Synthesis and photochemical reaction of tricyclo[7.2.2.0^{2,8}] tridecanes: a novel entry to the BCD carbon framework of phorbol

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Abstract

Synthesis of 10,10-dimethyltricyclo[7.2.2.0^{2,8}]tridec-12-ene-3,11-dione **5** *via* cycloaddition of a cyclohexa-2,4-dienone with cycloheptadiene and its photoreaction to tricyclic compound **3** containing BCD ring system of phorbol is presented.

Keywords: Cycloaddition, decarbonylation, photochemistry, Diels-Alder reaction

Introduction

Recently, there has been an upsurge of interest[1-5] in the tigliane diterpene phorbol **1** and its esters since some derivatives such as **2** exhibit potent tumor promotor. The tumor promoting activity of phorbol esters related to their control on intracellular signal transduction through protein kinase C (PKC). Other phorbol derivatives and structurally related daphnane diterpenes also elicit a wide variety of biological responses and exhibit anitumor, anti HIV and analgesic properties. The complex structure and striking biological properties of phorbol and its derivatives have prompted to devise methodology for constructing the framework of phorbol esters. Efficient construction of the complex tetracyclic network of phorbol is one of the many problems in addition to other structural and stereochemical features associated with its synthesis. It appears that introduction of the cyclopropane ring having *gem*-dimethyl group to daphnane framework (ABC ring system) also poses considerable synthetic problem in addition to the other functionalities present in the molecule. Several approaches involving oxyallyl[4+3]cycloaddition,[1a] tandem anioinic cyclization-Claisen,[1c] reductive coupling,[1d] intramolecular oxido-pyrylium-alkene cycloaddition,[2] transannular cyclization,[3] intramolecular nitrile oxide cycloaddition,[4] Diels-Alder reaction,[5] carbonyl ylide cyclization,[6] and and others have been employed to generate various rings of phorbol. The intramolecular oxido-pyrylium-alkene cycloaddition methodology[2] and oxyallyl cycloaddition[1b] has led to synthesis of phorbol.

In continuation of our studies towards development of new synthetic methods employing photoreaction of β,γ-enones[7] and the interest in phorbol, we considered it possible to generate a tricyclic system of type **3** having the BCD carbon framework of phorbol, *via* decarbonylation of an annulated bicyclo[2.2.2]octenone **5** on singlet excitation, either directly, or through the 1,3-acyl shift product **4**. We wish to report an efficient synthesis of the dione **5** and its photoreaction leading to the tricyclic compound **3** having the D, C and B rings of phorbol.[8]


1 $R_1 = R_2 = H$
2 $R_1 = COMe$,
  $R_2 = -CO(CH_2)_{12}Me$
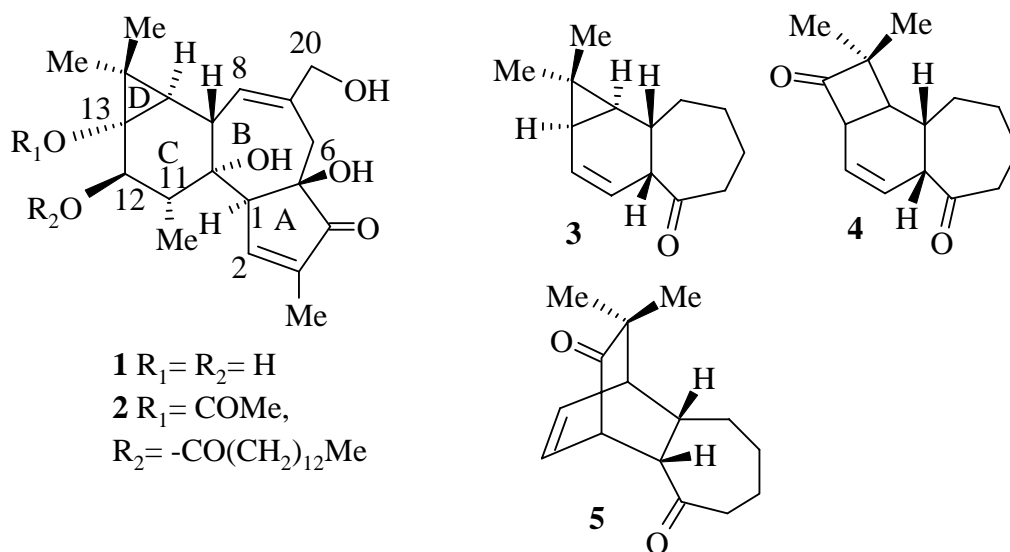
Figure 1

Results and Discussion

The dione **5** was synthesised from the readily available[9] dimer **6** and cyclohepta-1,3-diene *via* generation of cyclohexa-2,4-dienone **7** and cycloaddition with 1,3-cycloheptadiene followed by manipulation of the resulting adduct (Schemes 1 & 2). Thus, pyrolysis of **6** in *o*-dichlorobenzene containing 1,3-cycloheptadiene at ~140°C, for about 6h furnished the *endo* adduct **8** in good yield, whose structure was deduced from the following spectral data. Thus, the IR spectrum of **8** showed absorption bands at 3439 and 1718 cm^{-1} for hydroxyl and carbonyl groups respectively. Its ^{1}H NMR (300 MHz) spectrum displayed characteristic resonances at δ 6.5 (superimposed dd, $J_1=J_2=8$ Hz, 1H) and 6.28 (superimposed dd, $J_1=J_2=8$ Hz, 1H) for γ- and β-protons of the β,γ-enone moiety, respectively. The olefinic protons present in the seven-membered ring were observed at δ 5.6 (m, 1H) and 5.23 (m of d, J=9 Hz, 1H). The methylene protons of the oxirane ring exhibited resonance at δ 3.55 (part of an AB system, $J_{AB}=12$ Hz, 2H). It further showed signals at δ 3.28-3.18 (m, 2H, methine H)), 3.02 (d with structure, J=7.5 Hz, 1H), 2.71 (s, 1H, OH), 2.56 (t with structure, J=10 Hz, 1H, methine H), 2.20-1.94 (complex m, 2H, methylene H), 1.62-1.38 (m, 4H, methylene H). The ^{13}C NMR (75 MHz) spectrum also corroborated its structure since it displayed signal at δ 210.26 (CO), 136.12, 130.57, 128.63 and 127.97 for one

carbonyl carbon and four olefinic carbons respectively. It further exhibited resonances at δ 73.92, 53.81, 50.85, 48.66, 41.05, 35.30, 29.26, 25.06, 22.20 for quaternary, methine, and methylene carbons. The stereochemical orientation of the hydroxyl group is suggested on the basis of general tendency of the cyclohexa-2,4-dienones during their cycloaddition[8a] and by comparison with analogous compounds prepared in our laboratory.[8c] The stereochemistry at this centre would become inconsequential since the hydroxyl and chloromethyl groups would be next converted to *gem* dimethyl groups.
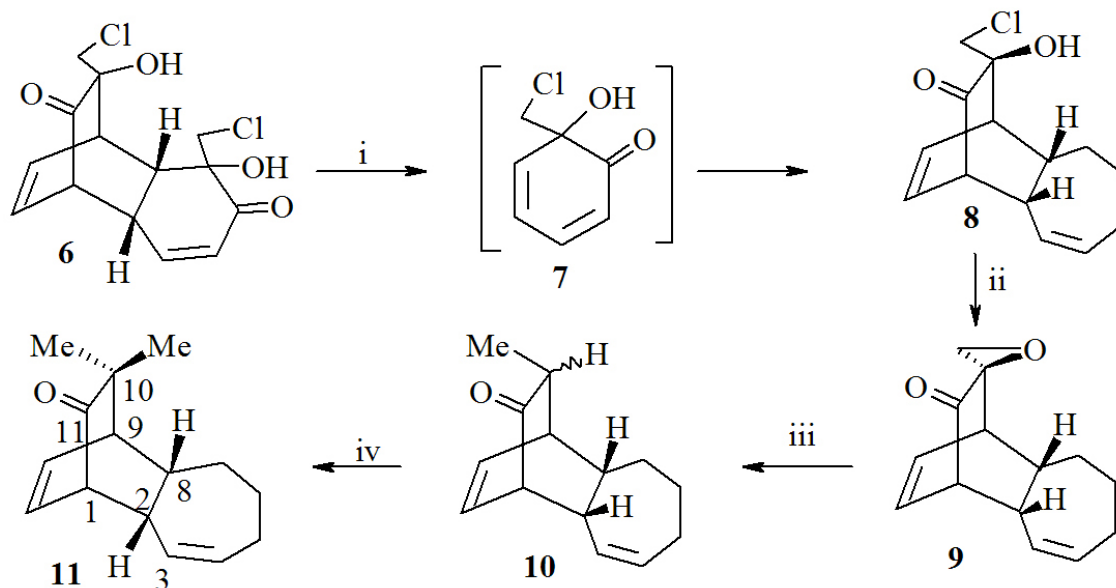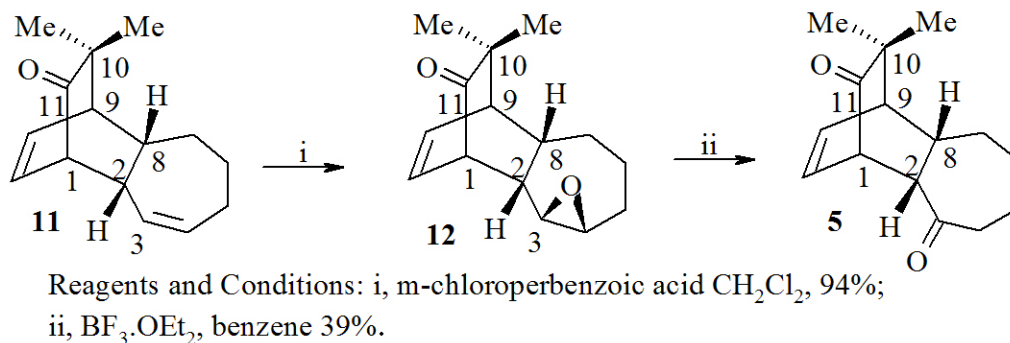

Reagents and Conditions: i, 1,3-cycloheptadiene, *o*-dichlorobenzene, 140 °C, 51%; ii, KOH(aq), CTAB, CHCl₃ , 93%; iii, Zn, NH₄Cl, Dioxane, Δ, 72%; iv, NaH, MeI, Δ, 78%.

Scheme 1

Treatment of **8** with aqueous KOH in chloroform readily gave the ketoepoxide **9** in quantitative manner.[8] The oxirane ring in **9** was transformed into geminal dimethyl group as shown in the scheme 1. Thus, the keto-epoxide **9** was subjected to reduction with zinc-NH₄Cl in dry dioxane[7c] which gave the monomethyl ketone **10** (as a mixture of *syn*: *anti* isomers) as a major product. Alkylation of **10** with methyl iodide in the presence of NaH-THF afforded the methylated ketone **11** in excellent yield whose structure was deduced from the following data. The IR spectrum of **11** showed an absorption band at 1720 cm⁻¹ for the carbonyl group. The ¹H NMR (300 MHz) spectrum displayed characteristic resonances at δ 6.48 (superimposed dd, $J_1=J_2=$ ~7.5 Hz, 1H) and 6.12 (superimposed dd, $J_1=J_2=$8.5 Hz, 1H) for γ- and β-protons of the β,γ-enone moiety, respectively. The olefinic protons were observed at δ 5.57 (m, 1H) and 5.22 (d with structure, J=~10 Hz, 1H). The signals due to other methine, methylene and methyl protons were observed at δ 3.13 (d with structure d, J=~6 Hz, 1H, methine H), 3.06 (br d, J=9.5 Hz, 1H, methine H), 2.42 (m of d, J=6 Hz, 1H, methine H), 2.28 (m, 1H, methine H), 2.16-2.04 (m, 1H,

methylene H), 2.02-1.92 (m, 1H, methylene H), 1.57-1.36 (complex m, 4H, methylene H), 1.15 (s, 3H, CH$_3$), 1.05 (s, 3H, CH$_3$). The ^{13}C NMR (75 MHz) spectrum of **11** also corroborated its structure since it exhibited signals at δ 217.09 and 138.98, 131.97, 127.94, 125.39 for one carbonyl carbon and four olefinic carbons respectively. It also showed signals at δ 55.85, 53.17, 43.74, 38.96, 37.46, 29.64, 27.72, 25.07, 24.13, 22.02 for other methine, methylene, quaternary and methyl carbons.

Regioselective epoxidation of **11** with *m*-chloroperbenzoic acid in CH$_2$Cl$_2$ at ambient temperature (~30°C) gave the epoxyketone **12** whose structure was discerned from the following data (Scheme 2). The ^{1}H NMR (300 MHz) spectrum exhibited only two signals at δ 6.59 (superimposed dd with structure, J$_1$=J$_2$~7.5 Hz, 1H) and 6.21 (superimposed dd with structure, J$_1$=J$_2$=7.5 Hz, 1H) corresponding to the olefinic protons of the β,γ-enone moiety. It also showed resonances at δ 3.39 (d with structure, J=~7.5 Hz, 1H) and 2.48 (m of d, J=7.5 Hz, 1H) due to bridgehead protons at C1 and C9 respectively. Furthermore, signals were observed at δ 2.94 (m, 1H), 2.74 (superimposed dd, J=4 Hz, 1H) corresponding to the protons at C4 and C3 respectively, in addition to resonances for methine, methylene and methyl protons. These assignments were confirmed with the help of a COSY spectrum which showed the following characteristic correlations. The resonance at δ 3.39 exhibited a strong correlation with the signal due to β-proton at δ 6.21 and a very weak correlation with the signal at δ 6.59 assigned to the γ-proton of the β,γ-enone moiety. On the other hand, the signal at δ 2.48 (assigned to the bridgehead proton at C9) showed a strong correlation with signal at δ 6.59 (assigned to the γ-proton of the β,γ enone moiety) and only a very weak correlation with the signal due to β-proton of the β,γ-enone group. Moreover, the signal at δ 2.74 (assigned to the proton at C3) exhibited COSY with the resonance at δ 2.94 (assigned to the proton at C4) and one of the signals at δ 2.28 (partly overlapped with another signal) due to methine proton. Similarly, the signal at δ 2.94 (assigned to the C4 proton) showed a strong COSY with the signals at δ 2.74 (assigned to the proton at C3) and δ 2.17 (dd of d, one of the methylene protons presumably at C5). These relationships between the protons and comparison of the spectral features with that of the precursor **11** clearly suggested that the olefinic linkage present in the seven membered ring of **11** had undergone a selective epoxidation. The observed selectivity is a manifestation of the homoconjugation of the olefinic moiety present in the bicyclo[2.2.2]octane framework. The *exo* orientation of the oxirane ring was suggested on the basis of the attack of the peracid from more accessible *exo* π-face. The ^{13}C NMR spectrum of the epoxide **12** also corroborated its formulation since it showed a signal at δ 215.65 for carbonyl group and 139.53, 125.37 for only two olefinic carbons of the bicyclo[2.2.2]octenone moiety. It further exhibited signals at δ 56.00, 54.29, 53.34, 52.66, 43.93, 40.57, 37.24, 29.60, 27.67, 26.73, 23.90, 23.70 for other quaternary, methylene and methyl carbons.

Reagents and Conditions: i, m-chloroperbenzoic acid CH_2Cl_2, 94%;
ii, $BF_3.OEt_2$, benzene 39%.

Scheme 2

At this juncture, rearrangement of the oxirane moiety to carbonyl group was attempted. Of the several reagents such as $BF_3.OEt_2$, $LiClO_4$, $HClO_4$ which are known to affect this transformation, we opted for $BF_3.OEt_2$ for the rearrangement of **12**. Thus, a solution of the epoxy-ketone **12** in dry benzene was treated with $BF_3.OEt_2$ at ~5 ^{0}C for about 2 hours (Scheme 2). Usual work-up and chromatography gave a dione to which the structure **5** was assigned on the basis of the following data. The presence of two carbonyl groups was clearly revealed from its ^{13}C NMR (75 MHz) spectrum that showed signals at δ 215.93 and 214.04 along with other resonances. The ^{1}H NMR (300 MHz) spectrum displayed characteristic signals at δ 6.39 (superimposed dd, $J_1=J_2=7$ Hz, 1H), 6.18 (d of superimposed dd, $J_1=J_2=7$ Hz, $J_3=1.5$ Hz, 1H) due to γ- and β-protons of β,γ-enone moiety, respectively. It also showed signals at δ 3.60 (d with structure, J=7 Hz, 1H) for the bridgehead proton at C1. Further signals were observed at δ 2.82 (m, 1H, partly overlapped with another multiplet) and 2.58 (d with structure, J ~7Hz, 1H) for the ring junction proton at C2 and the bridgehead proton at C9 respectively, in addition to the signals for other methine, methylene and methyl protons. These assignments were confirmed with the help of a COSY spectrum which revealed correlation between the signals at δ 6.39, 6.18 and 2.58. Similarly, the olefinic signal at δ 6.18, assigned to the β-proton of the β,γ-enone moiety, showed a correlation with resonances at δ 6.39 and 3.60. The signal at δ 2.82 (partly merged with another multiplet) was assigned to the ring junction proton at C2 since it showed correlation with the signal at δ 3.60 assigned to the bridgehead proton at C1 (which in turn, correlated with β-proton of the β,γ-enone moiety). The relationships between the various protons were further confirmed through NOESY spectrum. The signal at δ 6.39 exhibited NOESY with signals at δ 6.18, 2.58. The signal at δ 2.58 showed NOESY with signals at δ 2.90, 1.92 and the signal hidden under methyl groups. Furthermore, the signal at δ 2.90 showed NOESY with the signals at δ 2.82 in addition to other signals. The chemical shift and the relationship of the proton at C2 with other protons as revealed by COSY and NOESY spectra suggested the structure **5** for the above compound.

Though the mechanism of the epoxide rearrangement and the factors governing the regio-selectivity are not very clear, it appears that the 1,3-steric interactions between protons at C1 and C3 may be responsible for the preferential migration of the hydrogen from C3 to C4.

Rigid carbocyclic systems containing a β,γ-enone chromophore undergo two unique reactions upon excitation. The direct excitation in general, leads to 1,3-acyl migration while triplet sensitised irradiation follows a 1,2-migration or oxa-di-π-methane reaction.[10-12] The direct excitation (S1) of β,γ-unsaturated ketones containing the homo-conjugated carbonyl group in ethano bridge leads to the formation of cyclobutanone derivative as a result of 1,3-shift. In some cases decarbonylation is also observed.[13,14] We considered it possible to induce photodecarbonylation in **5** on direct irradiation in appropriate conditions.

Thus, a solution of the dione **5** in dry benzene was irradiated with a mercury vapour lamp (400 W, Applied photophysics) for 2h, in a Pyrex immersion well. Removal of the solvent followed by chromatography gave the tricyclic compound **3** in good yield (42%) as a result of decarbonylation, whose structure was clearly revealed from its spectral data (Scheme 3).
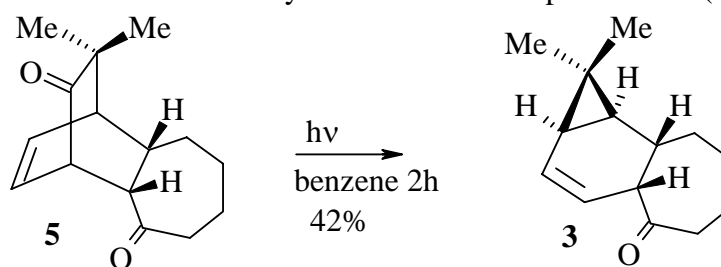
Scheme 3

The mechanism of formation of the decarbonylated product during the above photoreaction is difficult to suggest at this moment. Apparently, it proceeds through initial α-cleavage leading to the biradical **13** which cyclizes to give the 1,3-acyl shift product **4** that on subsequent decarbonylation gives the final product (Scheme 4).
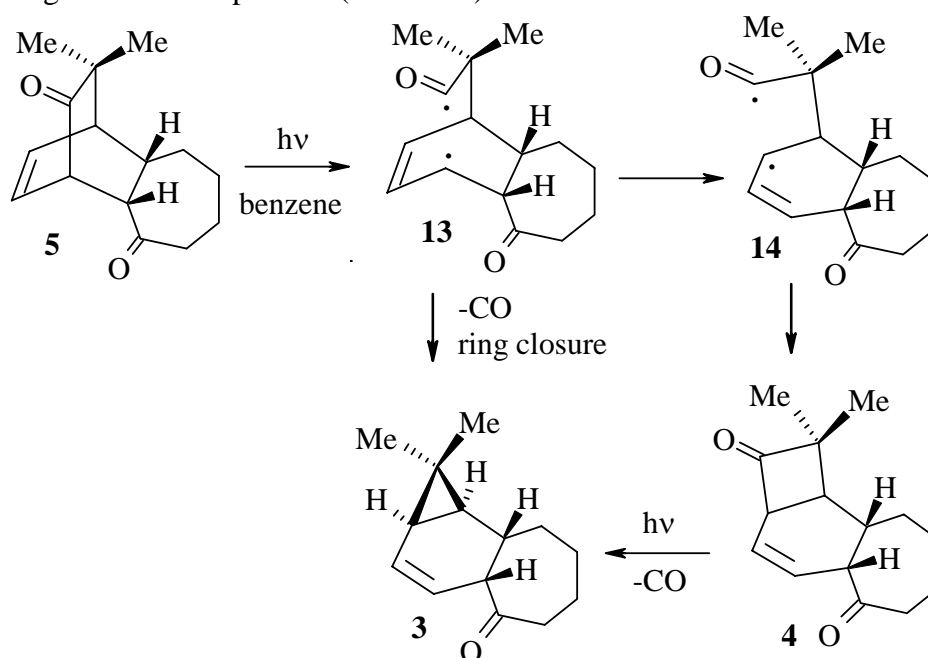
Scheme 4

This contention is based on the preliminary observation that 1,3-acyl shift product is formed (tlc, IR) during initial stages of the photoreaction that disappears after continued irradiation and the formation of the final product is observed. In this context it may be noted that cyclobutanones are known to undergo photo-decarbonylation upon excitation. However, the possibility of decarbonylation in biradicals **13** or **14** followed by ring closure can not be ruled out.

In summary, we have described a novel route to bicyclo[2.2.2]octenone annulated with a seven membered ring and its photochemical reaction directly leading to the tricyclic BCD framework of phorbol in a single stereoselective sequence.

Experimental Section

General Procedures. IR spectra were recorded on Nicolet Impact 400 FT-IR Instrument. UV spectra were recorded on Schimadzu 260 instrument. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were recorded on 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 HP GCD 1800A mass spectrometer. Microanalyses were done on a CEST 1106 instrument. Melting points were determined on a veego apparatus of Buchi type and are uncorrected. All the organic extracts were dried over anhydrous sodium sulphate. Reactions were monitored with 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). The elution was done with petroleum ether (60-80^{0}C) and ethyl acetate mixtures. The fractions eluted from column were concentrated at reduced pressure on a Buchi-RE 111 rotary evaporator.

10-Hydroxy-10-chloromethyl *endo* tricyclo[7.2.2.0^{2,8}]trideca-3,12-dien-11-one (8). A mixture of the dimer **6** (1.0g, 3.14 mmol) and 1,3-cycloheptadiene (2 mL) in *o*-dichlorobenzene (8 mL) was heated at ~140^{0}C for 6 hours. The reaction mixture was brought to room temperature and the excess cycloheptadiene and *o*-dicholoro benzene were distilled under vacuum. The residue thus obtained was chromatographed on silica gel. Elution with petroleum ether first gave the residual cycloheptadiene and *o*-dichlorobenzene. Continuted elution with petroleum ether-ethyl acetate (95:5) furnished the adduct **8** (0.8g, 51%) as a solid which was recrystallized from petroleum ether-ethyl acetate (98:2), mp 138-139^{0}C. IR (nujol) ν_{max}: 3439, 1718 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$) δ: 6.50 (superimposed dd, $J_1=J_2=8$ Hz, 1H, γ-proton of β,γ-enone moiety), 6.28 (superimposed dd, $J_1=J_2=8$ Hz, 1H, β-proton of β,γ-enone moiety), 5.60 (m, 1H, olefinic H), 5.23 (m of d, J=9 Hz, 1H, olefinic H), 3.55 (part of an AB system J$_{AB}$=12 Hz, 2H, -CH$_2$Cl), 3.28-3.18 (m, 2H, methine H), 3.02 (d with structure, J=7.5 Hz, 1H, methine H), 2.71 (s, 1H, OH), 2.56 (t with structure, J=10 Hz, 1H, methine H), 2.20-1.94 (complex m, 2H, methylene H), 1.62-1.38 (complex m, 4H, methylene H). ^{13}C NMR (75 MHz, CDCl$_3$) δ: 210.26 (CO), 136.12, 130.57, 128.63, 127.97, (four olefinic carbons), 73.92, 53.81, 50.85, 48.66, 41.05, 35.30, 29.26, 25.06,

22.20 (for other methine, methylene and quaternary carbons). Mass (m/z): 252 (M$^+$). Analysis Found: C, 66.47; H, 7.00%. Calculated for $C_{14}H_{17}O_2Cl$: C, 66.66; H, 6.74%.

10-Spiroepoxy *endo* tricyclo[7.2.2.0^{2,8}]trideca-3,12-dien-11-one (9). To a solution of adduct **8** (0.5g, 1.98 mmol) in chloroform (20ml) containing cetyltrimethylammonium bromide (CTAB) (0.005g) as a phase transfer catalyst, was added an aqueous solution of potassium hydroxide (1M, 2 mL). The reaction mixture was stirred at room temperature (~30 ^oC) for 6 hours, after which the organic phase was separated and the aqueous layer extracted with chloroform (3 x 20 mL). The combined organic extract was washed with brine (1 x 20 mL) and dried over anhydrous sodium sulphate. Removal of solvent followed by column chromatography [petroleum ether-ethyl acetate, (96:4)] of the residue on silica gel gave the epoxy ketone **9** (0.425g, 93%) as a solid that was recrystallized from petroleum ether-ethyl acetate (95:5), mp 124-125 ^oC. IR (nujol) ν_{max}: 1730 cm^{-1}. UV (MeOH) λ_{max}: 292.8 (w), 210.6 (s) nm. ^1H NMR (300 MHz, CDCl$_3$) δ: 6.54 (superimposed dd with structure, $J_1=J_2=7.5$ Hz, 1H, γ-proton of β,γ-enone moiety), 6.30 (superimposed dd, $J_1=J_2=7.5$ Hz, 1H, β-proton of β,γ-enone moiety), 5.63 (complex m, 1H, olefinic H), 5.29 (d with structure, J=10 Hz, 1H, olefinic H), 3.38 (m, 1H, methine H), 3.28 (br d with structure, J=~7.5 Hz, 1H, methine H), 3.14 (part of an AB system, J_{AB}=~7 Hz, 1H, -OC$\underline{H}_2$-), 2.84 (part of an AB system, J_{AB}=~7 Hz, 1H, -OC$\underline{H}_2$-), 2.39 (m, 2H, methine H), 2.21-1.97 (m, 2H, methylene H), 1.62-1.39 (m, 4H, methylene H). ^{13}C NMR (75 MHz, CDCl$_3$) δ: 205.69 (CO), 135.19, 130.36, 128.50, 128.16 (four olefinic carbons), 57.86, 54.12, 53.23, 46.90, 39.65, 38.55, 28.99, 24.90, 21.60. Mass (m/z): 202 (M$^+$). Analysis Found: C, 77.41; H, 7.46%. Calculated for $C_{14}H_{16}O_2$: C, 77.77; H, 7.40%.

10,10-Dimethyl *endo* tricyclo[7.2.2.0^{2,8}]trideca-3,12-dien-11-one (11). To a suspension of activated zinc (5g, excess) and ammonium chloride (1.2g, excess) in dry dioxane (20 mL) was added a solution of the compound **9** (1.0g, 4.62 mmol) in dry dioxane (10 mL). The reaction mixture was refluxed for 5 hours, after which it was cooled and filtered to remove zinc and washed with ethyl acetate. The filtrate was concentrated *in vacuo*, so as to remove most of the solvent and the residue was diluted with water (25 mL) and extracted with ethyl acetate (3 x 25 mL). The combined organic layer was washed with brine (1 x 25 mL) and dried over anhydrous sodium sulphate. The solvent was removed under vacuum, and the residue was chromatographed on silica gel. Elution with petroleum ether ethyl acetate (97:3) gave compound **10** (0.673g, 72%) as a *syn:anti* mixture[IR (neat) ν_{max} : 1722 cm^{-1}. UV (MeOH) λ_{max}: 295.0 (w), 213.8 nm. ^1H NMR (300 MHz, CDCl$_3$) δ : 6.57 (superimposed dd, $J_1=J_2=8$ Hz, 1H, γ-proton of β,γ-enone moiety), 6.19 (superimposed dd with structure, $J_1=J_2=8$ Hz, 1H, β-proton of β,γ-enone moiety), 5.57 (m, 1H, olefinic H), 5.24 (d with structure, J=~10 Hz, 1H, olefinic H), 3.13 (d with structure, J=~6 Hz, 1H, methine H), 2.98 (d, J=10 Hz, 1H, methine H), 2.58 (d with structure, J=6 Hz, 1H, methine H), 2.19-1.94 (complex m, 4H, methine H and methylene H), 1.59-1.38 (complex m, 4H, methylene H), 1.16 (d, J=~7.5 Hz, 3H, CH$_3$). (data for major isomer). Mass (m/z): 202 (M$^+$)]. The ketone **10** thus obtained was subjected to alkylation as follows.

Sodium hydride (0.356g of 60% w/w suspension in oil, excess) was placed in a dry two necked flask and washed with dry petroleum ether and tetrahydrofuran (10 ml) was added to it. A

solution of the ketone **10** (0.5g, 2.47 mmol) in tetrahydrofuran (5 mL) was slowly added to the reaction mixture and it was refluxed for 1 hour. Methyl iodide (5 mL, excess) was then added drop wise to the reaction mixture and the reaction mixture was further refluxed for 8 hours. The reaction mixture was cooled and quenched by careful addition of water, and it was filtered on a celite pad. The filtrate was concentrated under vacuum. The residue was diluted with water and extracted with ether (3 x 20 mL). The combined extract was washed with water (1 x 20 mL), brine (1 x 25 mL) and dried over anhydrous sodium sulphate. Removal of solvent and column chromatography [petroleum ether-ethyl acetate, (98:2)] of the residue on silica gel furnished the alkylated product **11** (0.425g, 78%). IR (neat) ν_{max}: 1720 cm^{-1}. UV (MeOH) λ_{max}: 293.8 (w), 216.8 (s) nm. ^{1}H NMR (300 MHz, CDCl$_3$) δ: 6.48 (superimposed dd, J_1=J_2=~7.5 Hz, 1H, γ proton of β, γ-enone moiety), 6.12 (superimposed dd, J_1=J_2=8.5 Hz, 1H, β-proton of β,γ-enone moiety), 5.57 (m, 1H, olefinic H), 5.22 (d with structure, J=~10 Hz, 1H, olefinic H), 3.13 (d with structure, J=~6 Hz, 1H, methine H), 3.06 (br d, J=~9.5 Hz, 1H, methine H), 2.42 (m of d, J=6 Hz, 1H, methine H), 2.28 (m, 1H, methine H), 2.16-2.04 (m, 1H, methylene H), 2.02-1.92 (m, 1H, methylene H), 1.57-1.36 (complex m, 4H, methylene H), 1.15 (s, 3H, CH$_3$), 1.05 (s, 3H, CH$_3$). ^{13}C NMR (75 MHz, CDCl$_3$) δ: 217.09 (CO), 138.98, 131.97, 127.94, 125.39, 55.85, 53.17, 43.74, 38.96, 37.46, 29.64, 27.72, 25.07, 24.13, 22. 02. Mass (m/z) : 216 (M$^+$).

10,10-Dimethyl-3,4-epoxy *endo* tricyclo[7.2.2.0^{2,8}]trideca-12-en-11-one (12). *m*-Chloroper-benzoic acid (0.237g, 1.37 mmol) was added to a solution of the compound **11** (0.3g, 1.37 mmol) in dry dichloromethane and the reaction mixture was stirred for 2 hours (tlc) at ambient temperature (~30°C). The reaction mixture was diluted with dichloromethane (25ml) and it was washed with saturated sodium bicarbonate solution (2 x 25 mL), water (1 x 25 mL) and brine (1 x 20 mL) and dried over anhydrous sodium sulphate. Removal of solvent gave a residue which was chromatographed on silica gel. Elution with petroleum ether-ethyl acetate (90:10) gave the compound **12** (0.30g, 94%) as a solid that was recrysrallised from petroleum ether-ethyl acetate (92:8), mp 94-95 °C. IR (film) ν_{max}: 1713 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$) δ: 6.59 (superimposed dd with structure, J_1=J_2=7.5 Hz, 1H, γ-proton of β,γ-enone moiety), 6.21 (superimposed dd with structure, J_1=J_2=7.5 Hz, 1H, β-proton of β, γ-enone moiety), 3.39 (d with structure, J=~7.5 Hz, 1H, methine H), 2.94 (m, 1H, methine H), 2.74 (superimposed dd, J_1=J_2=4 Hz, 1H, methine H), 2.48 (m of d, J=7.5 Hz, 1H, methine H), 2.36-2.24 (m, 2H, methine H), 2.17 (ddd, J_1=13.5 Hz, J_2=6 Hz, J_3=4Hz, 1H, methylene H), 1.80 - 1.43 (m, 4H, methylene H), 1.16-1.08 (m, merged with the singlet due to CH$_3$, 4H, CH$_3$ and one methylene proton), 1.05 (s, 3H, CH$_3$). ^{13}C NMR (75 MHz, CDCl$_3$) δ: 215.65 (CO), 139.53, 125.37 (two olefinic carbons), 56.00, 54.29, 53.34, 52.66, 43.93, 40.57, 37.24, 29.60, 27.67, 26.73, 23.90, 23.70. Mass (m/z): 232 (M$^+$). Analysis Found: C, 77.90; H, 8.96%. Calculated for C$_{15}$H$_{20}$O$_2$: C, 77.58; H, 8.62%.

10,10-Dimethyl *endo* tricyclo[7.2.2.0^{2,8}]trideca-12-en-3,11-dione (5). Boron trifluoride etherate (0.1 mL) was added to a solution of compound **12** (0.25g, 1.07 mmol) in dry benzene (10 mL) at ~ 5°C. The reaction mixture was stirred for 1.5 hours (tlc), after which it was diluted with benzene (30ml). The benzene layer washed with water (1 x 20 mL), brine (1 x 20 mL) and dried over anhydrous sodium sulphate. Removal of solvent followed by column chromatography

[petroleum ether-ethyl acetate, (95:5)] of the crude product on silica gel gave the dione **5** (0.097g, 39%) as a solid which was recrystallized from petroleum ether-ethyl acetate (96:4), mp 105-106 ^{0}C. IR (film) ν_{max}: 1713,1698 cm^{-1}. UV (MeOH) λ_{max}: 296.0 (w), 208.6 (s) nm. ^{1}H NMR (300 MHz, CDCl$_3$) δ: 6.39 (superimposed dd, J$_1$=J$_2$=7 Hz, 1H, γ-proton of β,γ-enone moiety), 6.18 (d of superimposed dd, J$_1$=7 Hz, J$_2$=1.5 Hz, 1H, β-proton of β,γ-enone moiety), 3.60 (d with structure, J=7 Hz, 1H, methine H), 2.90 (m, partly merged with another multiplet, 1H, methine H), 2.82 (m, partly merged with another multiplet, 1H, methine H), 2.58 (d with structure, J=~7 Hz, 1H, methine H), 2.17-1.94 (complex m, 2H, methylene H), 1.85 (m, 1H, methylene H), 1.49 (m, 1H, methylene H), 1.15 (s, 3H, CH$_3$), 1.14-1.09 (m, 4H, methylene H), 1.08 (s, 3H, CH$_3$). ^{13}C NMR (75 MHz, CDCl$_3$) δ: 215.93 (CO), 214.04 (CO), 137.48, 127.61, 50.52, 49.85, 46.38, 44.26, 43.95, 37.28, 30.45, 29.09, 27.79, 23.94, 18.23 (for other methine, methylene, quaternary and methyl carbons). Analysis Found: C, 77.42; H, 8.93%. Calculated for C$_{15}$H$_{20}$O$_2$: C, 77.58; H, 8.62%.

5,5-Dimethyl tricyclo[5.5.0.0^{4,6}]dodeca-2-en-12-one (3). A solution of the dione **5** (0.025 g, 0.107 mmol) in dry benzene (300 mL) was irradiated under nitrogen with a mercury vapour lamp (400W, Applied Photo Physics) in Pyrex immersion well for about 2 hours. The solvent was removed *in vacuo* and the residue was chromatographed on silica gel. Elution with petroleum ether-ethyl acetate, (98:2) furnished the tricyclic compound **3** (0.008g, 42%). Continued elution with petroleum ether-ethyl acetate (97:3) gave some unreacted starting material (0.003g). IR (neat) ν_{max}: 1711 cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$) δ: 6.06 (ddd, J$_1$=10 Hz, J$_2$=6 Hz, J$_3$=~3 Hz, 1H), 5.22 (dd, J$_1$=10 Hz, J$_2$=~2.5 Hz, 1H), 2.8 (br d, J=9 Hz, 1H), 2.48-2.30 (m, 2H), 2.04-1.94 (m, 1H), 1.66-1.58 (m, 1H), 1.24-1.18 (m, 1H), 1.12 (s, 3H, CH$_3$), 1.06-1.00 (m, 4H), 0.95 (s, 3H, CH$_3$), 0.90 (m, 1H, cyclopropyl proton), 0.82 (dd, J$_1$=6 Hz, J$_2$=~1 Hz, 1H, cyclopropyl proton). ^{13}C NMR (75 MHz, CDCl$_3$) δ: 128.54, 121.05, 50.59, 42.70, 34.11, 32.62, 30.87, 30.17, 29.87, 25.19, 22.43, 15.98, 14.73 (carbonyl carbon not observed). Mass (m/z): 204 (M$^+$).

Acknowledgements

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