

Intramolecular cycloaddition in cyclohexa-2,4-dienone and photochemical reactions: Synthesis of 12-methyl-3-oxa-*endo*-tricyclo[6.2.2.0^{1,6}]dodec-11-en-10-one, and pyran annulated bicyclo[3.3.0]octane and bicyclo[4.2.0]octane frameworks

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Synthesis of pyran annulated bicyclo[2.2.2]octane having a β,γ -enone chromophore and its photochemical reaction leading to diquinane-pyran hybrid and pyran annulated bicyclo[4.2.0]octane systems has been described.

Keywords: Cycloaddition, intramolecular, photoreaction, cyclohexa-2,4-dienone, oxa-di- π -methane rearrangement

There has been a considerable interest in the synthesis of diquinanes fused with heterocyclic rings because of their interesting biological properties^{1,2}. For example the tricyclic compounds **1-3** (**Figure 1**) having oxatriquinane framework exhibit cytotoxic activity and their analogs have proved to be useful for the treatment of breast cancer, and osteosarcoma^{2a,b}. Moreover, there is growing interest in design and synthesis of new molecular systems which combine structural features of different class of compounds³.

In view of the above and the continuing interest in this area⁴, we recently reported synthesis of oxatriquinanes^{4b}. In order to extend the methodology towards synthesis of new molecular entities, developing a synthetic route to new compound of type **4** containing a diquinane framework annulated with a pyran ring, and tricyclic system **5** in which a pyran ring is linearly fused to bicyclo[4.2.0] octane framework, present in enediandric acids^{5a,b} and sterpurnes^{5c,d} was further considered.

It was envisaged that a photochemical 1,2-acyl shift in tricyclic system having a β,γ -enone chromophore, such as **6**, would provide a direct entry to the pyran annulated diquinane of type **4** in a single stereoselective step. On the other hand, it was thought that a 1,3-acyl shift in **6** would furnish the tricyclic compound **5**. Furthermore, it was thought that the desired chromophoric system **6** could be derived from **7** which in turn can be obtained from the aromatic precursor of type **9** via its oxidation to spiroepoxy-

dienone **8** and subsequent intramolecular Diels-Alder reaction. (**Scheme I**).

Results and Discussion

In order to realize the aforementioned objectives, it was necessary to have a simple preparation of the aromatic precursor **9**. Initially, preparing the compound **9** via alkylation of the readily available precursor **10** with 4-bromobutene was considered followed by removal of the protecting group (**Figure 2**). However, the alkylation of **10** with 4-bromobutene was futile under various conditions. This is presumably due to propensity of 4-bromobutene to undergo elimination.

Therefore, the hydroxymethyl compound **10** was treated with PPh_3Br_2 (Ref. 6a) to give the known^{6b} benzylic bromide **12** in 56% yield (**Scheme II**). The alkylation of **12** with 3-buten-1-ol in the presence of NaH gave the O-alkylated product **11** in good yield which upon hydrolysis with HCl in THF-H₂O furnished the desired aromatic precursor **9** in 86% yield (**Scheme II**).

Having prepared the aromatic precursor **9**, it was subjected to oxidation for the generation of cyclohexadienone **8** and intra-molecular cycloaddition, following a procedure developed by this group⁷. Thus, a solution of **9** in acetonitrile was slowly oxidized with aqueous sodium metaperiodate at 5-10°C which gave the adduct **8** in low yield (28%) along with the dimer **13** as major product and the

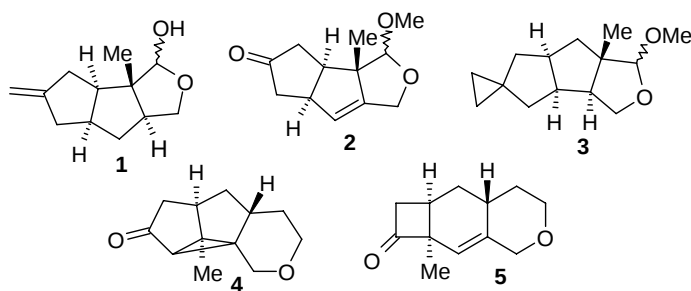
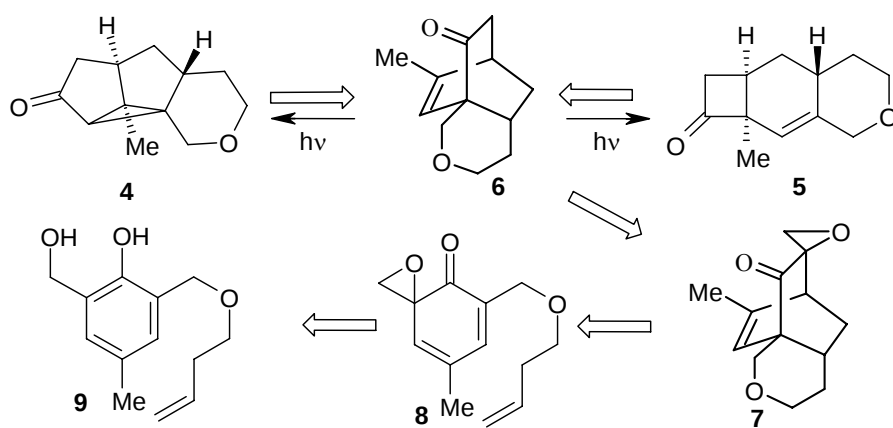


Figure 1



Scheme I

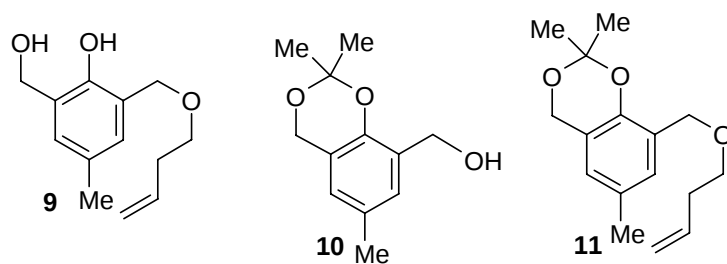
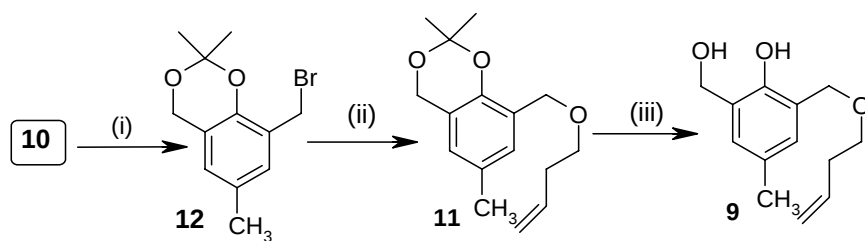
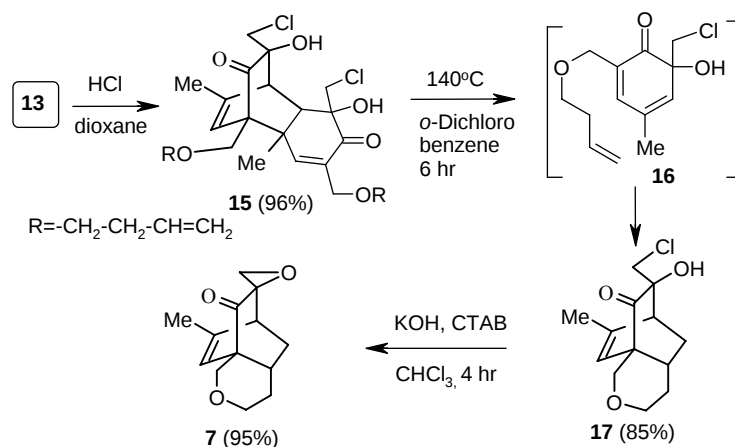
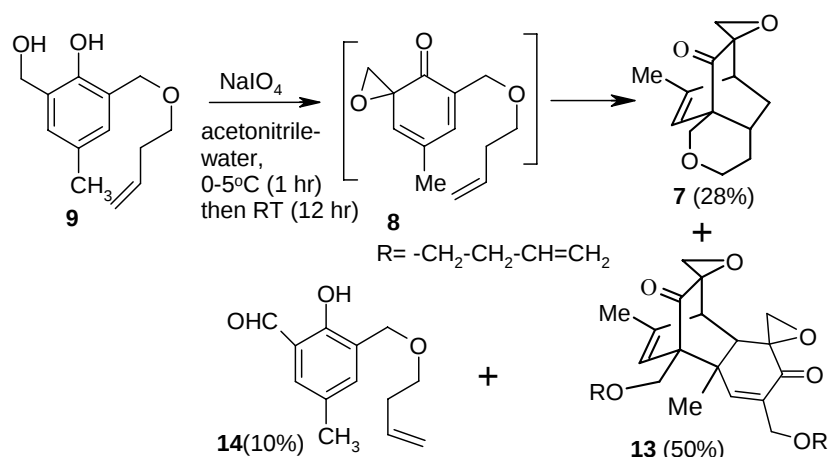


Figure 2



Scheme II — Reagents/conditions: (i) PPh_3 , Br_2 , 56%; (ii) 3-buten-1-ol, NaH , tetrabutylammonium iodide, THF, reflux, 62%; (iii) HCl , aq. THF, RT, 86%.



aldehyde **14** as a minor product (**Scheme III**). The formation of the dimer **13** as a major product in the above reaction suggested that the intermolecular Diels-Alder reaction between two moles of the spiroepoxy cyclohexadienone **8** is perhaps, more favorable than the intra-molecular interception of the cyclohexadienone moiety with internal alkene.

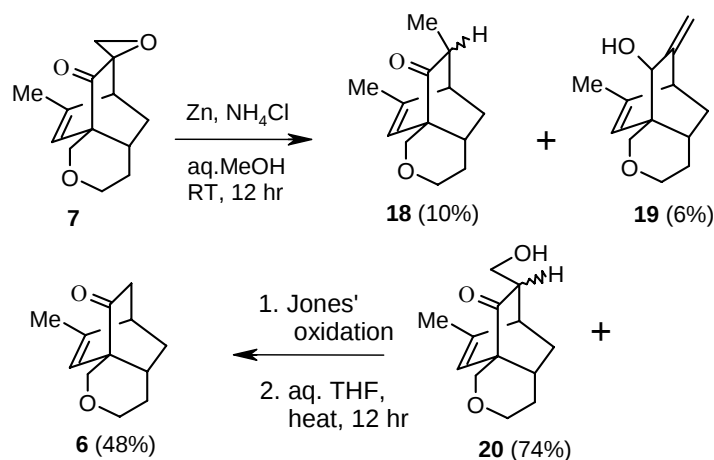
Therefore, it was thought to employ the dimer **13** for the synthesis of **7**. Hence, the epoxy dimer **13** was treated with HCl in dioxane to give the chlorohydroxy dimer **15** in excellent yield (96%). Pyrolysis of the chlorohydroxy dimer **15** in *o*-dichlorobenzene gave the adduct **17** in excellent yield (85%) as a result of retro Diels-Alder reaction of **15** leading to the monomer **16** followed by intra-molecular cycloaddition (**Scheme IV**).

The chlorohydroxy adduct **17** on treatment with 0.1M KOH in the presence of cetyltrimethylammo-

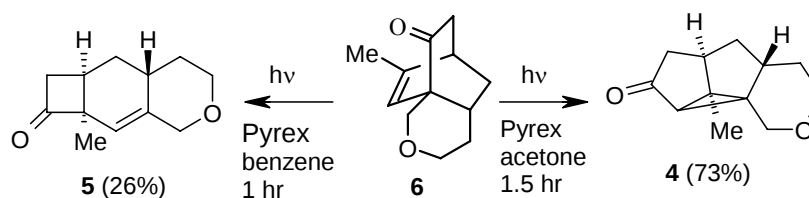
nium bromide (CTAB) as a phase transfer catalyst, gave the desired epoxy adduct **7** in excellent yield (95%) which was identical in all respects with that of the compound obtained earlier.

Towards synthesis of the desired chromophoric system **6**, manipulation of the oxirane ring present in the adduct **7** was required. Thus, the adduct **7** was treated with Zn and NH₄Cl at ambient temperature. Chromatography of the product mixture furnished the desired keto-alcohol **20** as a major product (74%), in addition to ketone **18** (10%) and the allylic alcohol **19** (6%) as minor products. Subsequently, the keto-alcohol **20** was oxidized with Jones' reagent and the resulting β -keto-acid was subjected to decarboxylation which gave the compound **6** in good yield (**Scheme V**).

Having synthesized the chromophoric system **6**, its photoreactions were explored. Photoreaction of



Scheme V



Scheme VI

β,γ -enones have stimulated intense interest because of their synthetic potential⁸⁻¹⁰. In general, triplet sensitized irradiation of rigid β,γ -enones leads to a 1,2-acyl shift whereas direct irradiation (singlet excitation) induces a 1,3-acyl shift. Though these reactions are quite characteristic of their excited states, the exact outcome depends on structure of the chromophoric system and presence of functional group in a subtle fashion. Keeping this in view, a solution of **6** in acetone (both as a solvent as well as sensitizer) was irradiated with a mercury vapour lamp (125 W Applied Photophysics) in a Pyrex immersion well for 1.5 hr. Removal of solvent followed by chromatography of the photolysate gave the tetracyclic ketone **4** in excellent yield (74%), as a result of 1,2-acyl shift (**Scheme VI**). Towards the singlet excitation, a solution of **6** in benzene was irradiated for 1 hr. Removal of solvent followed by chromatography furnished the linearly fused tricyclic compound **5** in a low yield (26%), along with unreacted starting material. Though the efficiency of 1,3-acyl shift is low, it provides stereoselective route to the tricyclic compound **5** which is not readily accessible otherwise.

Experimental Section

IR spectra were recorded on Perkin-Elmer 681 and Nicolet Impact 400 FT-IR instruments. ¹H and ¹³C NMR were recorded on Varian VXR 300 and Mercury Varian 400 NMR instruments. The samples were dissolved in CDCl₃ as solvent and tetramethyl silane as internal standard. The standard abbreviations s, d, t, m, dd and td refer to singlet, doublet, triplet, multiplet, doublet of doublet and triplet of doublet, respectively. Coupling constants are reported in Hertz. The high-resolution mass spectra were recorded on a Q-ToF micro instrument (YA-105). Melting points were determined on a Veego apparatus of Buchi type and are uncorrected. All the organic extracts were dried over anhydrous Na₂SO₄. Progress of reactions were monitored by thin layer chromatography, the spots were visualized with iodine vapour. Column chromatography was performed over SRL silica gel (60-120 or 100-200 mesh). The elution was done with petroleum ether (60-80°C) and ethyl acetate. The fractions eluted from column were concentrated under reduced pressure. The solvents used for all reactions were purified and dried by using standard procedures.

2,2,6-Trimethyl-8-(2-oxa-hex-5-enyl)-1,3-benzodioxine, **11**

Sodium hydride (1.32 g, 60% suspension in mineral oil) was placed in a round bottom flask and washed with petroleum ether (3×10 mL). THF (50 mL) and tetrabutylammonium iodide (0.1 g) were added. 3-Buten-1-ol (0.67 g, 0.8 mL, 9.3 mmole), was added by a syringe and the reaction-mixture was stirred until bubbling ceased. After which a solution of bromide **12** (1 g, 3.69 mmole) in THF (5 mL) was added by syringe. The reaction was stirred for 4 hr at RT. It was poured into an aqueous NH₄Cl solution (50 mL) and extracted with ether (3 × 50 mL). The combined organic extract was dried over anhydrous Na₂SO₄ and concentrated *in vacuo*. The residue was chromatographed over silica gel. Elution with petroleum ether-EtOAc (98:2) gave ether **11** as a colourless liquid (0.6 g, 62 %). IR (neat): 1640, 1611, 1481 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 7.07 (s, 1H), 6.69 (s, 1H), 5.92-5.81 (m, 1H), 5.14-5.03 (m, 2H), 4.81 (s, 2H), 4.49 (s, 2H), 3.56 (t, *J* = 8 Hz, 2H), 2.42-2.35 (m, 2H), 2.26 (s, 3H), 1.52 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 146.5, 129.2, 126.2, 118.8, 135.5, 128.1, 124.0, 116.3, 99.4, 69.8, 66.8, 61.0, 34.3, 24.8, 20.7; ESI HRMS: *m/z* Found: 285.1467 [M⁺+Na]. Calcd for C₁₆H₂₂O₃ Na: 285.1478.

2-Hydroxymethyl-4-methyl- 6-(2-oxa-hex-5-enyl) phenol, **9**

To a solution of **11** (2.42 g, 9.25 mmole) in THF-H₂O (1:1, 100 mL), was added HCl (110 mL, 1N) and the reaction mixture was stirred at ambient temperature for 18 hr. The organic solvent was removed under reduced pressure. The aqueous solution was extracted with ethyl acetate (3 × 30 mL). The combined organic layer was washed with NaHCO₃ (2 × 20 mL), brine (30 mL) and dried over anhydrous Na₂SO₄ and concentrated *in vacuo*. The crude product was chromatographed over silica gel. Elution with petroleum ether-EtOAc (88:12) provided the title compound **9** as a liquid (1.78 g, 86 %). IR (neat): 3368, 1640, 1483 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 6.96 (s, 1H), 6.81 (s, 1H), 5.87-5.77 (m, 1H), 5.16-5.09 (m, 2H), 4.69 (s, 2H), 4.66 (s, 2H), 3.61 (t, *J* = 6.4 Hz, 2H), 2.43-2.38 (m, 2H), 2.24 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 152.2, 134.7, 129.1, 129.0, 128.3, 127.4, 122.4, 117.4, 71.9, 70.0, 62.6, 34.1, 20.5; ESI HRMS: *m/z* Found 245.1154 [M⁺+Na]. Calcd for C₁₃H₁₈O₃Na: 245.1143.

12-Methyl-9-spiroepoxy-3-oxa-endo-tricyclo-[6.2.2.0^{1,6}]dodec-11-en-10-one, **7**, 2-formyl-4-methyl-6-(2-oxa-hex-5-enyl)phenol, **14** and 7,11-dimethyl-5,8-bis(2-oxa-hex-5-enyl)-3,10-bis(spiroepoxy)-endo-tricyclo[6.2.2.0^{2,7}]dodec-5,11-dien-4,9-dione, **13**

To a stirred solution of **9** (1.78 g, 8.02 mmole) in acetonitrile (75 mL) was added a solution of sodium metaperiodate (8 g in 75 mL of water, 37.28 mmole) drop wise over a period of 1 hr at 0-5°C. The reaction- mixture was stirred for 12 hr at ambient temperature. It was saturated with sodium chloride and extracted with EtOAc (3×40 mL). The combined organic extract was washed with brine (40 mL) and dried over anhydrous Na₂SO₄. The solvent was evaporated under reduced pressure and the residue was chromatographed over silica gel. Elution with petroleum ether-EtOAc (97:3) gave the aldehyde **14** in minor quantities (0.176 g, 10%). Further elution with petroleum ether-EtOAc (90:10) furnished the adduct **7** as a solid (0.492 g, 28%). Further elution with petroleum ether-EtOAc (85:20) gave the dimer **13** as a major product as a thick colourless liquid (0.88 g, 50%).

Data of the adduct 7. m.p. 122-24°C. IR(film): 1722 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 5.77 (broad s, 1H), 4.08 (part of an AB system, *J*_{AB} = 12 Hz, 1H), 3.92-3.71 (m, 1H), 3.74 (part of an AB system, *J*_{AB} = 12 Hz, 1H), 3.36-3.21 (m, 1H), 3.13 (part of an AB system, *J*_{AB} = 6 Hz, 1H), 2.87 (part of an AB system, *J*_{AB} = 6 Hz, 1H), 2.43- 2.35 (m, 1H), 2.31-2.28 (m, 1H), 2.18-2.10 (m, 1H), 1.95 (d, *J* = 1.8 Hz, 3H, CH₃), 1.60-1.43 (m, 2H), 1.13 (ddd, *J*₁ = 7.7 Hz, *J*₂ = 5.2 Hz, *J*₃ = 2.5 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃ + CCl₄): δ 205.5, 143.8, 122.7, 68.8, 67.7, 58.0, 52.2, 52.0, 43.2, 35.9, 31.3, 28.9, 20.5; ESI HRMS: *m/z* Found: 243.0991 [M⁺+Na]. Calcd for C₁₃H₁₆O₃Na: 243.0997.

Data for the aldehyde 14. IR (neat): 2859, 1655, 1460 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 11.07 (s, 1H, CHO), 9.86 (s, 1H), 7.48 (d with structure, 1H, *J* = 1.8 Hz), 7.27 (d with structure, 1H, *J* = 1.8 Hz), 5.93-5.79 (m, 1H), 5.016-5.04 (m, 2H), 4.59 (s, 2H), 3.61 (t, *J* = 6.5 Hz, 2H), 2.46-2.38 (m, 2H), 2.34 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 196.62 (CHO), 157.12, 137.16, 135.23, 132.57, 128.94, 126.93, 120.09, 116.53, 70.29, 66.42, 34.26, 20.42; ESI HRMS: *m/z* Found 221.1179 [M⁺+H]. Calcd for C₁₃H₁₇O₃: 221.1178.

Data for the dimer 13. IR (neat): 1726, 1691 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 6.76 (s, 1H), 5.89-5.72 (m, 3H), 5.14-5.02 (merged m, 4H), 4.12 (s, 2H), 3.87

(s, 2H), 3.56-3.48 (m, 4H), 3.16 (part of an AB system, J_{AB} = 5.8 Hz, 1H), 2.97 (part of an AB system J_{AB} = 5.8 Hz, 1H), 2.87-2.81 (m, 2H), 2.60 (t, J = 2.2 Hz, 1H), 2.38-2.32 (m, 4H), 2.20 (s, 1H), 1.9 (s, 3H), 1.4 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 204.1, 192.0, 148.0, 143.1, 136.6, 135.19, 135.11, 125.0, 116.6, 71.3, 70.4, 67.0, 66.3, 62.4, 58.6, 58.2, 58.1, 53.1, 48.3, 46.3, 45.7, 34.1, 34.0, 24.0, 20.9; ESI HRMS: m/z Found 479.1847 [$\text{M}^+ + \text{K}$]. Calcd for $\text{C}_{26}\text{H}_{32}\text{O}_6\text{K}$: 479.1836.

3,10-Bis(chloromethyl)-3,10-dihydroxy-7,11-dimethyl-5,8-bis(2-oxa-hex-5-enyl) *endo*-tricyclo[6.2.2.0^{2,7}]dodec-5,11-dien-4,9-dione, 15

To a solution of the spiroepoxy dimer **13** (1.37 g, 3.11 mmole) in dioxane (45 mL) was added HCl (8 mL, 50%) drop wise at 10-15°C. The reaction-mixture was stirred at RT. After completion of reaction (TLC, 6 hr), it was neutralized with solid sodium bicarbonate under cold conditions till the pH was slightly basic. Dioxane was removed under reduced pressure; the residue was diluted with water (30 mL) and extracted with EtOAc (3 $\times$ 50 mL). The combined organic extract was washed with brine (30 mL) and dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure and the residue was chromatographed over silica gel. Elution with petroleum ether-EtOAc (85:15) gave chlorohydroxydimer **15** as a colourless liquid (1.53 g, 96%). IR (neat): 3461, 1726, 1691 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 6.43 (br s, 1H), 5.87-5.73 (m, 2H), 5.54 (br s, 1H), 5.14-5.02 (m, 4H), 4.23 (s, 1H), 4.20-4.04 (m, 2H), 3.82-3.48 (cluster of m, 11 H), 2.85-2.79 (merged m, 2H), 2.38-2.28 (m, 4H), 1.78 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 208.2, 196.8, 145.8, 144.0, 135.1, 135.0, 134.0, 124.9, 116.6, 116.5, 76.2, 74.1, 71.2, 70.4, 67.0, 66.1, 62.4, 54.0, 50.0, 46.4, 46.0, 44.8, 34.1, 33.9, 24.0, 21.0; ESI HRMS: m/z Found 535.1628 [$\text{M}^+ + \text{Na}$]. Calcd for $\text{C}_{26}\text{H}_{34}\text{Cl}_2\text{O}_6\text{Na}$: 535.1630.

9-Chloromethyl-9-hydroxy-12-methyl-3-oxa-*endo*-tricyclo[6.2.2.0^{1,6}]dodec-11-en-10-one, 17

A mixture of chlorohydroxy dimer **15** (0.65 g, 1.26 mmole) and *o*-dichlorobenzene (7 mL) was heated in a sealed tube at ~160°C. After heating for 6 hr, the reaction-mixture was charged as such over silica gel. Elution with petroleum ether removed dichlorobenzene. Further elution with petroleum ether-EtOAc (85:15) gave the title compound **17** as a

solid (0.55 g, 85%), m.p. 116-18°C. IR (film): 3358, 1719 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 5.74 (broad d, J = 1.5 Hz 1H), 4.03 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.89-3.85 (m, 1H), 3.71 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.64 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.47 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.30 (dt, J_1 = 5.2 Hz, J_2 = 2.6 Hz, 1H), 3.0-2.86 (m, 1H), 2.67 (s, 1H), 2.54-2.44 (m, 1H), 2.08-2.01 (m, 1H), 1.97 (d, J = 1.65 Hz, 3H), 1.56-1.35 (m, 2H), 0.98-0.90 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ 209.2, 144.9, 121.8, 74.3, 68.6, 67.6, 51.3, 49.7, 43.9, 36.1, 31.3, 26.7, 20.8; ESI HRMS: m/z Found 279.0763 [$\text{M}^+ + \text{Na}$]. Calcd for $\text{C}_{13}\text{H}_{17}\text{ClO}_3\text{Na}$: 279.0764.

Synthesis of 12-methyl-9-spiroepoxy-3-oxa-*endo*-tricyclo[6.2.2.0^{1,6}]dodec-11-en-10-one, 7 from chlorohydroxy adduct, 17

To a solution of the adduct **17** (1.2 g, 4.67 mmole) in CHCl_3 (100 mL) was added 0.1M KOH (86 mg, 20 mL) and cetyltrimethylammonium bromide (80 mg) and the reaction-mixture was stirred for 4 hr (TLC) at ambient temperature. The organic layer was separated and the aqueous layer was extracted with CHCl_3 (3 $\times$ 20 mL) and the combined extract was dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure and the residue was chromatographed. Elution with petroleum ether-EtOAc (88:12) yielded the title compound **7** (0.977 g, 95%) as a solid, which was purified by recrystallization from petroleum ether-EtOAc mixture (95:5). It was found to be identical in all respects to the compound prepared by earlier method.

9,12-Dimethyl-3-oxa-*endo*-tricyclo[6.2.2.0^{1,6}]dodec-11-en-10-one, 18, 10-hydroxy-12-methyl-9-methylene-3-oxa-*endo*-tricyclo[6.2.2.0^{1,6}]dodec-11-ene, 19, and 9-hydroxymethyl-12-methyl-3-oxa-*endo*-tricyclo[6.2.2.0^{1,6}]dodec-11-en-10-one, 20

To a suspension of activated zinc (7 g, excess) in MeOH- H_2O (6:1, 35 mL) was added a solution of adduct **7** (0.9 g, 4.09 mmole) followed by addition of ammonium chloride (1 g, excess) and the reaction-mixture was stirred at RT for ~12 hr. It was filtered through a celite bed and the bed was washed with EtOAc (3 $\times$ 5 mL). The filtrate was concentrated under vacuum and the residue was diluted with water (25 mL), and extracted with EtOAc (4 $\times$ 25 mL). The combined organic layer was washed with brine (25 mL) and dried over anhydrous sodium sulfate. The

solvent was removed under reduced pressure and the residue was chromatographed over silica gel. Elution with petroleum ether-EtOAc (96:4) first gave the minor compound **18** (*syn:anti* mixture; 0.08 g, 10%) as a liquid. Further elution with petroleum ether-EtOAc (90:10) gave **19** (0.05 g, 6%) as a colourless liquid. Continued elution with petroleum ether-EtOAc (88:12) gave the desired alcohol **20** (*syn:anti* mixture, 2:1; 0.674 g, 74%).

Data for 18. IR (neat): 1712 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 5.65 (broad s, 1H), 4.06 (part of an AB system partly merged with another AB system, $J_{AB} = 12$ Hz, 1H), 3.86-3.83 (m, 1H), 3.67 (part of an AB system merged with another part of AB system, $J = 12$ Hz, 1H), 3.27 (merged t, $J_1 = 11.6$ Hz, 1H), 2.44-2.41 (m, 1H), 2.18 (m, 1H), 2.08-2.05 (m, 1H), 1.89 (d, $J = 1.5$ Hz, 3H), 1.86-1.81 (complex m, 1H), 1.52-1.36 (m, 2H), 1.09, 1.05 (two doublets, $J = 7.3$ Hz, total 3H), 0.94-0.88 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 215.1, 147.2, 121.2, 69.6, 67.7, 51.9, 42.8, 42.5, 35.3, 31.7, 27.1, 20.2, 14.7 (signals due to major isomer); ESI HRMS: m/z Found 207.1389 [M^+H]. Calcd for $\text{C}_{13}\text{H}_{19}\text{O}_2$: 207.1385.

Data for 19. IR (neat): 3430 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 5.69 (broad s, 1H), 4.96-4.95 (m, 2H), 3.90-3.82 (merged m, 2H), 3.74-3.66 (m, 2H), 3.37-3.33 (m, 1H), 2.79-2.77 (m, 1H), 2.18-2.12 (m, 1H), 2.08-2.05 (m, 1H), 1.80 (d, $J = 1.8$ Hz, 3H), 1.60 (br, 1H), 1.49-1.45 (m, 1H), 1.35-1.24 (m, 1H), 0.99-0.95 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 153.8, 142.0, 126.1, 107.5, 72.4, 71.4, 68.0, 46.1, 44.8, 35.2, 32.8, 28.9, 19.5; ESI HRMS: m/z Found 229.1200 [M^+Na]. Calcd for $\text{C}_{13}\text{H}_{18}\text{O}_2\text{Na}$: 229.1204.

Data for 20. IR (neat): 3429, 1705 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 5.68 (s, 1H), 4.06 (merged m, 1H), 3.88-3.78 (m, 2H), 3.72-3.54 (m, 2H), 3.33-3.23 (merged t, $J = 12$ Hz, 1H), 2.66-2.60 (m, 1H), 2.28-2.06 (m, 3H), 1.92 (d, $J = 1.46$ Hz, 3H), 1.57-1.36 (m, 2H), 1.12-0.89 (merged m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 214.4, 146.9, 121.3, 69.1, 67.6, 62.3, 51.7, 49.9, 39.1, 35.6, 31.5, 27.8, 20.0 (signals due to major isomer); ESI HRMS: m/z Found 223.1334 [M^+H]. Calcd for $\text{C}_{13}\text{H}_{18}\text{O}_3$: 223.1341.

12-Methyl-3-oxa-endo-tricyclo[6.2.2.0^{1,6}]dodec-11-en-10-one, **6**

To a solution of the β -keto-alcohol **20** (0.6 g, 2.7 mmole) in acetone (12 mL) was added freshly prepared Jones' reagent drop wise at $\sim 5^\circ\text{C}$. After completion of reaction (TLC, 45 min), acetone was removed under vacuum. The residue was diluted with water (10 mL)

and extracted with ethyl acetate (6×25 mL) and dried over anhydrous Na_2SO_4 . The solvent was removed under vacuum to give the crude carboxylic acid, which was subjected to decarboxylation as follows. The carboxylic acid thus obtained, was dissolved in THF- H_2O mixture (3:2, 15 mL) and refluxed for 12 hr. After which the aqueous layer was saturated with sodium chloride, extracted with ether (6×30 mL) and the combined extract was dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure and the residue was chromatographed. Elution with petroleum ether-EtOAc (90:10) provided the title compound **6** as a colourless liquid (0.25 g, 48%). IR (neat): 1716 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 5.66 (brs, 1H), 4.07 (part of an AB system, $J_{AB} = 12$ Hz, 1H), 3.86 (dd, $J_1 = 11.7$ Hz, $J_2 = 4$ Hz, 1H), 3.66 (part of an AB system, $J_{AB} = 12$ Hz, 1H), 3.28 (dt, $J_1 = 12$ Hz, $J_2 = 2.5$ Hz, 1H), 2.66-2.64 (m, 1H), 2.14-1.93 (m, 4H), 1.89 (d, $J = 1.5$ Hz, 3H, CH_3), 1.68-1.37 (m, 2H), 1.08-1.02 (m, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 211.6, 145.8, 120.9, 69.2, 67.3, 51.4, 39.9, 36.7, 34.6, 32.1, 31.4, 19.8; ESI HRMS: m/z Found 193.1221 [M^+H]. Calcd for $\text{C}_{12}\text{H}_{17}\text{O}_2$: 193.1229.

2-Methyl-11-oxa-tetracyclo[6.4.0.0^{1,3}.0^{2,6}]dodec-4-one, **4**

A solution of **6** (0.075 g, 0.39 mmole) in degassed acetone (100 mL, solvent as well as sensitizer) was irradiated with a mercury vapour lamp (125 W, Applied Photophysics) in a Pyrex immersion well for 1.5 hr, under nitrogen. Acetone was removed under vacuum and the residue was chromatographed. Elution with petroleum ether-EtOAc (97:3) gave unreacted starting material (0.014 g, 18%). Further elution with petroleum ether-EtOAc (85:15) afforded product **4** (0.055 g, 73%) as a colourless liquid.

IR (neat): 1725 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3): δ 3.94 (dt, $J_1 = 8.5$ Hz, $J_2 = 4.2$ Hz, 1H), 3.78 (d, $J = 12$ Hz, 1H), 3.47 (dt, $J_1 = 11.3$ Hz, $J_2 = 2.8$ Hz, 1H), 3.41 (d, $J = 12$ Hz, 1H), 2.71-2.61 (m, 2H), 2.58-2.43 (m, 1H), 2.18-2.04 (m, 1H), 1.91-1.71 (m, 3H), 1.56-1.46 (m overlapped with a s, total 4H), 1.33 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 215.2, 66.3, 65.6, 51.4, 50.2, 48.8, 46.5, 45.8, 43.6, 36.4, 32.9, 13.7; ESI HRMS: m/z Found 193.1232 [M^+H]. Calcd for $\text{C}_{12}\text{H}_{17}\text{O}_2$: 193.1229.

3-Methyl-11-oxa-tricyclo[6.4.0.0^{3,6}]dodec-1-en-4-one, **5**

A solution of **6** (0.075 g, 0.39 mmole) in benzene (100 mL) was irradiated with a mercury vapour lamp

(125 W, Applied Photophysics) in a Pyrex immersion well for 1 hr. Benzene was removed under reduced pressure and the photolysate was chromatographed. Elution with petroleum ether-EtOAc (92:8) afforded 1,3-acyl shift product **5** (0.02 g, 26%) as a colourless liquid. Further elution with petroleum ether-EtOAc (90:10) gave unreacted starting material (0.03 g, 40%).

IR (neat): 1774 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ 5.18 (s, 1H), 4.15 (part of an AB system, $J_{\text{AB}} = 13.1$ Hz, 1H), 4.08-4.02 (m, 1H), 3.98 (m of part of an AB system, $J_{\text{AB}} = 13.1$ Hz, 1H), 3.80-3.58 (m, 1H), 2.87 (d, $J = 8.8$ Hz, 2H), 2.40-2.25 (m, 2H), 1.94-1.80 (m, 2H), 1.55-1.43 (m, 1H), 1.37-1.32 (m, 1H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 209.1, 138.3, 119.8, 72.1, 68.2, 63.3, 46.0, 33.0, 31.2, 29.2, 28.2, 19.7; ESI HRMS: m/z Found 215.1054 [$\text{M}^+ + \text{Na}$]. Calcd for $\text{C}_{12}\text{H}_{16}\text{O}_2\text{Na}$: 215.1048.

Conclusion

A stereoselective route to pyran annulated diquinane and bicyclo[4.2.0]octane frameworks from a common precursor has been described. The current methodology involves *in-situ* generation and intramolecular cycloaddition of cyclohexa-2,4-dienone for the synthesis of 12-methyl-3-oxa-*endo*-tricyclo-[6.2.2.0^{1,6}]dodec-11-en-10-one and its photoreaction in triplet and singlet excited states as key features.

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