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BICYCLO[2.2.1]HEPTANE AS CYCLOPENTANE PRECURSOR. SYNTHESIS OF BENZHYDROPENTALENES ENROUTE TO TERPENOIDS

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Abstract - The synthesis of a bicyclo[2.2.1]heptane derivative 2 and its transformation to two different cyclopentanoid derivatives 9 and 18 through intramolecular functionalisation is described for entry into diterpene and sesquiterpene.

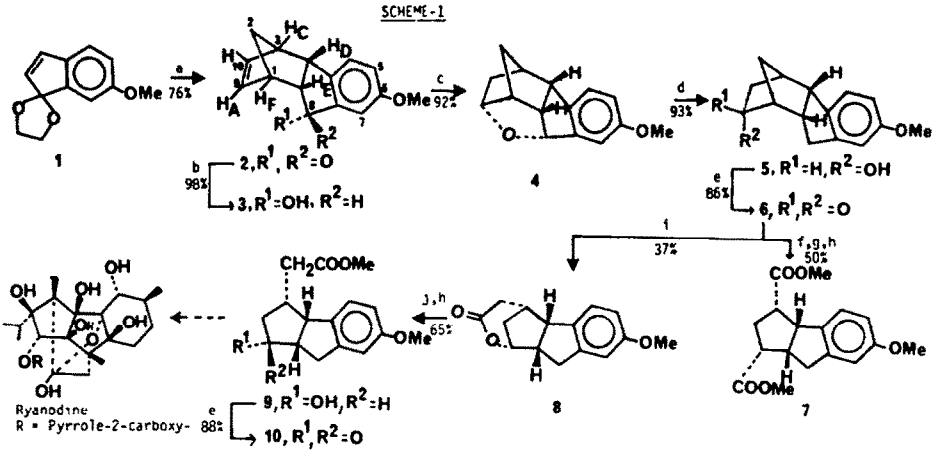
The fragmentation of bicyclo[2.2.1]heptanes for the regio and stereocontrolled delivery of substituted cyclopentanes is an inventive strategy for natural product elaboration[1,2]. The synthesis of prostaglandins[1a], monoterpene[1b] and triquinanes[1c] through oxidative fission of C-C double bond, $PGF_{2\alpha}$[1d] and diterpene[1e] through Baeyer-Villiger rearrangement, spirocyclic sesquiterpene hinesol[1f] through an anionic rearrangement of 1,3-diol monotosylate, antibiotic ikarugamycin[1g] through [3.3] sigmatropic rearrangement and our recent synthetic approach[2] to 5-5-6 and 5-7-6 tricyclic systems from appropriately functionalised bicyclo[2.2.1]heptanes are the representative examples of the various applications of this strategy. In this paper, we extend this concept to demonstrate how a single bicyclo[2.2.1]heptane derivative 2, through intramolecular functionalisation, may lead to two different cyclopentanoid derivatives 9 and 18, intermediates for our projected synthesis of the diterpene ryanodine[3] and the sesquiterpenes of the linear triquinane[4] family respectively.

The required bicyclo[2.2.1]heptane 2 m.p. 78°C was obtained in 76% yield as the sole product by a Diels-Alder cycloaddition between the indenone ketal 1[5] and cyclopentadine in aqueous acidic tetrahydrofuran (THF) (Scheme-1). The stereochemistry of the adduct 2 was readily assigned as endo from ^{1}H NMR analysis. The most characteristic feature of 2 in ^{1}H NMR is the absorption of the exo proton H_E at δ 3.19 as a doublet of doublet with J_{DE} = 6.6 Hz and J_{EF} = 4 Hz closely comparable with the coupling constant reported for the exo protons in norbornene derivatives[2a,6]. Transformation of the adduct 2 to the two different benzhydropentalenes 9 and 18 now requires cleavage of C_1-C_{10} bonds respectively. The C_1-C_9 bond in 2 was cleaved through Baeyer-Villiger oxidative ring opening of one of its derivative selectively functionalised at C_9 (Scheme-1) while C_3-C_{10} bond fission was achieved through a double oxidation sequence (Scheme-2), both the process being achieved through regioselective intramolecular transposition of the C_3 carbonyl function.

Reduction of the ketone 2 in refluxing ether with lithium aluminium hydride (LAH) afforded the syn-ol 3, m.p. 82°C in 98% yield (Scheme-1), the hydride being delivered from the less hindered β-face of the molecule. The syn-orientation of the hydroxyl group in 3 was established from the coupling constant of the C_8-benzylic hydrogen which appeared as a triplet at δ 5.11 (J=8.8 Hz) closely comparable with the value for an analogous compound[2a]. The syn-ol 3 when subjected to oxymercuration [$Hg(OAC)_2$-H_2O-THF-NaOH-$NaBH_4$] underwent smooth cyclisation to afford 4. The absence of D_2O exchangeable hydrogen in ^{1}H NMR of 4 and its resistance to Jones oxidation dictated this structural assignment to the oxymercuration product. Hydrogenolysis of 4 followed by

Jones oxidation afforded the ketone 6. That the C_3-carbonyl group in 2 has really been transposed to C_9 to afford 6 was established by degradation of 6 to the dimethyl ester 7. Baeyer-Villiger oxidation of the ketone 6 with m-chloroperbenzoic acid (mCPBA) afforded a mixture of

SCHEME-1

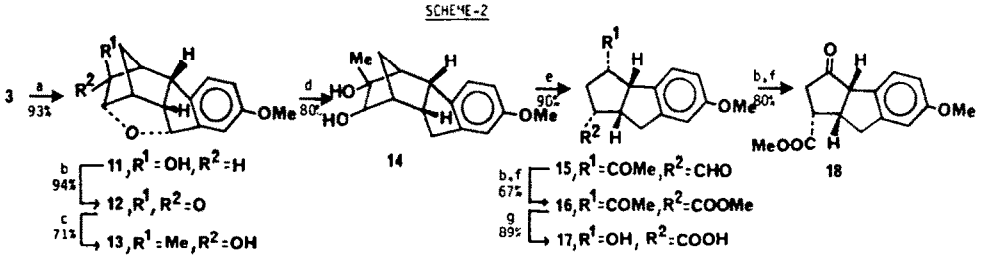


Reagents: a, Cyclopentadiene-THF-H_2O-HCl, rt. b, $LiAlH_4$-Et_2O-reflux. c, $Hg(OAc)_2$-THF-H_2O then NaOH-$NaBH_4$. d, 10% Pd-C, EtOH, 70% $HClO_4$. e, Jones reagent-acetone, 5°. f, NaH-C_6H_6-HCO_2Et. g, NaOH-30% H_2O_2. h, CH_2N_2-Et_2O. i, mCPBA-CH_2Cl_2-PTS, rt. j, KOH-EtOH-H_2O then HCl.

two regioisomeric lactones from which the major lactone 8 could be isolated in 37% yield through fractional crystallisation. On the other hand, direct saponification of the crude lactone mixture followed by esterification of the resulting hydroxy acids resulted in the cleavage of the C_1-C_9 bond producing the hydroxy ester 9 in 65% yield after crystallisation. Oxidation of 9 to the keto-ester 10 provided structural support to the former. Thus, with the synthesis of the hydroxy ester 9, having four contiguous chiral centres, a stereocontrolled approach towards the synthesis of ryanodine is realised as formation of a bond between C_9 and C_8 will provide the gross tetracyclic unit present in this diterpene.

For achieving the cleavage of C_3-C_{10} bond, introduction of a carbonyl function at C_{10} was necessary. Treatment of the syn-ol 3 with mCPBA in dichloromethane afforded the hydroxy ether 11, m.p. 82°C in 94% yield (Scheme-2). Oxidation of 11, m.p. 82°C in 94% yield (Scheme-2).

SCHEME-2



Reagents: a, mCPBA-CH_2Cl_2. b, Jones reagent-acetone. c, MeMgI-Et_2O. d, H_2, 10% Pd-C-EtOH-70% $HClO_4$. e, $NaIO_4$-CH_3CN-H_2O. f, CH_2N_2-Et_2O. g, KOH-H_2O-EtOH.

Oxidation of 11 provided the desired 10-oxo derivative 12. Reaction of 12 with excess of methyl magnesium iodide in ether afforded a mixture of exo and endo addition products from which the exo addition product 13, m.p. 118°C was isolated in 71% yield. Hydrogenolysis of 13 afforded the cis diol 14 cleavage of which was achieved with excess of sodium metaperiodate in aqueous acetonitrile to afford 15, m.p. 100°C in 98% yield. The dione 15, having two substituents of different oxidation level on the generated cyclopentane ring, was easily transformed to the methyl ester 16 through Jones oxidation followed by diazomethane treatment. Sequential reaction of 16 with

mCPBA and hydrolysis of the resulting acetoxy ester afforded the hydroxy acid 17, m.p. 116°C in 89% overall yield. Finally, Jones oxidation of 17 followed by diazomethane treatment afforded the keto-ester 18 in 80% yield. In the light of the direct transformation of an aromatic ring through its Birch reduction product to a cyclopentane ring[7], the keto-ester 18 can be considered as a procursor of linear triquinanes.

Experimental

Compounds described here are recemic mixtures. Melting points were determined for samples in open capillary tubes in a sulfuric acid bath. IR spectra were recorded on Perkin-Elmer model 298 in KBr pellet (for solids) and $CHCl_3$ solution (for liquids). ^1H NMR spectra were recorded at 200 MHz unless otherwise noted on a Varian XL-200 spectrometer with TMS as internal standard. Microanalyses were performed by Mr. P.P. Bhattacharyya of this laboratory. The procedure for 'usual work up' involved extraction of organic matter with a water-immiscible solvent (3-4 times), washing of the extract with brine, and drying with anhydrous Na_2SO_4. The solvent after work up was removed under reduced pressure. Petroleum and light petroleum refer to fractions of petroleum ether boiling in the ranges 60-80° and 40-60°C respectively. Column chromatography was performed on SiO_2 (60-120 mesh).

1β,3β,3aβ,8aβ-Tetrahydro-1,3-etheno-6-methoxybenz/e/pentalen-8 (2H)-one (2). A mixture of the 6-methoxy indenone ketal (1)[5] (1.75 g, 9.3 mmol), THF (8.7 mL), freshly distilled cyclopentadiene (8.8 mL), H_2O (0.9 mL) and conc. HCl (0.1 mL) was stirred magnetically in a stoppered flask at room temperature for 18-20 h until the disappearance of the ketal in TLC. Usual work up of the reaction mixture with ether followed by column chromatography (petroleum) afforded a white crystalline solid (2) (1.48 g, 76%). Recrystallisation from ether-petroleum furnished a pure sample, m.p. 78°C; IR 1695, 1610cm^{-1}; ^1H NMR δ 1.70-1.81 (2H), 3.19 (dd, H_E, J_{DE}=6.6 Hz, J_{EF}=4.0 Hz), 3.22 (s, H), 3.35 (brs, H), 3.78 (s, 3H), 3.85 (d, H, J=4.0 Hz), 5.48 (dd, H, J=6 and 3 Hz), 5.89 (dd , J=6 Hz and 3.2 Hz) and 7.0-7.34 (m, 3H). Anal. calcd. for $C_{15}H_{14}O_2$: C, 79.64; H, 6.19. Found: C, 79.43; H, 6.09.

1β,2,3β,3aβ,8β,8aβ-Hexahydro-1,3-etheno-8 -hydroxy-6-methoxybenz/e/pentalene (3). To a magnetically stirred refluxing suspension of LAH (640 mg, 17 mmol) in anhydrous ether (160 mL) was added dropwise a solution of the ketone (2) (2 g, 8.69 mmol) in ether (60 mL). Refluxing was continued for another 3.5 h after which it was cooled to 0°C and was decomposed by dropwise addition of saturated aqueous sodium sulfate solution. The precipitated white mass was filtered out and the filtrate was dried. Removal of solvent under reduced pressure afforded a white solid (3), (1.98 g, 98%), m.p. 76-80°C. Recrystallisation from ether - light petroleum furnished a pure sample, m.p. 82°C; IR 3510, 1610cm^{-1}; ^1H NMR δ 1.56-1.67 (3H), 3.08 (brs, H), 3.14 (brs, H), 3.25 (dd, 2H, J=9.6 and 4 Hz), 3.73-3.80 (dd, merged under - OMe signal), 3.75 (s, 3H), 5.11 (t, H, J=8.8 Hz), 5.54 (dd, H, J=5.6 and 3 Hz), 6.04 (dd, H, J=5.6 and 2.8 Hz), 6.77 (d, 2H, J=8 Hz), 7.02 (d, H, J=8 Hz). Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.95; H, 7.02. Found: C, 78.85; H, 7.17.

1β,2,3β,3aβ,8β,8aβ-Hexahydro-1,3-ethano-8,9-epoxy-6-methoxybenz/e/pentalene (4). A solution of the hydroxy compound (3) (500 mg, 2.19 mmol) in THF (4 mL) was added to a magnetically stirred yellow suspension of mercuric acetate (1.32 g, 4.14 mmol) in H_2O (6 mL) and THF (6 mL). The flask was stoppered and stirred at room temperature for 24 h. Aqueous NaOH (6 mL, 3 M) was then added followed by addition of a solution of $NaBH_4$ (125 mg, 3.30 mmol) in 3M aqueous NaOH (5 mL). After stirring for 30 minutes, the reaction mixture was saturated with NaCl and worked up with ether to afford a liquid which on sublimation afforded (4) (460 mg, 92%) as a colourless liquid b.p. 145°C (bath temperature) (0.3 mm). ^1H NMR δ 0.82-1.94 (4H), 2.29 (brs, H), 2.77 (t, H, J= 5 Hz), 3.24-3.66 (2H), 3.77 (s, 3H), 4.46 (dd, H, J=9.6 and 4 Hz), 5.11 (d, H, J=4.8 Hz), 6.83 (dd, H, J=9 and 2 Hz), 6.92 (d, H, J=2 Hz), 7.06 (d, H, J=9 Hz). Anal. calcd. for $C_{15}H_{16}O_2$: C, 78.95; H, 7.02. Found: C, 78.82; H, 7.29.

1β,2,3β,3aβ,8,8aβ-Hexahydro-1,3-(9-endo-hydroxyethano)-6-methoxybenz/e/pentalene (5). Hydrogenolysis of the compound (4) (480 mg, 2.1 mmol) was accomplished in EtOH (10 mL) using 10% Pd/C catalyst (100 mg) in presence of 70% $HClO_4$ (0.06 mL) for 5 h. After neutralization of the acid with powdered $NaHCO_3$, the reaction mixture was filtered through a short column of SiO_2 to remove the catalyst. Removal of solvent afforded a white solid (5) (440 mg, 93%); m.p. 102-106°C. Recrystallization from ether - light petroleum furnished the pure sample, m.p. 108°C; IR 3240, 1605cm^{-1}; ^1H NMR δ 0.58-1.06 (2H), 1.33-1.88 (3H), 2.36 (brs, H), 2.51 (t, H, J=6 Hz), 2.82-3.08 (2H), 3.42-3.58 (H), 3.66-3.90 (H), 3.78 (s, 3H), 4.24 (m, H), 6.76 (d, 2H, J=10 Hz), 7.03 (d, H, J=10 Hz). Anal. calcd. for $C_{15}H_{18}O_2$: C, 78.26; H, 7.82. Found: C, 77.95; H, 8.00.

1β,2,3β,3aβ,8,8aβ-Hexahydro-1,3-(9-oxo-ethano)-6-methoxybenz/e/pentalene (6). To a magnetically stirred cold (5-10°C) solution of 5 (440 mg, 1.91 mmol) in acetone (7 mL), Jones reagent (1.4 mL) was added dropwise. After stirring for additional 30 minutes, the reaction mixture was poured into water (30 mL). Usual work up with ether afforded a solid (6) (375 mg, 86%), m.p. 76-79°C. Recrystallization from ether-light petroleum furnished the pure compound, m.p. 80°C; IR 1730, 1605cm^{-1}; ^1H NMR δ 0.78-1.54 (2H), 1.7-2.08 (2H), 2.52-3.22 (5H), 3.66-4.0 (H), 3.73 (s, 3H), 6.66 (brs, H), 6.67 (dd, H, J=8 and 2 Hz) and 7.0 (d, H, J=8 Hz). Anal. calcd. for $C_{15}H_{16}O_2$: C, 78.95; H, 7.02. Found: C, 78.91; H, 7.35.

Methyl-1β,2,3β,3aβ,8,8aβ-hexahydro-6-methoxybenz/e/pentalene-1α,3α-dicarboxylate (7). A solution of the ketone (6) (150 mg, 0.7 mmol) in dry benzene (2 mL) was added to a stirred ice-cold suspension of NaH (980 mg, 20.3 mmol, 50%) (prewashed with petroleum) in benzene followed by a drop of MeOH under N_2. After stirring for 30 minutes, ethyl formate (0.6 mL, 6 mmol) was added

dropwise. The reaction mixture was left overnight after stirring at cold for 2 h. MeOH was added to cold reaction mixture until effervescences stopped. This was extracted with ether to remove any unreacted material. The basic aqueous part after acidification (10% aqueous HCl) was worked up with ether to afford a brown viscous liquid (130 mg).

The brown mass was dissolved in 10% aqueous NaOH (9.8 mL) and was oxidized at room temperature by adding H_2O_2 (8.4 mL, 30%) and aqueous NaOH (4.9 mL) in two lots with stirring for 5 h. The reaction mixture after acidification (6N HCl) was worked up with ether to afford the solid dicarboxylic acid, which on treatment with ethereal diazomethane afforded the dimethyl ester (7) (100 mg, 50%), m.p. 110°C; IR 1735cm^{-1}; ^{1}H NMR δ 2.01-2.30 (3H), 2.79-2.83 (H), 2.93-3.07 (2H), 3.38-3.50 (H), 3.53 (s, 3H), 3.74 (s, 3H), 3.75 (s, 3H), 3.97 (t, H, J=7.8 Hz), 6.66 (brs, 2H), 6.92 (d, H, J=8.8 Hz). Anal. calcd. for $C_{17}H_{20}O_5$: C, 67.10; H, 6.56. Found: C, 66.82; H, 6.85.

1β,2,3β,3aβ,8,8aβ-Hexahydro-6-methoxybenz/e/pentalen-1α→3α-methylene carboxy lactone (8). A solution of the ketone (6) (200 mg, 0.87 mmol) in CH_2Cl_2 (16 mL) was stirred with mCPBA (325 mg, 1.87 mmol) and $NaHCO_3$ (570 mg, 6.78 mmol) at room temperature for 30 h. The reaction mixture was successively washed with 5% aqueous Na_2SO_3 (3 x 5 mL), H_2O (2 x 5 mL), 5% aqueous $NaHCO_3$ (3 x 5 mL), brine (2 x 5 mL) and sried. Removal of solvent afforded a liquid which on filtration through a short column of neutral Al_2O_3 afforded a solid (160 mg, 75%) as a mixture of two regio-isomeric lactones. Repeated crystallization afforded the major lactone (8) (80 mg, 37%), m.p. 84°C; IR 1730, 1600cm^{-1}; ^{1}H NMR δ 0.80-1.24 (2H), 1.70-2.58 (3H), 2.80 (m, H), 2.92-3.36 (2H), 3.80 (s, 3H), 3.98 (t, H, J=8 Hz), 4.84 (brs, H), 6.78 (dd, 2H, J=10 and 2 Hz) and 7.05 (d, H, J=10 Hz). Anal. calcd. for $C_{15}H_{16}O_3$: C, 73.77; H, 6.55. Found: C, 74.02; H, 6.74.

1β,2,3β,3aβ,8,8aβ-Hexahydro-1α-hydroxy-3α-carbomethoxymethyl-6-methoxybenz/e/pentalene (9). The crude lactone mixture (75 mg, 0.30 mmol) obtained as above was hydrolyzed by refluxing for 3.5 h with 2.5% aqueous ethanolic KOH (4 mL). The reaction mixture after dilution with H_2O was extracted with ether to remove unhydrolyzed material. The basic aqueous part on acidification (6N HCl) was saturated with NaCl and worked up with ether to afford the hydroxy acid which was directly esterified with ethereal diazomethane. Crystallization of the crude methyl ester, from ether-light petroleum afforded the pure hydroxy ester (9) (55 mg, 65%), m.p. 94°C; IR 3420, 1735, 1610cm^{-1}; ^{1}H NMR δ 1.20-1.26 (2H), 1.91-2.14 (2H), 2.36-2.86 (3H), 3.16-3.25 (2H), 3.68 (s, 3H), 3.77 (s, H), 3.78 (s, 3H), 4.16-4.34 (H), 6.68 (dd, H, J=8.3 and 2.5 Hz), 6.75 (s, H), 6.94 (d, H, J=8.2 Hz). Anal. calcd. for $C_{16}H_{20}O_4$: C, 69.36; H, 7.24. Found: C, 69.15; H, 7.42.

2,3β,3aβ,8aβ-Tetrahydro-3α-carbomethoxymethyl-6-methoxybenz/e/pentalen-1-(8H)-one (10). To a magnetically stirred cold (5-10°C) solution of (9) (25 mg, 0.09 mmol) in acetone (2 mL), Jones reagent (0.15 mL) was added dropwise. After stirring for additional 1 h, the reaction mixture was poured into water (6 mL) and worked up with ether to afford a liquid (10) (22 mg, 88%); IR 1735cm^{-1}; ^{1}H NMR δ 1.64-1.76 (2H), 2.40-2.66 (2H), 2.81-3.13 (4H), 3.73 (s, 3H), 3.77 (s, 3H), 4.05 (t, H, J=6.4 Hz), 6.75 (d, 2H, J=8 Hz), 7.19 (d, H, J=8 Hz). Anal. calcd. for $C_{16}H_{18}O_4$: C, 70.07; H, 6.56. Found: C, 70.12; H, 6.37.

1β,2,3β,3aβ,8β,8aβ-Hexahydro-8α,9α-epoxy-1,3-(10-exohydroxy ethano)-6-methoxybenz/e/pentalene (11) A solution of the hydroxy compound (3) (3g, 13.15 mmol) in CH_2Cl_2 (90 mL) was stirred magnetically with mCPBA (2.55 g, 15 mmol) at room temperature for 18 h. The reaction mixture was successively washed with 5% aqueous Na_2SO_3 (3 x 25 mL), H_2O (2 x 25 mL), 5% aqueous $NaHCO_3$ (3 x 25 mL), brine and dried. Removal of solvent afforded a solid (11) (3 g, 93%), m.p. 108-110°C. Recrystallization from methylene chloride-light petroleum afforded the pure sample, m.p. 110°C; IR 3400, 1610cm^{-1}; ^{1}H NMR δ 1.68-1.98 (2H), 2.24-2.38 (2H), 2.83 (brs, H), 3.19 (s, H), 3.29-3.53 (2H), 3.83 (s, 3H), 4.14 (d, H, J=6 Hz), 5.15 (d, H, J=6 Hz), 6.89 (d, H, J=8 Hz), 6.92 (s, H), 7.16 (d, H, J=8 Hz). Anal. calcd. for $C_{15}H_{16}O_3$: C, 73.77; H, 6.55. Found: C, 73.82; H, 6.65.

1β,2,3β,3aβ,8β,8aβ-Hexahydro-8α,9α-epoxy-1,3-(10-oxoethano)-6-methoxybenz/e/pentalene (12). To a magnetically stirred cold (5-10°C) solution of (11) (320 mg, 1.31 mmol) in acetone (15 mL), Jones reagent (1 mL) was added dropwise. After stirring for additional 45 minutes the reaction mixture was poured into water (40 mL) and worked up with ether to afford a solid (12) (300 mg, 94%), m.p. 76-80°C. Recrystallization from CH_2Cl_2-light petroleum furnished the analytical sample, m.p. 82°C; IR 1750, 1610cm^{-1}; ^{1}H NMR δ 1.79-1.95 (H), 2.00-2.37 (2H), 3.07 (brs, H), 3.32 (brs, H), 3.81 (s, 3H), 3.91 (q, H, J=8 Hz), 5.57 (d, H, J=8 Hz), 5.89 (d, H, J=8 Hz), 6.92 (dd, H, J=8 and 2 Hz), 6.96 (d, H, J=2Hz), 7.20 (d, H, J=8 Hz). Anal. calcd. for $C_{15}H_{14}O_3$: C, 74.38; H, 5.78. Found: C, 74.44; H, 5.78.

1β,2,3β,3aβ,8β,8aβ-Hexahydro-8α,9α-epoxy-1,3-(10-exo-methyl-10-endo-hydroxyethano)-6-methoxybenz/e/pentalene (13). A solution of the ketone (12) (1.58 g, 6.5 mmol) in ether (60 mL) was added dropwise to a magnetically stirred ice-cold solution of MeMgI /prepared from Mg (1.7 g, 70.8 mg atom) and MeI (8 mL, 1.28 mmol) in ether (40 mL)/. After complete addition, the reaction mixture was stirred for additional 2 h at room temperature and left overnight. Then the reaction mixture was refluxed for 1 h. The cold reaction mixture was quenched with saturated aqueous NH_4Cl. The ether layer was separated and the aqueous part was extracted with ether (3 x 40 mL). The combined ether layer was washed with brine (2 x 20 mL), dried. Removal of solvent afforded a solid which was found to be a mixture of two components having Rt's 7.31 and 9.29 min in the ratio of 78:20 by GC. Repeated crystallization of the crude product mixture from ether-light petroleum afforded the desired endo-ol (13) (1.2 g, 71%), m.p. 118°C; IR 3540, 1605 cm^{-1}; ^{1}H NMR δ 1.17 (s, 3H), 1.67-1.86 (2H), 2.28 (brs, H), 2.90 (brs, H), 3.41-3.79 (3H), 3.79 (s, 3H), 3.87 (d, H, J=4.3 Hz), 5.22 (d, H, J=4.6 Hz), 6.87 (dd, H, J=8.2 and 2.5 Hz), 6.93 (d, H, J=2.4 Hz), 7.23 (d, H, J=8.2 Hz). Anal. calcd. for $C_{16}H_{18}O_3$: C, 74.71; H, 6.97. Found: C, 74.68; H, 7.15.

1β,2,3β,3aβ,8,8aβ-Hexahydro-1,3-(10-exo-methyl-9,10-endo-dihydroxyethano)-6-methoxybenz/e/pentalene (14). Hydrogenolysis of the compound (13) (1.4 g, 5.42 mmol) was accomplished in EtOH (25 mL) using 10% Pd/C (500 mg) in presence of $HClO_4$ (70%, 0.2 mL) for 9 h. After neutralization of the acid with powdered $NaHCO_3$, the reaction mixture was filtered to remove the catalyst. Removal of solvent from the filtrate afforded a white solid (14) (1.13 g, 80%). Recrystallization from ether-light petroleum furnished the pure sample, m.p. 130°C; IR 3520, 3350, 1600cm^{-1}; ^{1}H NMR δ 1.20 (s, 3H), 1.28 (m, H), 1.50 (m, H), 2.22 (brs, 2H), 2.45-3.10 (4H), 3.64-4.0 (3H), 3.78 (s, 3H), 6.79 (brs, 2H), 7.27 (d, H, J=9 Hz). Anal. calcd. for $C_{16}H_{20}O_3$: C, 73.84; H, 7.69. Found: C, 73.92; H, 7.65.

1β,2,3β,3aβ,8,8aβ-Hexahydro-3α-acetyl-6-methoxybenz/e/pentalen-1α-al (15). A solution of the compound (14) (1.05 g, 4.03 mmol) in acetonitrile (52 mL) and water (52 mL) was stirred with sodium metaperiodate (2.62 g, 12.3 mmol) at room temperature for 5 h. The reaction mixture was diluted with water and worked up with ether to afford a solid (15) (940 mg, 90%), m.p. 98-100°C. Recrystallization from ether-light petroleum afforded the pure sample, m.p. 100°C; IR 1700, 1600cm^{-1}; ^{1}H NMR δ 2.05 (s, 3H), 2.23-3.56 (6H), 3.90 (brs, H), 3.98-4.2 (H), 6.61 (brs, 2H), 6.83 (d, H, J=8 Hz), 9.67 (d, H, J=2 Hz). Anal. calcd. for $C_{16}H_{18}O_3$: C, 74.71; H, 6.97. Found: C, 74.98; H, 7.21.

Methyl-1β,2,3β,3aβ,8,8aβ-Hexahydro-3α-acetyl-6-methoxybenz/e/pentalene-1α-carboxylate (16). To a magnetically stirred cold (5-10°C) solution of 15 (930 mg, 3.6 mmol) in acetone (28 mL), Jones reagent (3 mL) was added dropwise. After stirring for additional 30 minutes, the reaction mixture was poured into water (80 mL) and worked up with ethylacetate. The organic layer was washed with 2% aqueous NaOH solution. The basic aqueous washing was acidified with 6N HCl and worked up with ethylacetate to afford the acid, m.p. 156-160°C which was esterified with ethereal diazomethane to afford the methyl ester (16) (700 mg, 67%), m.p. 82-85°C. Recrystallization from ether-light petroleum afforded the pure sample, m.p. 85°C; I.R. 1720, 1695, 1610cm^{-1}; ^{1}H NMR δ 1.91 (s, 3H), 1.92-2.25 (2H), 2.70-2.89 (H), 2.92-3.15 (3H), 3.34-3.49 (septet, H), 3.70 (s, 3H), 3.71 (s, 3H), 4.00 (dd, H, J=8.3 and 9.8 Hz), 6.58 (d, H, J=2.4 Hz), 6.63 (s, H), 6.84 (d, H, J=7.8 Hz). Anal. calcd. for $C_{17}H_{20}O_4$: C, 70.83; H, 6.94. Found: C, 71.11; H, 7.30.

1β,2,3β,3aβ,8,8aβ-Hexahydro-3α-hydroxy-6-methoxybenz/e/pentalene-1α-carboxylic acid (17). A solution of 16 (600 mg, 2.08 mmol) in CH_2Cl_2 (30 mL) was stirred magnetically with mCPBA (480 mg, 2.7 mmol) and PTS (70 mg, 0.37 mmol) at room temperature for 30 h. The reaction mixture was successively washed with 5% aqueous Na_2SO_3 (3 x 10 mL), H_2O (2 x 10 mL), 5% aqueous $NaHCO_3$ (3 x 10 mL), brine (2 x 10 mL) and dried. Removal of solvent followed by column chromatography of the residual oil afforded a white solid (520 mg, 82%), m.p. 56-58°C. Recrystallization from ether-light petroleum furnished the analytical sample, m.p. 58°C; IR 1725, 1695, 1610cm^{-1}; ^{1}H NMR δ 1.92-2.14 (2H), 2.27 (s, 3H), 2.62-2.78 (H), 2.94-3.13 (3H), 3.34-3.48 (H), 3.68 (s, 3H), 3.77 (s, 3H), 3.90 (H, dd, J=8.8 and 3.1 Hz), 6.66-6.77 (2H), 7.08 (d, H, J=8.2 Hz). Anal. calcd for $C_{17}H_{20}O_5$: C, 67.10; H, 6.57. Found: C, 67.32; H, 6.73.

A solution of the above acetate (120 mg, 0.39 mmol) in ethanol (6 mL) was stirred with aqueous KOH (6 mL, 10%) under N_2 at room temperature for 1 h followed by refluxing for 45 min. The reaction mixture after dulution with H_2O was extracted with ethylacetate to remove unhydrolyzed material. The basic aqueous part on acidification with 6N HCl was worked up with ethylacetate to afford solid hydroxy acid (17) (95 mg, 97%), m.p. 110-114°C. Recrystallization from ethylacetate-light petroleum afforded the pure sample, m.p. 116°C. IR 3420, 1700, 1605cm^{-1}; ^{1}H NMR (of methyl ester) δ 1.62 (brs, H), 2.0-2.16 (2H), 2.72-3.22 (4H), 3.34 (d, H, J=8 Hz), 3.49 (d, H, J=6.8 Hz), 3.64 (s, 3H), 3.74 (s, 3H), 6.72 (d, 2H, J=8 Hz), 7.06 (d, H, J=8 Hz). Anal. calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 68.00; H, 6.80.

Methyl-1β,3aβ,8,8aβ-Tetrahydro-3(2H)-oxo-6-methoxybenz/e/pentalene-1α-carboxylate (18). To a magnetically stirred cold (5-10°C solution of (17) (250 mg, 1.0 mmol) in acetone (7 mL), Jones reagent (0.85 mL) was added dropwise. After stirring for additional 1 h, the reaction mixture was poured into water (20 mL) and extracted with ethylacetate. The organic layer was washed with 2% aqueous NaOH solution. The chilled basic aqueous washing was then acidified with 6N HCl and worked up with ethylacetate to afford the keto acid (200 mg, 80%), m.p. 108°C; IR: 1695-1610cm^{-1}, which was converted to the corresponding methyl ester (18) by treatment with ethereal diazomethane; ^{1}H NMR δ 1.94-2.16 (2H), 2.60-3.40 (5H), 3.66 (s, 3H), 3.76 (s, 3H), 6.72 (d, 2H, J=8 Hz), 7.08 (d, H, J=8 Hz). Anal. calcd. for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20. Found: C, 69.03; H, 6.30.

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