Pergamon

Tetrahedron 56 (2000) 7785–7795

TETRAHEDRON

Molecular Complexity from Aromatics: Synthesis and Photoreaction of *endo*-Tricyclo[5.2.2.0^{2,6}]undecanes. Formal Total Syntheses of (±)-Coriolin

Vishwakarma Singh,[a,*] Biswajit Samanta[a] and Vinayak V. Kane[b]

[a]*Department of Chemistry, Indian Institute of Technology, Bombay, Mumbai 400 076, India*
[b]*Institut fur Organische Chemie, Technische Universitat Braunschweig, Hagenring 30, D-38106 Braunschweig, Germany*

Received 1 March 2000; revised 12 July 2000; accepted 27 July 2000

Abstract—Formal syntheses of coriolin **1**, a triquinane metabolite isolated from *Coriolus consors*, are described. Oxidation of 6-methyl saligenin **2** in the presence of cyclopentadiene gave the tricyclic keto epoxide **4** which was elaborated to tricyclo[5.2.2.0^{2,6}]undecenones **5** and **18** containing the major structural and stereochemical features of coriolin, in latent form. Triplet sensitized 1,2-acyl shifts in **5** and **18** gave tetracyclic compounds **6** and **19** in a stereoselective manner. Reductive cleavage of cyclopropane rings in **6** and **19** with H_2/Pd-C and TBTH-AIBN respectively, furnished the functionalised triquinanes **7** and **20b** which are known precursors for coriolin.

There has been an intense interest in the synthesis of linearly fused *cis:anti:cis* triquinane natural products and a plethora of methods have been developed for their synthesis.[1–4] Nevertheless, the search for new and efficient method for cyclopentane synthesis continues.[5] Coriolin **1**, a triquinane metabolite isolated from *Coriolus consors*,[6] has been a popular target for synthesis presumably due to its biological properties and unusually functionalized molecular architecture containing angular and geminal methyl groups. Several imaginative routes have been developed for synthesis of coriolin.[2,7] However, a majority of these generate the linearly fused *cis:anti:cis* triquinane framework in an iterative and non-stereoselective fashion. Recently, we reported an efficient and stereoselective method for the generation of molecular complexity from simple precursors.[8] In continuation of our interest in this area, we now wish to report a full account[9] of two formal syntheses of coriolin from 6-methylsaligenin **2**. The key features of our approach are the in situ generation of labile spiro-epoxycyclohexa-2,4-dienone **3**, its cycloaddition reaction with cyclopentadiene and triplet sensitized photochemical reaction of *endo* tricyclo[5.2.2.0^{2,6}]undecanes, as presented below (Fig. 1).

Strategy

Our strategy for the synthesis of coriolin is outlined in Scheme 1. Initially, we focused our attention on the synthesis of the triquinane intermediate **7** which is a precursor to coriolin.[10] The corner stone of our plan is the recognition of the structural and functional relationship between the triquinane **7** and the *endo* annulated tricyclo[5.2.2.0^{2,6}] undecenone **5**. It was envisaged that a photochemical 1,2-acyl shift in the tricyclic system **5** may furnish the tetracyclic system **6** which may in turn be converted to the triquinane **7** via cleavage of the peripheral cyclopropane bond. The crucial tricyclic system **5** was thought to be derived from the epoxy ketone **4** which appeared to be easily accessible from the oxidation of **2** and subsequent interception of the resulting spiro-epoxycyclohexa-2,4-dienone **3** following a procedure developed in our laboratory.[8]

Results and Discussion

Synthesis of the tricyclic precursor 4 and its transformation to the desired chromophoric system 5

The 6-methylsaligenin **2**, easily prepared from 6-methyl anisaldehyde[11] by demethylation and reduction, was

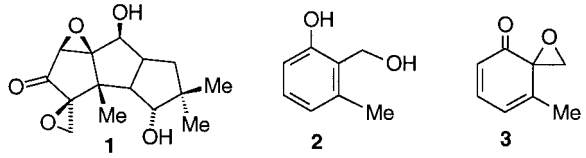
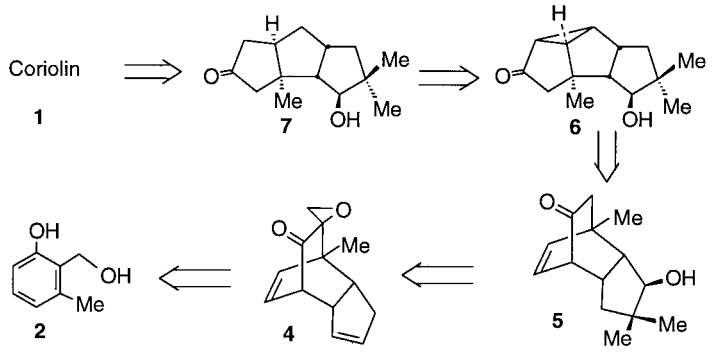


Figure 1.

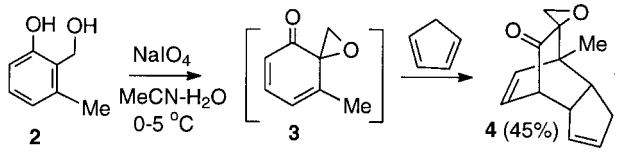
Keywords: cycloaddition; Diels–Alder reaction; photochemistry; polyquinanes.

* Corresponding author. Tel.: +91-22-576-7168; fax: +91-22-576-7152; e-mail: vks@ether.chem.iitb.ernet.in

0040–4020/00/$ - see front matter
PII: S0040-4020(00)00674-8



Scheme 1.



Scheme 2.

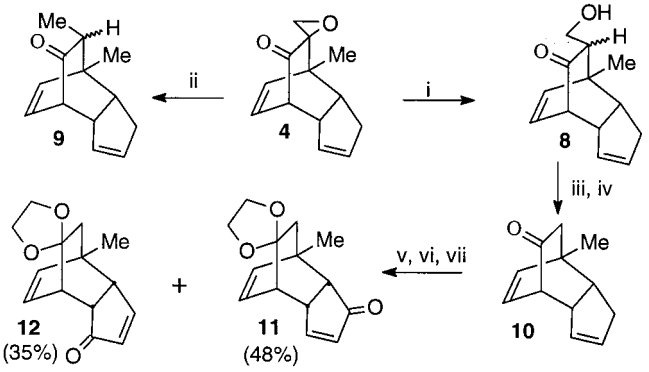
oxidized with sodium metaperiodate in aqueous acetonitrile containing cyclopentadiene to give the desired epoxy ketone **4** in reasonably good yield (Scheme 2). The structure of adduct **4** was deduced from its spectral and analytical data and by comparison with similar adducts previously prepared in our laboratory.[8]

The adduct **4** was reduced[12] with activated zinc in aqueous methanol containing NH_4Cl to give the keto-alcohol **8** as a major product [78%, as a *syn–anti* mixture, ^1H NMR (300MHz)] along with minor amounts of the ketone **9** (as a *syn–anti* mixture) (Scheme 3). It is interesting to note that the reduction of **4** in dry aprotic solvent (dioxane) selectively gave the ketone **9** in excellent yield (85%). Oxidation of the keto-alcohol **8** with Jones reagent followed by decarboxylation gave the tricyclic system **10**. Allylic oxidation[13] of **10** with SeO_2 and subsequent oxidation of the resulting alcohols with Jones' reagent[14] furnished an inseparable mixture of diene-diones which was converted to ketal-enones **11** and **12** and separated by careful column chromatography (Scheme 3).

Towards introduction of the *gem*-dimethyl group in the five-membered ring, the ketal enone **11** was treated with sodium borohydride, reducing both the double bond and carbonyl group. The resulting ketal alcohol was oxidized with PCC[15] to give the keto-ketal **13**. Alkylation of **13** with methyl iodide in the presence of potassium *tert*-butoxide smoothly gave the dialkylated compound **14**. Stereoselective reduction of the ketone **14** in THF–water mixture with sodium borohydride at ambient temperature (~30°C) furnished the desired alcohol **16** (73%) along with minor amounts of the undesired *endo* alcohol **15** (Scheme 4).

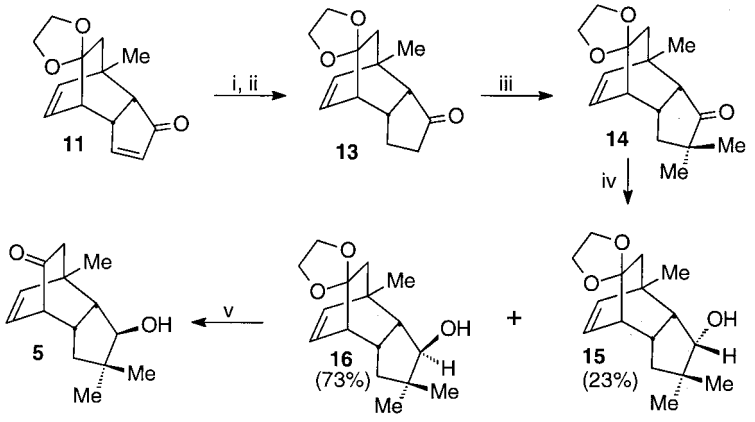
Photochemical reaction of 5 and reductive cleavage of tetracyclic precursor 6: synthesis of coriolin

Irradiation of a solution of compound **5** in acetone with a mercury vapor lamp (125W, Applied Photo Physics), in a Pyrex immersion well, gave the desired 1,2-acyl shift[16] product **6** as a crystalline solid (mp 117–118°C) in 68% yield (Scheme 5). Reductive opening of the cyclopropane ring was effected by catalytic hydrogenation using Pd-C catalyst (10%) and 165 psi hydrogen pressure. Fractional crystallization of the product mixture first gave compound **17** formed as a result of cleavage of the undesired cyclopropane bond (Scheme 5). Further recrystallization of the residue obtained by concentration of the mother liquor furnished the desired tricyclopentanoid **7** as a solid (mp, 118–119°C, lit. mp 118–120°C[10b] and 114–115°C[10a]).



Reagents/Conditions: i, Zn, NH_4Cl, MeOH-H_2O, r.t., 78%; ii, Zn, NH_4Cl, dry dioxane, Δ, 85%; iii, Jones' reagent, 91%; iv, THF-H_2O, Δ, 55%; v, SeO_2, KH_2PO_4,dioxane-H_2O, Δ, 57%; vi, Jones' reagent; acetone, ~5 °C, 89%; vii, p-TsOH, ethylene glycol, benzene, Δ, 83%.

Scheme 3.



Reagents/Conditions: i, $NaBH_4$, MeOH, r.t., 91%; ii, PCC, CH_2Cl_2 78%; iii, ^tBuOK, ^tBuOH, MeI, Δ, 60%; iv, $NaBH_4$, THF-H_2O, 96%; v, HCl(50%), acetone-H_2O, 92%.

Scheme 4.

Since the triquinane intermediate **7**, prepared earlier by Funk et al[10a] and Little and co-workers,[10b] is a precursor for coriolin, the formal synthesis of coriolin was complete.

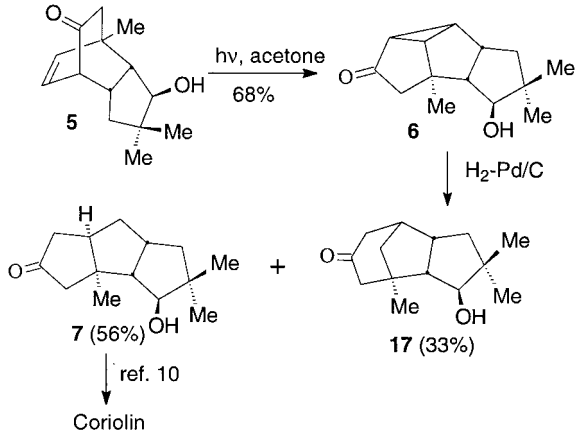
An Alternative Formal Synthesis of Coriolin

In the preceding section, synthesis of the triquinane intermediate **7** from the adduct **4** was described. However, it may be noted that one carbon was removed and two carbons were added during the transformation of **4** to the key chromophoric system **5**. Further, it may be recalled that the oxirane ring of the adduct **4** can be selectively reduced with Zn-NH_4Cl in aprotic solvent to give the ketone **9** (Scheme 3) in excellent yield, wherein all the thirteen carbons of the starting materials are retained. Therefore, we decided to elaborate the ketone **9** into a triquinane intermediate **20b** which is also a known intermediate for coriolin (Scheme 6).[17]

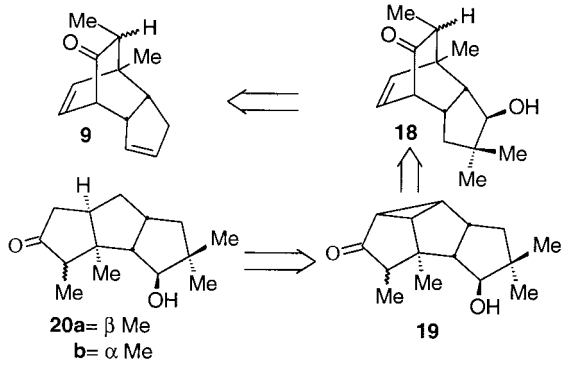
Elaboration of 9 to the tricyclic keto-alcohol 18 and photochemical rearrangement of 18

Reduction of the epoxy ketone **4** with Zn-NH_4Cl in dry dioxane gave **9** [as a *syn–anti* (*anti* isomer as major) mixture] in excellent yield (85%). The compound **9** was converted into a mixture of ketal alcohols **21** and **22** via oxidation, ketalization and reduction (Scheme 7) from which the desired ketal alcohol **21** was obtained in major amounts (60%) by careful column chromatography. Oxidation of the desired ketal alcohol **21** with PCC gave **23** which on alkylation with methyl iodide in the presence of potassium *tert*-butoxide furnished the alkylated compound **24** in 62% yield (Scheme 7). The tetramethyl ketone **24** thus obtained was reduced with sodium borohydride in THF-water mixture to give a mixture of alcohols from which the desired alcohol **26** was isolated in major amounts (70%) along with its *endo* isomer **25** (Scheme 7). In addition to the spectroscopic analysis, the stereochemical orientation of the hydroxyl group in **26** was further confirmed through its conversion to a known triquinane (vide infra).

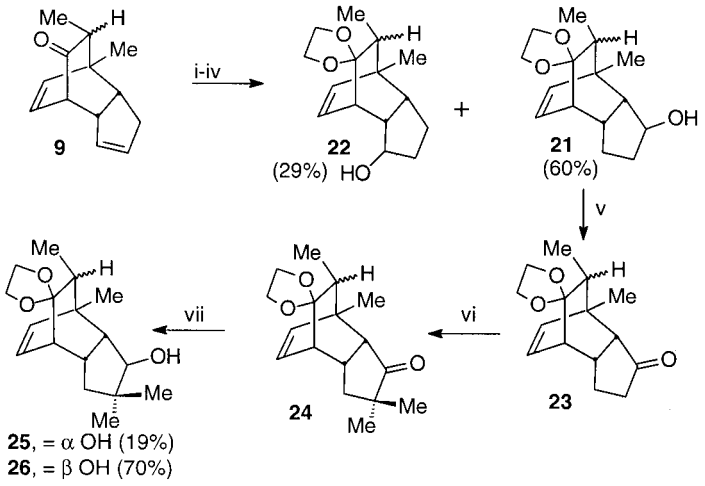
Hydrolysis of **26** with HCl (50%) in aqueous acetone readily gave the chromophoric system **18** in excellent yield (90%) (Scheme 8). Irradiation of **18** in acetone (solvent as well as sensitizer) with a mercury vapor lamp, (125 W, Applied Photo Physics) in a Pyrex immersion well gave the desired tetracyclic compound **19** in excellent isolated yield (65%) (Scheme 8).



Scheme 5.



Scheme 6.



Reagents/Conditions: i, SeO_2, KH_2PO_4, dioxane-H_2O, Δ, 55%; ii, Jones' reagent, acetone, 95%; iii, p-TsOH, Ethyleneglycol, benzene, Δ, 80%; iv, $NaBH_4$, MeOH, r.t., 89%; v, PCC, CH_2Cl_2, r.t., 98%; vi, KO^{t}Bu-BuOH, MeI, Δ, 62%; vii, $NaBH_4$, THF-H_2O, 89%.

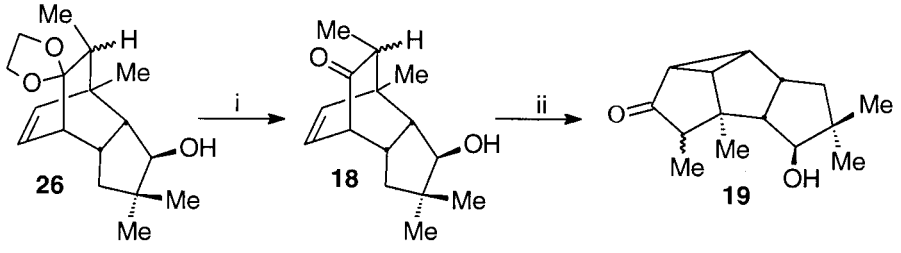
Scheme 7.

Cleavage of cyclopropane ring in the tetracyclic photoproduct 19: synthesis of the triquinane intermediate 20

At this juncture, cleavage of the peripheral cyclopropane sigma bond in the tetracyclic precursor **19** was required for the synthesis of the intermediate **20** for coriolin. Therefore, a solution of the compound **19** in methanol was stirred with Pd-C catalyst (10%) in an atmosphere of hydrogen for 11 hours (165 psi pressure). However, it gave quantitatively the undesired bridged tricyclic compound **27**, instead of the desired tricyclopentanoid **20** (Scheme 9).

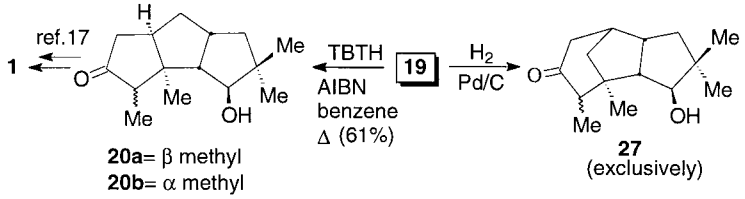
Therefore, we sought other methods for the cleavage of carbonyl conjugated cyclopropane ring such as photochemical electron transfer induced reduction,[18] electrophile assisted cleavage[19,20] and radical reduction by tributyltin hydride.[21] After careful scrutiny of these methods, a solution of the tetracyclic hydroxy-ketone **19** in benzene containing AIBN was treated with tributyltin hydride and refluxed for 3 hours (TLC) which gave the desired triquinane **20b** along with its epimer **20a** as a result of cleavage of peripheral cyclopropane bond (Scheme 9).

The structure of both the reduced products were established from their spectral data and comparison with data reported in literature.[17] Since the triquinane **20b** is a known precursor to coriolin, another formal synthesis was also complete.



Reagents/Conditions: i, HCl (50%), acetone, 90%; ii, hv, pyrex, acetone, 1.5 h, 65%.

Scheme 8.



Scheme 9.

Conclusion

In summary, two formal total syntheses of coriolin, a metabolite of *Coriolus consors*, from simple precursors have been reported. Cycloaddition of spiro-epoxy-5-methylcyclohexa-2,4-dienone and photochemical 1,2-acyl shift are the key features of our approach. The present routes constitute *a unique example of synthesis in which an aromatic ring and cyclopentadiene are combined in a manner so as to give the thirteen carbons of coriolin with desired connectivities and framework with correct stereochemical orientation in a highly efficient manner*. The requisite chromophoric systems **5** and **18** endowed with the important structural and stereochemical features of coriolin were derived from a common precursor **4** which itself was readily assembled in a single step from 6-methyl saligenin and cyclopentadiene. It is noteworthy that the adduct **4** contains the angular methyl group and the linearly fused *cis:anti:cis* triquinane framework in a latent fashion. Addition of two more carbons and hydroxyl group in each of the intermediates **10** and **9** led to the precursors **5** and **18**. Triplet sensitized photo-chemical rearrangement of **5** and **18** followed by cleavage of the cyclopropane ring led to the syntheses of highly embellished triquinanes **7** and **20b** respectively, which are known precursors for coriolin.

Experimental Section

General Remarks

IR spectra were recorded on a Nicolet Impact 400 FT-IR Instrument. UV spectra were recorded on a Shimadzu 260 instrument. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were recorded on a Varian VXR 300 instrument. Most of the samples were dilute solutions in $CDCl_3$ with $SiMe_4$ as internal standard. Mass spectra were recorded on a HP GCD 1800A mass spectrometer. Microanalyses were conducted on a CEST 1106 instrument. HRMS were determined by Finnigan Mat 8400. Melting points were determined on a veego apparatus of Buchi type and are uncorrected. All the organic extracts were dried over anhydrous sodium sulfate. Reactions were monitored using thin layer chromatography and spots were visualized with iodine vapour. Column chromatography was performed using Acme/SRL silica gel (60–120 and 100–200 mesh). Elution was done with petroleum ether (60–80°C) and ethyl acetate mixtures.

1-Methyl-9-spiro-epoxy-*endo*-tricyclo[5.2.2.0^{2,6}]undeca-4,10-diene-8-one (4). To a solution of 6-methylsaligenin **2** (2.0 g, 14.49 mmol) in acetonitrile (40 ml) was added freshly cracked cyclopentadiene (10 ml, excess), and the reaction mixture was cooled in an ice bath (0–5°C). A solution of $NaIO_4$ (12 g, 56.07 mmol) in water (40 ml) was then added dropwise to the reaction mixture with stirring. After stirring for 2 h, it was brought to room temperature (~30°C), and further stirred for 6 h. The reaction mixture was filtered and organic layer was separated and the aqueous layer was extracted with ether (3×50 ml). The combined organic extract was washed with brine (30 ml) and dried over anhydrous sodium sulfate. Removal of solvent gave a residue which was chromatographed on silica gel. Elution with petroleum ether first gave unreacted cyclopentadiene dimer. Continued elution with petroleum ether-ethyl acetate, (95:5) furnished the adduct **4** (1.31 g, 45%) as a colourless solid which was recrystallized from petroleum ether-ethyl acetate (96:4), mp 79–80°C. IR (film) ν_{max}: 1737 cm^{-1}. UV (MeOH) λ_{max}: 304, 212 nm. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.16–6.04 (m, 2H, γ and β protons of β, γ-enone moiety), 5.72 (m of d, J=6 Hz, 1H, olefinic H), 5.51 (m of d, J=6 Hz, 1H, olefinic H), 3.36–3.10 (m, 2H, C*H*), 3.04 (part of an AB system, J_{AB}=6 Hz, 1H, –OCH_2–), 2.93 (part of an AB system, J_{AB}=6 Hz, 1H, –OCH_2–), 2.79 (ddd, J_1=J_2=10.5 Hz, J_3=5 Hz, 1H, C*H*), 2.50 (m of dd, J_1=18 Hz, J_2=10 Hz, 1H, CH_2), 2.10 (m of d, J=18 Hz, 1H, CH_2), 1.1 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 205.85 (CO), 138.17, 133.33, 129.68, 128.01 (four olefinic carbons), 59.78, 51.87, 51.25, 49.76, 42.36, 42.24, 36.99, 15.15. Mass (m/z): 202 (M^+). Analysis Found: C, 77.00; H, 6.92%. Calcd, for $C_{13}H_{14}O_2$: C, 77.22; H, 6.93%.

1-Methyl-*endo*-tricyclo[5.2.2.0^{2,6}]undeca-4,10-dien-8-one (10). To a suspension of activated zinc (15 g, excess) in methanol-water (2:8, 120 ml) was added a solution of epoxy ketone **4** (3 g, 14.85 mmol) in methanol (10 ml) and then ammonium chloride (3.3 g, excess) was also added to it. The reaction mixture was stirred at ambient temperature (~30°C) for 7 h (TLC). The reaction mixture was filtered through a celite bed to remove zinc and the residue was washed with ethyl acetate. The filtrate was concentrated under vacuum, diluted with water (30 ml) and extracted with ethyl acetate (3×50 ml). The combined extract was washed with water (2×30 ml), brine (40 ml) then dried. Removal of solvent followed by chromatography [petroleum ether-ethyl acetate, (96:4)] on silica gel first gave the compound **9** as a colourless liquid (0.36 g, 13%, as a *syn:anti* mixture). Further elution with petroleum ether-ethyl acetate (80:20) furnished the keto alcohol **8** as a viscous colourless liquid [IR (neat) ν_{max}: 3463, 1716 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.11–6.02 (m, 2H, β and γ protons of β, γ-enone moiety), 5.66 (m of d, J=6 Hz, 1H, olefinic H), 5.47 (m of d, J=6 Hz, 1H, olefinic H), 3.90 (ddd, J_1=11 Hz, J_2=8.5 Hz, J_3=4.5 Hz, 1H), 3.75 (ddd, J_1=11 Hz, J_2=8.5 Hz, J_3=2.5 Hz, 1H), 3.20–3.12 (m, 2H), 2.63–2.54 (m, 1H), 2.39 (m of dd, J_1=16 Hz, J_2=9.5 Hz 1H, CH_2), 2.06–1.95 (overlapped m, 2H), 1.18 (s, 3H, CH_3). (data for major isomer). Mass (m/z): 204 (M^+)] as a mixture of *syn:anti* isomers (2.3 g, 78%) which was subjected to oxidation and decarboxylation as follows.

To a solution of the keto alcohol **8** (2.0 g, 9.8 mmol) in acetone (50 ml) was added Jones' reagent dropwise at ~5°C. After the reaction was complete (TLC), acetone was removed under vacuum and the residue was diluted with water (30 ml) and extracted with ethyl acetate (3×40 ml). The combined extract was washed with water (2×25 ml), brine (30 ml) and dried over anhydrous Na_2SO_4. Removal of solvent under vacuum gave a β-keto acid [(1.94 g, 91%), (IR)] which was dissolved in THF-water mixture (1:1, 40 ml) and the reaction mixture was refluxed for 6 h (TLC). Tetrahydrofuran was removed in vacuo, and the aqueous medium was extracted with ether (3×25 ml). The combined extract was washed with sodium bicarbonate solution (30 ml), water(2×40 ml) and dried. The solvent was removed and the residue was chromatographed. Elution with petroleum ether-ethyl acetate (97:3) gave the title

compound **10** (0.85 g, 55%) as a colourless liquid. IR (neat) ν_{max}: 1729 cm^{-1}. UV (MeOH) λ_{max}: 294, 214 nm. ^1H NMR (300 MHz, $CDCl_3$) δ: 6.08–6.01 (m, 2H, γ and β protons of β, γ-enone moiety), 5.65 (m of d, J=6 Hz, 1H, olefinic H), 5.46 (m of d, J=6 Hz, 1H, olefinic H), 3.26–3.19 (m, 1H, C*H*), 3.13–3.08 (m, 1H, C*H*), 2.52–2.36 (overlapped m, 2H, C*H* and CH_2), 2.00 (m of d, partly overlapped with part of an AB system, J=16 Hz, 1H, allylic CH_2), 1.96 (AB system partly overlapped with a m, J_{AB}=17 Hz, 2H, $COCH_2$), 1.29 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 212.78 (CO), 139.46, 132.62, 130.28, 127.46 (olefinic carbons), 52.94, 50.94, 47.05, 46.26, 40.75, 36.78, 22.30. Mass (m/z) : 174 (M^+).

1-Methyl-*endo*-tricyclo[5.2.2.0^{2,6}]-undeca-8-(1,3-dioxolane)-4,10-dien-3-one (11) and 1-methyl-*endo*-tricyclo-[5.2.2.0^{2,6}]-undeca-8-(1,3-dioxolane)-3,10-dien-5-one (12). To a stirred suspension of selenium dioxide (3.17 g, 28.5 mmol) in dioxane–water (5:1, 12 ml) was added potassium dihydrogenphosphate (1.95 g, 14.3 mmol). A solution of the compound **10** (1.0 g, 5.7 mmol) in dioxane (10 ml) was added to the reaction mixture and it was heated at 90°C for 17 h. The reaction mixture was then brought to room temperature, filtered over a celite pad, and washed with ethyl acetate. The filtrate was concentrated under reduced pressure and the residue was diluted with water (25 ml) and extracted with ethyl acetate (3×30 ml). The combined extract was washed with water (2×25 ml), brine (30 ml) and dried. The solvent was removed and the residue was chromatographed. Elution with petroleum ether-ethyl acetate (70:30) furnished a mixture of hydroxy ketones (0.622 g, 57%) [IR and ^1H NMR, (60 MHz)] which was subjected to further oxidation with Jones' reagent as follows.

To a solution of the above mixture of hydroxy ketones (0.622 g, 3.27 mmol) in acetone (25 ml) was added freshly prepared Jones' reagent dropwise at ~5°C. After the oxidation was complete (TLC), acetone was removed under vacuum and the residue was diluted with water (30 ml) and extracted with ether (3×25 ml). The combined extract was washed with saturated sodium bicarbonate solution (2×25 ml), water (2×20 ml) and brine (25 ml) and dried. The solvent was removed in vacuo and the residue was chromatographed on a short column of silica gel. Elution with petroleum ether-ethyl acetate (85:15) furnished a mixture of diene–diones (0.547 g, 89%) which was subjected to ketalization as described below.

A mixture of ethylene glycol (1 ml, excess) and *p*-toluene sulphonic acid (7 mg) in dry benzene (60 ml) was refluxed in a Dean–Stark apparatus, in order to remove traces of water. After which the mixture of diene–diones (0.547 g, 29.0 mmol) was added to it and the reaction mixture was refluxed for 3 h (TLC). The reaction mixture was then brought to room temperature and the benzene layer was separated. It was washed with sodium bicarbonate solution (25 ml), water (2×20 ml), brine (25 ml) and dried. Solvent was removed in vacuo and the residue was chromatographed on silica gel. Elution with petroleum ether-ethyl acetate (90:10) first gave the ketal-enone **11** (0.324 g, 48%) as a colourless solid which was recrystallized from petroleum ether-ethyl acetate (98:2), mp 94–95°C. IR (nujol) ν_{max}: 1686 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.37 (dd, J_1=6 Hz, J_2=2.5 Hz, 1H, –C*H*=CH–CO), 6.14 (dd, J_1=6 Hz, J_2=2 Hz, 1H, –CH=C*H*–CO), 5.88–5.80 (m, 2H, olefinic H), 4.00–3.92 (m, 4H, $(CH_2O)_2$), 3.53–3.48 (m, 1H, C*H*), 2.76–2.72 (m, 1H, C*H*), 2.18 (d, J= 6 Hz, 1H, COC*H*), 1.71 (part of an AB system, J_{AB}= 14 Hz, 1H, CH_2), 1.58 (part of an AB system J_{AB}=14 Hz, 1H, CH_2), 1.46 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 209.91 (CO), 164.39 (d), 136.96 (d), 136.51 (d), 127.69 (d) (four olefinic carbons), 113.10 (s), 64.32 (t), 64.18 (t), 52.45 (d), 48.41 (t), 43.49 (d), 42.72 (d), 40.05 (s), 21.44 (q). Mass (m/z): 232 (M^+). Analysis Found: C, 72.74; H, 7.07%. Calcd, for $C_{14}H_{16}O_3$: C, 72.41; H, 6.89%.

Continued elution with the same solvent furnished the minor isomeric ketal-enone **12** as a viscous liquid (0.236 g, 35%). IR (neat) ν_{max}: 1703 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.55 (dd, J_1=6 Hz, J_2=2.5 Hz 1H, –C*H*=CH–CO), 6.22 (dd, J_1=6 Hz, J_2=2.5 Hz, 1H, –CH=C*H*–CO), 5.97 (dd, J_1=8.5 Hz, J_2=6.5 Hz, 1H, olefinic H), 5.72 (d, J=8.5 Hz, 1H, olefinic H), 4.01–3.92 (m, 4H, $(CH_2O)_2$), 3.03 (dd, J_1=6.5 Hz, J_2=2.5 Hz, 1H, C*H*), 2.88–2.80 (m, 2H, C*H*), 1.80 (part of an AB system, J_{AB}=13.5 Hz, 1H, CH_2), 1.71 (part of an AB system, J_{AB}=13.5 Hz, 1H, CH_2), 1.51 (s, 3H, CH_3). HRMS: M^+, Found, 232.1096. $C_{14}H_{16}O_3$ requires 232.1099.

1-Methyl-*endo*-tricyclo[5.2.2.0^{2,6}]undeca-8-(1,3-dioxolane)-10-ene-3-one (13). Sodium borohydride (0.150 g, 3.94 mmol) was added in small portions to a solution of the ketal-enone **11** (0.80 g, 3.44 mmol) in methanol (10 ml) at ambient temperature (~30°C) during 1 h, after which the reaction was found to be complete (TLC). The solvent was removed in vacuo, and the residue was diluted with water (20 ml) and extracted with ethyl acetate (3×25 ml). The combined organic extract was then washed with brine (20 ml) and dried over anhydrous sodium sulfate. Removal of solvent followed by column chromatography of the residue [petroleum ether-ethyl acetate, (80:20)] furnished the alcohol as a colourless liquid [(0.740 g, 91%),IR (neat) ν_{max}: 3497 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 6.30 (d, J=8.5 Hz, 1H, olefinic H), 6.15 (superimposed dd, J_1=J_2=8.5 Hz, 1H, olefinic H), 4.22 (br m, 1H, *H*–C–OH), 3.95–3.89 (m, 4H $(CH_2O)_2$), 2.72–2.61 (m, 2H, C*H*), 2.04 (dd, J_1=10.5 Hz, J_2=6 Hz, 1H, C*H*), 1.81–1.70 (m, 1H, CH_2), 1.65–1.38 (overlapped m, 6H, CH_2 and O *H*), 1.30 (s, 3H, CH_3), 1.20–1.03 (m, 1H, CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 140.92, 130.28 (olefinic carbons), 74.69, 64.25, 63.96, 55.77, 49.05, 43.09, 41.73, 38.63, 35.92, 29.78, 27.55, 22.82. Mass (m/z): 236 (M^+)] which was oxidized with PCC to give **13** as follows.

To a suspension of PCC (1.09 g, 5.05 mmol) in dichloromethane (10 ml) was added a solution of the above alcohol (0.6 g, 2.96 mmol) in dichloromethane (10 ml). The reaction mixture was stirred for 5 h (TLC) at ambient temperature (~30°C). It was charged on to a short column of silica gel and eluted with ether. Removal of ether under vacuum gave a residue which was again chromatographed on silica gel. Elution with petroleum ether-ethyl acetate (85:15) furnished the ketone **13** (0.541 g, 78%) as a colourless solid which was recrystallized from petroleum ether-ethyl acetate (94:6), mp. 59–60°C. IR (nujol) ν_{max}: 1731 cm^{-1}.

UV (MeOH) λ_{max}: 300, 202 nm. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.26 (superimposed dd, J_1=J_2=8 Hz, 1H, olefinic H), 5.98 (d, J=8 Hz, 1H, olefinic H), 3.92 (m, 4H, $(CH_2O)_2$), 3.05 (m, 1H, C*H*), 2.67 (dd, J_1=6 Hz, J_2=3 Hz, 1H, C*H*), 2.19 (d, J=9.5 Hz, 1H, C*H*), 2.10–2.18 (merged multiplets, 3H, CH_2), 1.64 (part of an AB system partly overlapped with the signal due to H_2O in $CDCl_3$, J_{AB}=14.5 Hz, 1H, CH_2), 1.64–1.55 (multiplet partly merged with signal due to H_2O present in $CDCl_3$, 1H, CH_2), 1.50 (part of an AB system, J_{AB}=14.5 Hz, 1H, C*H*), 1.38 (s, 3H, CH_3). ^{13}C NMR (75 MHz) $CDCl_3$ δ: 220.77(CO), 138.85, 130.53 (olefinic carbons), 113.16, 64.29, 64.04, 55.96, 48.66, 45.33, 40.11, 39.15, 35.65, 24.82, 21.85. Mass (m/z): 234 (M^+). Analysis Found: C, 71.38; H, 7.53%. Calcd, for $C_{14}H_{18}O_3$: C, 71.79; H, 7.69%.

1,4,4-Trimethyl-*endo*-tricyclo[5.2.2.0^{2,6}]undeca-8-(1,3-dioxolane)-10-en-3-one (14). Potassium *tert*-butoxide (2.73 g, 21.36 mmol) was placed in a three necked flask equipped with reflux condenser and nitrogen inlet, and *tert*-butanol (5 ml) was added to it. A solution of the ketone **13** (0.50 g, 2.13 mmol) in *tert*-butyl alcohol (10 ml) was then added slowly through a syringe, to the stirred reaction mixture. Methyl iodide (5 ml, excess) was then added. The reaction mixture was refluxed for 6 h, after which it was cooled and quenched by careful addition of water (~3 ml). *tert*-Butyl alcohol was removed under vacuum and the residue was diluted with water (30 ml) and extracted with ether (3×30 ml). The combined ether layer was washed with brine (30 ml) and dried. Removal of solvent followed by chromatography [petroleum ether-ethyl acetate, (98:2)] of the residue on silica gel gave the alkylated product **14** as a colourless liquid (0.335 g, 60%). IR (neat) ν_{max}: 1732 cm^{-1}. UV(MeOH) λ_{max}: 286, 206 nm. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.11–6.04 (m, 2H, olefinic H), 3.98–3.80 (m, 4H, $(CH_2O)_2$), 3.15–2.90 (m, 1H, C*H*), 2.65–2.61 (m, 1H, C*H*), 2.43 (d, J=10 Hz, 1H, C*H*), 1.87 (dd, J_1=13 Hz, J_2=9.5 Hz, 1H, CH_2), 1.63 (part of an AB system, J_{AB}=14 Hz, 1H, CH_2), 1.49 (part of an AB system, J_{AB}=14 Hz, 1H, CH_2), 1.48 (s, merged with part of an AB system, 3H, CH_3), 1.24 (dd, J_1=13 Hz, J_2=9 Hz 1H, CH_2), 1.00 (s, 3H, CH_3), 0.95 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 222.03 (CO), 139.35, 130.53 (olefinic carbons), 113.19, 64.27, 64.04, 53.16, 49.64, 46.37, 44.00, 40.10, 38.99, 32.65, 26.42, 22.09, 21.88. Mass (m/z): 262 (M^+).

1,4,4-Trimethyl-3-*endo*-hydroxy-*endo*-tricyclo[5.2.2.0^{2,6}]-undeca-8-(1,3-dioxolane)-10-ene (15) and 1,4,4-trimethyl-3-*exo*-hydroxy-*endo*-tricyclo[5.2.2.0^{2,6}]undeca-8-(1,3-dioxolane)-10-ene (16). To a solution of **14** (0.380 g, 1.14 mmol) in tetrahydrofuran–water (9:1, 10 ml) was added sodium borohydride (0.086 g, 2.26 mmol) in small portions, and the reaction was stirred at ambient temperature for ~8 h (TLC). The reaction mixture was concentrated in vacuo and water (25 ml) was added to the residue and the aqueous medium was extracted with ethyl acetate (3×20 ml). The combined organic layer was washed with water (2×20 ml), brine (25 ml) and dried. Removal of solvent and column chromatography [petroleum ether-ethyl acetate, (92:8)] of the residue on silica gel first gave the minor alcohol **15** as a colourless liquid (0.069 g, 23%). IR (neat) ν_{max}: 3456 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.27 (d, J=8 Hz, 1H, olefinic H), 6.16 (superimposed dd, J_1=J_2=8 Hz, 1H, olefinic H), 3.95–3.88 (m, 4H, $(CH_2O)_2$), 3.54 (dd, J_1=10.5 Hz, J_2=6 Hz, 1H, *H*–C–OH), 2.88–2.78 (m, 1H, C*H*), 2.56 (br d, J=6.3 Hz, 1H, C*H*), 2.33 (dd, J_1=11 Hz, J_2=6.3 Hz, 1H, C*H*), 1.63 (part of an AB system, J_{AB}=12.5 Hz, 1H, CH_2), 1.52 (part of an AB system J_{AB}=12.5 Hz, 1H, CH_2), 1.42 (dd, J_1=12.5 Hz, J_2=8 Hz, 1H, CH_2), 1.30 (s, 3H, CH_3), 1.24 (d, J=11 Hz, 1H), 1.04 (superimposed dd, J_1=J_2=11 Hz, 1H, CH_2), 0.95 (s, 3H, CH_3), 0.91 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ:141.22, 130.51 (olefinic carbons), 114.31, 81.90, 64.27, 63.93, 54.75, 49.04, 44.27, 42.93, 40.73, 40.40, 38.85, 22.87, 22.83, 22.65. HRMS: M^+, Found 264.1719. $C_{16}H_{24}O_3$ requires 264.1724.

Further elution of the column with petroleum ether-ethyl acetate (85:15) furnished the desired alcohol **16** as a colourless liquid (0.220 g, 73%). IR (neat) ν_{max}: 3431 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.18 (superimposed dd, J_1=J_2=8.5 Hz, 1H, olefinic H), 6.04 (d, J=8.5 Hz, 1H, olefinic H), 3.96–3.87 (m, 4H, $(CH_2O)_2$), 3.18 (dd, J_1= 8 Hz, J_2=6 Hz, 1H, *H*–C–OH), 2.79–2.68 (m, 1H, C*H*), 2.44 (m of d, J=7 Hz, 1H, C*H*), 1.78 (dd, J_1=10 Hz, J_2=7 Hz, 1H, C*H*), 1.58–1.46 (m, partly merged with the signal due to H_2O present in the $CDCl_3$, C*H* and CH_2), 1.25 (s, partly merged with another signal, total 4H, CH_3+1H), 0.99–0.90 (m, merged with signal due to CH_3, total 4H, CH_3 and CH_2), 0.88 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 139.34, 131.80 (olefinic carbons), 114.15, 83.60, 64.21, 63.90, 55.35, 48.75, 43.61, 41.64, 41.05, 38.87, 37.06, 26.20, 22.61, 21.16. Mass (m/z): 264 (M^+).

1,4,4-Trimethyl-3-*exo*-hydroxy-*endo*-tricyclo[5.2.2.0^{2,6}]-undeca-10-en-8-one (5). To a solution of the compound **16** (0.20 g, 0.75 mmol) in acetone–water (90:10, 10 ml) was added two drops of HCl (50%), and the reaction mixture was stirred for 2 h at ambient temperature (~30°C). Acetone was removed under vacuum and water (20 ml) was added to the residue and extracted with ether (3×20 ml). The combined organic extract was washed with brine (25 ml) and dried. Removal of solvent and chromatography of the residue [petroleum ether-ethyl acetate, (90:10)] gave the compound **5** (0.150 g, 92%) as a colourless solid which was recrystallized from petroleum ether-ethyl acetate (96:4), mp 72–74°C. IR (nujol) ν_{max}: 3509, 1720 cm^{-1}. UV (MeOH) λ_{max}: 292, 208 nm. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.23–6.09 (m, 2H, β and γ protons of β,γ-enone moiety), 3.26 (d, J=8 Hz, 1H, *H*–C–OH), 2.99 (m of d, J=8Hz,1H, C*H*), 2.78–2.58 (m, 1H, C*H*), 1.99–1.89 (m, partly merged with another signal, 3H, C*H* and CH_2), 1.60 (dd, partly merged with the peak due to H_2O present in $CDCl_3$, J_1=11.5 Hz, J_2=7Hz, 1H, methylene H), 1.41 (br s, 1H, –O*H*), 1.35 (s, 3H, CH_3), 1.06 (dd, J_1=11.5 Hz, J_2=10 Hz, 1H, CH_2), 0.96 (s, 3H, CH_3), 0.90 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 212.96 (CO), 141.69, 128.37 (olefinic carbons), 83.47, 55.55, 53.46, 47.01, 41.47, 41.30, 40.00, 39.26, 26.04, 22.06, 21.12. Mass (m/z): 220 (M^+).

1,7,10,10-Trimethyl-9-hydroxy tetracyclo[6.3.0.0.^{2,4}0^{3,7}]-undeca-5-one (6). A solution of the compound **5** (0.10 g, 0.45 mmol) in acetone (solvent as well as sensitizer) was irradiated with a mercury vapour lamp (125 W, Applied Photo Physics) in a Pyrex immersion well under nitrogen

for 1.5 h. Acetone was removed in vacuo and the residue was chromatographed on silica gel. Elution with petroleum ether-ethyl acetate (90:10) first gave some unchanged starting material (0.008 g). Further elution with petroleum ether-ethyl acetate (88:12) furnished the desired tetracyclic compound **6** (0.068 g, 68%) as a colourless solid, which was recrystallised from petroleum ether-ethyl acetate (95:5), mp 117–118°C. IR(nujol) ν_{max}: 3470, 1705 cm^{-1} UV (MeOH) λ_{max}: 284, 209 nm. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.62 (dd, J_1=10 Hz, J_2=6 Hz, 1H, *H*–C–OH), 2.58–2.50 (m, 1H), 2.43–2.38 (m, 2H), 2.10–1.93 (m, 4H), 1.68–1.61 (m, hidden under the signal due to H_2O present in $CDCl_3$, 1H), 1.49 (s, 3H, C*H*$_3$), 1.38 (d, *J*=6 Hz, 1H), 1.24 (dd, J_1=14 Hz, J_2=6 Hz, 1H), 1.05 (s, 3H, C*H*$_3$), 0.83 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 214.63 (CO), 81.12, 66.82, 58.17, 47.03, 44.78, 42.62, 39.78, 39.61, 39.24, 38.43, 26.94, 21.83, 20.86. Mass (m/z): 220 (M^+). Analysis Found: C, 76.28; H, 9.36%. Calcd, for $C_{14}H_{20}O_2$: C, 76.36, H, 9.09%.

4,4,7-Trimethyl-5-hydroxy tricyclo[5.3.1.0^{2,6}]undeca-9-one (17) and 7,10,10-trimethyl-9-hydroxy tricyclo-[6.3.0.0^{3,7}]undeca-5-one (7). A solution of the tetracyclic keto-alcohol **6** (0.03 g, 0.13 mmol) in methanol (30 ml) was stirred at ambient temperature with palladium on carbon (7 mg, catalytic amount) in an atmosphere of hydrogen (165 psi pressure) for 8 h in a Parr autoclave. The catalyst was removed by filtration and washed with methanol. The filtrate was concentrated and the residue was chromatographed on silica gel. Elution with petroleum ether-ethyl acetate (88:12) gave a mixture of two products (0.027 g, 90%). Fractional crystallisation of the mixture from petroleum ether-ethyl acetate (96:4) first furnished the undesired product **17** (0.010 g, 33%) (mp 115–116°C). Further recrystallisation of the solid obtained from evaporation of the mother liquor gave the desired tricyclopentanoid **7** (0.017 g, 56%) as a colourless crystalline solid, mp 118–119°C (lit. mp 114–115°C[10a] and 118–120°C[10b]).

Data for compound **17**. IR (nujol) ν_{max}: 3433, 1692 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.37 (dd, J_1=9 Hz, J_2=5 Hz, 1H, *H*–C–OH), 2.35–2.20 (m, 4H), 2.06–2.01 (m, 1H), 1.88–1.78 (m, 2H), 1.72 (dd, J_1=12.5 Hz, J_2=8.5 Hz, 1H), 1.60–1.51 (m, partly hidden under the signal due to H_2O present in $CDCl_3$, 2H), 1.27 (br d, *J*=5 Hz, 1H), 1.20 (s, 3H, CH_3), 0.99 (s, 3H, CH_3), 0.94 (dd, partly merged with singlet due to CH_3, J_1=12.5 Hz, J_2=9.5 Hz, 1H), 0.83 (s, 3H, CH_3). Mass (m/z): 222 (M^+).

Data for compound **7**, mp. 118–119°C. IR(nujol) ν_{max}: 3441, 1726 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 3.52 (dd, J_1=8.7 Hz, J_2=5 Hz, 1H), 2.78–2.64 (m, 1H), 2.48–2.32 (m, 2H), 2.24 (t, *J*=8.8 Hz, 1H), 2.15 (d, *J*=18 Hz, 1H), 2.08 (s, 2H), 1.82 (dd, J_1=12.5 Hz, J_2=8.8 Hz, 1H), 1.65 (ddd, J_1=14 Hz, J_2=7.5 Hz, J_3=1.5 Hz, 1H), 1.53–1.44 (m, 1H), 1.33 (br d, *J*=5 Hz, 1H), 1.22 (s, 3H, C*H*$_3$), 1.08–0.98 (m, partly hidden under the signal due to methyl, 1H), 1.02 (s, 3H, C*H*$_3$), 0.89 (s, 3H, C*H*$_3$). Mass (m/z): 222 (M^+). These spectral features compared well with the literature.[10] Analysis Found: C, 75.33; H, 9.95%. Calcd, for $C_{14}H_{22}O_2$: C, 75.67, H, 9.90%.

1,9-Dimethyl-*endo*-tricyclo[5.2.2.0^{2,6}]undeca-4,10-dien-8-one (9). To a suspension of activated zinc (8.0 g, excess) and ammonium chloride (2.20 g, excess) in dry dioxane (25 ml) was added a solution of the compound **4** (2.0 g, 9.9 mmol) in dry dioxane (10 ml). The reaction mixture was refluxed for 5 h (TLC), after which it was cooled and filtered to remove zinc and washed with ethyl acetate. The filtrate was concentrated in vacuo, and the residue was diluted with water (25 ml) and extracted with ethyl acetate (3×25 ml). The combined ethyl acetate layer was washed with water (2×20 ml), brine (25 ml) and dried. The solvent was removed under vacuum and the residue was chromatographed. Elution with petroleum ether-ethyl acetate (97:3) gave the compound **9** as a colourless liquid (1.58 g, 85%), as a *syn:anti* mixture (*anti* as major). IR (neat) ν_{max}: 1730 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 6.09–5.98 (m, 2H, β and γ protons of β,γ-enone moiety), 5.66 (m of d, *J*=6 Hz, 1H, olefinic H), 5.44 (m of d, *J*=6 Hz, 1H, olefinic H), 3.12–3.03 (m, 2H, C*H*), 2.66 (d of t, J_1=9 Hz, J_2=6 Hz 1H, C*H*), 2.40 (m of dd, J_1=16 Hz, J_2=10 Hz, 1H, C*H*$_2$), 2.04 (m of d, *J*=16Hz, 1H, C*H*$_2$), 1.86 (q, *J*=7.5 Hz, *H*–C–C*H*$_3$), 1.27 (s, 3H, C*H*$_3$), 1.10 (d, *J*=7.5 Hz, C*H*$_3$). Mass (m/z): 188 (M^+). (Data for major isomer). Mass (m/z): 188(M^+).

1,9-Dimethyl-3-hydroxy-*endo*-tricyclo[5.2.2.0^{2,6}]undeca-8-(1,3-dioxolane)-10-ene (21) and 1,9-Dimethyl-5-hydroxy-*endo*-tricyclo[5.2.2.0^{2,6}]undeca-8-(1,3-dioxolane)-10-ene (22). The ketone **9** (1.0 g, 5.3 mmol) was oxidised with selenium dioxide (2.9 g, 26.12 mmol) in dioxane–water mixture (80:20, 20 ml) containing potassium dihydrogen-phosphate (1.8 g, 13.2 mmol) as described earlier. Usual work-up and chromatography [petroleum ether-ethyl acetate (65:35)] afforded a mixture of hydroxy–ketones (0.596 g, 55%) which was further oxidized with Jones' reagent. To a solution of the above mixture of hydroxy ketones (0.596 g, 2.92 mmol) in acetone (20 ml) was added freshly prepared Jones' reagent dropwise at ~5°C. After the oxidation was complete (TLC), acetone was removed under vacuum and the residue was diluted with water and extracted with ether (3×20 ml). The ether extract was washed with saturated sodium bicarbonate solution (2×20 ml), water (30 ml), and brine (25 ml) and dried over anhydrous sodium sulphate. Removal of solvent followed by chromatography [petroleum ether-ethyl acetate (85:15)] furnished a mixture of the diene-diones (0.560 g, 95%) which were subjected to ketalization.

A mixture of ethylene glycol (0.8 ml, excess) and *p*-toluene sulphonic acid (8 mg, catalytic amount) in dry benzene (50 ml) was refluxed in a Dean–Stark apparatus in order to remove traces of water. The mixture of above diene-diones (0.560 g, 2.41 mmol) in dry benzene (10 ml) was added to it, and the reaction mixture was then refluxed until completion of the reaction (TLC, 4 h). The reaction mixture was brought to room temperature, and the benzene layer was separated. It was washed with sodium bicarbonate solution (30 ml), water (25 ml) and brine (20 ml) and dried. Removal of solvent furnished a mixture of ketal enones (0.545 g, 80%) which was further reduced with sodium borohydride as follows:

To a solution of the above mixture of ketal-enones (0.545 g, 2.21 mmol) in methanol (15 ml) was added sodium borohydride (0.126 g, 3.31 mmol) in small portions at ambient temperature (~30°C) during 2.5 h, after which the reaction

was found to be complete (TLC). Methanol was removed in vacuo and the residue was diluted with water (40 ml) and extracted with ethyl acetate (3×30 ml). The combined extract was washed with brine (30 ml) and dried. Solvent was removed under vacuum and the residue was chromatographed. Elution with petroleum ether-ethyl acetate (95:5) first gave the desired ketal alcohol **21** (0.332 g, 60%) as a colourless liquid. IR(neat) ν_{max}: 3519 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 6.33 (d, J=8 Hz, 1H, olefinic H), 6.11 (superimposed dd, $J_1=J_2$=8 Hz, 1H, olefinic H), 4.22–4.14 (m, 1H, *H*–C–OH), 4.00–3.82 (m, 4H, $(CH_2O)_2$), 2.60–2.47 (m, 2H, C*H*), 2.14 (dd, J_1=11 Hz, J_2=6 Hz, 1H, C*H*), 1.78–1.67 (m, 1H, CH_2), 1.64–1.36 (m, 4H, C*H*, CH_2 and O *H*), 1.25 (s, 3H, CH_3), 1.19–1.03 (m, 1H, CH_2), 0.86 (d, J=7.5 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 143.48, 129.56 (olefinic carbons), 114.25, 75.10, 65.14, 63.43, 48.62, 47.80, 43.42, 41.24, 40.99, 35.99, 27.71, 20.82, 9.55. Mass (m/z): 250 (M^+).

Further elution with petroleum ether-ethyl acetate (85:15) furnished the ketal alcohol **22** (0.160 g, 29%) in minor amounts, as a colourless solid which was recrystallized from petroleum ether-ethyl acetate (92:8), mp 87–89°C. IR(nujol) ν_{max}: 3362 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 6.32 (dd, J_1=8 Hz, J_2=6.5 Hz, 1H, olefinic H), 6.01 (d, J=8 Hz, 1H, olefinic H), 4.22 (br s, 1H, *H*–C–OH), 4.00–3.82 (m, 4H, $(CH_2O)_2$), 2.67 (m of d, J=6Hz, 1H, C*H*), 2.58 (merged ddd, J_1=10.5Hz, J_2=5Hz, $J_{3=}$2Hz, 1H, C*H*), 2.20 (q, J=8 Hz, 1H, *H*–C–CH_3), 1.70–1.44 (series of m, merged with the signal due to H_2O present in $CDCl_3$, 4H, C*H* and CH_2), 1.35 (d, J=9 Hz, 1H, O *H*), 1.21–1.05 (m, merged with signal due to CH_3, 4H, CH_3 and CH_2), 0.88 (d, J=8 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 141.03, 131.50 (olefinic carbons), 114.12. 76.33, 65.06, 63.44, 47.71, 46.11, 43.65, 41.43, 41.01, 35.83, 26.38, 21.29, 9.50. Mass (m/z) 250 (M^+). Analysis Found: C, 71.62; H, 8.89%. Calcd, for $C_{15}H_{22}O_3$: C, 72.00; H, 8.80%.

1,9-Dimethyl-*endo*-tricyclo[5.2.2.0^{2,6}]undeca-8-(1,3-dioxolane)-10-en-3-one (23). To a suspension of PCC (1.376 g, 6.4 mmol) in dichloromethane (5 ml) was added a solution of the alcohol **21** (0.8 g, 3.2 mmol) in dichloromethane (10 ml). The reaction mixture was stirred at ambient temperature (~30°C) for 3 h (TLC). After which it was charged on to a short column of silica gel and eluted with ether. Removal of ether under vacuum gave a residue which was chromatographed. Elution with petroleum ether-ethyl acetate (80:20) yielded the ketone **23** as a colourless liquid (0.77 g, 98%). IR (neat) ν_{max}: 1729 cm^{-1}. UV (MeOH) λ_{max}: 295, 211 nm. ^1H NMR (300 MHz, $CDCl_3$) δ: 6.23 (superimposed dd, $J_1=J_2$=8 Hz, 1H, olefinic H), 6.00 (d, J=8 Hz, 1H, olefinic H), 4.02–3.81 (m, 4H, $(CH_2O)_2$), 2.97–2.87 (m, 1H, C*H*), 2.61 (m of d, J=6Hz, 1H, C*H*), 2.29 (d, J=10 Hz, 1H, C*H*), 2.10–1.94 (m, 3H, CH_2), 1.69–1.56 (m, 1H, CH_2),1.51 (q, 1H, J=7.5 Hz, C*H*), 1.32 (s, 3H, CH_3), 0.98 (d, J=7.5 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 222.38 (CO), 141.13, 129.94 (olefinic carbons), 113.08, 65.19, 63.58, 50.12, 48.00, 45.76, 42.70, 39.35, 35.38, 25.01, 20.52, 10.05. Mass (m/z): 248 (M^+).

1,4,4,9-Tetramethyl-*endo*-tricyclo[5.2.2.0^{2,6}]undeca-8-(1,3-dioxolane)-10-en-3-one (24). A solution of the ketone **23** (0.80 g, 3.22 mmol) in ^{t}butyl alcohol (10 ml) was treated with potassium *tert*-butoxide (2.70 g, 24.10 mmol) and methyl iodide (5 ml, excess) as described earlier. Usual work-up followed by chromatography [petroleum ether-ethyl acetate, (97:3)] of the residue furnished the alkylated product **24** (0.552 g, 62%) as a solid which was recrystallized from petroleum ether, mp 99–100°C. IR (film) ν_{max}: 1724 cm^{-1}. UV (MeOH) λ_{max}: 300.4 (w), 207.2 (s) nm. ^1H NMR (300 MHz, $CDCl_3$) δ: 6.09–6.01 (m, 2H, olefinic H), 4.04–3.83 (m, 4H, $(CH_2O)_2$), 2.92–2.86 (m, 1H, C*H*), 2.60–2.50 (m, 2H, C*H*), 1.85 (dd, J_1=13 Hz, J_2=9 Hz, 1H, CH_2), 1.50 (q, J=7.5 Hz, 1H, *H*–C–CH_3), 1.41 (s, 3H, CH_3), 1.26 (dd, J_1=13 Hz, J_2=9 Hz, 1H, CH_2), 0.99 (s, 3H, CH_3), 0.91 (s, 3H, CH_3), 0.86 (d, J=7.5 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 223.79 (CO), 141.88, 129.96 (olefinic carbons), 113.31, 65.27, 63.61, 48.77, 47.10, 46.44, 44.40, 41.53, 40.37, 32.51, 26.68, 22.31, 20.50, 9.84. Mass (m/z): 276 (M^+). Analysis Found: C, 74.20; H, 9.03%. Calcd, for $C_{17}H_{24}O_3$: C, 73.91; H, 8.69%.

1,4,4,9-Tetramethyl-3-*endo*-hydroxy-*endo*-tricyclo-[5.2.2.0^{2,6}]undeca-8-(1,3-dioxolane)-10-ene (25) and 1,4,4,9-tetramethyl-3-*exo*-hydroxy-*endo*-tricyclo[5.2.2.0^{2,6}]-undeca-8-(1,3-dioxolane)-10-ene (26). Sodium borohydride (0.27 g, 7.24 mmol) was added in small portions to a solution of compound **24** (0.50 g, 1.81 mmol) in tetrahydrofuran-water (90:10, 20 ml) and the reaction mixture was stirred at ambient temperature (~30°C) till the reaction was complete (TLC, 9 h). The reaction mixture was concentrated under reduced pressure and the residue was diluted with water (30 ml) and extracted with ethyl acetate (3×25 ml). The combined extract was washed with water (2×20 ml), brine (25 ml) and dried over anhydrous sodium sulfate. Removal of solvent under vacuum followed by chromatography of the residue [petroleum ether-ethyl acetate (93:7)] first gave the undesired alcohol **25** as a colourless liquid (0.095 g, 19%) in minor amounts. IR (neat) ν_{max}: 3517 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 6.32 (d, J=8 Hz, 1H, olefinic H), 6.04 (superimposed dd, $J_1=J_2$=8 Hz, 1H, olefinic H), 4.00–3.81 (m, 4H, $(CH_2O)_2$), 3.50 (dd, J_1=12 Hz, J_2=6 Hz, 1H, *H*–C–OH), 2.74–2.64 (m, 1H, C*H*), 2.52–2.41 (m, 2H, C*H*), 1.51 (q, J=7 Hz, 1H, *H*–C–CH_3), 1.40 (dd, J_1=12 Hz, J_2=7.5 Hz, 1H), 1.29 (d, J=12 Hz, 1H), 1.25 (s, 3H, CH_3), 1.04 (superimposed dd, $J_1=J_2$=12 Hz, 1H), 0.95 (s, 3H, CH_3), 0.90 (s, 3H, CH_3), 0.88 (d, J=7Hz, partly overlapped with another signal, 3H, CH_3). Mass (m/z): 278 (M^+).

Further elution with petroleum ether-ethyl acetate (90:10) furnished desired alcohol **26** as a colourless liquid (0.352 g, 70%). IR (neat) ν_{max}: 3477 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 6.16–6.04 (m, 2H, olefinic H), 3.97–2.80 (m, 4H, $(CH_2O)_2$), 3.24 (dd, J_1=8 Hz, J_2=6 Hz, 1H, *H*–C–OH), 2.68–2.56 (m, 1H, C*H*), 2.38 (m of d, J=6 Hz, 1H, C*H*), 1.93 (dd, J_1=11 Hz, J_2=10 Hz, 1H, C*H*), 1.58 (q partly overlapped with the signal due to H_2O in $CDCl_3$, J=8 Hz, 1H, *H*–C–CH_3), 1.47 (dd, J_1=12 Hz, J_2=7.5 Hz, 1H, CH_2), 1.26 (br d, J=6 Hz, 1H, O *H*), 1.20 (s, 3H, CH_3), 0.97 (d, J=11 Hz, 1H, CH_2), 0.92 (s, 3H, CH_3), 0.88 (s, 3H, CH_3), 0.86 (d, J=8 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 141.95, 131.03 (olefinic carbons), 114.04, 83.46, 65.18, 63.45, 48.03, 47.58, 44.01, 41.88, 41.26, 41.14, 36.84, 26.28, 21.24, 20.99, 9.37. HRMS: M^+, Found, 278.1875. $C_{17}H_{26}O_3$ requires 278.1882.

1,4,4,9-Tetramethyl-3-*exo*-hydroxy-*endo*-tricyclo[5.2.2.0^{2,6}]-undeca-10-en-8-one (18). To a solution of ketal alcohol **26** (0.30 g, 1.07 mmol) in acetone-water (90:10, 10 ml) mixture was added 3 drops of hydrochloric acid (50%) and stirred for 3 h at ambient temperature (~30°C). The reaction was worked-up as described earlier and the residue was chromatographed [petroleum ether-ethyl acetate, (91:9)] to give the compound **18** as a colourless liquid (0.226 g, 90%). IR(neat) ν_{max}: 3460, 1716 cm^{-1}. UV (MeOH) λ_{max}: 295, 214 nm. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.23 (d, J=8 Hz, 1H, γH of β,γ-enone moiety), 6.12 (superimposed dd, J_1=J_2=8 Hz, 1H, β H of β,γ-enone moiety), 3.36 (dd, J_1=9 Hz, J_2=6 Hz, 1H, *H*–C–OH), 2.97 (m of d, J=6 Hz, 1H, C*H*), 2.57–2.45 (m, 1H, C*H*), 2.12 (dd, J_1=12 Hz, J_2=9 Hz, 1H, C*H*), 1.82 (q, J=8 Hz, 1H, *H*–C–CH_3), 1.59 (dd, J_1=12 Hz, J_2=9 Hz, 1H, CH_2), 1.43 (br d, J=6 Hz, 1H), 1.32 (s, 3H, CH_3), 1.05 (d, J=8 Hz overlapped with another multiplet, 4H, CH_3 and CH_2), 0.96 (s, 3H, CH_3), 0.89 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 215.57(CO), 143.81, 127.97 (olefinic carbons), 83.17, 53.17, 49.24, 47.51, 42.52, 41.64, 41.53, 39.59, 26.12, 21.19, 20.24, 10.83. HRMS: M^+, Found 234.1616. $C_{15}H_{22}O_2$ requires 234.1620.

6,7,10,10-Tetramethyl-9-hydroxy tetracyclo[6.3.0.0^{2,4}0^{3,7}]-undeca-5-one (19). A solution of compound **18** (0.150 g, 0.64 mmol) in acetone (100 ml) was irradiated under nitrogen with a mercury vapour lamp (125 W, Applied Photo Physics) in a Pyrex immersion well for about 1.5 h. Acetone was removed in vacuo and the residue was chromatographed. Elution with petroleum ether-ethyl acetate (92:8) first gave the unchanged starting material (0.020 g). Continued elution with petroleum ether-ethyl acetate (90:10) furnished the tetracyclic compound **19** (0.097 g, 65%) as a solid which was recrystallized from petroleum ether-ethyl acetate (97:3), mp 97–98°C. IR (nujol) ν_{max}: 3402, 1701 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.68 (dd, J_1= 9.5 Hz, J_2=6 Hz, 1H, *H*–COH), 2.34–2.17 (m, 3H), 2.08–1.98 (m, 2H), 1.94 (dd, J_1=13.5 Hz, J_2=9.5 Hz, 1H), 1.59 (dd, partly merged with signal due to H_2O present in $CDCl_3$, J_1=9.5 Hz, J_2=6 Hz, 1H), 1.47 (s, 3H, CH_3), 1.30 (q, J=7.5Hz, 1H), 1.24 (dd, J_1=13.5 Hz, J_2=6 Hz, 1H),1.05 (s, 3H, CH_3), 0.89 (d, J=7.5 Hz, 3H, CH_3), 0.82 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 215.07 (CO), 80.96, 59.84, 58.66, 50.38 (quaternary), 44.72, 42.35, 38.30, 38.17, 37.20, 37.11, 27.07, 21.26, 21.02, 8.86. Mass (m/z): 234 (M^+). Analysis Found: C, 76.93; H, 9.63%. Calcd, for $C_{15}H_{22}O_2$: C, 76.92; H, 9.40%.

4,4,7,8-Tetramethyl-5-hydroxy tricyclo[5.3.1.0^{2,6}]undeca-9-one (27). A solution of the tetracyclic keto-alcohol **19** (0.03 g, 0.128 mmol) in methanol (50 ml) was stirred at room temperature with palladium on carbon (10%) in an atmosphere of hydrogen (150 psi pressure) for 12 h in a Parr autoclave. The catalyst was removed by filtration and washed with methanol (15 ml). The filtrate was concentrated in vacuo and the residue was chromatographed on silica gel. Elution with petroleum ether-ethyl acetate, (88:12) yielded the compound **27** as a solid which was recrystallized from petroleum ether-ethyl acetate (97:3), mp 154–155°C (0.027 g, 99%). IR (film) ν_{max}: 1689 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.36 (dd, J_1=9 Hz, J_2=7.5 Hz, 1H, *H*–C–OH), 2.46–2.26 (m, 3H), 2.17 (q, J=9 Hz, 1H, C*H*), 2.00 (dd, J_1=9 Hz, J_2=3 Hz, 1H), 1.91–1.83 (m, 2H), 1.75–1.65 (m, 2H), 1.27 (br s, 1H), 1.20 (s, 3H, CH_3), 1.01 (d, J=6 Hz, 3H, CH_3), 0.99 (s, 3H, CH_3), 0.92–0.84 (m, 1H), 0.83 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 212.34 (CO), 82.27, 56.94, 51.91, 49.40, 47.47, 44.21, 43.93, 43.37, 41.84, 39.64, 26.28, 20.07, 19.51, 8.61. Mass (m/z): 236 (M^+). Analysis Found: C, 74.61; H,10.36%. Calcd, for $C_{15}H_{24}O_2$: C, 76.27; H, 10.16%.

6,7,10,10-Tetramethyl-9-hydroxy tricyclo[6.3.0.0^{3,7}]-undeca-5-one (20a & 20b). Tributyltin hydride (0.15 ml) was added to a solution of tetracyclic compound **21** (0.05 g, 0.213 mmol) in dry benzene containing AIBN. The reaction mixture was refluxed for 3 h (TLC) under an atmosphere of nitrogen, after which it was brought to room temperature (~30°C). Benzene was removed under vacuum and the residue was chromatographed on silica gel. Elution with petroleum ether first gave some tin impurities. Continued elution with petroleum ether-ethyl acetate (88:12) furnished the triquinane **20a** (0.022 g, 44%) as a solid which was recrystallized from petroleum ether-ethyl acetate (96:4), mp 73–75°C. IR (nujol) ν_{max}: 3459, 1730 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.60 (dd, J_1=9 Hz, J_2=7.5 Hz, 1H, *H*–COH), 2.75– 2.36 (m, 3H), 2.19 (dq, J_1=7.5 Hz, J_2=1.5 Hz, 1H), 1.96–1.84 (m, 2H), 1.80–1.71 (m, 2H). 1.60–1.49 (m, hidden under the signal due to H_2O present in $CDCl_3$, 1H), 1.26 (s, 3H, CH_3), 1.16–1.10 (m, 1H), 1.07 (d, J=7.5 Hz, 3H, CH_3), 1.02 (s, 3H, CH_3), 0.88 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 220.36 (CO), 81.03, 56.65, 52.93, 51.12, 50.13, 46.13, 45.91, 41.59, 39.56, 36.21, 26.78, 23.23, 19.95, 10.07. Mass (m/z): 236 (M^+).

Further elution with the same solvent gave **20b** (0.009 g, 17%) as a colourless solid which was recrystallized from petroleum ether-ethyl acetate (94:6), mp 161–162°C (lit.[17] mp 162°C). IR (nujol) ν_{max}: 3502, 3467, 1724 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.51 (dd, J_1=8 Hz, J_2=~6 Hz, 1H, *H*–COH), 2.76–2.64 (m, 1H), 2.40–2.16 (complex m, 3H), 2.0 (q, J=6 Hz, 1H), 1.83 (dd, J_1=12 Hz, J_2=9 Hz, 1H), 1.76–1.55 (m, 2H, partly hidden under signal due to H_2O in $CDCl_3$), 1.30 (d, J=6 Hz, 1H, OH), 1.1 (m, 2H, partly hidden under signals due to methyls), 1.03 (s, 3H, CH_3), 0.99 (s, 3H, CH_3), 0.97 (d, J=6 Hz, 3H, CH_3), 0.90 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 220.88 (CO), 81.93, 57.39, 51.92, 51.80, 45.99, 43.43, 42.68, 41.26, 39.25, 37.40, 26.47, 19.48, 16.43, 7.94 Mass (m/z): 236 (M^+). These spectral features are in good agreement with the literature data.[17]

Acknowledgements

We are thankful to RSIC, I.I.T. Bombay for high field NMR spectra and mass spectra. One of us (B. S.) is thankful to I.I.T. Bombay for a fellowship. We are also indebted to the Department of Science and Technology, New Delhi, for continued research support.

References

1. Paquette, L. A.; Doherty, A. M. In *Polyquinane Chemistry*; Springer Verlag: New York, 1987; 26, pp 1–225.

2. Mehta, G.; Srikrishna, A. *Chem. Rev.* **1997**, *97*, 671–719.
3. Singh, V.; Thomas, B. *Tetrahedron* **1998**, *54*, 3647–3692.
4. a) Santora, V. J.; Moore, H. W. *J. Am. Chem. Soc.* **1995**, *117*, 8486–8487. (b) Paquette, L. A.; Morwick, T. *J. Am. Chem. Soc.* **1995**, *117*, 1451–1452. (c) MacDougall, J. M.; Moore, H. W. *J. Org. Chem.* **1997**, *62*, 4554–4555. (d) Jung, M. E.; Rayle, H. L. *J. Org. Chem.* **1997**, *62*, 4601–4609. (e) Tormo, J.; Moyano, A.; Pericas, M. A.; Riera, A. *J. Org. Chem.* **1997**, *62*, 4851–4856.
5. a) Masuya, K.; Domon, K.; Tanino, K.; Kuwajima, I. *J. Am. Chem. Soc.* **1998**, *120*, 1724–1731. (b) Lautens, M.; Blackwell, J. *Synthesis* **1998**, 537–546. (c) Krishnamurthy, V.; Rawal, V. H. *J. Braz. Chem. Soc.* **1998**, *9*, 341–344. (d) Wei, X.; Taylor, R. J. K. *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 409–412.
6. a) Takeuchi, T.; Iinuma, H.; Iwanaga, J.; Takahashi, H.; Umezawa, H. *J. Antibiot.* **1969**, *22*, 215–217. (b) Nishimura, Y.; Koyama, Y.; Umezawa, S.; Takeuchi, T.; Ishizuka, M.; Umezawa, H. *J. Antibiot.* **1980**, *33*, 404.
7. a) Mizuno, H.; Domon, K.; Masuya, K.; Tanino, K.; Kuwajima, I. *J. Org. Chem.* **1999**, *64*, 2648–2656. (b) Domon, K.; Masuya, K.; Tanino, K.; Kuwajima, I. *Tetrahedron Lett.* **1997**, *38*, 465–468. For earlier references on synthesis of coriolin see Ref. 2.
8. Singh, V. *Acc. Chem. Res.* **1999**, *32*, 324–333.
9. Singh, V.; Samanta, B. Preliminary communication. *Tetrahedron Lett.* **1999**, *40*, 383–386.
10. a) Funk, R. L.; Bolton, G. L.; Daggett, J. U.; Hansen, M. M. *Tetrahedron* **1985**, *41*, 3479–3495. (b) Hijfte, L. V.; Little, R. D.; Petersen, J. L.; Moeller, K. D. *J. Org. Chem.* **1987**, *52*, 4647–4661.
11. Carter, S. D.; Wallace, T. W. *Synthesis* **1983**, 1000–1002.
12. For a discussion on the mechanism and stereochemical out come of this reduction: Singh, V.; Deota, P. T. *J. Chem. Res.* **1989**, 390–391 and Ref. 8.
13. House, H. O. *Modern Synthetic Reactions*; W. A. Benzamin: Menlo Park, California, 1972; pp 407–411.
14. Fieser, L. L.; Fieser, M. *Reagents for Organic Synthesis*; John Wiley and Sons: New York, 1967.
15. Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647–2648.
16. a) Zimmerman, H. E.; Armesto, D. *Chem. Rev.* **1996**, *96*, 3065–3112. (b) Wilsey, S.; Bearpark, M. J.; Bernardi, F.; Olivucci, M.; Robb, M. A. *J. Am. Chem. Soc.* **1996**, *118*, 176–184. (c) Demuth, M. In *Organic Photochemistry*, Padwa, A. Ed., Marcell Dekkar, Inc: New York, 1991; Vol. 11, pp 37–97.
17. a) Mehta, G.; Murthy, A. N.; Reddy, D. S.; Reddy, A. V. *J. Am. Chem. Soc.* **1986**, *108*, 3443–3452. (b) Mehta, G.; Reddy, A. V.; Murthy, A. N.; Reddy, D. S. *J. Chem. Soc., Chem. Commun. 1982*, 540–541.
18. Pandey, B.; Rao, A. T.; Dalvi, P. V.; Kumar, P. *Tetrahedron* **1994**, *50*, 3843–3848.
19. Wong, H. N. C.; Hon, M. Y.; Tse, C. W.; Yip, Y. C.; Tanko, J.; Hudlicky, T. *Chem. Rev.* **1989**, *89*, 165–198.
20. Imanishi, T.; Matsui, M.; Yamashita, M.; Iwata, C. *Tetrahedron Lett.* **1986**, *27*, 3161–3164.
21. (a) Enholm, E. J.; Jia, Z. J. *Tetrahedron Lett.* **1995**, *36*, 6819. (b) Enholm, E. J.; Jia, Z. J. *J. Org. Chem.* **1997**, *62*, 174–181.