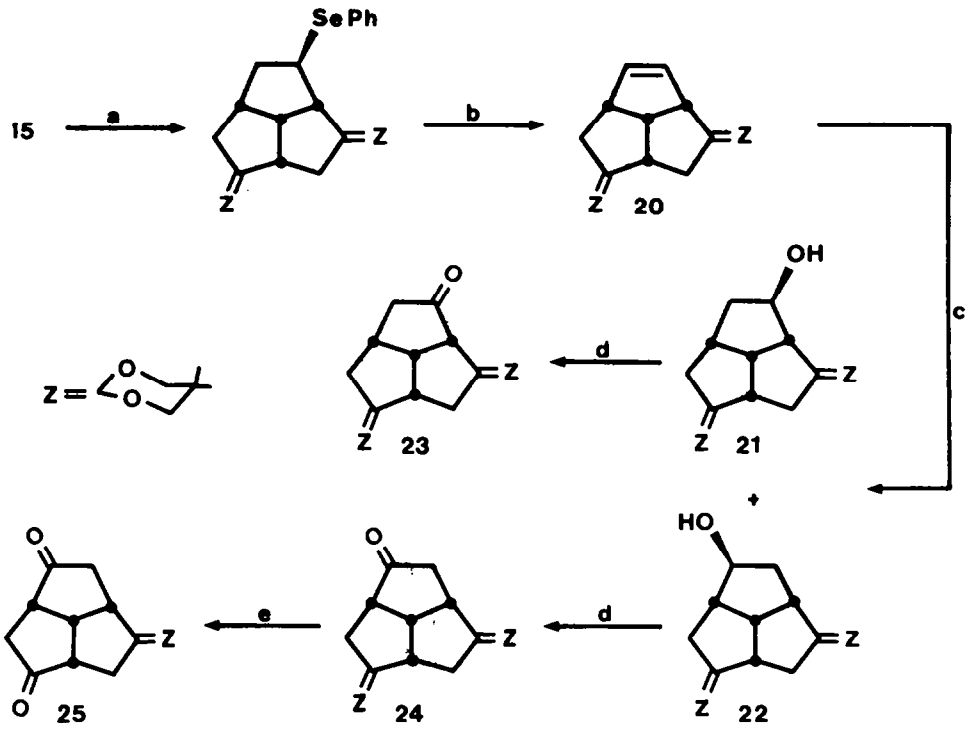
From a mechanistic point of view, the fact that the endo-methanesulfonate 13 leads to the exo-selenide 15 can be explained assuming S_N2 mechanism as generally accepted,[7] while the transformation of the exo-methanesulphonate 14 to the exo-selenide must take place either by a S_N1 or by an elimination-addition mechanism. Since the endo-selenide is recovered unchanged when it was submitted under the substitution conditions, any possible equilibration to the more stable exo-selenide must be excluded.

The oxidation/elimination sequence directly applied to the selenide 15 may lead, through a syn-elimination, to two isomeric unsaturated ketones, 18 and 3 (Scheme 5). However, when the selenide 15 was treated with sodium metaperiodate only the conjugated ketone 18 was obtained in yields higher than 80%. As previously reported in the case of the corresponding monoketone 2,[1a] the unconjugated ketone 3 could be obtained by protecting the functional groups as an acetal before the elimination reaction, protection that was indeed necessary in the hydroboration step.



Scheme 5

Accordingly, transacetalization of the selenide 15 leads to the bis-acetal 19, in 93% yield, which was oxidized with MCPBA affording, after thermolysis of the intermediate selenoxide, the unsaturated bis-acetal 20, in 96% yield (see Scheme 6). Hydroboration of newly created double bond with $BH_3.SMe_2$ in THF, followed by oxidation with H_2O_2, led to a mixture of monoalcohols that were separated by column chromatography and identified as 21 and 22, in a 40:60 relative ratio, the total yield being 92%. The structural assignments were made on the bases of the corresponding triketones resulting from an oxidation/deprotection sequence. While oxidation of 21 with PCC led to the ketone bis-acetal 23 in 71% yield, the oxidation of 22 afforded 24 in 93% yield. The ^{13}C NMR spectra corroborated also the structural assignments, since the chemical shift of C-1 was higher in 23 than in 24, as observed in some related bicyclic and tricyclic models (see Chart1).[1,8,9] Final confirmation was obtained when the bis-acetal 24 was treated with HCl in THF to give, in 94% yield, the diketone monoacetal 25, which had been previously characterized and transformed to triketone 4 by further acid hydrolysis.[1]



Scheme 6

a) 2,2,5-Trimethyl-1,3-dioxane/ p-$MeC_6H_4SO_2OH$; b) MCPBA/CH_2Cl_2 - $NHEt_2/CCl_4$; c) $BH_3.SME_2$/THF - H_2O_2/NaOH; d) CCP/CH_2Cl_2; e) HCl/THF.

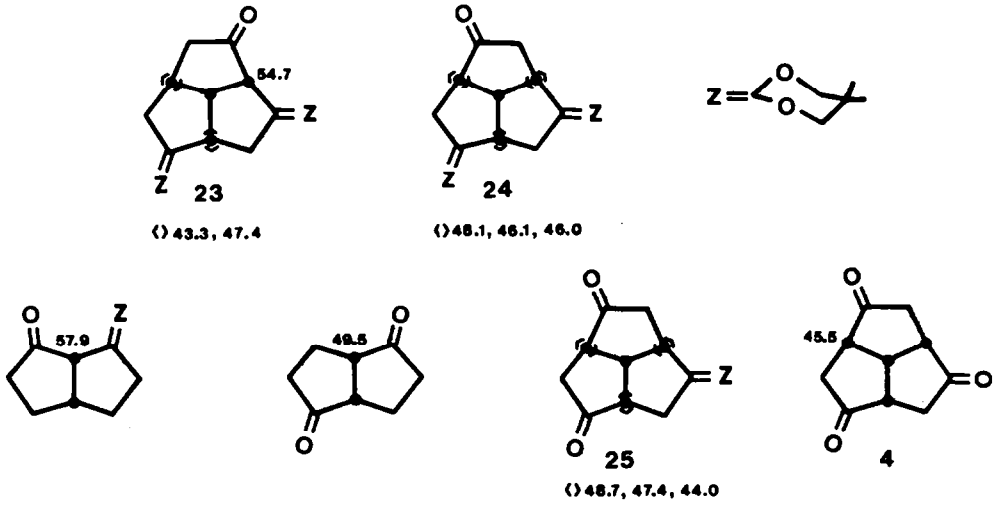


Chart 1

X-Ray Diffraction Analysis of Structure 10.- In order to confirm the sterochemistry of the tricyclic aldols, which was assigned on the basis of the ^1H NMR data, a X-ray diffraction analysis of the predominant endo-isomer 10 was also performed, and a brief discussion of the most salient structural details of this compound follows.

In the first place, it is observed that practically all the C-C bonds distances are in the range of the standard values, 1.53 ± 0.02 Å, with the exception of the C(7)-C(3) bond that is longer than those values: 1.567 Å (Table 1). Regarding to the internal angles of the cyclopentane rings, all of them are in the range 102.9-114.9° (Table 1), and it is also observed that, of the three condensed cyclopentane rings, the ring B (C(3)-C(4)-C(5)-C(6)-C(7)) is practically a perfect envelope, as shown by the 0.96° value for the dihedral angle C(4)-C(3)-C(7)-(6). On the other hand, though the ring C (C(6)-C(7)-C(8)-C(9)-C(10)) is roughly a perfect envelope too, with a value of 3.19° for the dihedral angle C(8)-C(9)-C(10)-C(6), the ring A (C(1)-C(2)-C(3)-C(7)-C(8)) which holds the OH group at the endo configuration, shows a skew envelope directing the oxygen atom towards the inside of the convex face of the triquinacene polycyclic system.

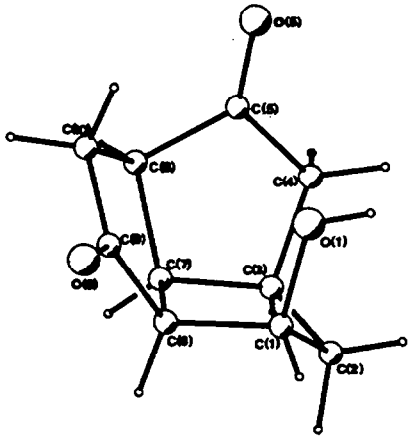


Fig. 1 X-Ray drawing of compound 10

Table 1. Selected bond distances and angles for compound 10 with e.s.d.s in parentheses

Distances (Å)		Angles (°)	
C(1)-O(1)	1.433 (0.002)	C(2)-C(1)-O(1)	111.6 (0.2)
C(1)-C(2)	1.522 (0.003)	C(8)-C(1)-O(1)	106.3 (0.2)
C(1)-C(8)	1.539 (0.003)	C(8)-C(1)-C(2)	102.9 (0.2)
C(2)-C(3)	1.538 (0.003)	C(3)-C(2)-C(1)	105.2 (0.2)
C(3)-C(4)	1.535 (0.003)	C(7)-C(3)-C(2)	103.8 (0.2)
C(3)-C(7)	1.567 (0.002)	C(7)-C(3)-C(4)	105.9 (0.2)
C(4)-C(5)	1.508 (0.003)	C(5)-C(4)-C(3)	107.2 (0.1)
C(5)-O(5)	1.218 (0.003)	C(6)-C(5)-C(4)	109.2 (0.2)
C(5)-C(6)	1.515 (0.002)	C(7)-C(6)-C(5)	104.9 (0.1)
C(6)-C(7)	1.554 (0.003)	C(10)-C(6)-C(7)	107.5 (0.2)
C(6)-C(10)	1.521 (0.003)	C(6)-C(7)-C(3)	107.8 (0.1)
C(7)-C(8)	1.538 (0.003)	C(8)-C(7)-C(3)	106.9 (0.2)
C(8)-C(9)	1.517 (0.003)	C(8)-C(7)-C(6)	105.4 (0.2)
C(9)-O(9)	1.210 (0.003)	C(7)-C(8)-C(1)	105.2 (0.1)
C(9)-C(10)	1.513 (0.003)	C(9)-C(8)-C(7)	106.2 (0.2)
		C(10)-C(9)-C(8)	110.1 (0.2)
		C(9)-C(10)-C(6)	106.2 (0.2)

EXPERIMENTAL

M.ps. are uncorrected and have been determined in a melting point BÜchi 510 apparatus. UV, IR and ^1H NMR spectra were recorded on Perkin-Elmer instruments, models Lambda 5, 681 and R-24, respectively, and the 200 MHz ^1H NMR and ^{13}C NMR with a varian XL-200. Mass spectra were run in a Hewlett-Packard 5930A spectrometer and high resolution MS with an updated AIE instrument, model 902 S. Evaporative distillations were performed with a BÜchi Kugelrohrofen GKR-50 and, unless otherwise stated, all chromatographic purifications were performed on silica gel, using hexane-EtOAc mixtures of increasing polarity as eluent. All solvents were dried and distilled before use, and reactions were usually run under an atmosphere of dry N_2.

endo-4,7-Dioxo-cis-bicyclo(3.3.0)octane-2-acetaldehyde, (7)2,2-dimethyltrimethylene)acetal, 9.

A) From lactone 6 by DIBAL reduction: i) To a solution of lactone 6 (1.47 g, 5.5 mmol) in a 5:3 mixture of benzene:ether (80 mL), cooled at -5°C, a 20% solution of DIBAL in hexane (7.32 mL, 7.17 mmol) was added via syringe and the reaction mixture stirred at low temperature for 35 min. Water (5 mL) was then added to destroy the excess of hydride and the resulting mixture diluted with dichloromethane (500 mL), dry and the solvents evaporated to give the hydroxyaldehyde 7 (1.58 g) in quantitative yields. The product was used for the next operation without any further purification. IR (film), 3500, 2730, 1730, 1065 and 1030 cm^{-1}; ^1H NMR 60 MHz ($CDCl_3$): 0.97 (s, 6H), 1.2-2.7 (complex multiplet, 11H), 3.45 (s, 4H), 4.22 (m, 1H) and 9.75 (m, 1H).

ii) The above crude hydroxyaldehyde 7 was dissolved in dichloromethane (30 mL), cooled at 0°C, and pyridinium chlorochromate (1.78 g, 8.26 mmol) and celite (1.78 g) were added. The mixture was stirred at room temperature for 6 h, diluted with ether (100 mL), filtered through a column of silica gel (15 g) and washing with ether (500 mL). Evaporation of the solvent gave a colorless oily material which was purified by column chromatography (40 g of silica gel), to afford the ketoaldehyde 9 (0.850 g) in 58% overall yield from lactone 6. The analytical sample was prepared by evaporative distillation at 210°C/0.25 torr. IR ($CHCl_3$): 2960, 2870, 2730, 1740, 1730, 1470, 1400, 1330, 1110 and 1010 cm^{-1}; ^1H NMR 60 MHz ($CDCl_3$): 0.89 (s, 3H), 1.05 (s, 3H), 1.30-3.00 (complex m, 11H), 3.30 (s, 2H), 3.40 (s, 2H) and 9.72 (s, 1H); MS m/e (%): 266 (M^+, 67), 249 (18), 238 (29), 167 (42), 154 (82), 128 (75), 41 (100). Anal. calcd. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.57; H, 8.60%.

B) From lactone 6 by $LiAlH_4$ reduction: i) To a stirred suspension of lithium aluminum hydride (4.56 g. 120 mmol) in anhydrous ether (120 mL), cooled with an ice bath, a solution of lactone 6 (11.26 g, 42 mmol) in THF (180 mL) was added dropwise. The reaction mixture was stirred at room temperature for 2 h, it was then cooled with an ice bath and diluted with dichloromethane. The intermediate complex was destroyed by adding dropwise a saturated solution of sodio-potassium tartrate (15 mL). The excess of water was eliminated by anhydrous sodium sulphate, filtration and evaporation of the solvents under vacuum to give the dihydroxy compound 8 (11.48 g) in quantitative yield. IR (KBr): 3300, 2960, 2860, 1115, 1070 and 1020 cm^{-1}; ^1H NMR 60 MHz ($CDCl_3$): 0.96 (s broad, 6H), 1.0-3.0 (complex m, 17H), 3.45 (s broad, 4H), 3.60 (m, 3H), 4.10 (m, 1H).

ii) To a solution of the above dihydroxy compound in dichloromethane (80 mL), cooled at 0°C, pyridinium chlorochromate (28 g, 130 mmol) and celite (30 g) were added and the mixture stirred at room temperature for 8h. In order to remove the chromium salts, the reaction mixture was then diluted with ether (600 mL), filtered through a column of silica gel and washing with ether (1 L), and the combined organic solution evaporated under vacuum to afford the ketoaldehyde 9 (8.26 g, 73% overall yield from lactone 6).

exo- and endo-9-Hydroxytricyclo(5.2.1.$0^{4,10}$)decan-2,5-dione, 10 and 11.

A) To a solution of ketoaldehyde 9 (7.3 g, 27.4 mmol) in acetone (500 mL), aqueous 3M HCl (90 mL) was added and the mixture stirred at room temperature for 3 days; it was then neutralized with sodium bicarbonate (25 g), filtered and the acetone removed under vacuum. The resulting aqueous solution was extracted with dichloromethane, the combined organic extracts dried, the solvent evaporated under vacuum and the residue chromatographed on silica gel (150 g) to give:

i) the acetal 12 (1.45 g), in 20% yield, as a colorless solid, m.p. 119-121°C. The analytical sample was prepared by recrystallization from dichloromethane:hexane. IR ($CHCl_3$): 2960, 1740, 1470, 1170, 1150, 1130, 1115, 1020, and 980 cm^{-1}; ^1H NMR 200 MHZ ($CDCl_3$): 0.73 (s, 3H), 1.19 (s, 3H), 1.8-3.2 (complex m, 11H), 3.44 (d, J_{AB} = 11.1Hz, 2H), 3.62 (d, J_{AB} = 11.1Hz, 2H), 4.51 (t, J = 4.6Hz, 1H); MS, m/e (%) : 266 (M^+, 3), 265 (1), 238 (0.5), 181 (7), 163 (5), 137 (5), 135 (8), 115 (100), 97 (5), 82 (4), 69 (55), 56 (22), and 41 (15). Anal. calcd. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.43; H, 8.42%.

ii) the endo-aldol 10 (1.56 g), in 32% yield, as a colorless solid, m.p. 165-166°C (from ethyl acetate). IR ($CHCl_3$): 3600, 3550, 2950, 1740, 1400, 1170, 1090, and 1000 cm^{-1}; ^1H NMR 200 MHz ($CDCl_3$): 1.73 (half part of an AB system, J_1 = 9.5Hz, J_2 = J_3 = 1.3Hz, H_{10} endo), 2.01 (half part of an AB system, J_1 = 9.5Hz, J_2 = 5.4Hz, J_3 = 2.5Hz, H_{10}, exo), 2.27-3.19 (complex m, 7H), 3.62 (q, J = 7.1Hz, 1H), and 4.40 (dd of d, J_1 = 4.2Hz, J_2 = 2.5Hz, J_3 = 1.3Hz, 1H, CHOH); MS, m/e (%): 180 (M^+, 32), 162 (85), 134 (73), 121 (50), 107 (30), 92 (55), 91 (65), 83 (100), 79 (71), 77 (52), 66 (86), 55 (98), 53 (77), 41 (54), and 39 (63). Anal. calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.75; H, 7.05%.

iii) the exo-aldol 11 (0.876 g) in 18% yield, as colorless crystals, m.p. 144-145°C. IR ($CHCl_3$): 3600, 3450, 2950, 1740, 1400, 1170, 1090, and 1010 cm^{-1}; ^1H NMR 200MHz ($CDCl_3$): 0.94 (half part of an AB system, J_1 = 6.9Hz, J_2 = 5.2Hz, J_3 = 1.8Hz, $1H_{10}$ endo), 2.01 (half part of an AB system, J_1 = 6.9Hz, J_2 = 3.2Hz, J_3 = 1.0Hz, H_{10}, exo), 2.1-3.3 (complex m, 7H), 3.70 (q, J =

5.5Hz, 1H), 4.46 (d of t, J_1 = 1.8Hz, J_2 = J_3 = 1.0Hz, 1H, CHOH); MS, m/e (%): 180 (M^+, 23), 162 (10), 134 (8), 121 (7), 98 (14), 91 (12), 83 (52), 82 (100), 66 (15), 55 (34), and 41 (22). Anal. calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.82; H, 6.92%.

B) In a similar operation (starting from 5.67 g of ketoaldehyde 9), in which the reaction time was lenghtened for 10 days, besides the acetal 12 (0.484 g, 8% yield) and the mixture of exo and endo aldols, 10 and 11 (1.423 g, 37% yield), a third aldol 17 (X =OH) (0.134 g), m.p. 206-208°C (from ethyl acetate) was isolated in 3% yield. IR ($CHCl_3$): 3450, 2960, 1750, 1410, 1160, and 1070 cm^{-1}; ^1H NMR 200 MHz ($CDCl_3$): 1.69 (half part of an AB system, J_1 = 12.4Hz, J_2 = 11.3Hz, J_3 = 3.4Hz, J_4 = 1.7Hz, H_{10}), 2.06 (half part of an AB system, J_1 = 12.4Hz, J_2 = 6.2Hz, J_3 = 2.8Hz, J_4 = 1.1Hz, $H_{10'}$), 2.24-2.98 (complex m, 9H), 4.02 (dd of d, J_1 = 11.3Hz, J_2 = 6.2Hz, J_3 = 4.5Hz, 1H, CHOH); MS, m/e (%): 180 (M^+, 3), 153 (0.3), 138 (13), 121 (2), 102 (6), 91 (18), 79 (21), and 60 (100). Anal. calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.30; H, 7.03%.

exo-and endo-9-Phenylselenotricyclo(5.2.1.$0^{4,10}$)decan-2,5-dione, 15 and 16.

A) A mixture of the aldols 10 and 11 (2.4 g, 13.5 mmol) was dissolved in dichloromethane (100 mL), triethylamine (3.6 mL) added and, under stirring and cooling by means of an ice bath, methanesulfonyl chloride (2.39 mL, 30.6 mmol) was added dropwise. The reaction mixture was stirred at 0°C for 5 h, in the dark, and then diluted with dichloromethane and washed with 2M HCl, saturated sodium bicarbonate and saturated sodium chloride solutions. The organic layer was dried and the solvent evaporated under vacuum to afford a crude material (6.70 g) that was used for the next operation (see B).

For the spectroscopic characterization of the methanesulphonates, 13 and 14, a similar operation starting from 0.630 g of ketoaldehyde 9 was performed. The methanesulfonates were prepared from the crude mixture of aldols and using pyridine as the base; purification by column chromatography on silica gel (15 g) gave:

i) acetal 12 (0.034 g) in 5% overall yield from ketoaldehyde 9,

ii) endo-methanesulfonate 13 (0.106 g), colorless crystals, m.p. 133-134°C , in 17% overall yield. IR ($CHCl_3$): 3020, 2960, 1750, 1350, 1180, 950 and 900 cm^{-1}; ^1H NMR 200 MHz ($CDCl_3$): 2.0-3.4 (complex m, 9H), 2.95 (s, 3H), 3.75 (q, J = 9.6Hz, 1H), 5.36 (d of t, J_1 = 6.4Hz, J_2 = J_3 = 3.2Hz, 1H, $CHSO_3CH_3$); MS, m/e (%): 258 (M^+, 3), 179 (0.8), 162 (100), 136 (53), 135 (53), and 120 (50). Anal. calcd. for $C_{11}H_{14}O_5S$: C, 51.16; H, 5.43. Found: 51.11; H, 5.36%.

iii) exo-methanesulfonate 14 (0.054 g), colorless crystals, m.p. 185-186°C (9% overall yield). IR ($CHCl_3$): 3030, 2960, 1750, 1360, 1110, 960, 920, and 850 cm^{-1}; ^1H NMR 200 MHz ($CDCl_3$): 1.08 (dd of d, J_1 = 14Hz, J_2 = 12Hz, J_3 = 4Hz, 1H), 1.8-3.3 (complex m, 9H), 3.11 (s, 3H), 3.77 (q, J = 10Hz, 1H), and 5.16 (d, J = 4Hz, CHO_3SCH_3); MS, m/e (%): 258 (M^+, 4), 179 (3), 169 (19), 160 (48), and 83 (100). Anal. calcd. for $C_{11}H_{14}O_5S$: C, 51.16; H, 5.43. Found: 51.23; H, 5.45%.

iv) methanesulfonate 17 (X = OMs) (0.035 g), as colorless crystals, m.p. 188-190°C (6% overall yield). IR ($CHCl_3$): 3015, 2970, 1750, 1360, 1170, 1010, 960, 920, and 840 cm^{-1}; ^1H NMR 200 MHz ($CDCl_3$): 1.9-3.0 (complex m, 10H), 3.11 (s, 3H), 4.99 (dd of d, J_1 = 11.2Hz, J_2 = 6.9Hz, J_3 = 4.3Hz, CHO_3SCH_3); ^{13}C NMR (d-acetone): 32.73 (t), 36.74 (d), 39.06 (q), 39.64 (t), 40.71 (d), 47.45 (t), 53.63 (d), 55.70 (d), 75.90 (d), 211.94 (s), and 215.59 (s); MS, m/e (%): 258 (M^+, 10), 216 (7), 174 (17), 162 (17), 138 (62), and 91 (100). Anal. calcd. for $C_{11}H_{14}O_5S$: C, 51.16; H, 5.43. Found: C, 51.19; H, 5,43%.

B) To a solution of diphenyl diselenide (4.22 g, 13.5 mmol) in THF (100 mL), 50% aqueous hypophosphorous acid (7.13 g, 135 mmol) was added and the mixture heated under reflux for 20 min. It was then cooled at room temperature, diluted with benzene (400 mL), dried over magnesium sulphate, and filtered under an atmosphere of N_2. 1.6M n-butyllithium in hexane (18.6 mL, 29.7 mmol) was introduced via syringe, the mixture stirred at room temperature for 10 min, and a solution of the mixture of crude methanesulphonates (6.7 g) in THF (20 mL) was then added, and stirring continued for 5 h. The reaction mixture was washed with saturated ammonium chloride solution, dried, and the solvents evaporated under vacuum. The resulting crude material (6.9 g) that was chromatographed on silica gel (120 g) to afford two fractions:

i) exo-selenide 15 (3.00 g), as a colorless solid, m.p. 138-139°C (70% overall yield from aldols). IR (KBr): 2960, 2820, 1740, 1730, 1570, 1435, 1250, 1150, 1010, 730, and 690 cm^{-1}; ^1H NMR 200 MHz ($CDCl_3$): 1.24 (dd of d, J_1 = 14.7Hz, J_2 = 12.2Hz, J_3 = 5.6Hz, 1H), 2.06 (dd of t, J_1 = 14.7Hz, J_2 = 7.0Hz, J_3 = 1.4Hz, 1H), 2.0-3.4 (complex m, 7H), 3.65 (q, J = 10.0Hz, apical H), 4.0 (d of t, J_1 = 5.6Hz, J_2 = J_3 = 1.4Hz, CHSePh), 7.27 (m, 3H), and 7.52 (m, 2H); ^{13}C NMR ($CDCl_3$): 37.95 (d), 39.85 (t), 40.57 (t), 43.19 (t), 43.93 (d), 45.34 (d, 2C), 59.30 (d), 127.77 (d), 129.30 (d, 2C), 129.42 (s), 133.96 (d, 2C), 216.83 (s), and 218.42 (s); MS, m/e (%): 320/318 (M^+, 7/4), 163 (19), 159/157 (9/6), and 135 (100).

ii) endo-selenide 16 (0.299 g), as a heavy oily material, in 7% overall yield from the aldols. IR ($CHCl_3$): 3000, 2960, 1740, 1570, 1470, 1440, 1410, 1155, and 690 cm^{-1}; ^1H NMR 200 MHz ($CDCl_3$): 1.2 (t of d, J_1 = 12.0Hz, J_2 = J_3 = 11.4Hz, 1H), 2.2-3.1 (complex m, 8H), 3.56 (q, J = 10.8Hz, apical H), 3.60 (dd of d, J_1 = 12.0Hz, J_2 = 8.4Hz, J_3 = 6.0Hz, CHSePh), 7.27 (m, 3H), and 7.55 (m, 2H); MS, m/e (%): 320/318 (M^+, 9/5), 279 (1.7), 234 (11), 180 (7), 162 (51), 135 (32), 134 (100), 119 (13), 105 (12), 95 (27), 85 (28), and 83 (50).

Tricyclo(5.2.1.$0^{4,10}$)decan-9-en-2,5-dione, 18.

To a stirred solution of sodium periodate (0.33 g, 1.54 mmol) in water (3 mL), the exo-selenide 15 (0.237 g, 0.74 mmol), dissolved in methanol (13 mL), was added dropwise and the mixture stirred at room temperature for 1 h. A saturated solution of sodium bicarbonate was then added, extracted with dichloromethane, the organic layer dried and the solvents evaporated off, to give the conjugated ketone 18 (0.100 g) as a colorless oily material, in 83% yield. The analytical sample was prepared by t.l.c. on silica gel and eluting with a 3:7 mixture of hexane:ethyl acetate. UV (ethanol), λ_{max} = 244.8 nm (ϵ = 1860); IR ($CHCl_3$): 2940, 1735, 1720, 1620, 1435, 1400, 1165, 1110, 980, and 910 cm^{-1}; ^1H NMR 60 MHz ($CDCl_3$): 1.1-4.1 (complex m, 9H) and 6.4 (m, 1H); MS, m/e (%): 162 (M^+, 100), 134 (31), 133 (18), 119 (34), 106 (27), and 105 (29).

exo-9-Phenylselenotricyclo(5.2.1.0^{4,10})decan-2,5-dione, bis(2,2-dimethyltrimethylene)acetal, 19.

A mixture of the exo-selenide 15 (1.516 g, 3.62 mmol) 2-ethyl-2,5,5-trimethyl-1,3-dioxane (16.33 g, 103.3 mmol), 2,2-dimethyl-1,3-propanediol (0.31 g, 2.98 mmol), and a few crystals of p-toluenesulfonic acid, was stirred at room temperature for 7 days. It was then diluted with benzene (100 mL), neutralized with triethylamine, dried, the solvents evaporated under vacuum, and the excess of 2-ethyl-2,5,5-trimethyl-1,3-dioxane eliminated under high vacuum. The resulting residue was chromatographed on silica gel (65 g) to afford the bis-acetal 19 (2.147 g), as colorless crystals of m.p. 130-133°C, in 92% yield. IR (CCl_4): 2960, 2870, 1470, 1400, 1340, 1220, 1110, 1020, 1000, 910, and 700 cm^{-1}; ^{1}H NMR 200 MHz ($CDCl_3$): 0.84 (s, 3H), 0.93 (s, 3H), 0.99 (s, 3H), 1.03 (s, 3H), 1.2-3.0 (complex m, 10H), 3.5 (m, 9H), 7.27 (m, 3H), 7.59 (m, 2H); MS, m/e (%): 492-490 (M^+, 0.6/0.4), 335 (100), 269 (5), 249 (12), 205 (6), 163 (37), and 135 (63). Anal. calcd. for $C_{26}H_{36}O_4Se$: C, 63.53; H, 7.38. Found: C, 63.51; H, 7.40%

Tricyclo(5.2.1.0^{4,10})dec-8-ene-2,5-dione, bis(2,2-dimethyltrimethylene)acetal, 20.

To a stirred solution of the bis-acetal 19 (2.085 g, 4.25 mmol) in dichloromethane (60 mL), cooled at -78°C, 85% MCPBA (1.056 g, 5.20 mmol) in the same solvent (25 mL) was added dropwise and the mixture stirred at low temperature for 2 h, the reaction being monitored by t.l.c. It was then poured into refluxing CCl_4, in which diethylamine (1.6 mL) had been previously added, and the reflux was continued for 30 min. After cooling at room temperature the reacción mixture was washed with 2M HCl and saturated solution of sodium bicarbonate. The organic layer was dried, the solvents evaporated off and the residue chromatographed on silica gel (60 g) to afford the olefin 20 (1.359 g), as a colorless solid, m.p. 122-125°C, in 96% yield. IR (CCl_4): 2960, 2860, 1470, 1400, 1335, 1310, 1120, 1110, and 1090 cm^{-1}; ^{1}H NMR 200 MHz ($CDCl_3$): 0.83 (s, 3H), 0.93 (s, 3H), 0.95 (s, 3H), 0.99 (s, 3H), 1.1-3.1 (complex m, 8H), 3.5 (m, 8H), 5.54 (half of an AB system, J_1 = 5.4Hz, J_2 =J_3 = 1.8Hz, 1H), and 5.80 (half of an AB system, J_1 = 5.4Hz, J_2 = J_3 = 1.8Hz, 1H); MS, m/e (%): 334 (M^+, 20), 319 (5), 268 (5), 255 (3), 248 (5), 219 (42), 205 (6), 192 (7), 179 (12), 154 (39), 141 (52), and 128 (41). Anal. calcd. for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Found: C, 71.70; H, 9.24%.

Hydroboration/Oxidation of olefin 20: exo-8-Hydroxy- and exo-9-Hydroxytricyclo(5.2.1.0^{4,10})decane-2,5-dione, bis(2,2-dimethyl-trimethylene)acetal, 22 and 21.

To a solution of the olefin 20 (0.125 g; 0.37 mmol) in THF (2 mL), cooled at 0°C, 11.9M $BH_3.SMe_2$ complex (40 L, 0.48 mmol) was added via syringe and the mixture stirred for 4h. It was then hydrolyzed with water (2 mL), 30% hydrogen peroxide (0.5 mL) added, and the mixture stirred at 40°C for 1h. The aqueous solution was saturated with sodium chloride and extracted several times with ethyl acetate. The organic solution was dried and the solvent evaporated off and the resulting crude material (0.160 g) was chromatographed on silica gel (10 g) to give, in a 92% overall yield, the two monohydroxy derivatives in a relative ratio of 40:60:

i) the exo-9-hydroxy derivative 21 (54 mg), as a colorless solid, m.p. 217-218°C. IR (CCl_4): 3600, 2940, 2860, 1470, 1390, 1360, 1330, 1215, 1100, 1060, 1020, 990, and 900 cm^{-1}; ^{1}H NMR 200 MHz ($CDCl_3$): 0.88 (s, 3H), 0.90 (s, 3H), 1.01 (s, 3H), 1.04 (s, 3H), 1.1-2.6 (complex m, 8H), 2.72 (q, 1H), and 3.0 (q, 1H); MS, m/e (%): 352 (M^+, 6), 337 (1), 335 (1), 334 (1), 324 (1), 284 (1), 266 (24), 154 (59), 141 (38), 128 (61), and 69 (100). Anal. calcd. for $C_{20}H_{32}O_5$: C, 68.15; H, 9.15. Found: C, 67.96; H, 9.34%.

ii) the exo-8-hydroxy derivative 22 (79 mg), as a colorless solid, m.p. 183-186°C. IR (CCl_4): 3620, 2950, 2830, 1470, 1400, 1340, 1210, 1110, 1015, 990, and 900 cm^{-1}; ^{1}H NMR 60 MHz ($CDCl_3$): 0.80 (s, 3H), 0.83 (s, 3H), 1.5 (s, 6H), 1.2-3.2 (complex m, 10H), 3.4 (m, 8H), 4.15 (m, 1H, CHOH); MS, m/e (%): 352 (M^+, 23), 337 (9), 334 (11), 267 (9), 265 (11), 255 (9), 248 (20), 237 (55), 179 (36), and 167 (100).

Oxidation of the exo-9-hydroxy derivative 21: Tricyclo (5.2.1.0^{4,10})decane-2,5,9-trione, (2,5)bis-(2,2-dimethyltrimethylene)acetal, 23.

A solution of the exo-hydroxy derivative 21 (0.120 g, 0.48 mmol) in dichloromethane (10 mL) was cooled at 0°C, and pyridinium chlorochromate (0.134 g, 0.62 mmol) and celite (0.140 g) were added, and the mixture stirred at room temperature for 12 h. The reaction mixture was then diluted with ether (50 mL) and the organic solution separated from the insoluble chromium salts which were thoroughly washed with ether. The combined ether extracts were filtered through silica gel, the solvent evaporated off, and the residue (0.100 g) purified by column chromatography on silica gel (5 g), to give the monoketone 23 (84 mg), as colorless crystals, m.p. 226-228°, in 71% yield. IR (CCl_4): 2920, 2830, 1725, 1450, 1305, 1290, 1200, 1100, 1080, 1000, and 880 cm^{-1}; ^{1}H NMR 200 MHz ($CDCl_3$): 0.87 (s, 3H), 0.88 (s, 3H), 1.05 (s, 3H), 1.07 (s, 3H), 1.5-3.3 (complex m, 10H), and 3.3 (m, 8H); ^{13}C NMR ($CDCl_3$): 22.2 (q, 2C), 22.5 (q, 2C), 29.9 (s, 2C), 32.2 (d), 39.0 (t), 41.5 (t), 43.3 (d), 46.6 (t), 47.4 (d), 54.7 (d), 71.0 (t), 71.7 (t), 72.8 (t), 72.9 (t), 109.7 (s), 109.8 (s), and 216.9 (s); MS, m/e (%): 350 (M^+, 41), 335 (7), 322 (21), 281 (38), 265 (8), 235 (59), 209 (30), 179 (13), 167 (13), 128 (48), and 41 (100). Anal. calcd. for $C_{20}H_{30}O_5$: C, 68.54; H, 8.63. Found: C, 68.83; H, 8.63%.

Oxidation of the exo-8-hydroxy derivative 22: Tricyclo(5.2.1.0^{4,10})decane-2,5,8-trione, (2,5)-bis(2,2-dimethyltrimethylene)acetal, 24.

A solution of the exo-8-hydroxy derivative 22 (79 mg, 0.26 mmol) in dichloromethane (5 mL) was cooled at 0°C, and pyridinium chlorochromate (0.100 g, 0.46 mmol) and celite (0.115 g) were added, and the mixture stirred at room temperature for 6 h. The reaction mixture was then diluted with ether (50 mL) and the organic solution separated from the insoluble chromium salts which were thoroughly washed with ether. The combined ether extracts were filtrated through silica gel, the

solvent evaporated off, and the residue (85 mg) purified by column chromatography on silica gel (5 g), to give the monoketone 24 (73 mg), as colorless crystals, m.p. 174-176°C, in 93% yield. IR (CCl_4): 2950, 2860, 1740, 1460, 1390, 1340, 1110, 1100, and 1020 cm^{-1}; ^1H NMR 200 MHz ($CDCl_3$): 0.91 (s, 3H), 0.96 (s, 3H), 0.966 (s, 3H), 0.974 (s, 3H), 1.9-3.0 (complex m, 9H), 3.2 (m, 1H), 3.38 (half of an AB system, J_{AB} = 8Hz, 2H), 3.40 (half of an AB system, J_{AB} = 8Hz, 2H), 3.49 (s, 2H), and 3.54 (s, 2H); ^{13}C NMR ($CDCl_3$): 22.34 (q), 22.42 (q), 22.51 (q), 22.54 (q), 29.90 (s), 29.97 (s), 32.74 (t), 35.99 (t), 39.12 (t), 42.27 (d), 46.04 (d), 46.07 (d), 48.12 (d), 71.45 (t), 71.61 (t), 72.57 (t, 2C), 109.15 (s), 110.28 (s), and 220.73 (s); MS, m/e (%): 350 (M^+, 17), 335 (1), 322 (0.3), 294 (6), 264 (4), 234 (6), 167 (11), 154 (35), 128 (20), and 41 (100). Anal. calcd. for $C_{20}H_{30}O_5$: C, 68.54; H, 8.63. Found: C, 68.59; H, 8.76%.

Tricyclo(5.2.1.$0^{4,10}$)decane-2,5,8-trione, 4.

To a solution of ketone bis-acetal 24 (0.31 g, 0.88 mmol) in THF (20 mL), 2M HCl (10 mL) was added and the mixture stirred at room temperature for 48 h. It was then neutralized with sodium bicarbonate, the two layers separated and the aqueous one extracted several times with ethyl acetate. The combined organic extracts were dried and the solvents evaporated off to afford the monoacetal 25 (0.220 g) in 94% yield, which was converted by further acid hydrolysis to the trione 4 as described in a previous communication.[1]

X-Ray diffraction analysis of compound 10.-Crystal data.

Compound 10: $C_{10}H_{12}O_3$, F_w = 180.2, monoclinic, a = 11.501(3), b = 11.858(3), c = 6.259(2) Å, β = 97.17(2)°, V = 846.9(57) $Å^3$, $P2_1/n$, D_x = 1.413 g cm^{-3}, Z = 4, F(000) = 384, λ(Mo K_α) = 0.71069 Å, μ = 1.12 cm^{-1}. 288°K.

A prismatic crystal (0.1 x 0.1 x 0.15 mm) was selected and mounted on a Philips PW-1100 four circle diffractometer. Unit-cell parameters were determined from 25 reflections ($4 \leqslant \theta \leqslant 12°$) and refiend by least-squares method. Intensities were collected with graphite monochromatized Mo K_α radiation, using the ω-scan technique, with scan width 0.8° and scan speed 0.03° s^{-1}. 1349 independent reflections were measured in the range $2 \leqslant \theta \leqslant 25°$; 1238 of which were assumed as observed applying the condition $I \geqslant 2.5\ \sigma(I)$. Three reflections were measured every two hours as orientation and intensity control, significant intensity decay was not observed. Lorentz-polarization, but not absorption, corrections were made.

The structure was solved by direct methods, using the MULTAN84 system of computer programs[10] and refined by full-matrix least-squares, using SHELX76 program.[11] The function minimized was $\sum\omega\,||Fo| - |Fc||^2$, where $w = (\sigma^2(Fo) + 0.014\ |Fo|^2)^{-1}$. All hydrogen atoms were located from a difference synthesis and refined with an overall isotropic temperature factor and anisotropically the remaining atoms. The final R values was 0.056 (wR = 0.060) for all observed reflections.

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REFERENCES

1. a) E. Carceller, M.Ll. García, A. Moyano, M.A. Pericàs, and F. Serratosa, Tetrahedron, 1986, 42, 1831; b) C. Almansa, E. Carceller, A. Moyano, and F. Serratosa, Tetrahedron, 1986, 42, 3637.
2. M.O. Osborn, S. Kuroda, J.L. Muthard, J.D. Kramer, P. Engel, and L.A. Paquette, J. Org. Chem., 1981, 46, 3379.
3. F. Serratosa, "Dodecahedrane: A Synthetic Objective", Main Section Lecture delivered at ESOC II, Stresa (Italy), 1981.
4. E. Carceller, M.Ll. García, A. Moyano, and F. Serratosa, J. Chem. Soc., Chem. Commun., 1984, 824.
5. P. Deslongchamps, U.O. Cheriyan, Y. Lambert, J.C. Mercier, L. Ruest, R. Russo, and P. Sovey, Can. J. Chem., 1978, 56, 1687.
6. A.B. Smith III and R.M. Scarborough, Tetrahedron Letters, 1978, 1649.
7. D.L.J. Clive, Tetrahedron, 1978, 34, 1049.
8. J.K. Whitesell and R.S. Matthews, J. Org. Chem., 1977, 42, 3878.
9. M.Ll. García, Ph. D. Thesis (in preparation); unreported results.
10. P. Main, S.L. Fiske, S.E. Hull, L. Lessinger, G. Germain, J.P. Declerçq, and M.M. Woolfson, '1984 MULTAN: A system of computer programs for crystal structure determination from X-ray diffraction data. University of York (U.K.) and University of Louvain (Belgium)'.
11. G.M. Sheldrick, 'SHELX: A computer program for crystal structure detrmination', 1976, University of Cambridge (U.K.).