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SYNTHESIS OF TRICYCLO(5.2.1.$0^{4,10}$)DECANE-2,5,8-TRIONE FROM DESLONGCHAMPS'S DIKETONE

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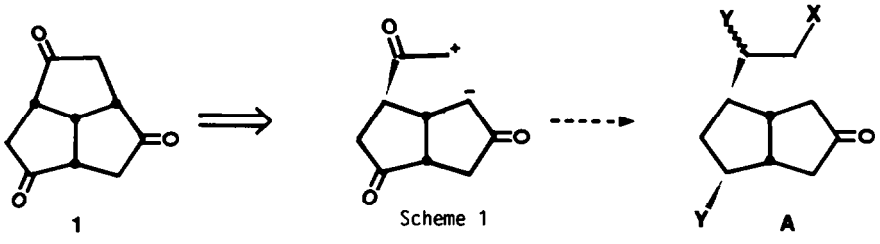
Abstract.- Tricyclo(5.2.1.$0^{4,10}$)decane-2,5,8-trione (1) has been synthesized by base-induced cyclization of intermediates of type A readily available from Deslongchamps's diketone 2.

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

In a previous publication[1] we have discussed some different strategies we have developed for the preparation of triketone 1 which include: i) the regioselective functionalization of either triquinacene or some of its simple derivatives; ii) the "two-bond disconnection", and iii) the "three-bond disconnection" strategies. In the present communication we give full experimental details of the so-called "one-bond disconnection strategy" that proceeds through intermediates of type A, in which X is a good leaving group -such as a halide or a sulfonyloxy- and Y a latent carbonyl group (Scheme 1).

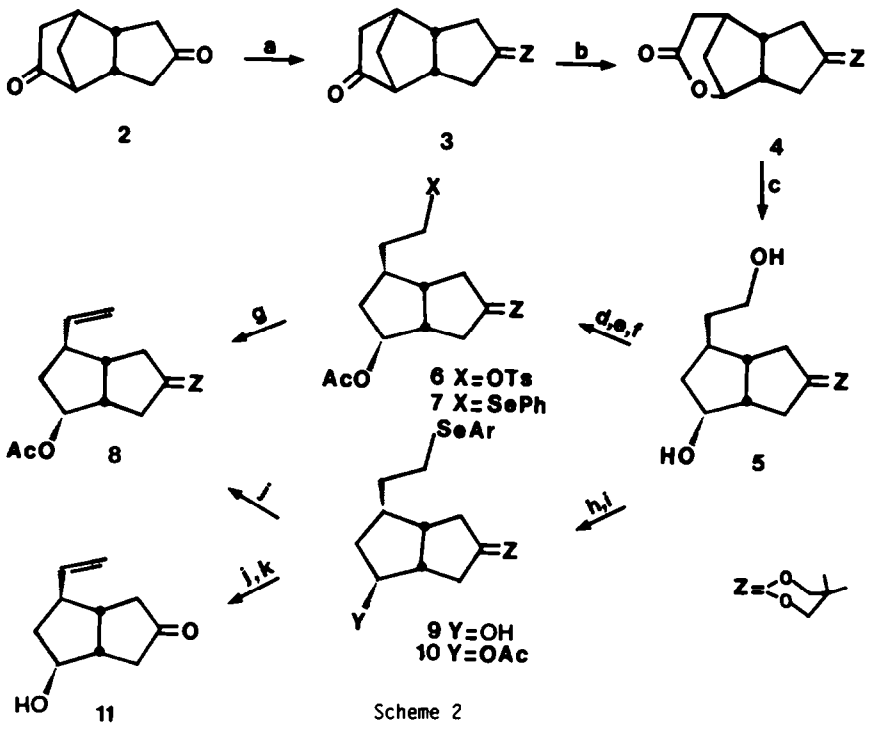


Scheme 1

The starting point of this synthetic approach is the so-called "Deslongchamps's diketone" (2), which we prepared from endo-dicyclopentadiene as previously reported.[2,3]

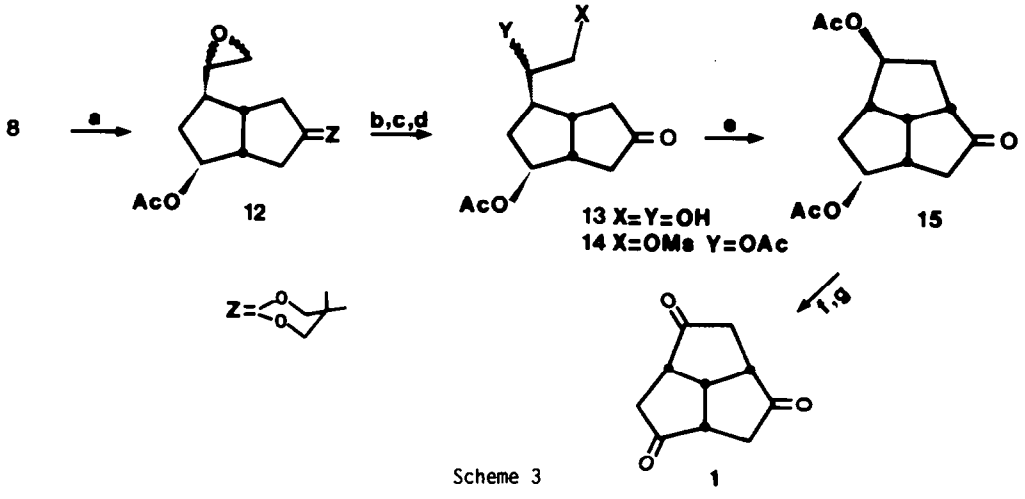
Diketone 2 was monoprotected as the cyclic acetal 3 (Scheme 2), then oxidized with MCPBA to lactone 4 and finally reduced to diol 5 with lithium aluminum hydride as described.[4] The primary alcohol was selectively activated as the tosylate and the secondary one protected as the acetate (5 ⟶ 6). Since the direct elimination of the tosyloxy group gave poor results, it was replaced by the phenylselenide group[5] (6 ⟶ 7) and then eliminated, after oxidation with MCPBA, to afford the olefin 8 in 39% overall yield from 4. Much better results were obtained when the primary hydroxyl group of diol 5 was directly converted, in 86% yield, into the corresponding o-nitrophenylselenide

9 by reaction with o-nitrophenylselenocyanate in the presence of tributylphosphine, according to the method reported by Grieco.[6] It is worthwhile to emphasize here the great chemoselectivity of this method which allows the reaction of a primary alcohol in the presence of an unprotected secondary hydroxyl group. Protection of this hydroxy group as the acetate (9 ⟶ 10) and oxidation with 30% hydrogen peroxyde afforded the olefin 8 in 73% overall yield from lactone 4.



Scheme 2

a) $(CH_3)_2C(CH_2\text{-}OH)_2$/TsOH/benzene; b) MCPBA/$CH_2Cl_2$; c) $LiAlH_4$/THF/ether; d) TsCl/pyr/CH_2Cl_2; e) Ac_2O/pyr; f) PhSeSePh/BuLi/benzene; g) MCPBA/CH_2Cl_2 $HNPr_2$-i/CCl_4; h) $NO_2PhSeCN/Bu_3P$/THF; i) Ac_2O/pyr; j) H_2O_2/THF; k) TsOPyr/acetone.



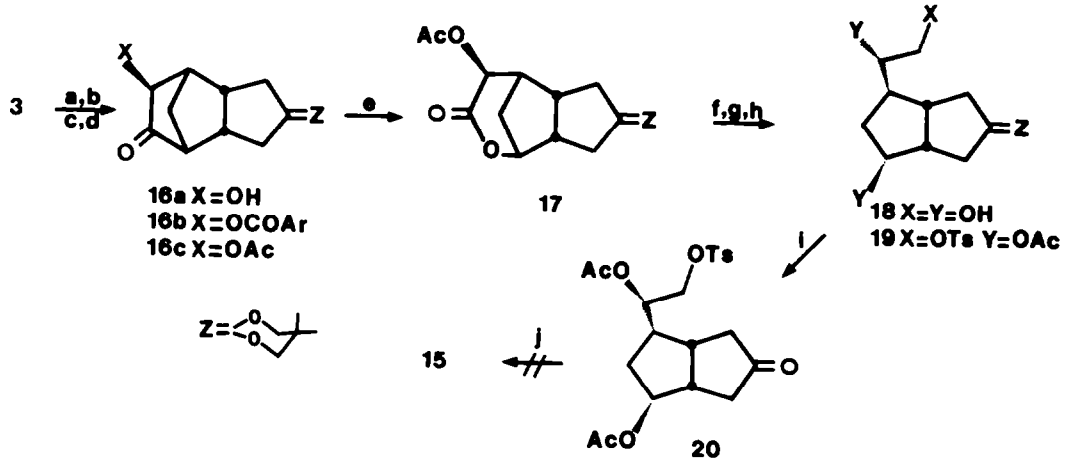
Scheme 3

a) MCPBA/CH_2Cl_2; b) Tartaric acid/H_2O; c) MsCl/pyr; d) Ac_2O/pyr; e)$KOBu^t$/THF; f) K_2CO_3/CH_3OH; g) PCC/CH_2Cl_2

Hydroxylation of the double bond with MCPBA gave a 60:40 mixture of diastereomeric epoxides 12 which was treated with aqueous tartaric acid for 5 days to afford the free diols 13 (Scheme 3). The primary hydroxy group was again activated as a mesylate and the secondary one protected as the corresponding acetate leading to a 70:30 mixture of mesylates 14 : base-induced cyclization with potassium tert-butoxide gave the tricyclic compound 15 in about 45% yield (10% from olefin 8), the less predominant diastereomer being recovered unchanged. Transesterification with methanol in the presence of p-toluenesulfonic acid and oxidation with PCC afforded the triketone 1 in 42% yield.

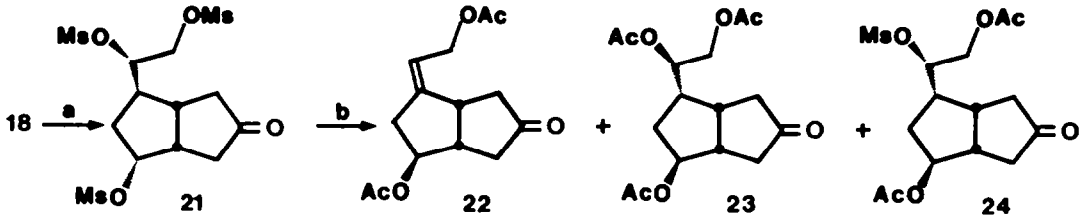
However, since only one of the two diastereomers 14 underwent cyclization under basic conditions, next we planned a completely stereoselective synthesis of this intermediate (Scheme 4). The monoprotected Deslongchamps's diketone 3 was hydroxylated at the alpha position of the free carbonyl group via the silyl enol ether and the corresponding epoxide[7], and then acetylated (3 ⟶ 16c), the acetoxy being at the exo side of the norbornane bridged system. Baeyer-Villiger oxidation with MCPBA, followed by lithium aluminum hydride reduction afforded a triol (18) in 65% overall yield from 16c. Once again, the primary hydroxyl group was activated as a tosylate and the secondary ones protected as acetates: only one diastereomer is now present, the stereochemistry of the secondary hydroxyl group on the side-chain being the one shown (19). All the attempts to induce cyclization of this diastereomer, after acid hydrolysis of the acetal group (19 ⟶ 20), failed. It seems clear that this diastereomer is the same one that was recovered unchanged in the cyclization step of the route previously reported. Most probably, eclipsing of the two oxy groups, in the transition state leading to the tricyclic compound, prevents cyclization to take place (20 ⟶ 15).

The solution to this problem was, in theory, very easy: making just the pertinent stereochemical correction of configuration by means of a S_N2 reaction (Scheme 5). For this, the trimesylate 21 was prepared from triol 18 and then heated under reflux with a solution of tetraethylammonium acetate in acetone for 12 h. Although some inversion was observed, the method is of little synthetic value since fully substitution (triacetate 23, 25% yield) competes with elimination (olefinic diacetate 22, 42% yield) and partial substitution (monomesylate 24, 25% yield), and the mixture could be only separated by careful column chromatography.



Scheme 4

a) BuLi/Me_3SiCl; b) MCPBA/CH_2Cl_2; c) $Et_3NH^+F^-/CH_2Cl_2$; d) Ac_2O/pyr; e) MCPBA/CH_2Cl_2; f) $LiAlH_4$/THF/ether; g) TsCl/pyr; h) Ac_2O/pyr; i) TsOH/acetone; j) $KOBu^t/Bu^tOH$

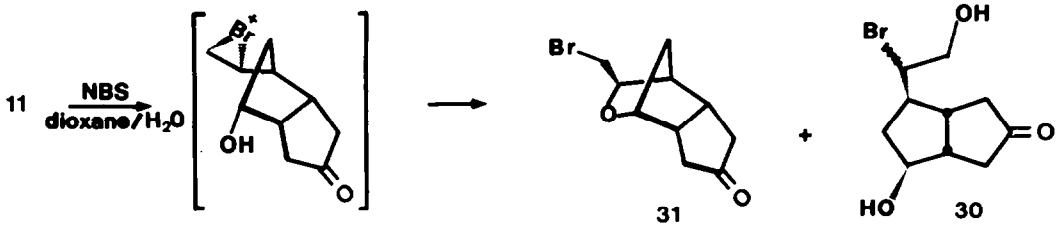


Scheme 5

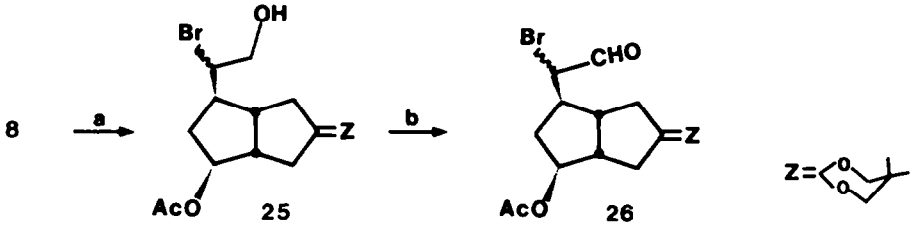
a) MsCl/pyr; b)$Et_4N^+OAC^-$/acetone

In view of this failure, we turned out our interest to the previously reported route from olefin 8 or, alternatively, 11, the bromohydrin formation from the double bond being studied under a variety of conditions.

In the first place, treatment of the hydroxy olefin 11 with NBS in dioxane/H_2O led in 46% yield to a tricyclo derivative 31 -which must be formed by an intramolecular attack of the endo-hydroxy group to the intermediate bromonium ion (Scheme 6)-, together with a 29% yield of bromo-hydrin 30, the structure of which was clear from the results obtained in the hydrobromination of the acetoxy olefin 8, which was also performed in order to prevent the observed intramolecular attack. Under the same conditions (Scheme 7), the acetoxy olefin 8 afforded a mixture of two diastereomeric bromohydrins 25 having the unwanted regiochemistry in which the bromine is at the secondary position of the side chain and the hydroxy group at the primary one as evidenced by the ^{13}C NMR spectrum and its oxidation to the aldehyde 26. Although the substituted secondary carbonium ion should be more stable than the primary one, owing to the steric hindrance of C-1 of the side chain, the nucleophilic attack takes place on the C-2 position to give the 1-bromo-2-hydroxyethyl 25 instead of the expected 1-hydroxy-2-bromoethyl derivative.



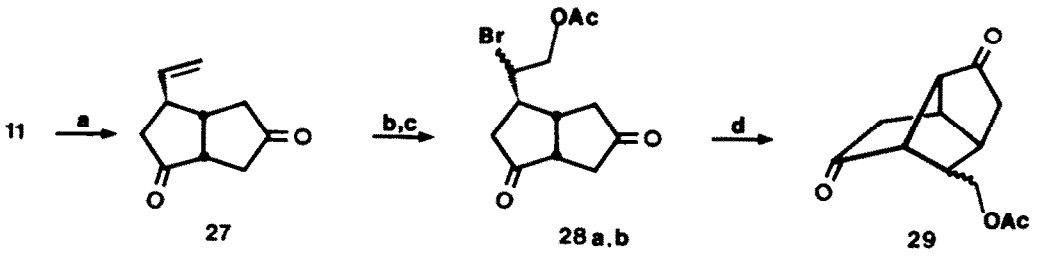
Scheme 6



Scheme 7

a) NBS/dioxane/H_2O; b) PCC/CH_2Cl_2

In order to reduce the steric hindrance resulting from the endo-hydroxy group attached to the bicyclic skeleton, it was oxidized to a carbonyl group (11 ⟶ 27) (Scheme 8). However, the resulting bromohydrins were again the unwanted regioisomers 28a and 28b, the base-induced cyclization of which led to a new polycyclic compound to which the structure 29 was tentatively assigned on the bases of its analytical and spectral data (see Experimental).

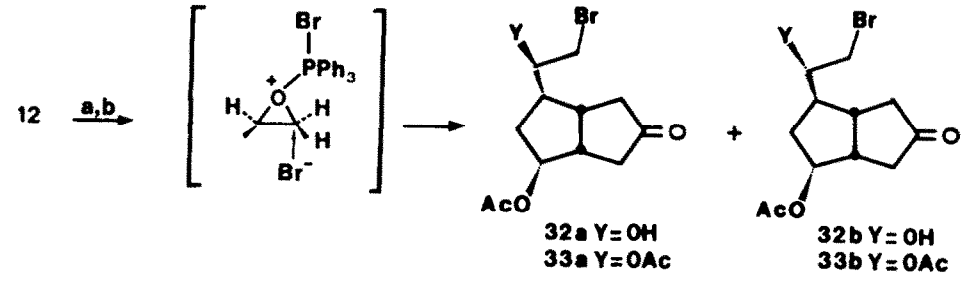


Scheme 8

a) PCC/CH_2Cl_2; b) NBS/dioxane/H_2O; c) Ac_2O/pyr; d) KOBu^t/THF

The bromohydrin 32, with the proper functionalization, could be finally prepared by the regioselective opening of oxiranes 12 with bromine in the presence of triphenylphosphine as reported by Palumbo and his coworkers. According to this method, the nucleophile attacks the less hindered position assisted by the bromotriphenylphosphonium ion (Ph_3P^+-Br), which plays the role of a Lewis acid and coordinates with the oxygen atom, being observed that the bulkier the nucleophile the higher the regioselectivity attained.[8]

The bromohydrin 32 was obtained as a mixture of two diastereomers which could be separated by column chromatography, followed by acetylation, affording 12% yield of 33a and 32% yield of the epimer 33b (Scheme 9).



Scheme 9

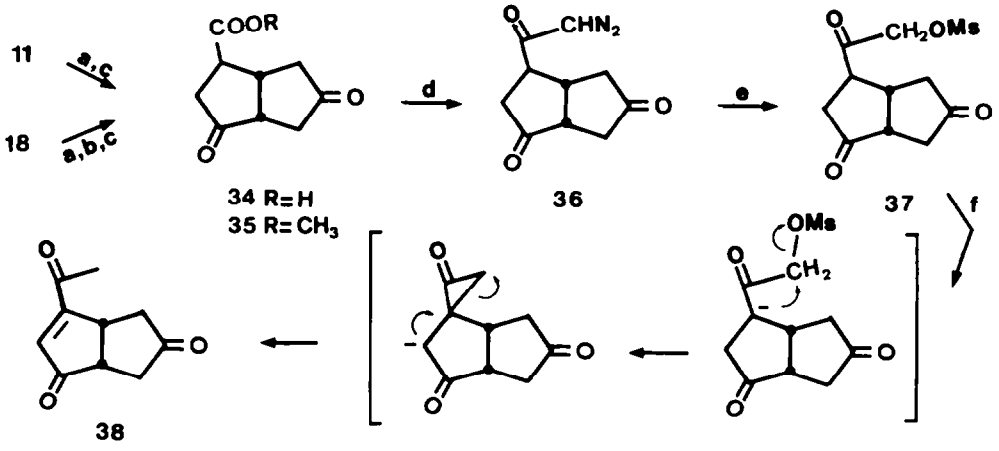
a) $Br_2/PPh_3/CH_2Cl_2$; b) Ac_2O/pyr

The less predominant isomer, with the proper stereochemistry at the C-1 position of the side chain, underwent an easy base-induced cyclization, promoted by potassium tert-butoxide, to the tricyclic compound 15 in very high yield (80%; 10% from olefin 8), which was isolated, after

chromatographic purification, as white crystals, m.p. 78-79°C, identical with the compound prepared from mesylate 14. Acid-induced methanolysis of the acetoxy groups and oxidation of the resulting diol with pyridinium chlorochromate/celite afforded in 42% yield the triketone 1 as white crystals, m.p. 170-172°C, identical in all respects with an authentic sample.[1,9]

Since the configuration of the secondary alcohol in the side chain of compound 13 is just irrelevant with regard to the desired final triketone 1, one way to obviate all the stereochemical inconveniences deriving from it is to abolish it in the synthetic intermediates. However, oxidation to a carbonyl group would present some problems in the cyclization step since it would activate the side chain in front of bases. For this reason, either the olefin 11 or the triol 18 were oxidized to the acid 34 by using Sharpless's reagent,[10] which is claimed does not affect the configuration of the carbon atom at the alpha position. The acid 34 (Scheme 10) was treated with oxalyl chloride and then with etheral solution of diazomethane to afford the corresponding diazoketone 36. When a highly pure sample of diazoketone was heated with a variety of metal catalysts, such as copper(II) sulfate, or rhodium(II) acetate, a complex mixture containing no less than eight products (t.l.c.) was always formed. Since related structures have been synthesized by this method in very high yields,[11] in the present case the failure must be ascribed either to some electronic effects of the carbonyl group at the alpha position of the C-H bond to which the carbenoid species should be inserted, or to an inversion of configuration in same stage of the sequence, so that we were dealing with the exo carboxylic acid rather than the endo isomer. Although an X-ray diffraction analysis of this compound would be the ultimate prove of such an assumption, the fact that the methyl ester 35 does not epimerize in the presence of lithium hydroxide is a good indication that it is probably the more stable exo-isomer.[12]

On the other hand, the attempted acid-induced cyclization of diazoketone 36 with methanesulfonic acid in benzene solution, through the protonated methyldiazonium salt, gave only the corresponding methanosulfoniloxy derivative 37 that, on treatment with triethylamine, underwent a Favorskii-type rearrangement to the unsaturated methylketone 38.



Scheme 10

a) $RuCl_3.3H_2O/NaIO_4/CCl_4/CH_3CN/H_2O$; b) acetone/1.2N HCl; c) CH_2N_2/ether; d) benzene/oxalyl chloride/CH_2N_2/THF/ether; e) MsOH/benzene; f) Et_3N/benzene

EXPERIMENTAL

M.Ps. are uncorrected and have been determined in a melting point Büchi 510 apparatus. IR spectra were recorded with a Perkin-Elmer spectrophotomer, model 681. ^{1}H NMR spectra, unless otherwise stated, were recorded with a 60 MHz Perkin-Elmer spectrometer, model R-24, and 200 MHz ^{1}H NMR and ^{13}C NMR spectra with a Varian XL-200. Mass spectra were run in a Hewlett-Packard 5930A spectrometer. Chromatographic purifications were performed on silica gel, using hexane/ethyl acetate mixtures of increasing polarity as eluent. All solvents were dried and distilled before using, and reactions were usually run under atmosphere of nitrogen.

endo-6-Acetoxy-endo-8-(2-p-toluenesulfonyloxyethyl)-cis-bicyclo-(3.3.0)octan-3-one, 2,2-dimethyltrimethylene acetal, 6.

The acetal diol 5 (5.01 g, 18.5 mmol), prepared from Deslongchamps's diketone (2) as previously described,[4] was dissolved in a mixture of dichloromethane (250 mL) and pyridine (50 mL). After cooling at -40°C, a solution of p-toluenesulfonyl chloride (3.8 g, 20 mmol) in dichloromethane (20 mL) was added dropwise and the reaction mixture kept at -4°C for 3 days. It was then washed with saturated $NaHCO_3$ solution and dried. The solvent was evaporated off under vacuum and the resulting residue dissolved in a mixture of pyridine (10 mL) and acetic anhydride (10 mL) and stirred at room temperature for 12 h. The reaction mixture was washed with saturated $NaHCO_3$ solution, dried and evaporated to dryness under vacuum. The residue was chromatographed to give a diacetate (1.18 g, 20% yield) and the tosylate 6 (4.90 g, 57% yield). IR ($CHCl_3$): 1730, 1600, 1365, 1250, 1190, 1180, 1110 cm^{-1}; ^{1}H NMR ($CDCl_3$): 0.90 (s, 3H), 0.95 (s, 3H), 2.00 (s, 3H), 2.45 (s, 3H), 1 - 3 (complex m, 11H), 4.0 (t, J = 6Hz, 2H), 4.80 (m, 1H), 7.3 and 7.6 (AA'XX' system, 4H); MS, m/e: 466 (M$^+$), 407, 406, 354, 311, 295, 294, 207, 167, 149.

endo-6-Acetoxy-endo-8-phenylseleno-cis-bicyclo(3.3.0)octan-3-one, 2,2-dimethyltrimethylene acetal, 7.

To a solution of diphenyl diselenide (0.280 g, 0.88 mmol) in THF (3 mL) 50% aq hypophosphorous acid (0.8 mL) was added and the mixture refluxed for 20 min. After cooling at room temperature, benzene (20 mL) was added and dried over $MgSO_4$. The benzene solution was filtered through a pad of $MgSO_4$ and transferred to a dry reaction vessel fitted with septum, condenser and N_2 inlet. Lithium phenylselenide was generated via addition of 1.6 M solution of n-butyl lithium in hexane (1.1 mL, 1.7 mmol). After 10 min at room temperature, the reaction vessel was charged with the tosylate 6 (1.137 g, 2.1 mmol) dissolved in benzene (15 mL) containing 12-crown-4 (0.1 mL), and the reaction mixture refluxed for 6 h. After cooling at room temperature, it was diluted with ether and washed with saturated NH_4Cl solution and dried. Evaporation of solvents gave an oily residue (1.46 g) that was chromatographed to give the phenylseleno derivative 7 (0.72 g, 70% yield), together with minor amounts of a diselenide (60 mg, 5% yield). Phenylseleno derivative 7, IR ($CHCl_3$): 1730, 1250, 1110 cm^{-1}; ^{1}H NMR ($CDCl_3$): 0.90 (s, 3H), 0.95 (s, 3H), 2.05 (s, 3H), 1-3 (complex m, 11H), 2.80 (t, J = 7Hz, 2H), 3.35 (s, 4H), 4.85 (m, 1H), 7.20 (m, 5H).

endo-6-Hydroxy-endo-8-(2-o-nitrophenylselenoethyl)-cis-bicyclo(3.3.0)octan-3-one, 2,2-dimethyltrimethylene acetal, 9.

To a stirred solution of acetal diol 5 (2.13 g, 7.9 mmol) and o-nitrophenylselenocyanate[5] (2.13 g, 9.4 mmol) in THF (25.4 mL), tributylphosphine (2.32 mL, 9.4 mmol) was introduced via syringe and the reaction mixture stirred at room temperature for 45 min. Evaporation of solvent gave a residue that was chromatographed to give the o-nitrophenylseleno derivative 9 (3.09 g, 86% yield) as yellow crystals, m.p. 128-130°C (from chloroform/hexane). IR (KBr): 3280, 2950, 2860, 1600, 1500, 1330, 1120 cm^{-1}; ^{1}H NMR ($CDCl_3$): 1.00 (s, 6H), 1.5-2.8 (complex m, 11H), 2.88 (t, 2H), 3.48 (s, 4H), 4.30 (m, 1H), 7.40 (m,3H), 8.20 (m, 1H); MS, m/e: 455/453 (M$^+$), 438/436, 352/350, 333/331, 269, 253, 202, 167 (100%), 139, 128, 107. Anal. calcd. for $C_{21}H_{29}NO_5Se$: C, 55.50; H, 6.43; N, 3.08. Found: C, 55.73; H, 6.71; N,3.07%.

endo-6-Acetoxy-endo-8-(2-o-nitrophenylselenoethyl)-cis-bicyclo(3.3.0)octan-3-one, 2,2-dimethyltrimethylene acetal, 10.

The acetal alcohol 9 (2.22 g, 4.9 mmol) was dissolved in a mixture of pyridine (9.2 mL) and acetic anhydride (4.6 mL) and stirred at room temperature for 12 h. It was then evaporated to dryness under vacuum and the residue dissolved in chloroform (50 mL), washed with saturated solution of NH_4Cl (10 mL x 3) and dried. Evaporation of solvent gave the acetoxy acetal 10 as a yellow oily product (2.3 g, 100% yield). IR (film): 2960, 2860, 1735, 1600, 1520, 1450, 1330, 1250, 1115, 1050 cm^{-1}; ^{1}H NMR ($CDCl_3$): 0.95 (s, 3H), 1.02 (s, 3H), 1-2.9 (complex m, 10H), 2.00 (s, 3H), 2.90 (t, J = 8Hz, 2H), 3.48 (s, 4H), 4.90 (m, 1H), 7.35 (m, 3H), 8.25 (m, 1H); MS, m/e: 497/495 (M$^+$), 467/465, 438, 437/435, 411/409, 375/373, 311 (100%), 295, 251, 202, 167, 149, 128.

endo-6-Acetoxy-endo-8-vinyl-cis-bicyclo(3.3.0)octan-3-one, 2,2-dimethyltrimethylene acetal, 8.

a) From phenylseleno derivative 7: To a solution of phenylseleno derivative 7 (2.06 g, 4.4 mmol) in dichloromethane (25 mL), cooled at -78°C, 85% MCPBA (0.974 g, 4.8 mmol) was added and the reaction mixture stirred for 30 min. It was then added to a refluxing solution of diisopropylamine (1.42 mL, 10 mmol) in carbon tetrachloride (125 mL). After 5 min, the solution was allowed to cool at room temperature, the solvent evaporated and the resulting yellow oily residue was purified by chromatography to afford the olefin acetal 8 (1.268 g, 98% yield).

b) From o-nitrophenylseleno derivative 10: To a stirred solution of the arylseleno derivative 10 (2.83 g, 5.71 mmol) in THF (15 mL), cooled with an ice bath, 30% hydrogen peroxide (5 mL) was added dropwise and stirred at room temperature overnight. The solution was poured then into water (100 mL) and extracted with ether (15 mL x3). The combined ether extracts were washed with saturated $NaHCO_3$ and NaCl solutions and dried. The solvents were evaporated off to give the olefin

acetal 8 as a yellow oil (1.42 g, 85% yield). The analytical sample was prepared by evaporative distillation at 190°C/0.3 torr. IR ($CHCl_3$): 3090, 2970, 2880, 1730, 1645, 1250, 1115, cm^{-1}; ^1H NMR ($CDCl_3$): 0.95 (s, 6H), 1-3 (complex m, 9H), 2.00 (s, 3H), 3.50 (s, 4H), 5.00 (m, 3H), 5.70 (m, 1H); MS, m/e: 294 (M^+), 279 , 253, 251, 235, 234, 207, 193, 167, 128, 121, 81, 69. Anal. calcd. for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.44; H, 9.01%.

endo-6-Hydroxy-endo-8-vinyl-cis-bicyclo(3.3.0)octan-3-one, 11.

From o-nitrophenylseleno acetal 9 (1.0 g, 2.2 mmol) the corresponding olefin acetal (0.530 g, 96% yield) was obtained as described above (see 10 ⟶ 8), which was hydrolyzed to the olefin ketone 11 (74% yield) by pyridinium p-toluenesulfonate in acetone under reflux for 12 h. The crude reaction product was recrystallized from a mixture of benzene/hexane to give colorless crystals, m.p. 62°C. IR (KBr): 3400, 3080, 2940, 1740, 1640, 1400, 1015, 1000, 910 cm^{-1}; ^1H NMR ($CDCl_3$): 1.2-3.1 (complex m), 4.4 (m, 1H), 5.05 (m, 2H), 5.8 (m, 1H). Anal. calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.35; H, 8.54%.

endo-6-Acetoxy-endo-8-(1,2-epoxyethyl)-cis-bicyclo(3.3.0)octan-3-one, 12.

To a solution of olefin acetal 8 (0.980 g, 3.33 mmol) in dichloromethane (4 mL), MCPBA (0.79 g, 4 mmol) in the same solvent (10 mL) was added and the reaction mixture stirred at room temperature for 6 h. Anhydrous KF (0.98 g) was then added, the mixture stirred for 1 h, the solid filtered off and the filtrate washed with saturated $NaHCO_3$ solution and dried. Evaporation of solvent gave a 60:40 mixture of diastereomeric epoxides 12 (1.0 g, 3.24 mmol), as shown by the 200Hz NMR spectrum (see below). IR ($CHCl_3$): 1735, 1250, 1110, 1050, 1020 cm^{-1}; ^1H NMR ($CDCl_3$): 0.94 (s, 60%, 3H), 0.96 (s, 40%, 3H), 0.98 (s, 40%, 3H), 1.00 (s, 60%, 3H), 1.2-2.1 (complex m, 9H), 2.04 (s, 60%, 3H), 2.05 (s, 40%, 3H), 2.48 (q, J_{gem} = 4.8Hz, J_{trans} = 2.4Hz, 40%, 1H), 2.57 (q, J_{gem} = 4.8Hz, J_{trans} = 2.4Hz, 60%, 1H), 2.74 (q, J_{gem} = 4.8Hz, J_{cis} = 4.0Hz, 40%, 1H), 2.82 (q, J_{gem} = 4.8Hz, J_{cis} = 4.0Hz, 60%, 1H), 2.92 (m, 1H), 3.49 (s, 4H), 4.80 (m, 1H); MS, m/e: 310 (M^+), 295, 280, 250, 168, 128.

endo-6-Acetoxy-endo-8-(1,2-dihydroxyethyl)-cis-bicyclo(3.3.0)oc-tan-3-one, 13.

The mixture of crude epoxides 12 (1.0 g, 3.24 mmol) was dissolved in DME (7 mL), a saturated aq solution of tartaric acid (5.3 mL) added, and the mixture stirred at room temperature for 7 days. It was then poured into saturated $NaHCO_3$ solution and thoroughly extracted with ethyl acetate. The combined organic extracts were dried, solvents evaporated off under vacuum and the resulting residue (0.97 g) chromatographed to give a diastereomeric mixture of diols 13 (0.390 g, 48% yield) as a colorless oily material. IR (film): 3460, 2960, 2880, 1745, 1250 cm^{-1}; ^1H NMR ($CDCl_3$): 2.00 (s, 3H), 2.3 (complex m, 6H), 2.90 (complex m, 4H), 3.55 (complex m, 4H), 5.20 (m, 1H).

endo-6-Acetoxy-endo-8-(1-acetoxy-2-methanesulfonyloxyethyl)-cis-bicyclo(3.3.0)octan-3-one, 14.

The mixture of diols 13 (0.390 g, 1.64 mmol) was dissolved in dichloromethane (25 mL) and, after cooling at -40°C, pyridine (4.2 mL) and methanesulfonyl chloride (0.14 mL, 1.8 mmol) were added and the reaction mixture kept at 4°C for 36 h. It was then poured into water, the organic layer separated, washed with $NaHCO_3$ solution and dried. Evaporation of solvent under vacuum gave a residue that was dissolved in a mixture of pyridine (3 mL) and acetic anhydride (1.5 mL) and the solution stirred at room temperature for 60 h. After the working up, the resulting residue (0.411 g) was chromatographed to give a 70:30 mixture of mesylate diacetates 14 (0.273 g, 47% yield). IR (film): 1750, 1370, 1240, 1180 cm^{-1}; ^1H NMR ($CDCl_3$): 2.01 (s, 3H), 2.10 (s, 3H), 1.5-3 (complex m, 9H), 3.04 (s, 3H), 4.22 (1/2 AB part of a ABX system, $J_{1,2}$ = 12Hz, $J_{1,3}$ = 4Hz, 70%, H_1), 4.26 (1/2 AB part of a ABX system, $J_{1',2'}$ = 12Hz, $J_{1',3'}$ = 4Hz, 30%, $H_{1'}$), 4.44 (1/2 AB part of a ABX system, $J_{1',2'}$ = 12Hz, $J_{2',3'}$ = 2.8Hz, 30%, $H_{2'}$), 4.50 (1/2 AB part of a ABX system, $J_{1,2}$ = 12Hz, $J_{2,3}$ = 2.8Hz, 70%, H_2), 5.00 (d-q, $J_{1,3}$ = 4Hz, $J_{2,3}$ = 2.8Hz, $J_{3,5}$ = 9.6Hz, 70%, H_3), 5.08 (m, 30%, $H_{3'}$), 5.30 (m, 1H); MS, m/e: 362 (M^+), 344, 320, 308, 302, 284, 206, 182, 164, 146.

endo-5-exo-8-Diacetoxytricyclo(5.2.1.$0^{4,10}$)decan-2-one, 15.

To a solution of the diastereoisomeric mesylates 14 (0.120 g, 0.34 mmol), in a mixture of anhydrous tert-butyl alcohol (5 mL) and THF (2 mL), $KOBu^t$ (0.081 g, 0.72 mmol) in tert-butyl alcohol/THF (2 mL of a 1:1 mixture) was added at room temperature and the reaction mixture stirred for 24 h. The solvents were removed under vacuum, the residue dissolved in ether, and the resulting solution washed with 0.1M buffered aq solution of phosphates (pH = 7), and then dried over $MgSO_4$. The ether was evaporated to give the crude material (0.150 g) which was chromatographed to afford the tricyclic ketone 15 (0.041 g, 44.5% yield) as a colorless oil (see below from 32a), together with one of the starting mesylates 14 (0.060 g).

exo-9-Acetoxy-endo-tricyclo(5.2.1.$0^{2,6}$)decane-4,8-dione, (4)2,2-dimethyltrimethylene acetal, 16c.

a) To a solution of 1.6 M n-BuLi in hexane (23 mL, 37 mmol), diluted with THF (30 mL) and cooled with an ice bath, a solution of i-Pr_2NH (4.8 mL, 37 mmol) in THF (30 mL) was added. After stirring for 5 min, a solution of monoacetal 3 (4.71 g, 19 mmol) in THF (60 mL) was added and the reaction mixture stirred for 1 h at room temperature. The mixture was cooled again, trimethylsilyl chloride (7 mL) added, stirred for 15 min at room temperature and finally poured into a saturated solution of $NaHCO_3$ and thoroughly extracted with ether. The combined ether extracts were dried and solvents removed under vacuum to afford the corresponding enol silyl ether (8.6 g) as a yellow solid compound.

b) To a solution of the above enol silyl ether (7.50 g, 17 mmol) in dichloromethane (50 mL), cooled with an ice bath, 85% MCPBA (5.07 g, 25 mmol) was added and then stirred for 2 h, a white precipitate being formed. The solid material was filtered off and triethylammonium fluoride (15 g) was added and reaction mixture stirred at room temperature for 14 h. It was then washed with saturated Na_2CO_3 solution, 1 M HCl and saturated $NaHCO_3$ solution, and dried. Evaporation of solvents and column chromatography of the resulting residue (5.5 g) afforded the alfa-hydroxy ketone 16a (3.0 g, 66% yield) as a colorless solid, together with some starting material (0.53 g) and m-chlorobenzoyloxy ketone 16b (0.69 g, 10% yield), which was hydrolyzed to the hydroxy ketone 16a in

95% yield. IR (KBr): 3470, 1745, 1115 cm^{-1}; ^1H NMR ($CDCl_3$): 0.90 (s, 3H), 1.00 (s, 3H), 1-3 (complex m, 13 H), 3.30 (s, 2H), 3.40 (s, 2H), 3.85 (d, J = 3Hz, 1H).

c) The hydroxy ketone 16a (0.50 g, 1.88 mmol) was dissolved in a mixture of pyridine (5 mL) and acetic anhydride (2.5 mL), and stirred for 12 h at room temperature. It was then evaporated to dryness under vacuum, the residue dissolved in chloroform, washed with $NaHCO_3$ solution and dried. Evaporation of solvent afforded a crude material (0.60 g) which was purified by flash chromatography to give the acetoxy ketone 16c (0.47 g, 81% yield) as colorless crystals, m.p. 111°C. IR (CCl_4): 1758, 1752, 1230, 1120 cm^{-1}; ^1H NMR ($CDCl_3$): 0.90 (s, 3H), 1.00 (s, 3H), 2.11 (s, 3H), 1-3 (complex m, 12H), 3.32 (s, 2H), 3.40 (s, 2H), 5.00 (d, J = 3Hz, 1H); ^{13}C MNR ($CDCl_3$) : 20.90 (q), 22.41 (q), 22.54 (q), 30.05 (s), 33.26 (t), 35.02 (t), 38.11 (t), 39.82 (d), 41.98 (d), 43.20 (d), 54.05 (d), 71.57 (t), 72.30 (t), 72.93 (d), 110.67 (s), 170.02 (s), 212.19 (s); MS, m/e: 308 (M^+), 249, 221, 208, 180, 167, 128, 81, 69. Anal. calcd. for $C_{17}H_{24}O_5$: C, 66.21; H, 7.84. Found: C, 66.42; H, 8.03%.

exo-10-Acetoxy-8-oxa-endo-tricyclo(5.3.1.0^{2,6})undecane-4,9-dione, (4)2,2-dimethyltrimethylene acetal, 17.

A mixture of acetoxy ketone 16c (4.0 g, 12.8 mmol), $LiCO_3$ (1.60 g, 21.8 mmol), 85% MCPBA (5.30 g, 25.8 mmol) and a trace of 1,6-di-tert-butyl-4-methylphenol in dichloromethane (150 mL) was heated under reflux for 36 h. The reaction mixture was then diluted with more dichloromethane (100 mL), washed with saturated solution of $NaHCO_3$ and dried. Evaporation of solvent under vacuum afforded a 67:33 mixture of two regioisomeric lactones (5.10 g) from which lactone 17 was separated (2.69 g, 65% yield) by selective hydrolysis with 1 M NaOH (17 mL) in THF (200 mL) for 3 days. The analytical sample was prepared by recrystallization from hexane/ether, giving colorless crystals, m.p. 144-146°C. IR (KBr): 1750, 1240, 1110, 1035 cm^{-1}; ^1H NMR ($CDCl_3$): 0.85 (s, 3H), 1.00 (s, 3H), 2.10 (s, 3H), 1-3 (complex m, 13H), 3.45 (s, 2H), 3.49 (s, 2H), 4.70 (m, 1H), 5.45 (m, 1H); ^{13}C NMR ($CDCL_3$): 20.91 (q), 22.32 (q), 22.61 (q), 30.01 (s), 31.96 (t), 34.69 (t), 35.64 (t), 40.73 (d 2), 46.23 (d), 70.83 (t), 70.93 (d), 72.55 (t), 81.72 (d), 110.34 (s), 166.95 (s), 169.33 (s); MS, m/e: 324 (M^+), 281, 165, 197, 179, 167, 128, 69, 55, 43. Anal. calcd. for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46. Found: C, 62.73; H, 7.52%.

rel-(1R,5S,6R,8S)-6-Hydroxy-8(1S)-(1,2-dihydroxyethyl)bicyclo(3.3.0)octan-3-one, 2,2-dimethyltrimethylene acetal, 18.

A solution of acetoxy lactone 17 (1.36 g, 4.2 mmol) in THF (50 mL) was added dropwise to a suspension of $LiAlH_4$ (0.480 g, 12.5 mmol) in ether (50 mL) cooled with an ice bath, and the reaction mixture stirred at room temperature for 4 h. It was diluted with dichloromethane (160 mL) and then a saturated solution of sodium potassium tartrate (3.5 mL) was added dropwise. The water was eliminated by addition of $NaSO_4$, the salts filtered off and the solvent evaporated under vacuum to give the triol acetal 18 as a colorless solid material (1.36 g, 100% yield). IR (KBr): 3400, 1100, 1060, 1010, 995 cm^{-1}; ^1H NMR ($CDCl_3$): 0.93 (s, 3H), 1.00 (s, 3H), 1-3 (complex m, 12H), 3.50 (br s, 2H), 3.52 (br s, 2H), 3.55 (m, 3H), 4.28 (m, 1H).

rel-(1R,5S,6R,8S)-6-Acetoxy-8-((1S)-1-acetoxy-2-p-toluenesulfonyloxyethyl)bicyclo(3.3.0)octan-3-one, 2,2-dimethyltrimethylene acetal, 19.

The triol acetal 18 (1.2 g, 4.2 mmol) was dissolved in a mixture of dichloromethane (100 mL) and pyridine (20 mL), cooled at -40°C, and a solution of p-toluenesulfonyl chloride (1.04 g, 5.4 mmol) in dichloromethane (30 mL) was added dropwise. The reaction mixture was kept at -4°C for 2 days, then diluted with ether (200 mL), washed with saturated $NaHCO_3$ solution and extracted with ether. The combined ether extracts were dried and the solvent evaporated off under pressure to give an oily material that was dissolved in a mixture of pyridine (8 mL) and acetic anhydride (5 mL) and stirred at room temperature for 36 h. After the usual working up and purification by chromatography the diacetoxy tosylate 19 was isolated (0.896 g, 40.7% yield). IR (KBr), 1740, 1360, 1240; ^1H NMR ($CDCl_3$): 0.90 (s, 3H), 1.00 (s, 3H), 1.95 (s, 3H), 1-3 (complex m, 9H), 2.00 (s, 3H), 2.45 (s, 3H), 3.40 (s, 4H), 4.10 (AB part of a ABX system, 2H), 4.85 (m, 2H), 7.23 and 7.66 (AA'XX' system, 4H).

rel-(1R,5S,6R,8S)-6-Acetoxy-8-((1S)-1-acetoxy-2-p-toluenesulfonyloxyethyl)bicyclo(3.3.0)octan-3-one, 20.

To a solution of diacetoxy tosylate acetal 19 (0.280 g, 0.53 mmol) in anhydrous acetone (40 mL), p-toluensulfonic acid (30 mg) was added and the reaction mixture stirred at room temperature for 5 days. K_2CO_3 (80 mg) was added and the mixture stirred for 20 min, the solid material filtered off and solvents evaporated under vacuum. The residue was chromatographed to yield the diacetoxy tosylate ketone 20 (0.168 g, 73.5% yield) as colorless crystals. IR (KBr): 1730 (br), 1360, 1230, 1180, 1170 cm^{-1}; ^1H NMR ($CDCl_3$): 2.00 (s, 6H), 2-2.4 (m, 5H), 2.45 (s, 3H), 2.70 (m, 4H), 4.10 (AB part of a ABX system, 2H), 4.80 (m, 1H), 5.20 (m, 1H), 7.3 and 7.7 (AA'XX' system, 4H); MS, m/e: 378 (M^+), 318, 279, 267, 266, 206, 172, 164, 155, 146, 108, 107,91.

Reaction of rel-(1R,5S,6R,8S)-6-methanesulfonlyloxy-8-((1S)-1,2-dimethanesulfonlyloxyethyl)bicyclo(3.3.0)octan-3-one (21) with tetraethylammonium acetate.

A solution of trimesylate 21 (0.325 g, 0.75 mmol) - prepared from triol 18 by mesylation with excess of methanesulfonyl chloride and pyridine, followed by deprotection- and tetraethylammonium acetate monohydrated (1.5 g, 7.5 mmol) in acetone (50 mL) was heated under reflux for 18 h. After the usual working up and purification of the crude residue (0.30 g) by column chromatography the following compounds were isolated:

i) Diacetoxy olefin 22 (0.065 g, 42% yield), IR ($CHCl_3$): 1740, 1250 cm^{-1}; ^1H NMR ($CDCl_3$): 1.9-3 (complex m, 8H), 2.03 (s, 6H), 3.46 (m, 1H), 4.50 (AB part of a ABX system, 2H), 4.90 (m, 1H), 5.50 (m, 1H); MS, m/e: 206 (M^+-CH_3COOH), 164, 146, 121, 118, 105, 104, 91, 79, 77, 43.

ii) Triacetoxy 23 (0.050 g, 25% yield), IR ($CHCl_3$): 1740, 1240 cm^{-1}; ^1H NMR ($CDCl_3$): 2.00 (s, 9H), 2-3 (complex m, 9H), 4.15 (AB part of a ABX system, 2H), 4.95 (m, 2H).

iii) Diacetoxy nonomesylate 24 (0.057 g, 25% yield), IR ($CHCl_3$): 1745, 1360, 1240, 1175 cm^{-1}; ^1H NMR ($CDCl_3$): 2.00 (s, 3H), 2.10 (s, 3H), 1.5-3 (complex m, 9H), 3.00 (s, 3H), 4.00 (AB part of a

ABX system, 2H), 4.70 (m, 2H).

Hydroxybromination of endo-6-hydroxy-endo-8-vinyl-cis-bicyclo(3.3.0)octan-3-one, (11 ⟶ 30 + 31).

To a solution of olefin 11 (0.505 g, 3 mmol) in dioxane (2 mL), N-bromosuccinimide (1.083 g, 6 mmol), calcium carbonate (0.304 g, 3 mmol) and H_2O (1 mL) were added and the mixture stirred at room temperature for 4 h. The reaction mixture was then poured into ethyl acetate (50 mL) and filtered. The resulting solution was washed with water and 5% aq solution of sodium thiosulfate, dried and the solvent evaporated to give a crude material (1.0 g) that was purified by column chromatography. Elution with a 75:25 mixture of hexane/ethyl acetate gave 9-bromomethyl-8-oxa-endo-tricyclo(5.2.1.$0^{2,6}$)decan-4-one, 31 (0.336 g, 46% yield). The analytical sample was recrystallized from dichloromethane/hexane to afford colorless crystals, m.p. 62-63°C. IR ($CHCl_3$): 2995, 2950, 1735, 1400, 1165, 995, 955, 905 cm^{-1}; ^1H NMR ($CDCl_3$): 1.4-2.0 (m, 2H), 2.0-2.9 (complex m, 7H), 3.05 (m, 2H), 3.6 (q, 1H), 4.15 (br s, 1H); ^{13}C NMR ($CDCl_3$): 32.41 (t), 36.22 (t), 37.02 (t), 38.05 (d), 38.55 (t), 41.25 (d), 44.65 (d), 75.97 (d), 79.73 (d), 219.38 (s); MS, m/e: 246/244 (M^+), 163/161, 151 (100%), 133, 123, 111, 105, 95, 91, 81, 54, 41. Anal. calc. for $C_{10}H_{13}O_2Br$: C, 49.00; H, 5.34. Found: C, 49.11; H, 5.26%.

Further elution with a 60:40 mixture of the same solvents gave the bromohydrin 30 (0.237 g, 29% yield). IR (film): 3440, 2960, 2920, 2870, 1730, 1460, 1290, 1260, 1180, 1120 cm^{-1}; ^1H NMR ($CDCl_3$): 1.1-4.7 (complex m, 15H).

endo-6-Acetoxy-endo-8-(1-bromo-2-hydroxyethyl)-cis-bicyclo(3.3.0)octan-3-ona, 2,2-dimethyltrimethylene acetal, 25.

To a solution of olefin 8 (0.20 g, 0.5 mmol) in dioxane (2 mL), calcium carbonate (0.051 g, 0.5 mmol), H_2O (1 mL) and N-bromosuccinimide (0.182 g, 1 mmol) were added and the mixture stirred at room temperature for 2 h. The reaction mixture was then poured into H_2O (25 mL), filtered and extrated with ether. The etheral layer was washed with H_2O and 5% aq sodium thiosulfate solution, dried and solvents removed under vacuum to afford a crude material (0.280 g) that was purified by column chromatography to give some unreacted olefin (0.061 g, 30% yield) and a mixture of diastereomeric bromohydrins 25 (0.124 g, 47% yield). IR ($CHCl_3$): 3440, 2990, 2940, 2860, 1725, 1370, 1240, 1100, 1040 cm^{-1}; ^1H NMR ($CDCl_3$): 1.0 (s, 6H), 1.0-3.2 (complex m, 9H), 2.0 (s, 3H), 3.45 (s, 4H), 3.9 (m, 4H), 5.0 (m, 1H); ^{13}C NMR ($CDCl_3$): 20.86 (q), 22.49 (q), 30.18 (t), 32.12 (t), 32.75 (t), 33.64 (t), 34.01 (t), 34.46 (t), 34.85 (t), 40.08 (d), 41.08 (d), 41.62 (d), 41.93 (d), 42.40 (d), 42.75 (d), 60.61 (d), 61.06 (d), 66.26 (t), 66.68 (t), 71.42 (t), 73.29 (t), 73.67 (d), 75.03 (d), 108.07 (s), 170.52 (s); MS, m/e: 375/373 (M^+-OH), 332/330, 311, 256, 251, 207, 192, 165, 160, 147, 139, 128, 105, 96, 69, 64 (100%), 43.

endo-6-Acetoxy-endo-8-(1-bromo-2-oxoethyl)-cis-bicyclo(3.3.0)octan-3-one, 2,2-dimethyltrimethylene acetal, 26.

A solution of the above mixture of bromohydrins 25 (0.150 g, 0.38 mmol) in dichloromethane (10 mL) was treated with pyridinium chlorochromate (0.123 g, 0.57 mmol) and the mixture stirred for 18 h. After the usual working-up and column chromatography of the crude reaction product, the aldehyde 26 (0.094 g, 65% yield) was isolated as a yellow oil. IR ($CHCl_3$): 2960, 2865, 1730, 1240, 1110 cm^{-1}; ^1H NMR ($CDCl_3$): 0.95 (s, 6H), 1.0-3.3 (complex m, 9H), 2.05 (s, 3H), 3.5 (br s, 4H), 3.15 (m, 1H), 5.05 (m, 1H), 9.4 (d, 1H); MS, m/e: 330/328 (M^+-CH_3COOH), 309, 249, 223, 181, 163 (100%), 135, 128, 121, 83, 69, 55, 43.

endo-8-Vinyl-cis-tricyclo(3.3.0)octane-3,6-dione, 27.

To a solution of olefin 11 (0.800 g, 4.8 mmol) in dichloromethane (15 mL), cooled with an ice bath, pyridinium chlorochromate (1.551 g, 7.2 mmol) and celite (1.551 g) were added and the mixture stirred at room temperature for 18 h. It was then diluted with ether (100 mL) and filtered through silica gel and the solvent removed under vacuum to give the olefin 27 (0.760 g) as an yellow oily material in 95% yield. IR ($CHCl_3$): 3000, 2960, 1740, 1650, 1400, 1145, 915 cm^{-1}; ^1H NMR ($CDCl_3$): 1.0-3.5 (complex m, 9H), 4.8-6.2 (m, 3H).

endo-8-(2-Acetoxy-1-bromoethyl)-cis-bicyclo(3.3.0)octan-3,6-dione, 28.

To a solution of olefin 27 (0.760 g, 4.6 mmol) in dioxane/H_2O (5 mL/2.5 mL), calcium carbonate (0.463 g, 4.6 mmol) and N-bromosuccinimide (1.650 g, 9.27 mmol) were added and the mixture stirred at room temperature for 4 h. It was then poured into H_2O, filtered and the clear solution extracted with ether. The combined ether extracts were washed with 5% aq sodium thiosulfate solution and saturated aq sodium chloride solution, dried and the solvent evaporated under vacuum to give a crude material (1.2 g).

The above crude reaction mixture was treated with acetic anhydride (5 mL) and pyridine (10 mL), and the mixture stirred at room temperature for 24 h. The solution was evaporated under vacuum and the solid residue dissolved in dichloromethane. The resulting solution was washed with saturated aq solution of ammonium and sodium chloride, dried and the solvent evaporated to give the crude acetoxy derivative (1.160 g) which was chromatographed to afford 24% yield from the olefin (0.350 g) of the epimer 28a and 13% yield (0.196 g) of the epimer 28b.

Epimer 28a, IR (film): 2950, 2910, 1740, 1400, 1370, 1240, 1050 cm^{-1}; ^1H NMR ($CDCl_3$): 1.3-3.7 (complex m, 9H), 2.1 (s, 3H), 4.0 (m, 3H); ^{13}C NMR ($CDCl_3$): 20.6 (q), 37.1 (t), 39.1 (t), 39.4 (t), 40.6 (d), 41.6 (d), 50.7 (d), 52.1 (d), 67.1 (t), 170.2 (s), 214.3 (s), 216.0 (s); MS, m/e: 304/302 ($M^{+\cdot}$), 251, 244/242, 223, 181, 163 (100%), 135, 121, 107, 93, 91, 79, 67, 55, 43.

Epimer 28b, IR (film): 2941, 1740, 1400, 1370, 1240, 1050 cm^{-1}; ^1H NMR ($CDCl_3$): 1.7-3.3 (complex m, 9H), 2.1 (s, 3H), 4.0 (m, 1H), 4.35 (m, 2H); ^{13}C NMR ($CDCl_3$): 20.7 (q), 37.4 (t), 38.7 (t), 40.3 (d), 41.2 (t), 41.8 (d), 51.9 (d), 52.4 (d), 66.5 (t), 170.2 (s), 213.9 (s), 214.9 (s); MS, m/e: 304/302 ($M^{+\cdot}$), 251, 244/242, 223, 181, 163 (100%), 135, 121, 107, 93, 91, 79, 55, 43.

Cyclization of endo-8-(1-acetoxy-2-bromoethyl)-cis-bicyclo(3.3.0) octan-3,6-dione, 28a, to 2-acetoxymethyltricyclo(4.3.0.$0^{3,7}$)nonane-4,8-dione, 29.

To a solution of potassium tert-butoxide (0.062 g, 0.55 mmol) in anhydrous THF (10 mL), cooled with acetone/dry ice, acetylated bromhydrin 28a (0.168 g, 0.55 mmol) dissolved in THF (5 mL) was

added dropwise in a 2 h period and the mixture stirred for 3 h. It was then poured into a buffered cold solution of phosphates (20 mL), extracted with ether, the combined ether extracts dried and evaporated under vacuum. The residue was chromatographed to give 26% of the unreacted bromhydrin (0.043 g) and 33% of the cyclization product (0.040 g), 29. IR ($CHCl_3$): 3010, 1950, 1740, 1380, 1240, 1150, 1030, 900, 880 cm^{-1}; ^1H NMR ($CDCl_3$): 0.8-2.0 (complex m, 2H), 2.0 (s, 3H), 2.0-3.6 (complex m, 7H), 3.9 (d, J = 6.5 Hz, 2H); ^{13}C NMR ($CDCl_3$): 20.75 (q), 22.17 (d), 31.96 (d), 34.57 (d), 34.84 (d), 40.38 (t), 42.50 (t), 45.56 (d), 64.49 (t), 170.67 (s), 211.07 (s), 216.38 (s); MS, m/e: 222 ($M^{+\cdot}$), 180, 162, 134, 121, 107, 106, 91, 79, 55, 43 (100%).

endo-6-Acetoxy-endo-8-(1-acetoxy-2-bromoethyl)-cis-bicyclo(3.3.0)octan-3-one, 33a and 33b.

To a solution of bromine (0.27 mL, 4.84 mmol) in dichloromethane (130 mL), triphenylphosphine (1.26 g, 4.84 mmol) was added and to the resulting colorless solution a mixture of epoxides 12 (1.36 g, 4.4 mmol) in dichloromethane (10 mL) was then added and stirred at room temperature for 45 min. The solution was poured into aq 1N $NaHCO_3$ (250 mL) the two layers separated and the aq one extracted with dichloromethane. The combined organic layers were dried and the solvent evaporated off to give a crude material (3.59 g), which was dissolved in acetone (100 mL), a few crystals of p-toulenesulfonic acid added and the solution stirred for 3 days. Elimination of solvents and chromatography of the residue afforded:

a) 14% yield (0.185 g, from olefin) of bromhydrin 32a.IR (film): 3470, 2950, 1730, 1240 cm^{-1}; ^1H NMR ($CDCl_3$): 1.0-3.3 (complex m, 10H), 2.0 (s, 3H), 3.3-4 (m, 3H), 5.15 (m, 1H).

b) a mixture of the corresponding epimer 32b of the above bromhydrin with triphenylphosphine (1.435 g). IR (film): 3420, 3050, 2950, 1735, 1450, 1240, 1175, 1120, 720, 690 cm^{-1}; ^1H NMR ($CDCl_3$): 1.0-3.5 (complex m, 13H), 2.0 (s, 3H), 5.15 (m, 1H), 7.5 (m, $OPPh_3$); ^{13}C NMR ($CDCl_3$): 20.84 (q), 34.43 (t), 38.25 (t), 39.07 (t), 39.86 (t), 42.16 (d), 43.11 (d), 44.28 (d), 72.12 (d), 75.31 (d), 128.38 (s, $OPPh_3$), 131.98 (d, $OPPh_3$), 170.13 (s), 218.24 (s).

The two fractions were acetylated separately with acetic anhydride/pyridine, to afford:

a) 12.1% yield (0.185 g, from olefin) of rel-(1R, 5S, 6R, 8S)-6-acetoxy-8(1R)-(1-acetoxy-2-bromoethyl)bicyclo (3.3.0)octan-3-one (33a). IR ($CHCl_3$): 2940, 1740, 1370, 1240, 1030 cm^{-1}; ^1H NMR ($CDCl_3$): 0.8-3.2 (complex m, 9H), 2.05 (s, 3H), 2.15 (s, 3H), 3.55 (m, 2H), 5.15 (m, 2H); MS, m/e: 348/346 (M^+) 330/328, 288/286, 246/244, 225, 207, 183, 165, 147 (100%), 119, 111, 105, 91, 79, 55, 43.

b) 32% yield (from olefin, 0.489 g) of the corresponding epimer 33b. IR (film): 2940, 1735, 1365, 1230, 1020 cm^{-1}; ^1H NMR ($CDCl_3$): 1.0-3.2 (complex m, 9H), 2.0 (s, 3H), 2.1 (s, 3H), 3.55 (m, 2H), 5.1 (m, 2H); MS, m/s: 348/346 (M^+), 330/328, 288/286, 270/268, 246/244, 225, 207, 165, 147 (100%), 119, 111, 105, 91, 79, 43.

endo-5-exo-8-Diacetoxytricyclo(5.2.1.0^{4,10})decan-2-one, 15.

To a solution of potassium tert-butoxide (74 mg, 0.66 mmol) in THF (6 mL), cooled at -78°C and operating under an atmosphere of nitrogen, a solution of the epimer 32a (0.185 g, 0.53 mmol) in THF (12 mL) was added in a 2.5 h period. The mixture was stirred at -78°C for 4 h, then poured into a chilled buffered solution of phosphates (20 mL, pH = 7) and worked up as usual to give a crude material (0.142 g). Purification by column chromatography afforded the pure product (0.115 g) in 81% yield. The analytical sample was prepared by recrystallization from benzene, yielding white crystals, m.p. 78-79°C. IR ($CHCl_3$): 1735, 1230 cm^{-1}; ^1H NMR 200 MHz ($CDCl_3$): 1.0-3.0 (complex m, 9H), 2.02 (s, 6H), 3.35 (q br, J = 10,5 Hz, 1H), 5.02 (m, 1H), 5.09 (d of t, J = 5.8Hz, J = 7.3Hz, 1H); ^{13}C NMR ($CDCl_3$): 20.91, 21.25, 34.44, 35.10, 39.15, 39.83, 48.40 (2), 50.37, 76.60, 81.70, 170.30, 170.46; MS, m/e: 266 (M^+), 249, 206, 189, 164, 146, 105. Anal. calcd. for $C_{14}H_{18}O_2$: C, 63.16; H, 6.77. Found: C, 63.37; H, 6.91%.

Tricyclo(5.2.1.0^{4,10})decan-2,5,8-trione, 1.

To a solution of the above diacetoxy tricycloderivative 15 (0.115 g, 0.43 mmol) in methanol (20 mL), aq potassium carbonate (0.607 g in 10 mL H_2O) was added and the solution stirred at room temperature for 5 h. After neutralization with 2M HCl and the usual working up, the resulting diol was dissolved in dichloromethane (10 mL), and treated with pyridinium chlorochromate (0.283 g, 1.32 mmol) and celite (0.283 g). After stirring for 18 h, the reaction mixture was filtered through a column of silica gel, washing with ether and ethyl acetate, to give a crude material (75 mg) which was purified by column chromatography, affording pure triketone 1 (32 mg), m.p. 170-172°C in 42% yield, identical in all respects with an authentic sample.[1]

endo-4,7-Dioxo-cis-bicyclo(3.3.0)octane-2-carboxylic acid, 34.

a) From olefin ketone 11: To a solution of olefin ketone 11 (0.450 g, 2.7 mmol) in a 1:1 mixture of carbon tetrachloride and acetonitrile (12 mL), cooled with an ice bath, a solution of $NaIO_4$ (3.0 g, 14 mmol) and $RuCl_3.3H_2O$ (90 mg) in water (8 mL) was added and the reaction mixture kept at room temperature for 12 h. It was then diluted with chloroform, the layers separated and the aq one extracted with ethyl acetate and dried. Evaporation of the solvent under vacuum gave the crude acid (566 mg) which was purified by chromatography to afford the pure acid (347 mg, 71% yield). Recrystallization from dichloromethane/methanol gave colorless crystals, m.p. 180°C. IR (KBr): 3500-2500 (br), 1750, 1710, 1270, 1180, 1160, 1140 cm^{-1}; ^1H NMR (CD_3OD): 2.1 (complex m, 6H), 3.0 (complex m, 3H), 4.4 (s, 1H); ^{13}C NMR (CD_3OD): 39.35 (t), 40.42 (t), 40.60 (t), 41.13 (d), 43.11 (d), 51.78 (d), 176.46 (s), 218.70 (s), 219.70 (s); MS, m/e: 182 (M^+), 164, 154, 137, 136, 100, 82. Anal. calcd. for $C_9H_{10}O_4$: C, 59.34; H, 5.53. Found:C, 59.37; H, 5.43%.

b) From triol 18 (1.2 g, 4.1 mmol) and proceeding similarly the acid was obtained as the corresponding monoacetal, which was then hydrolyzed to the acid diketone 34 (36% yield), identical in all respects with the one prepared from olefin ketone 11.

endo-4-(2-Diazo-1-oxoethyl)-cis-bicyclo(3.3.0)octan-2,7-dione, 36.

To a solution of acid diketone 34 (0.310 g, 1.7 mmol) in benzene (10 mL) oxalyl chloride (2 mL) was added and the reaction mixture stirred for 12 h at room temperature. It was then evaporated under vacuum, the crude acid chloride dissolved in THF (15 mL) and a 0.4 M solution of diazomethane in ether (25 mL) was added dropwise in 1 h 30 min period, with stirring. Evaporation to dryness and

chromatography of the residue afforded the pure diazoketone 36 (0.320 g, 91% yield) as a yellow oil. IR ($CHCl_3$): 2120, 1750, 1645 cm^{-1}; ^1H NMR ($CDCl_3$): 2-4 (complex m, 9H), 5.36 (s, 1H).

Methyl endo-4,7-Dioxo-cis-bicyclo(3.3.0)octane-2-carboxylate, 35.

The acid 34 (0.095 mg, 0,52 mmol) was treated with 0.3M etheral solution of diazomethane (25 ml). After 12 h the ether was evaporated to give the crude methyl ester 35, which was purified by column chromatography (0.090 mg). IR ($CHCl_3$): 1745, 1240, 1180 cm^{-1}; ^1H NMR ($CDCl_3$): 2-3.5 (complex m, 9H), 3.75 (s, 3H); MS, m/e: 196 (M^+), 165, 137, 114.

Attempted acid-induced cyclization of diazoketone 36: endo-4-(2-methanosulfoniloxy-1-oxoethyl)-cis-bicyclo(3.3.0)octane-2,7-dione, 37.

To a solution of diazoketone 36 (0.200 g, 1.0 mmol) in benzene (30 mL), cooled with an ice bath, a solution of methanesulfonic acid (0.060 g, 0,53 mmol), in the same solvent (20 mL), was added in an atmosphere of nitrogen and the mixture stirred at room temperature for 12 h. Since the IR spectrum showed the presence of unreacted diazoketone more methanesulfonic acid (0.065 g, 0,58 mmol) was added and the mixture heated under reflux for 0.5 h. The solvents were removed and the residue purified by column chromatography to give the endo-4-(2-methanesulfoniloxy-1-oxoethyl)-cis-bicyclo(3.3.0)octane-2,7-dione (0.166 g), 37. IR ($CHCl_3$): 2940, 1740, 1350, 1170 cm^{-1}; ^1H NMR ($CDCl_3$): 4.9 (br s, 2H), 3.2 (s, 3H), 1.5-4 (complex m, 9H).

4-(1-Oxoetil)-cis-bicyclo(3.3.0)oct-3-ene-2,7-dione, 38.

To a solution of methanesulfoniloxy derivative 37 (0.166 g, 0.7 mmol) in benzene (100 mL), triethylamine (2 mL) was added and the mixture refluxed under nitrogen for 18 h. The solvent was evaporated and the residue chromatographed to give the unsaturated methylketone 38 (0,090 g), as white crystals, m.p. 77°C. IR ($CDCl_3$): 1745, 1715, 1685, 1400, 1370, 1165 cm^{-1}; ^1H NMR ($CDCl_3$): 2.5 (s, 3H), 1.5-4 (complex m, 6H), 6.7 (s, 1H); MS, m/e: 178 ($M^{+\cdot}$), 163, 150, 136, 121, 107, 93, 79, 65, 43. Anal. calcd. for $C_{10}H_{10}O_3$: C, 67.40; H, 5.65. Found: C, 67.42; H, 5.63%.

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