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Regioselective Synthesis of Substituted Pterocarpans and Pterocarpenes. Lewis Acid Ti (IV) Promoted Formal (3+2) Cycloaddition Reactions.

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Abstract: A synthesis of novel pterocarpans (**8a-e, 10a-c** and **11a-e**) and pterocarpenes (**7a-d** and **9a-c**) has been carried out. This method involves the Lewis acid Ti (IV) promoted formal (3+2) cycloaddition reaction of 2-alkoxy-1,4-benzoquinones (**6a-c**) with appropriately substituted 2*H*-chromenes (**1a-b**, **2a-b** and **5**) at -78^{0}C.

Recently there has been considerable interest in the synthesis of furan and related ring systems,[1] which are commonly present in many natural products and pharmaceutical agents.[2] Pterocarpans, a class of naturally occurring phytoalexins possessing a furan ring system, have gained more importance due to their biological activity. A large number of pterocarpans and pterocarpenes, both simple and complex possessing 2,2-dimethyl-2*H*-pyrano or 2,2-dimethyl-3,4-dihydropyrano moiety, were isolated from natural sources and reported to posses antifungal,[3] antitumor[4] and potent activity against snake venoms.[5] The literature includes a variety of synthetic approaches to the pterocarpan unit, the most commonly used route involves a rearrangement of chalcones using thallium (III) nitrate.[6] Recently Engler et al[7] reported that the formation of the pterocarpan ring was achieved in one step by formal (3+2) cycloaddition reaction of 2-alkoxy-1,4-benzoquinone with appropriately substituted 2*H*-chromenes. The resultant adduct serves as a key intermediate in the synthesis of many naturally occurring pterocarpans. It was also noted that the alkoxy substituent at C_3 and C_9 and the hydroxyl function at C_8 carbon in the pterocarpan unit are essential for exhibiting anti-**HIV** activity.[8]

In the continuation of our work on the synthesis of novel pterocarpans,[9] we have utilised Engler's methodology for the regioselective synthesis of variously substituted pterocarpans and pterocarpenes by formal (3+2) cycloaddition reaction.

RESULTS AND DISCUSSION:

Several examples of the (3+2) cycloaddition reactions of 2*H*-chromenes (**1**, **2** and **5**) with 2-alkoxy-1,4-benzoquinones (**6a-c**) are tabulated (Table-1). The reaction was carried out at -78^{0}C in the presence of Ti (IV) solid, prepared by premixing titanium (IV) chloride and titanium (IV) propoxide in CH_2Cl_2 at 0-5^{0}C, by the addition of a solution of 2,2-dimethyl-2*H*-chromenes (**1a-b**, **2a-b** & **5**) in methylene chloride to a well stirred solution of quinones (**6a-c**) in the same solvent. The reaction mixture was initially maintained at -78^{0}C for 4 h, subsequently it was allowed to stay at room temperature for 24 h after the addition of a catalytic amount of *p*-

toluene sulfonic acid so as to afford the desired (3+2) cycloadducts after the usual workup (Scheme-1 & 2). The products were further purified by column chromatography.

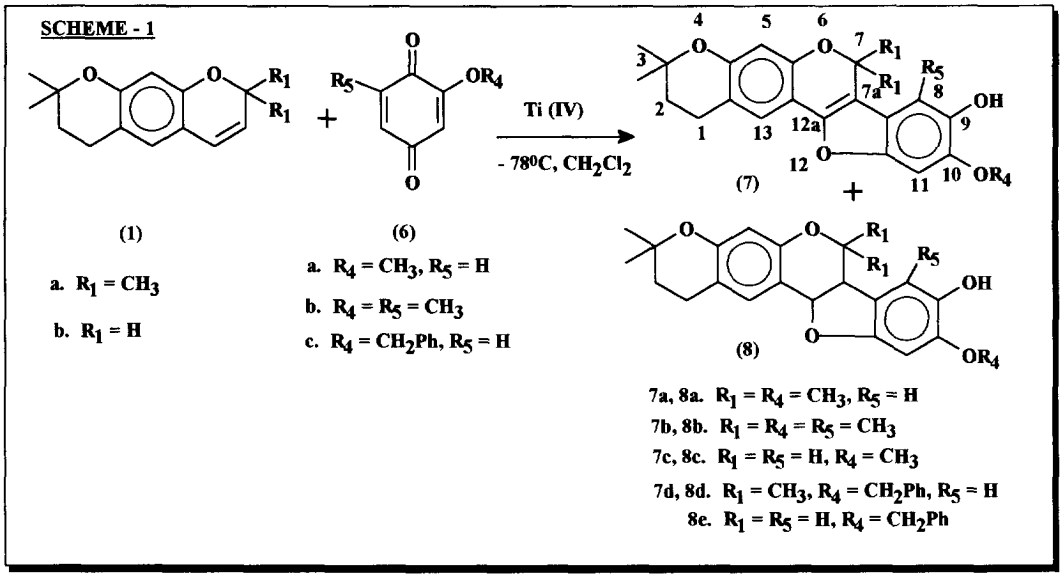


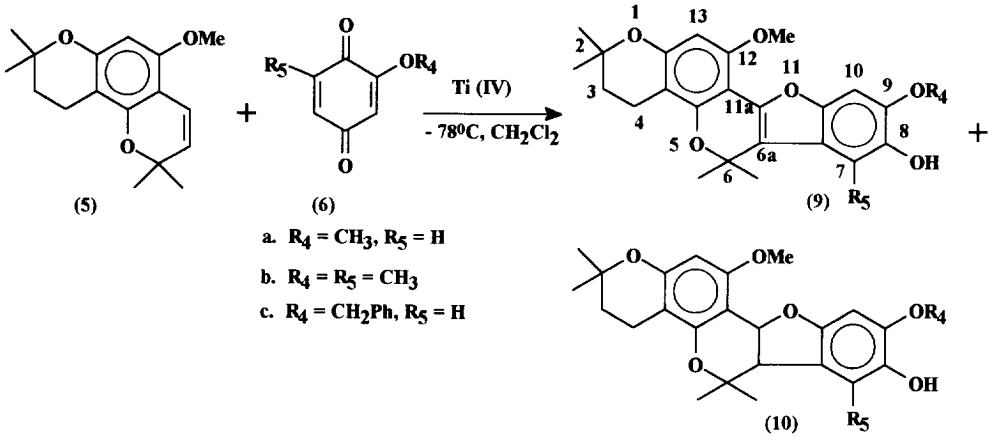
Table 1. Titanium (IV) catalysed reaction of 2,2-dimethyl-2*H*-chromenes with 2-alkoxy-1,4-benzoquinones.

Entry	Chromene	Quinone	$TiCl_4$:$Ti(OiPr)_4$	Pterocarpene (Yield %)	Pterocarpan (Yield %)
1.	1a	6a	2 : 1	7a (19 %)	8a (63 %)
2.	1a	6b	2 : 1	7b (12 %)	8b (55 %)
3.	1b	6a	2 : 1	7c (19 %)	8c (31 %)
4.	1a	6c	1.5 : 1	7d (21 %)	8d (60 %)
5.	1b	6c	1.5 : 1	—	8e (54 %)
6.	5	6a	2 : 1	9a (27 %)	10a (60 %)
7.	5	6b	2 : 1	9b (26 %)	10b (64 %)
8.	5	6c	1.5 : 1	9c (29 %)	10c (60 %)
9.	2a	6a	1.5 : 1	—	11a (62 %)
10.	2a	6b	1.5 : 1	—	11b (56 %)
11.	2a	6c	1.5 : 1	—	11c (51 %)
12.	2b	6a	1.5 : 1	—	11d (45 %)
13.	2b	6c	1.5 : 1	—	11e (48 %)

Formation of pterocarpans (**8**) were confirmed by the appearance of a hydroxyl function (about 3,500 cm^{-1}) in the IR spectrum and the appearance of two one proton doublets at about δ 3.2 & 5.5 (J=7.0 Hz) in their ^1H NMR (multiplet at around δ 3.4 in case of compounds **8c** and **8e**). The cis ring fusion of dihydrobenzofurans was ascertained by comparing the coupling constants ($J_{7a,12a}$=7.0 Hz). The absence of two doublets at around δ 3.2 & 5.5 in the ^1H NMR of pterocarpene (7) and two carbon peaks at δ 76.15 & 76.56 in ^{13}C NMR (for C_{7a} & C_{12a}) confirms the formation of pterocarpenes (Scheme-**1** & **2**). These

deductions were further supported by the mass spectral analysis. In order to suppress the formation of pterocarpene, the reactions were carried out under a variety of conditions and the best results were obtained by quenching the reaction one minute after the addition of chromene (entry-4, 5 and 8-13). As is evident from the table, formation of pterocarpan was achieved in about 45-60 % yield (Scheme-3) (entry- 4, 5 & 8-13) and in a few cases formation of pterocarpene (20-25 %) was unavoidable (entry- 4 & 8). Formation of the (2+2) cycloadduct was not observed in this case.

SCHEME - 2



(5) (6) (9) (10)

a. $R_4 = CH_3$, $R_5 = H$

b. $R_4 = R_5 = CH_3$

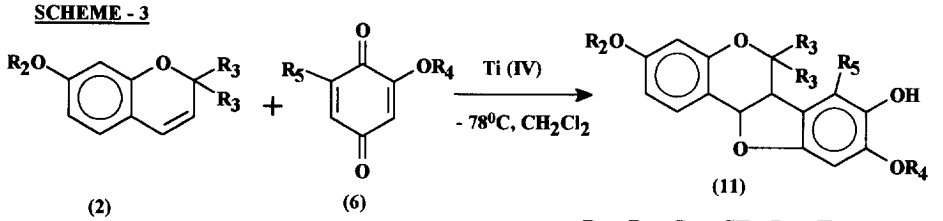
c. $R_4 = CH_2Ph$, $R_5 = H$

9a, 10a. $R_4 = CH_3$, $R_5 = H$

9b, 10b. $R_4 = R_5 = CH_3$

9c, 10c. $R_4 = CH_2Ph$, $R_5 = H$

SCHEME - 3



(2) (6) (11)

a. $R_2 = R_3 = CH_3$

b. $R_2 = CH_2Ph$, $R_3 = CH_3$

a. $R_4 = CH_3$, $R_5 = H$

b. $R_4 = R_5 = CH_3$

c. $R_4 = CH_2Ph$, $R_5 = H$

a. $R_2 = R_3 = R_4 = CH_3$, $R_5 = H$

b. $R_2 = R_3 = R_4 = R_5 = CH_3$

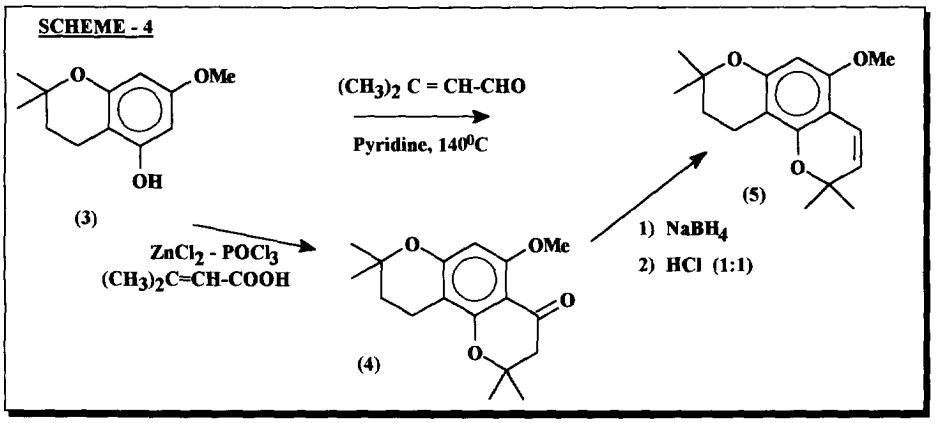
c. $R_2 = R_3 = CH_3$, $R_4 = CH_2Ph$, $R_5 = H$

d. $R_2 = CH_2Ph$, $R_3 = R_4 = CH_3$, $R_5 = H$

e. $R_2 = R_4 = CH_2Ph$, $R_3 = CH_3$, $R_5 = H$

The required chromenes (**1** and **2**) were prepared by sodium borohydride reduction of the corresponding chromanone to chromanols and *in situ* dehydration of chromanols using hydrochloric acid (1:1) in overall yield of 70-75 %.[10]

The chromene (**5**) was conveniently synthesised by the base catalysed reaction of 7-methoxy-5-hydroxy chroman (**3**) with 3-methyl-2-butenal in pyridine at 140°C for 4 h in about 84 % yield (Scheme-4).[11] Appearance of two one proton doublets at δ 5.37 and 6.54 (J=9.8 Hz) in the ^{1}H NMR spectrum confirms the formation of compound (**5**). It was also synthesised by reduction of chromanone (**4**) prepared by the reaction of 7-methoxy-5-hydroxy chroman (**3**) with 3,3-dimethyl acrylic acid in the presence of $ZnCl_2$ - $POCl_3$, followed by dehydration using hydrochloric acid (1:1) in about 81% yield (Scheme-4). The appearance of a carbonyl peak at 1680 cm^{-1} in the IR spectrum and the appearance of one proton singlet at δ 2.66 in the ^{1}H NMR spectrum confirms the formation of the chromanone (**4**).



2-Methoxy-1,4-benzoquinone (**6a**)[12] and 6-methyl-2-methoxy-1,4-benzoquinone (**6b**)[13] were prepared by oxidation of vanillin and 3,5-dimethoxy toluene (Orcinol) using aqueous H_2O_2. 2-Benzyloxy-1,4-benzoquinone (**6c**)[14] was prepared in about 82 % yield by oxidation of 2-benzyloxy phenol using Fremy's salt.

EXPERIMENTAL:

Diphenyldiselenide was purchased from Fluka Chemical Co. and titanium tetrachloride and titanium isopropoxide were purchased from Aldrich Chemical Co. All melting points are uncorrected. TLC Analyses were carried out on glass plates coated with TLC grade silica gel. Silica gel (100-200 mesh) was used for column chromatography. Laboratory solvents were purified and pre-dried before use according to standard procedures. Petroleum ether of b.p. 60-80°C was used for column chromatography.

IR spectra were recorded on a Perkin Elmer 688 Spectrometer. NMR were recorded either on Bruker Am 500, Varian VXR 300S, Bruker-200, or Varian FT 60A using $CDCl_3$ as the solvent containing TMS as an internal standard with chemical shifts (δ) expressed as ppm downfield with respect to TMS. J values are given in Hz. Elemental analyses were performed on a CEST 1106 elemental analyser. Mass spectra were recorded either on a Finnigan MAT-1020-B 70 eV or Hewlett Packard MS Engine 5989-A mass spectrometer.

2,3,9,10-Tetrahydro-2,2,8,8-tetramethyl-5-methoxy-2*H*,8*H*-benzo [1,2-*b*:3,4-*b*'] pyran-4-one (4).

A mixture of 7-methoxy-5-hydroxy-2,2-dimethylchroman (**3**) (3.5 g, 17 mmol), 3,3-dimethyl acrylic acid (2 g, 26 mmol), fused $ZnCl_2$ (7 g, 50 mmol) and phosphorous oxychloride (15 mL, 160 mmol) was kept aside

at room temperature under anhydrous conditions for 24 h and then poured onto ice with stirring. The brownish oily product was extracted with ether (3×30 mL) and the extract washed with water, brine, dried (Na_2SO_4) and evaporated to give a dark residue. The residue was chromatographed over silica gel and eluted with pet. ether / ethyl acetate (95:5). Removal of the solvent and crystallisation of the solid from pet. ether gave colorless needles (3.5 g, 71%). m.p. 70-72°C; IR (nujol): ν_{max} 1680, 1620, 1560, 1480, 1460, 1380, 1360, 1300, 1160, 1160, 1110 cm^{-1}; ^1H NMR (60 MHz): δ 1.35 & 1.43 (2 × s, 12H, C_2- & C_8 -$(CH_3)_2$), 1.8 (t, 2H, J=7.0 Hz, C_9-H), 2.61 (t, 2H, J=7.0 Hz, C_{10}-H), 2.66 (s, 2H, C_3-H), 3.80 (s, 3H, -OCH_3), 5.90 (s, 1H, C_6-H). Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.31; H, 7.64. Found: C, 70.48; H, 7.69.

9,10-Dihydro-2,2,8,8-tetramethyl-5-methoxy-2*H*,8*H*-benzo [1,2-*b*:3, 4-*b'*] pyran (5).

Method-A: To a solution of the chromanone (**4**) (2.6 g, 8.9 mmol) in dry methanol (25 mL) was added sodium borohydride (1 g, 26 mmol) and the mixture was refluxed on a boiling water bath for 3 h. The solvent was distilled off and the resultant residue washed with hydrochloric acid (1:1), extracted with ether (3×40 mL), the extract washed with water and then dried (Na_2SO_4). Evaporation of the solvent gave a residue which was chromatographed over silica gel and eluted with pet. ether / ethyl acetate (97:3) affording the title compound (**5**) as a colorless semisolid (2 g, 81%).

Method-B: 3-Methyl-2-butenal (2 mL, 20 mmol) was added during 1 h to a stirred mixture of 5-hydroxy-7-methoxy chroman (**3**) (3 g, 14 mmol) and dry pyridine (4 mL, 50 mmol) at 140°C. After heating for 3 h, 3-methyl-2-butenal (2 mL, 20 mmol) was again added and heating was continued for 6 h. The mixture was evaporated to dryness and the residue was chromatographed over silica gel and eluted with pet. ether / ethyl acetate (97:3) gave chromene (**5**) as a colorless semisolid (2.98 g, 84 %); IR (nujol): ν_{max} 1620, 1550, 1480, 1450, 1370, 1350 cm^{-1}; ^1H NMR (300 MHz): δ 1.31 & 1.40 (2 × s, 12H, C_2- & C_8 -$(CH_3)_2$), 1.74 (t, 2H, J=6.6 Hz, C_9-H), 2.55 (t, 2H, J=6.6 Hz, C_{10}-H), 3.74 (s, 3H, -OCH_3), 5.37 (d, 1H, J=9.8 Hz, C_3-H), 5.92 (s, 1H, C_6-H), 6.54 (d, 1H, J=9.8 Hz, C_4-H). ^{13}C NMR (50 MHz): δ 16.4, 26.7, 27.9, 32.4, 55.4, 74.4, 75.9, 92.3, 102.2, 103.2, 117.1, 125.0, 151.6, 154.3, 154.9. Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.41; H, 8.09. Found: C, 74.44; H, 8.39.

General Procedure for Synthesis of Compounds 7a-c, 8a-c, 9a-c and 10a-c.

Titanium (IV) chloride and titanium (IV) isopropoxide (2:1) were combined in dichloromethane (2 mL) at 0-5°C, and the solution was stirred for 1 h and then cooled to -78°C. A solution of quinone in dichloromethane (10 mL) was added, followed, after 20 min, by a solution of the 2,2-dimethyl-2*H*-chromene in CH_2Cl_2 (10 mL). The reaction mixture was maintained at -78°C for 4 h and subsequently it was allowed to stay at room temperature for 24 h after the addition of a catalytic amount of *p*-toluene sulfonic acid. Addition of saturated aqueous sodium bicarbonate quenched the reaction and was extracted with CH_2Cl_2. The extract was washed with water, brine, dried (Na_2SO_4) and evaporated.

Synthesis of compounds 7a and 8a.

2,2-Dimethyl-2*H*-chromene (**1a**) (1 g, 4.1 mmol) and 2-methoxy-1,4-benzoquinone (**6a**) (0.56 g, 4.1 mmol) undergo a cyclisation reaction in the presence of Ti (IV) catalyst to give a crude violet colored residue,

which was extracted with CH_2Cl_2, washed with water, brine, dried (Na_2SO_4) and concentrated under vacuum. The crude residue was chromatographed over silica gel and eluted with pet. ether / ethyl acetate (96:4) and (91:9) to give two fractions (i) and (ii), identified as (**7a**) and (**8a**).

1,2,-Dihydro-9-hydroxy-10-methoxy-3,3,7,7-tetramethyl-3*H*,7*H*-benzofuro [3,2-*c*] pyrano [3,2-*g*] [1] benzopyran (7a): Removal of the solvent from fraction (i) gave compound (**7a**) which crystallised from pet. ether / ethyl acetate as white cubes (0.3 g, 19%). m.p. 165-167°C; IR (nujol): ν_{max} 3510, 1600, 1380 cm^{-1}; ^1H NMR (300 MHz): δ 1.35 & 1.75 (2 × s, 12H, C_3- & C_7-$(CH_3)_2$), 1.80 (t, 2H, J=7.0 Hz, C_2-H), 2.65 (t, 2H, J=7.0 Hz, C_1-H), 3.90 (s, 3H, -OCH_3), 5.50 (s, 1H, -OH), 6.30 (s, 1H, C_{11}-H), 6.90 (s, 1H, C_5-H), 7.00 (s, 1H, C_{13}-H), 7.20 (s, 1H, C_8-H). Anal. Calcd for $C_{23}H_{24}O_5$: C, 72.61; H, 6.36. Found: C, 72.65; H, 6.38.

1,2,7a,12a-Tetrahydro-9-hydroxy-10-methoxy-3,3,7,7-tetramethyl-3*H*,7*H*-benzofuro-[3,2-*c*]pyrano [3,2-*g*] [1] benzopyran (8a): Removal of the solvent from fraction (ii) gave compound (**8a**) which crystallised from pet. ether as white needles (1 g, 63%). m.p. 170-172°C; IR (nujol): ν_{max} 3510, 1610, 1380 cm^{-1}; ^1H NMR (300 MHz): δ 0.85 (s, 3H, C_{7eq}-CH_3), 1.25 & 1.45 (2 × s, 6H, C_3-$(CH_3)_2$), 1.55 (s, 3H, C_{7ax}-CH_3), 1.70 (t, 2H, J=7.0 Hz, C_2-H), 2.60 (t, 2H, J=7.0 Hz, C_1-H), 3.25 (d, 1H, J=7.0 Hz, C_{7a}-H), 3.85 (s, 3H, -OCH_3), 5.25 (s, 1H, -OH), 5.42 (d, 1H, J=7.0 Hz, C_{12a}-H), 6.38 (s, 1H, C_{11}-H), 6.45 (s, 1H, C_5-H), 6.85 (s, 1H, C_{13}-H), 7.20 (s, 1H, C_8-H). ^{13}C NMR (75 MHz): δ 20.17, 21.83, 26.86, 27.56, 32.91, 49.51, 56.1, 74.43, 76.4, 77.42, 79.0, 94.24, 105.55, 110.97, 112.13, 114.7, 119.32, 130.1, 139.67, 146.75, 152.5, 153.63, 155.34. MS m/e: M^+ 382 (100%), 367 (96.5%), 229 (14.2%). Anal. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.35; H, 7.00.

Synthesis of Compounds 7b and 8b.

2,2-Dimethyl-2*H*-chromene (**1a**) (1 g, 4.1 mmol) and 2-methoxy-6-methyl-1,4-benzoquinone (**6b**) (0.62 g, 4.1 mmol) undergo a cyclisation reaction in the presence of Ti (IV) catalyst to give a crude violet colored residue, which was extracted with CH_2Cl_2, washed with water, brine, dried (Na_2SO_4) and concentrated under vacuum. The crude residue was chromatographed over silica gel and eluted with pet. ether / ethyl acetate (93:7) and (90:10) to give two fractions (i) and (ii), identified as (**7b**) and (**8b**).

1,2,-Dihydro-9-hydroxy-10-methoxy-3,3,7,7,8-pentamethyl-3*H*,7*H*-benzofuro-[3,2-*c*]pyrano[3,2-*g*] [1] benzopyran (7b): Removal of the solvent from fraction (i) gave compound (**7b**) which crystallised from pet. ether / ethyl acetate as white cubes (0.2 g, 12%). m.p. 169-171°C; IR (nujol): ν_{max} 3510, 1605, 1380 cm^{-1}; ^1H NMR (300 MHz): δ 1.40 & 1.70 (2 × s, 12H, C_3- & C_7-$(CH_3)_2$), 1.80 (t, 2H, J=7.0 Hz, C_2-H), 2.15 (s, 3H, -CH_3), 2.65 (t, 2H, J=7.0 Hz, C_1-H), 3.90 (s, 3H, -OCH_3), 5.50 (s, 1H, -OH), 6.30 (s, 1H, C_{11}-H), 6.90 (s, 1H, C_5-H), 7.00 (s, 1H, C_{13}-H). Anal. Calcd for $C_{24}H_{26}O_5$: C, 73.06; H, 6.65. Found: C, 73.10; H, 6.68.

1,2,7a,12a-Tetrahydro-9-hydroxy-10-methoxy-3,3,7,7,8-pentamethyl-3*H*,7*H*-benzofuro-[3,2-*c*] pyrano [3,2-*g*] [1] benzopyran (8b): Removal of the solvent from fraction (ii) gave compound (**8b**) which crystallised from pet. ether as white needles (0.9 g, 55%). m.p. 189-191°C; IR (nujol): ν_{max} 3500, 1610, 1385 cm^{-1}; ^1H NMR (300 MHz): δ 0.90 (s, 3H, C_{7eq}- CH_3), 1.30 & 1.45 (2 × s, 6H, C_3-$(CH_3)_2$), 1.55 (s, 3H, C_{7ax}- CH_3), 1.70 (t, 2H, J=7.0 Hz, C_2-H), 2.10 (s, 3H, -CH_3), 2.60 (t, 2H, J=7.0 Hz, C_1-H), 3.20 (d, 1H, J=7.0 Hz, C_{7a}-H), 3.80 (s, 3H, -OCH_3), 5.30 (s, 1H, -OH), 5.42 (d, 1H, J=7.0 Hz, C_{12a}-H), 6.30 (s, 1H, C_{11}-

H), 6.45 (s, 1H, C_5-H), 6.85 (s, 1H, C_{13}-H). ^{13}C NMR (50 MHz): δ 14.59, 20.23, 21.86, 26.92, 29.54, 3304, 48.37, 56.18, 74.40, 79.61, 92.10, 105.4, 111.84, 114.54, 119.79, 120.82, 130.28, 138.29, 146.14, 152.80, 153.26, 155.54. MS m/e: M^+ 396 (56.4%), 381 (100%), 183 (22.7%), 105 (33.6%). Anal. Calcd for $C_{24}H_{28}O_5$: C, 72.69; H, 7.2. Found: C, 72.72; H, 7.28.

Synthesis of Compounds 7c and 8c.

2,2-Dimethyl-2*H*-chromene (**1b**) (1 g, 4.6 mmol) and 2-methoxy-1,4-benzoquinone (**6a**) (0.63 g, 4.6 mmol) undergo a cyclisation reaction in the presence of Ti (IV) catalyst to give a crude violet colored residue, which was extracted with CH_2Cl_2, washed with water, brine, dried (Na_2SO_4) and concentrated under vacuum. The crude residue was chromatographed over silica gel and eluted with pet. ether / ethyl acetate (95:5) and (91:9) to give two fractions (i) and (ii), identified as (**7c**) and (**8c**).

1,2,-Dihydro-9-hydroxy-10-methoxy-3,3-dimethyl-*3H*,7*H*-benzofuro-[3,2-*c*]pyrano[3,2-*g*][1]benzopyran (7c): Removal of the solvent from fraction (i) gave compound (**7c**) which crystallised from pet. ether / ethyl acetate as white cubes (0.3 g, 19%). m.p. 150-153°C; IR (nujol): ν_{max} 3530, 1600, 1585, 1380 cm^{-1}; ^1H NMR (300 MHz): δ 1.35 (s, 6H, C_3-$(CH_3)_2$), 1.80 (t, 2H, J=7.0 Hz, C_2-H), 2.65 (t, 2H, J=7.0 Hz, C_1-H), 3.90 (s, 3H, -OCH_3), 5.20 (s, 1H, -OH), 5.50 (s, 2H, C_7-H), 6.30 (s, 1H, C_{11}-H), 6.65 (s, 1H, C_5-H), 7.00 (s, 1H, C_{13}-H), 7.20 (s, 1H, C_8-H). Anal. Calcd for $C_{21}H_{20}O_5$: C, 71.56; H, 5.72. Found: C, 71.6; H, 5.71.

1,2,7a,12a-Tetrahydro-9-hydroxy-10-methoxy-3,3-dimethyl-3*H*,7*H*-benzofuro-[3,2-*c*]pyrano[3,2-*g*][1] benzopyran (8c): Removal of the solvent from fraction (ii) gave compound (**8c**) which crystallised from pet. ether as white needles (0.3g, 31%). m.p. 168-170°C; IR (nujol): ν_{max} 3530, 1590, 1380 cm^{-1}; ^1H NMR (300 MHz): δ 1.35 & 1.45 (2 × s, 6H, C_3-$(CH_3)_2$), 1.70 (t, 2H, J=7.0 Hz, C_2-H), 2.65 (t, 2H, J=7.0 Hz, C_1-H), 3.40 (m, 1H, C_{7a}-H), 3.60 (t, 1H, J=10.8 Hz, C_{7ax}-H), 3.80 (s, 3H, -OCH_3), 4.19 (m, 1H, C_{7eq}-H), 5.20 (s, 1H, -OH), 5.40 (d, 1H, J=7.0 Hz, C_{12a}-H), 6.30 (s, 1H, C_{11}-H), 6.50 (s, 1H, C_5-H) , 6.80 (s, 1H, C_{13}-H), 7.15 (s, 1H, C_8-H). ^{13}C NMR (75 MHz): δ 21.89, 26.59, 27.18, 32.92, 40.46, 56.22, 66.58, 74.63, 78.42, 94.76, 104.89, 110.47, 112.1, 115.32, 118.23, 131.34, 139.92, 146.91, 152.87, 154.83, 155.42. MS m/e: M^+ 354 (100%), 307 (8.47%), 299 (14.1%). Anal. Calcd for $C_{21}H_{22}O_5$: C, 71.16; H, 6.26. Found: C, 71.22; H, 6.29.

Synthesis of Compounds 9a and 10a.

2,2-Dimethyl-2*H*-chromene (**5**) (1 g, 3.65 mmol) and 2-methoxy-1,4-benzoquinone (**6a**) (0.5 g, 3.65 mmol) undergo a cyclisation reaction in the presence of Ti (IV) catalyst to give a crude violet colored residue, which was extracted with CH_2Cl_2, washed with water, brine, dried (Na_2SO_4) and concentrated under vacuum. The crude residue was chromatographed over silica gel and eluted with pet. ether / ethyl acetate (93:7) and (89:11) to give two fractions (i) and (ii), identified as Compound (**9a**) and (**10a**).

3,4-Dihydro-8-hydroxy-9,12-dimethoxy-2,2,6,6-tetramethyl-2*H*,6*H*-benzofuro[3,2-*c*]pyrano[2,3-*f*][1] benzopyran (9a): Removal of the solvent from fraction (i) gave compound (**9a**) which crystallised from pet. ether / ethyl acetate as white cubes (0.4 g, 27%). m.p. 180-183°C; IR (nujol): ν_{max} 3520, 1640, 1610, 1580, 1340 cm^{-1}; ^1H NMR (200 MHz): δ 1.35 & 1.70 (2 × s, 12H, C_2-& C_6-$(CH_3)_2$), 1.80 (t, 2H, J=7.0 Hz, C_3-H), 2.65 (t, 2H, J=7.0 Hz, C_4-H), 3.85 & 3.95 (2 × s, 6H, 2 × -OCH_3), 5.65 (s, 1H, -OH), 6.15 (s, 1H, C_{10}-H), 6.95 (s, 1H, C_{13}-H), 7.15 (s, 1H, C_7-H). ^{13}C NMR (50 MHz): δ 16.82, 26.57, 27.8, 32.24, 55.82, 56.24, 74.63, 78.90, 93.45, 95.41, 98.42, 102.46, 103.08, 112.92, 117.70, 142.4, 143.97, 146.36, 149.25,

151.73, 153.58, 155.19. MS m/e: M^+ 410 (71.79%), 395 (100%), 339 (55.14%). Anal. Calcd for $C_{24}H_{26}O_6$: C, 70.23; H, 6.38. Found: C 70.29; H, 6.40.

3,4,6a,11a-Tetrahydro-8-hydroxy-9,12-dimethoxy-2,2,6,6-tetramethyl-2*H*,6*H*,-benzofuro[3,2-*c*] pyrano [2,3-*f*][1]benzopyran (10a). Removal of the solvent from fraction (ii) gave compound (**10a**) which crystallised from pet. ether as white needles (0.9 g, 60%). m.p. 195-197°C; IR (nujol): ν_{max} 3500, 1610, 1590, 1380 cm^{-1}; ^1H NMR (200 MHz): δ 0.90 (s, 3H, C_{6eq}-CH_3), 1.40 & 1.50 (2 × s, 6H, C_2-$(CH_3)_2$), 1.55 (s, 3H, C_{6ax}-CH_3), 1.70 (t, 2H, J=7.0 Hz, C_3-H), 2.65 (t, 2H, J=7.0 Hz, C_4-H), 3.20 (d, 1H, J=7.0 Hz, C_{6a}-H), 3.80 & 3.95 (2 × s, 6H, 2 × -OCH_3), 5.30 (s, 1H, -OH), 5.55 (d, 1H, J=7.0 Hz, C_{11a}-H), 6.15 (s, 1H, C_{10}-H), 6.60 (s, 1H, C_{13}-H), 6.90 (s, 1H, C_7-H). ^{13}C NMR (50 MHz): δ 16.54, 20.04, 25.89, 27.11, 27.35, 32.28, 48.53, 55.64, 55.94, 74.35, 76.15, 76.56, 92.58, 94.56, 100.14, 102.03, 110.68, 118.93, 139.3, 146.6, 152.19, 153.81, 155.49, 158.34. MS m/e: M^+ 412 (77.9%), 397 (100%), 341 (62.3%). Anal. Calcd for $C_{24}H_{28}O_6$: C, 69.89; H, 6.84 . Found : C, 69.91; H, 6.84.

Synthesis of Compounds 9b and 10b.

2,2-Dimethyl-2*H*-chromene (**5**) (1 g, 3.65 mmol) and 2-methoxy-6-methyl-1,4-benzoquinone (**6b**) (0.55 g, 3.65 mmol) undergo a cyclisation reaction in the presence of Ti (IV) catalyst to give a crude violet colored residue, which was extracted with CH_2Cl_2, washed with water, brine, dried (Na_2SO_4) and concentrated under vacuum. The crude residue was chromatographed over silica gel and eluted with pet. ether / ethyl acetate (96:4) and (92:8) to give two fractions (i) and (ii), identified as (**9b**) and (**10b**).

3,4-Dihydro-8-hydroxy-9,12-dimethoxy-2,2,6,6,7-pentamethyl-2*H*,6*H*-benzofuro[3,2-*c*]pyrano[2,3-*f*] [1] benzopyran (9b). Removal of the solvent from fraction (i) gave compound (**9b**) which crystallised from pet. ether / ethyl acetate as white cubes (0.4 g, 26%). m.p. 187-189°C; IR (nujol): ν_{max} 3520, 1640, 1580, 1350 cm^{-1}; ^1H NMR (300 MHz): δ 1.35 & 1.70 (2 × s, 12H, C_2-& C_6-$(CH_3)_2$), 1.80 (t, 2H, J=7.0 Hz, C_3-H), 2.20 (s, 3H, C_7-CH_3), 2.65 (t, 2H, J=7.0 Hz, C_4-H), 3.85 & 3.95 (2 × s, 6H, 2 × -OCH_3), 5.60 (s, 1H, -OH), 6.15 (s, 1H, C_{10}-H), 6.95 (s, 1H, C_{13}-H). Anal. Calcd for $C_{25}H_{28}O_6$: C, 70.74; H, 6.65. Found: C, 70.74; H, 6.66.

3,4,6a,11a-Tetrahydro-8-hydroxy-9,12-dimethoxy-2,2,6,6,7-pentamethyl-2*H*,6*H*-benzofuro[3,2-*c*] pyrano [2,3-*f*] [1] benzopyran (10b): Removal of the solvent from fraction (ii) gave compound (**10b**) which crystallised from pet. ether as white needles (0.94 g, 64%). m.p. 210-212°C; IR (nujol): ν_{max} 3500, 1610, 1585, 1380 cm^{-1}; ^1H NMR (300 MHz): δ 0.85 (s, 3H, C_{6eq}-CH_3), 1.30 & 1.45 (2 × s, 6H, C_2-$(CH_3)_2$), 1.55 (s, 3H, C_{6ax}-CH_3), 1.70 (t, 2H, J=7.0 Hz, C_3-H), 2.15 (s, 3H, C_7-CH_3), 2.65 (t, 2H, J=7.0 Hz, C_4-H), 3.25 (d, 1H, J=7.0 Hz, C_{6a}-H), 3.80 & 3.90 (2 × s, 6H, 2 × -OCH_3), 5.30 (s, 1H, -OH), 5.45 (d, 1H, J=7.0 Hz, C_{11a}-H), 6.15 (s, 1H, C_{10}-H), 6.60 (s, 1H, C_{13}-H). Anal. Calcd for $C_{25}H_{30}O_6$: C, 70.0; H, 7.09. Found: C, 70.01; H, 7.13.

Synthesis of Compounds 9c and 10c.

2,2-Dimethyl-2*H*-chromene (**5**) (0.64 g, 2.33 mmol) and 2-benzyloxy-1,4-benzoquinone (**6c**) (0.5 g, 2.33 mmol) undergo a cyclisation reaction in the presence of Ti(IV) catalyst to give a crude yellowish colored residue, which was extracted with CH_2Cl_2, washed with water, brine, dried (Na_2SO_4) and concentrated under vacuum. The crude residue was chromatographed over silica gel and eluted with pet. ether / ethyl acetate (92:8) and (90:10) to give two fractions (i) and (ii), identified as (**9c**) and (**10c**).

3,4-Dihydro-8-hydroxy-9-benzyloxy-12-methoxy-2,2,6,6-tetramethyl-2*H*,6*H*-benzofuro[3,2-*c*] pyrano [2,3-*f*] [1] benzopyran (9c). Removal of the solvent from fraction (i) gave compound (**9c**) which crystallised from pet. ether as white solid (0.32 g, 29%). m.p. 90-92°C; IR (nujol); ν_{max} 3550, 3024, 2975, 2407, 1614, 1578, 1466, 1333 cm^{-1}; ^1H NMR (500 MHz): δ 1.35 & 1.73 (2 × s, 12H, C_2-& C_6-$(CH_3)_2$), 1.80 (t, 2H, J=6.75 Hz, C_3-H), 2.65 (t, 2H, J=6.75 Hz, C_4-H), 3.91 (s, 3H, -OCH_3), 5.14 (s, 2H, -OCH_2-), 5.66 (s, 1H, -OH), 6.08 (s, 1H, C_{10}-H), 6.99 (s, 1H, C_{13}-H), 7.19 (s, 1H, C_7-H), 7.35-7.44 (s, 5H, 5 × Ar-H). ^{13}C NMR (125 MHz): δ 17.18, 26.96, 28.15, 32.59, 56.22, 71.92, 75.05, 79.26, 93.74, 97.3, 98.72, 102.94, 103.46, 113.28, 118.49, 127.97, 128.65, 129.0, 136.41, 142.97, 143.29, 146.93, 149.44, 152.14, 153.92, 155.59. MS m/e: M^+ 486 (29.3%), 395 (100%), 381 (10.7%), 339 (24.8%). Anal. Calcd for $C_{30}H_{30}O_6$: C, 74.06; H, 6.21. Found: C, 74.11; H, 6.22.

3,4,6a,11a-tetrahydro-8-hydroxy-9-benzyloxy-12-methoxy-2,2,6,6-tetramethyl-2*H*,6*H*-benzofuro [3,2-*c*] pyrano [2,3-*f*] [1] benzopyran (10c). Removal of the solvent from fraction (ii) gave compound (**10c**) which crystallised from pet. ether as white amorphous solid (0.65 g, 60%). m.p. 99-101°C; IR (nujol); ν_{max} 3552, 3019, 2979, 2407, 1624, 1597, 1499, 1347, 1097 cm^{-1}; ^1H NMR (500 MHz): δ 0.92 (s, 3H, C_{6eq}-CH_3), 1.32 & 1.35 (2 × s, 6H, C_2-$(CH_3)_2$), 1.51 (s, 3H, C_{6ax}-CH_3), 1.77 (t, 2H, J=6.65 Hz, C_3-H), 2.60 (t, 2H, J=6.65 Hz, C_4-H), 3.15 (d, 1H, J=7.0 Hz, C_{6a}-H), 3.85 (s, 3H, -OCH_3), 5.05 (s, 2H, -OCH_2-), 5.39 (s, 1H, -OH), 5.53 (d, 1H, J=7.0 Hz, C_{11a}-H), 6.07 (s, 1H, C_{10}-H), 6.61 (s, 1H, C_{13}-H), 6.89 (s, 1H, C_7-H), 7.37-7.41 (s, 5H, 5 × Ar-H). ^{13}C NMR (125 MHz): δ 16.94, 20.43, 26.26, 27.54, 27.74, 32.64, 48.88, 56.04, 71.58, 74.77, 76.51, 77.08, 92.95, 96.36, 100.45, 102.42, 111.27, 119.87, 128.07, 128.62, 128.95, 136.48, 139.95, 146.0, 152.57, 154.05, 155.87, 158.68. MS m/e: M^+ 488 (79.0%), 473 (42.3%), 397 (100%), 382 (13.5), 341 (25.0%). Anal. Calcd for $C_{30}H_{32}O_6$: C, 73.75; H, 6.60. Found: C, 73.76; H, 6.59.

General Procedure for Synthesis of Compounds 7d, 8d-e and 11a-e.

Titanium (IV) chloride and titanium (IV) isopropoxide (1.5:1) were combined in CH_2Cl_2 (5 ml) at $0\text{-}5^0$ C and stirred for 1 h at -78^0C. A solution of quinone in dichloromethane (10 mL) was added, followed, after 10 min, by a solution of 2,2-dimethyl-2*H*-chromene in dichloromethane (10 mL). The reaction mixture was quenched one minute after the addition of chromene by adding isopropanol and saturated aqueous sodium bicarbonate. The reaction mixture was extracted with CH_2Cl_2 and washed with water, brine, dried (Na_2SO_4) and concentrated under vaccum.

Synthesis of Compounds 7d and 8d.

2,2-Dimethyl-2*H*-chromene (**1a**) (2.28 g, 9.3 mmol) and 2-benzyloxy-1,4-benzoquinone (**6c**) (2.0 g, 9.34 mmol) undergo a cyclisation reaction in the presence of Ti (IV) catalyst to give a crude violet colored residue, which was extracted with CH_2Cl_2, washed with water, brine, dried (Na_2SO_4) and concentrated under vacuum. The crude residue was chromatographed over silica gel and eluted with pet. ether / ethyl acetate (93:7) and (91:9) gave two fractions (i) and (ii), identified as (**7d**) and (**8d**).

1,2,-Dihydro-9-hydroxy-10-benzyloxy-3,3,7,7-tetramethyl-3*H*,7*H*-benzofuro-[3,2-*c*]pyrano[3,2-*g*] [1] benzopyran (7d). Removal of the solvent from fraction (i) gave compound (**7d**) which crystallised from pet. ether as white needles (0.89 g, 21%). m.p. 150-151°C; IR ($CHCl_3$): ν_{max} 3550, 3024, 2982, 2933, 2407, 1649, 1593, 1487, 1368, 1291, 1158 cm^{-1}; ^1H NMR (300 MHz): δ 1.33 & 1.71 (2 × s, 12H, C_3- & C_7-$(CH_3)_2$), 1.79 (t, 2H, J=6.8 Hz, C_2-H), 2.73 (t, 2H, J=6.8 Hz, C_1-H), 5.15 (s, 2H, -OCH_2-), 5.62 (s, 1H, -

OH), 6.35 (s, 1H, C_{11}-H), 6.98 (s, 1H, C_5-H), 7.10 (s, 1H, C_{13}-H), 7.14 (s, 1H, C_8-H), 7.30-7.47 (m, 5H, 5 × Ar-H). MS m/e: M^+ 456 (20.68%), 441 (6.03%), 365 (100%), 309 (10.7%). Anal. Calcd for $C_{29}H_{28}O_5$: C, 76.28; H, 6.19. Found: C, 76.31; H, 6.24.

1,2,7a,12a-Tetrahydro-9-hydroxy-10-benzyloxy-3,3,7,7-tetramethyl-3*H*,7*H*-benzofuro[3,2-*c*] pyrano [3,2-*g*] [1] benzopyran (8d). Removal of the solvent from fraction (ii) gave compound (**8d**) which crystallised from pet. ether as white needles (2.56 g, 60%). m.p. 158-160°C; IR ($CHCl_3$): ν_{max} 3552, 3019, 2979, 2940, 2400, 1630, 1591, 1505, 1347, 1123 cm^{-1}; ^1H NMR (300 MHz): δ 0.88 (s, 3H, C_{7eq}-CH_3), 1.3 (s, 6H, C_3-$(CH_3)_2$), 1.51 (s, 3H, C_{7ax}-CH_3), 1.79 (t, 2H, J=6.7 Hz, C_2-H), 2.76 (t, 2H, J=6.7 Hz, C_1-H), 3.29 (d, 1H, J=7.5 Hz, C_{7a}-H), 5.07 (s, 2H, -OCH_2-), 5.31 (b, 1H, -OH), 5.44 (d, 1H, J=7.5 Hz, C_{12a}-H), 6.34 (s, 1H, C_{11}-H), 6.54 (s, 1H, C_5-H), 6.89 (s, 1H, C_{13}-H), 7.18 (s, 1H, C_8-H), 7.30-7.44 (m, 5H, 5 × Ar-H). MS m/e: M^+ 458 (70.9%), 443 (82.0%), 367 (100%), 353 (42%). Anal. Calcd for $C_{29}H_{30}O_5$: C, 75.55; H, 6.60. Found: C, 75.61; H, 6.62.

1,2,7a,12a-Tetrahydro-9-hydroxy-10-benzyloxy-3,3-dimethyl-3*H*,7*H*-benzofuro-[3,2-*c*]pyrano[3,2-*g*] [1] benzopyran (8e).

2,2-Dimethyl-2*H*-chromene (**1b**) (0.50 g, 2.33 mmol) and 2-benzyloxy-1,4-benzoquinone (**6c**) (0.50 g, 2.33 mmol) undergo a cyclisation reaction in the presence of Ti (IV) catalyst to give a dark brown residue, which was chromatographed over silicagel and eluted with pet. ether / ethyl acetate (91:9) affording compound (**8e**) which crystallised from pet. ether / ethyl acetate as white cubes (0.53 g, 54%). m.p. 184-185°C; IR ($CHCl_3$): ν_{max} 3420, 3026, 2400, 1630, 1499, 1341, 1222, 762 cm^{-1}; ^1H NMR (300 MHz): δ 1.30 & 1.33 (2 × s, 6H, C_3-$(CH_3)_2$), 1.78 (t, 2H, J=6.8 Hz, C_2-H), 2.75 (t, 2H, J=6.8 Hz, C_1-H), 3.48 (m, 1H, C_{7a}-H), 3.56 (m, 1H, C_{7ax}-H), 4.20 (m, 1H, C_{7eq}-H), 5.05 (s, 2H, -OCH_2-), 5.30 (s, 1H, -OH), 5.43 (d, 1H, J=6.32 Hz, C_{12a}-H), 6.37 (s, 1H, C_{11}-H), 6.52 (s, 1H, C_5-H) , 6.84 (s, 1H, C_{13}-H), 7.18 (s, 1H, C_8-H), 7.33-7.40 (m, 5H, 5 × Ar-H). MS m/e: M^+ 430 (28.2%), 339 (74.0%), 283 (74%), 91 (100%). Anal. Calcd for $C_{27}H_{26}O_5$: C, 75.33; H, 6.09. Found: C, 75.35; H, 6.12.

6a,11a-Dihydro-8-hydroxy-3,9-dimethoxy-6,6-dimethyl-6*H*-benzofuro [3,2-*c*] [1] benzopyran (11a).

7-Methoxy-2,2-dimethyl-2*H*-chromene (**2a**) (1.06 g, 5.43 mmol) and 2-methoxy-1,4-benzoquinone (**6a**) (0.7 g, 5.43 mmol) undergo a cyclisation reaction in the presence of Ti (IV) catalyst to afford a crude violet colored oil, which was chromatographed over silicagel and eluted with pet. ether / ethyl acetate (93:7) yielding compound (**11a**) which crystallised from pet. ether as white needles (1.1 g, 62%). m.p. 100-101°C; IR (nujol): ν_{max} 3460, 1624, 1591, 1499, 1466, 1347 cm^{-1}; ^1H NMR (300 MHz): δ 0.90 (s, 3H, C_{6eq}-CH_3), 1.52 (s, 3H, C_{6ax}-CH_3), 3.30 (d, 1H, J=7.5 Hz, C_{6a}-H), 3.79 (s, 3H, -OCH_3), 3.85 (s, 3H, -OCH_3), 5.30 (b, 1H, -OH), 5.44 (d, 1H, J=7.5 Hz, C_{11a}-H), 6.46 (d, 1H, J=2.5 Hz, C_4-H), 6.48 (s, 1H, C_{10}-H), 6.61 (dd, 1H, J=2.5, 8.5 Hz, C_2-H), 6.87 (s, 1H, C_7-H), 7.40 (d, 1H, J=8.5, C_1-H). MS m/e: M^+ 328 (42.7 %), 313 (100 %), 298 (9.4 %). Anal. Calcd for $C_{19}H_{20}O_5$: C, 69.5; H, 6.14. Found: C, 69.8; H, 6.17.

6a,11a-Dihydro-8-hydroxy-3,9-dimethoxy-6,6,7-trimethyl-6*H*-benzofuro [3,2-*c*] [1] benzopyran (11b).

7-Methoxy-2,2-dimethyl-2*H*-chromene (**2a**) (0.64 g, 3.28 mmol) and 6-methyl-2-methoxy-1,4-benzoquinone (**6b**) (0.5 g, 3.28 mmol) undergo a cyclisation reaction in the presence of Ti (IV) catalyst to give a crude violet colored oil, which was chromatographed over silicagel and eluted with pet. ether / ethyl acetate (92:8) yielding compound (**11b**) which crystallised from pet. ether as white cubes (0.63 g, 56%). m p. 60-62° C; IR ($CHCl_3$): ν_{max} 3522, 1628, 1593, 1480, 1361 cm^{-1}; ^1H NMR (300 MHz): δ 0.97 (s, 3H, C_{6eq}-CH_3), 1.51 (s, 3H, C_{6ax}-CH_3), 2.30 (s, 3H, - CH3), 3.30 (d, 1H, J=6.6 Hz, C_{6a}-H), 3.79 (s, 3H, -OCH_3), 3.94 (s,

3H, -OCH_3), 5.36 (d, 2H, J=6.6 Hz, C_{11a}-H, -OH), 6.39 (s, 1H, C_{10}-H), 6.46 (d, 1H, J=2.5 Hz, C_4-H), 6.61 (dd, 1H, J=2.5, 8.4 Hz, C_2-H), 7.39 (d, 1H, J=8.23 Hz, C_1-H). ^{13}C NMR (50 MHz): δ 14.6, 20.1, 29.4, 48.1, 55.3, 56.1, 78.1, 79.3, 92.1, 102.1, 108.4, 112.2, 119.7, 120.7, 130.8, 138.2, 146.1, 153.2, 154.5, 161.1. MS m/e: M^+ 342 (81.8 %), 327 (100 %), 285 (18.9 %).

6a,11a-Dihydro-8-hydroxy-3-methoxy-9-benzyloxy-6,6-dimethyl-6*H*-benzofuro[3,2-*c*] [1] benzopyran (11c).

7-Methoxy-2,2-dimethyl-2*H*-chromene (**2a**) (0.45 g, 2.33 mmol) and 2-benzyloxy-1,4-benzoquinone (**6c**) (0.5 g, 2.33 mmol) undergo a cyclisation reaction in the presence of Ti (IV) catalyst to give a crude yellowish colored residue, which was chromatographed over silicagel and eluted with pet. ether / ethyl acetate (91:9) affording compound (**11c**) which crystallised from pet. ether as white amorphous solid ((0.48 g, 51%). m.p 58-60°C; IR ($CHCl_3$): ν_{max} 3552, 3026, 2400, 1630, 1584, 1492, 1354 cm^{-1}; ^1H NMR (300 MHz): δ 0.90 (s, 3H, C_{6eq}-CH_3), 1.56 (s, 3H, C_{6ax}-CH_3), 3.31 (d, 1H, J=7.5 Hz, C_{6a}-H), 3.79 (s, 3H, -OCH_3), 5.07 (s, 2H, -OCH_2-), 5.31 (b, 1H, -OH), 5.44 (d, 1H, J=7.5 Hz, C_{11a}-H), 6.46 (d, 1H, J=2.5 Hz, C_4-H), 6.55 (s, 1H, C_{10}-H), 6.61 (dd, 1H, J=2.5, 8.6 Hz, C_2-H), 6.89 (s, 1H, C_7-H), 7.35-7.42 (m, 6H, 5 × Ar-H, C_1-H). ^{13}C NMR (50 MHz): δ 20.2, 27.5, 49.4, 55.3, 71.4, 76.8, 78.8, 95.8, 102.3, 108.6, 111.2, 112.6, 119.7, 127.8, 128.4, 128.7, 130.6, 136.1, 140, 146, 147, 148, 160.1. MS m/e: M^+ 404 (100%), 389 (37.8%), 313 (92.6%).

6a,11a-Dihydro-8-hydroxy-3-benzyloxy-9-methoxy-6,6-dimethyl-6*H*-benzofuro[3,2-*c*] [1] benzopyran (11d).

7-Benzyloxy-2,2-dimethyl-2*H*-chromene (**2b**) (0.5 g, 1.87 mmol) and 2-methoxy-1,4-benzoquinone (**6a**) (0.25 g, 1.87 mmol) undergo a cyclisation reaction in the presence of Ti (IV) catalyst to give a violet colored residue, which was chromatographed over silicagel and eluted with pet. ether / ethyl acetate (92:8) to yield compound (**11d**) which crystallised from pet. ether / ethyl acetate as white crystals (0.33 g, 45%). m.p. 58-60° C; IR ($CHCl_3$): ν_{max} 3550, 3024, 2400, 1628, 1586, 1494, 1452, 1347, 1221, 1171 cm^{-1}; ^1H NMR (500 MHz): δ 0.92 (s, 3H, C_{6eq}-CH_3), 1.53 (s, 3H, C_{6ax}-CH_3), 3.31 (d, 1H, J=7.45 Hz, C_{6a}-H), 3.85 (s, 3H, -OCH_3), 5.05 (s, 2H, -OCH_2-), 5.32 (s, 1H, -OH), 5.46 (d, 2H, J=7.45 Hz, C_{11a}-H), 6.49 (s, 1H, C_{10}-H), 6.56 (d, 1H, J=2.45 Hz, C_4-H), 6.70 (dd, 1H, J=2.5, 8.5 Hz, C_2-H), 6.88 (s, 1H, C_7-H), 7.33-7.44 (s, 6H, 5 × Ar-H, C_1-H). ^{13}C NMR (125 MHz): δ 22.11, 27.15, 28.45, 33.19, 71.99, 74.82, 79.58, 96.98, 103.43, 105.6, 109.01, 113.83, 114.3, 119.23, 120.75, 128.08, 128.75, 129.05, 136.33, 143.15, 143.67, 147.15, 149.37, 152.72, 155.44. MS m/e: M^+ 404 (100%), 389 (60.4%), 313 (21.4%). Anal. Calcd for $C_{25}H_{24}O_5$: C, 74.24; H, 5.98. Found: C, 74.23; H, 5.96.

6a,11a-Dihydro-8-hydroxy-3,9-dibenzyloxy-6,6-dimethyl-6*H*-benzofuro[3,2-*c*] [1] benzopyran (11e).

7-Benzyloxy-2,2-dimethyl-2*H*-chromene (**2b**) (0.62 g, 2.33 mmol) and 2-benzyloxy-1,4-benzoquinone (**6c**) (0.5 g, 2.33 mmol) undergo a cyclisation reaction in the presence of Ti (IV) catalyst to give a dark brown colored residue, which was chromatographed over silicagel and eluted with pet. ether / ethyl acetate (90:10) yielding compound (**11e**) which crystallised from pet. ether as white crystals (0.53 g, 48%). m.p. 58-60°C; IR ($CHCl_3$): ν_{max} 3559, 3026, 2407, 1624, 1591, 1499, 1347, 1216, 1163 cm^{-1}; ^1H NMR (200 MHz): δ 0.96 (s, 3H, C_{6eq}-CH_3), 1.57 (s, 3H, C_{6ax}-CH_3), 3.35 (d, 1H, J=6.6 Hz, C_{6a}-H), 5.07 (s, 4H, 2 × -OCH_2-), 5.46 (d, 2H, J=6.6 Hz, C_{11a}-H, -OH), 6.55 (s, 2H, C_{10}-H, C_4-H), 6.75 (dd, 1H, J=2.6, 8.4 Hz, C_2-H), 6.96 (s, 1H, C_7-H), 7.42-7.47 (s, 11H, 10 × Ar-H, C_1-H). ^{13}C NMR (50 MHz): δ 20.3, 27.6, 49.5, 70.0, 71.4, 77.2, 72.8,

78.8, 95.9, 103.5, 109.4, 111.4, 113.0, 119.8, 127.5, 127.9, 128.0, 128.5, 128.6, 128.8, 130.8, 136.2, 136.9, 140.17, 146.1, 154.4, 160.3. MS m/e: M^+ 480 (100%), 465 (45.1%), 425 (42.6%), 389 (82.9%).

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