A one pot synthesis of fused chromenones

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DOI: http://dx.doi.org/10.3998/ark.5550190.0014.302

Abstract

A new class of compounds, 7-hydroxy-9,10-dihydroindeno[5,4-*c*]chromene-6,11-dione **2a-e**, 7-hydroxy-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione **2f-j** and 7-hydroxy-10,10-dimethyl-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione **2k-o** have been synthesized by reacting various 1-(2-oxo-2-(2-oxo-2*H*-chromen-3-yl)ethyl)pyridinium bromides **1a-e** with 1,3-cyclopentandione, 1,3-cyclohexandione and dimedone respectively in the presence of sodium acetate in refluxing glacial acetic acid. Thus, new fused chromenones derivatives are synthesized and characterized by analytical and spectral data.

Keywords: 1-(2-Oxo-2-(2-oxo-2*H*-chromen-3-yl)ethyl)pyridinium bromide , indeno[5,4-*c*]chromene, naphtho[2,1-*c*]chromene

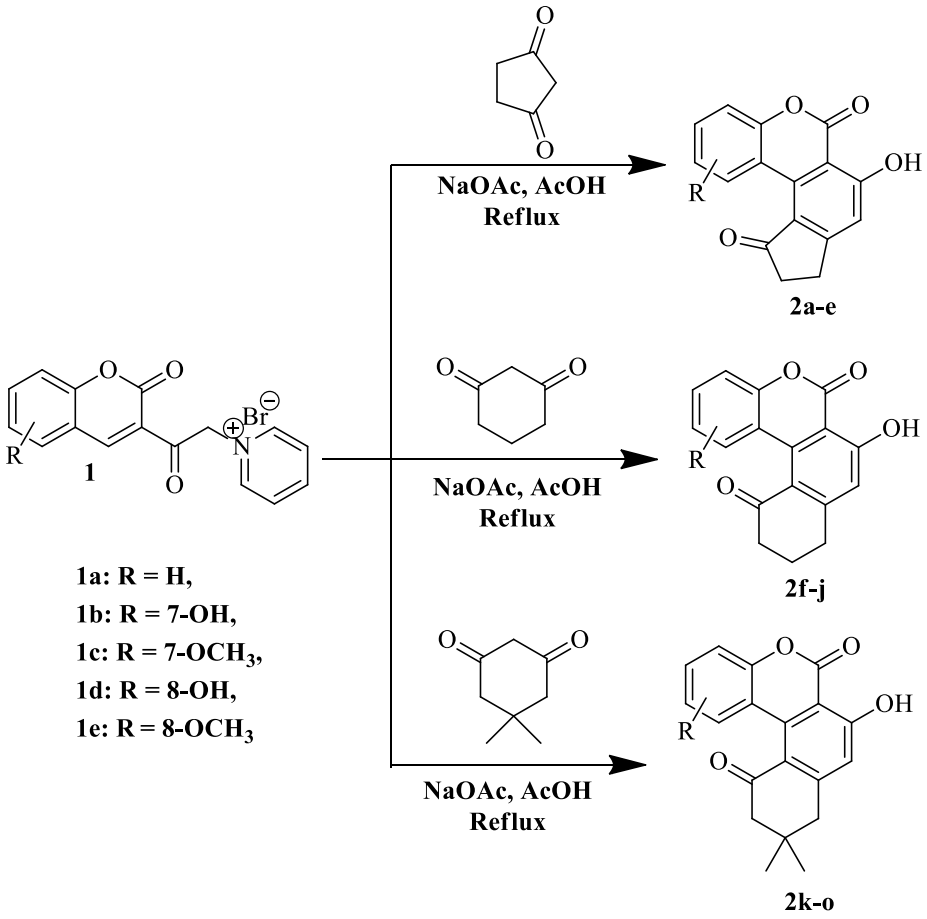
Introduction

During the last twenty years, the study of the biological activities of chromene derivatives has drawn the attention of many scientists.[1-10] Recently, the anticoagulant, antibacterial, anti-helminthic, hypothermal and vasodilatory properties of chromene have been reviewed.[1] Fused chromenones are interesting due to their significant antibacterial[11-15] and novobiocin[16,17] activities. Recently, Selectfluor[18] has been used as an alternative to conventional catalysts for the synthesis of substituted chromenones via Pechmann condensation of phenols with β-ketoesters under solvent-free conditions. Some of the co-workers developed simple and efficient synthesis of polyfunction heterocyclics from readily available starting materials.[19,20] They have reported the synthesis of chromenopyridine and thiopyranochromene derivatives by cycloaddition of active methylene compounds with chromene-3-(4-aminosulfonyl) carbanilide[19] or coumarin-3-thiocarboxamide.[20] Thus, considering the above synthetic methodology to prepare chromenones and its biological importance it was thought worthwhile to incorporate chromenone nucleus as a fuse group with indanone and naphthelenone. Therefore, in the present work we report a one pot

synthesis of 7-hydroxy-9,10-dihydroindeno[5,4-*c*]chromene-6,11-dione **2a-e,** 7-hydroxy-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione **2f-j** and 7-hydroxy-10,10-dimethyl-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione **2k-o** utilizing inexpensive and easily available starting materials.

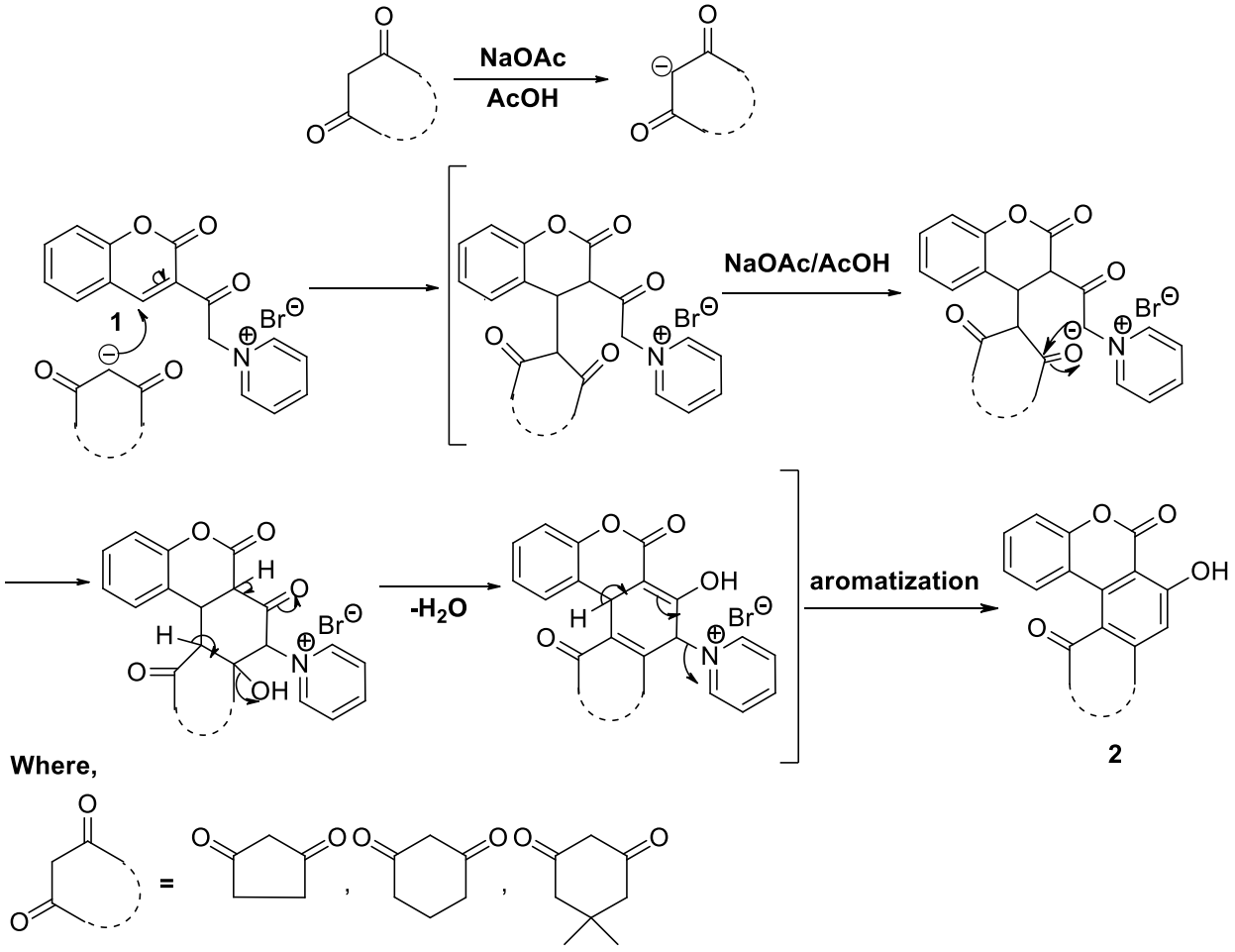
Result and Discussion

In this work, 1-(2-oxo-2-(2-oxo-2*H*-chromen-3-yl)ethyl)pyridinium bromide **1a-e** were reacted with appropriate diketone compound such as 1,3-cyclopentandione, 1,3-cyclohexandione and dimedone respectively in the presence of sodium acetate in refluxing acetic acid to afford 7-hydroxy-9,10-dihydroindeno[5,4-*c*]chromene-6,11-dione **2a-e**, 7-hydroxy-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione **2f-j** and 7-hydroxy-10,10-dimethyl-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione **2k-o** respectively (Scheme 1).



Scheme 1

Compound **1** was allowed to react with the 1,3-diketone under acidic conditions, to obtain fused chromenones **2**. The reaction pathway is assumed to proceed by Michael addition of the active methylene function of 1-(2-oxo-2-(2-oxo-2*H*-chromen-3-yl) ethyl) pyridinium bromide on 1,3-diketone, resulting in the formation of intermediate having 1,5-dione functionality. The active methylene group (flanked by carbonyl ketone and pyridine moiety) then gets cyclized with carbonyl group of 1,3-diketone and the resultant intermediate finally aromatized to afford the product **2**. The proposed mechanism is shown in Scheme 2.



Scheme 2

The structures of all the synthesized compounds were established on the basis of IR, ^{1}H-NMR, ^{13}C-NMR, DEPT-135 spectral data, elemental analysis and molecular weights of some selected compounds **2a**, **2f** and **2k** were confirmed by mass spectrometry.

The IR spectrum of **2a**–**o** showed characteristic bands around 1670, 1715, 2926, 1610, and 3020 cm^{-1} for carbonyl stretching vibrations of δ-lactone ring, carbonyl stretching vibrations of 1,3-diketone ring, aliphatic C–H stretching vibrations of CH_2 groups, aromatic C=C and C-H stretching vibrations respectively. The decrease in C=O stretching frequency of δ-lactone ring

from the normal value (~1710 cm^{-1}) is due to hydrogen bonding with C_7-OH. A broad band observed around 3440 cm^{-1} is due to phenolic-OH stretching.

The NMR spectrum of compounds **2a–e** showed two triplets around δ 3.08 and δ 3.13 each integrating for two protons attached at C_9 and C_{10} respectively. A singlet appeared around δ 8.10 is due to C_8–H and –OH proton was seen as a broad singlet around δ 11.35, which was conformed by D_2O exchanged spectrum. The remaining aromatic protons appeared at appropriate positions and with appropriate multiplicity. The ^{13}C-NMR spectra of compounds **2a–e** showed signals around δ 28.0 and 29.0 due to C_9 and C_{10}, respectively. This was further confirmed by DEPT-135 spectra in which these signals got inverted. This supports the incorporation of indanone ring in the compounds **2a–e**. The carbonyl carbon signals in indanone ring and δ-lactone ring appeared around δ 200.0 and δ 163.0 respectively. The aromatic carbons appeared between δ 105.0 and 161.6. The signal around δ 161.6 is due to C_7-OH. Mass spectra of compound **2a** gave molecular ion peak at 266.0 (M^+) corresponding to molecular formula $C_{16}H_{10}O_4$.

The NMR spectrum of compounds **2f–j** showed a multiplet around δ 2.25 integrating for two protons attached at C_{10}. Two triplets appeared around δ 2.70 and δ 2.95 each integrating for two protons attached at C_9 and C_{11} respectively. A singlet appeared around δ 8.15 is due to C_8–H and –OH proton was seen as a broad singlet around δ 11.40, which was conformed by D_2O exchanged spectrum. The remaining aromatic protons appeared as expected. The ^{13}C-NMR spectra of compounds **2f–j** showed signals around δ 23.0, 30.0 and 35.0 due to C_9, C_{10} and C_{11} respectively. This was further confirmed by DEPT-135 spectra in which these signals got inverted. This supports the incorporation of naphthalenone ring in the compounds **2f-j**. The carbonyl carbon signals in naphthalenone ring and δ-lactone ring appeared around δ 197.0 and δ 163.0 respectively. The aromatic carbons appeared between δ 107.0 and 161.9. The signal around δ 161.9 is due to C_7-OH. Mass spectra of compound **2f** gave molecular ion peak at 280.0 (M^+) corresponding to molecular formula $C_{17}H_{12}O_4$.

The NMR spectrum of compounds **2k-o** showed three singlets around δ 1.11, 2.70 and 2.90 due to six protons of two methyl groups attached at C_{10}, two protons attached at C_9 and C_{11} respectively. A singlet appeared around δ 8.20 is due to C_8–H and –OH proton was seen as a broad singlet around δ 11.40, which was confirmed as stated earlier. The remaining aromatic protons appeared as expected. The ^{13}C-NMR spectra of compounds **2k-o** showed signals around δ 28.5, 33.6, 44.7 and 54.5 due to two methyl group attached at C_{10}, C_{10} (itself), C_9 and C_{11} respectively. This was further confirmed by DEPT-135 spectra in which C_9 and C_{11} signals got inverted. The incorporation of naphthalenone ring in the compounds **2k-o** is this supported. The carbonyl carbon signals in naphthalenone ring and δ-lactone ring appeared around δ 200.0 and δ 163.0 respectively. The aromatic carbons appeared between δ 108.0 and 162.0. The signal around δ 162.0 is due to C_7-OH. Mass spectra of compound **2k** gave molecular ion peak at 308.1 (M^+) corresponding to molecular formula $C_{19}H_{16}O_4$.

All other compounds gave satisfactory spectral data which are given in experimental section.

Conclusions

In summary, a simple, convenient and general method has been developed for the preparation of fused chromenes utilizing easily accessible and inexpensive starting materials. This synthetic approach includes some important aspects such as high yields and mild reaction conditions, which make this synthetic protocol a useful and an attractive procedure for the synthesis of indanone and naphthalenone fused chromenones derivatives. This reaction can be regarded as a new approach for the preparation of synthetically and pharmaceutically relevant heterocyclic systems.

Experimental Section

General. Reagents and solvents were obtaind from commercial sources and used without further purification. All melting points were taken in open capillaries and are uncorrected. Thin-layer chromatography (TLC, on aluminum plates coated with silica gel 60 F_{254}, 0.25 mm thickness, Merck) was used for monitoring the progress of all reactions, purity and homogeneity of the synthesized compounds. Elemental analysis (% C, H, N) was carried out by Perkin-Elmer 2400 series-II elemental analyzer at Sophisticated Instrumentation Centre for Applied Research & Training (SICART), Vallabh Vidhyanagar and result obtained for those elements are within ±0.4% of the theoretical values. The FTIR spectra were recorded using potassium bromide disc on a Shimadzu FTIR 8401 spectrophotometer and only the characteristic peaks are reported. ^{1}H-NMR and ^{13}C-NMR spectra were recorded using DMSO-d_6 solvent on a Bruker Avance 400 (MHz) spectrometer using solvent peak as internal standard at 400 and 100 MHz, respectively. Chemical shifts are reported in parts per million (ppm). Mass spectra were scanned on a Shimadzu LCMS 2010 spectrometer. 1-(2-oxo-2-(2-oxo-2*H*-chromen-3-yl) ethyl) pyridinium bromide **1(a-e)** was prepared according the literature procedures[21].

General procedure for the synthesis of fused chromenones (2a-o). In a round bottom flask (100 mL), a solution of appropriate diketone (1,3-cyclopentandione or 1,3-cyclohexandione or dimedone) (0.0058 mol) was taken in glacial acetic acid (15 mL). To this solution, sodium acetate (0.06 mol) and an appropriate 1-(2-oxo-2-(2-oxo-2*H*-chromen-3-yl) ethyl) pyridinium bromide **1a-e** (0.006 mol) in acetic acid (10 mL) were added with stirring. The reaction mixture was stirred at room temperature for 45 minutes and then refluxed in an oil bath at 140-145˚C for 6 hours and left overnight. It was then poured in water (75 mL) and the crude solid obtained was extracted with chloroform (3 x 50 mL). The organic layer was washed with 10% sodium bicarbonate solution (50 mL), water (50 mL) and dried over anhydrous sodium sulfate. Distillation of chloroform in vacuum gave gummy material which was subjected to column

chromatography using ethyl acetate-pet.ether (60-80) (2:8) as an eluent to afford product **2a-o** respectively. The product was recrystallized from chloroform-hexane.

7-Hydroxy-9,10-dihydroindeno[5,4-*c*]chromene-6,11-dione (2a). Yield 62%; mp 222-224 ºC; white crystalline solid; Selected IR frequencies (KBr): 3445 (broad, -OH), 2926 (C-H, aliphatic), 1670 (C=O, δ-lactone), 1710 (C=O, indanone), 1615 (C=C, aromatic) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.08 (2H, t, C_9-H, *J* 6.8 Hz), 3.15 (2H, t, C_{10}-H, *J* 6.8 Hz), 7.33-7.61 (4H, m, Ar-H), 8.07 (1H, s, C_8-H), 11.30 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 28.0 (CH_2), 29.0 (CH_2), 105.0 (C), 114.7 (CH), 117.8 (CH), 118.4 (C), 123.3 (CH), 127.2 (CH), 129.8 (C), 130.6 (CH), 136.5 (C), 139.2 (C), 150.2 (C), 161.6 (C_7), 163.0 (C=O, δ-lactone), 200.0 (C=O, indanone); Anal. Calcd. for $C_{16}H_{10}O_4$: C, 72.18; H, 3.79%. Found: C, 72.08; H, 3.51%. MS: 266.0 (M^+).

3,7-Dihydroxy-9,10-dihydroindeno[5,4-*c*]chromene-6,11-dione (2b). Yield 57%; mp 176-178 ºC; white crystalline solid; Selected IR frequencies (KBr): 3442 (broad, -OH), 2935 (C-H, aliphatic), 1680 (C=O, δ-lactone), 1720 (C=O, indanone), 1610 (C=C, aromatic) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.05 (2H, t, C_9-H, *J* 6.7 Hz), 3.13 (2H, t, C_{10}-H, *J* 6.7 Hz), 7.34-7.59 (3H, m, Ar-H), 8.09 (1H, s, C_8-H), 11.30 (1H, s, -OH proton, D_2O exchangeable), 11.83 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 28.5 (CH_2), 29.8 (CH_2), 105.7 (C), 113.2 (CH), 116.7 (CH), 118.7 (C), 123.4 (CH), 127.5 (CH), 129.8 (C), 135.7 (C), 140.3 (C), 150.2 (C), 159.7 (C), 160.7 (C_7), 163.3 (C=O, δ-lactone), 199.9 (C=O, indanone); Anal. Calcd. for $C_{16}H_{10}O_5$: C, 68.09; H, 3.57%. Found: C, 68.23; H, 3.42%.

7-Hydroxy-3-methoxy-9,10-dihydroindeno[5,4-*c*]chromene-6,11-dione (2c). Yield 63%; mp 228-230 ºC; off-white solid; Selected IR frequencies (KBr): 3439 (broad, -OH), 2948 (C-H, aliphatic), 1670 (C=O, δ-lactone), 1730 (C=O, indanone), 1622 (C=C, aromatic), 1055 (asymmetric and symmetric C-O-C stretching) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.07 (2H, t, C_9-H, *J* 6.8 Hz), 3.11 (2H, t, C_{10}-H, *J* 6.8 Hz), 3.94 (3H, s, OCH_3), 7.32-7.55 (3H, m, Ar-H), 8.11 (1H, s, C_8-H), 11.42 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 28.4 (CH_2), 28.8 (CH_2), 56.2 (OCH_3), 106.7 (C), 114.1 (CH), 116.4 (CH), 119.5 (C), 122.2 (CH), 126.4 (CH), 129.2 (C), 136.8 (C), 140.1 (C), 150.4 (C), 158.8 (C), 161.7 (C_7), 163.5 (C=O, δ-lactone), 200.1 (C=O, indanone); Anal. Calcd. for $C_{17}H_{12}O_5$: C, 68.92; H, 4.08%. Found: C, 68.83; H, 3.97%.

4,7-Dihydroxy-9,10-dihydroindeno[5,4-*c*]chromene-6,11-dione (2d). Yield 64%; mp 195-198 ºC; white crystalline solid; Selected IR frequencies (KBr): 3437 (broad, -OH), 2933 (C-H, aliphatic), 1680 (C=O, δ-lactone), 1715 (C=O, indanone), 1617 (C=C, aromatic) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.08 (2H, t, C_9-H, *J* 6.7 Hz), 3.10 (2H, t, C_{10}-H, *J* 6.7 Hz), 7.30-7.57 (3H, m, Ar-H), 8.08 (1H, s, C_8-H), 11.35 (1H, s, -OH proton, D_2O exchangeable), 11.78 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 28.8 (CH_2), 29.4 (CH_2), 105.2 (C), 113.2 (CH), 116.9 (CH), 118.7 (C), 122.1 (CH), 127.8 (CH), 130.2 (C), 135.2 (C), 140.5 (C), 151.8 (C), 159.1 (C), 160.1 (C_7), 163.8 (C=O, δ-lactone), 200.0 (C=O, indanone); Anal. Calcd. for $C_{16}H_{10}O_5$: C, 68.09; H, 3.57%. Found: C, 68.11; H, 3.71%.

7-Hydroxy-4-methoxy-9,10-dihydroindeno[5,4-*c*]chromene-6,11-dione (2e). Yield 67%; mp 173-176 ºC; off-white solid; Selected IR frequencies (KBr): 3445 (broad, -OH), 2933 (C-H, aliphatic), 1670 (C=O, δ-lactone), 1720 (C=O, indanone), 1621 (C=C, aromatic), 1050

(asymmetric and symmetric C-O-C stretching) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.03 (2H, t, C_9-H, *J* 6.8 Hz), 3.13 (2H, t, C_{10}-H, *J* 6.8 Hz), 3.97 (3H, s, OCH_3), 7.29-7.49 (3H, m, Ar-H), 8.13 (1H, s, C_8-H), 11.44 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 28.2 (CH_2), 28.6 (CH_2), 56.24 (OCH_3), 105.9 (C), 114.3 (CH), 117.1 (CH), 120.3 (C), 122.2 (CH), 126.7 (CH), 128.9 (C), 136.9 (C), 139.9 (C), 150.7 (C), 152.7 (C), 162.3 (C_7), 163.0 (C=O, δ-lactone), 200.2 (C=O, indanone); Anal. Calcd. for $C_{17}H_{12}O_5$: C, 68.92; H, 4.08%. Found: C, 68.89; H, 4.11%.

7-Hydroxy-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione (2f). Yield 61%; mp 180-182 ºC; white solid; Selected IR frequencies (KBr): 3430 (broad, -OH), 2900 (C-H, aliphatic), 1665 (C=O, δ-lactone), 1720 (C=O, naphthalenone), 1610 (C=C, aromatic) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.25 (2H, m, C_{10}-H), 2.76 (2H, t, C_9-H, *J* 5.5 Hz), 2.95 (2H, t, C_{11}-H, *J* 5.5 Hz), 7.33-7.62 (4H, m, Ar-H), 8.15 (1H, s, C_8-H), 11.42 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 23.8 (CH_2), 30.2 (CH_2), 35.6 (CH_2), 107.9 (C), 111.3 (C), 116.3 (CH), 120.7 (CH), 122.6 (CH), 125.7 (C), 128.3 (CH), 135.4 (CH), 140.1 (C), 149.5 (C), 158.7 (C), 161.3 (C_7), 163.2 (C=O, δ-lactone), 197.2 (C=O, naphthalenone); Anal. Calcd. for $C_{17}H_{12}O_4$: C, 72.85; H, 4.32%. Found: C, 72.71; H, 4.25%. MS: 280.0 (M^+).

3,7-Dihydroxy-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione (2g). Yield 69%; mp 210-213 ºC; white solid; Selected IR frequencies (KBr): 3440 (broad, -OH), 2930 (C-H, aliphatic), 1660 (C=O, δ-lactone), 1710 (C=O, naphthalenone), 1615 (C=C, aromatic) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.20 (2H, m, C_{10}-H), 2.71 (2H, t, C_9-H, *J* 5.5 Hz), 2.93 (2H, t, C_{11}-H, *J* 5.5 Hz), 7.34-7.59 (3H, m, Ar-H), 8.09 (1H, s, C_8-H), 11.39 (1H, s, -OH proton, D_2O exchangeable), 11.83 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 23.3 (CH_2), 29.8 (CH_2), 34.8 (CH_2), 107.3 (C), 111.7 (C), 116.8 (CH), 121.3 (CH), 121.8 (CH), 125.5 (C), 128.2 (C), 134.9 (CH), 140.8 (C), 151.4 (C), 158.9 (C), 161.7 (C_7), 163.8 (C=O, δ-lactone), 197.8 (C=O, naphthalenone); Anal. Calcd. for $C_{17}H_{12}O_5$: C, 68.92; H, 4.08%;. Found: C, 68.79; H, 4.18%.

7-Hydroxy-3-methoxy-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione (2h). Yield 64%; mp 190-194 ºC; off-white solid; Selected IR frequencies (KBr): 3435 (broad, -OH), 2940 (C-H, aliphatic), 1670 (C=O, δ-lactone), 1730 (C=O, naphthalenone), 1622 (C=C, aromatic), 1050 (asymmetric and symmetric C-O-C stretching) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.27 (2H, m, C_{10}-H), 2.73 (2H, t, C_9-H, *J* 5.5 Hz), 2.97 (2H, t, C_{11}-H, *J* 5.5 Hz), 3.40 (3H, s, OCH_3), 7.31-7.60 (3H, m, Ar-H), 8.08 (1H, s, C_8-H), 11.44 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 23.4 (CH_2), 30.1 (CH_2), 35.2 (CH_2), 56.4 (OCH_3), 107.8 (C), 111.5 (C), 116.7 (CH), 120.9 (CH), 122.3 (CH), 125.4 (C), 128.4 (C), 135.7 (CH), 141.2 (C), 151.5 (C), 157.8 (C), 161.9 (C_7), 162.8 (C=O, δ-lactone), 197.7 (C=O, naphthalenone); Anal. Calcd. for $C_{18}H_{14}O_5$: C, 69.67; H, 4.55%. Found: C, 69.79; H, 4.35%.

4,7-Dihydroxy-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione (2i). Yield 67%; mp 203-207 ºC; white crystalline solid; Selected IR frequencies (KBr): 3440 (broad, -OH), 2925 (C-H, aliphatic), 1650 (C=O, δ-lactone), 1715 (C=O, naphthalenone), 1610 (C=C, aromatic) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.22 (2H, m, C_{10}-H), 2.77 (2H, t, C_9-H, *J* 5.5 Hz), 2.95 (2H, t, C_{11}-H, *J* 5.5 Hz), 7.33-7.61 (3H, m, Ar-H), 8.11 (1H, s, C_8-H), 11.42 (1H, s, -OH proton, D_2O exchangeable), 11.86 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 22.9 (CH_2), 30.2

(CH_2), 35.1 (CH_2), 107.2 (C), 111.8 (C), 116.5 (CH), 120.8 (CH), 121.6 (CH), 125.3 (C), 128.4 (C), 135.1 (CH), 141.1 (C), 151.6 (C), 158.7 (C), 161.2 (C_7), 163.5 (C=O, δ-lactone), 197.2 (C=O, naphthalenone); Anal. Calcd. for $C_{17}H_{12}O_5$: C, 68.92; H, 4.08%;. Found: C, 68.75; H, 3.98%.

7-Hydroxy-4-methoxy-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione (2j). Yield 61%; mp 183-186 ºC; off-white solid; Selected IR frequencies (KBr): 3450 (broad, -OH), 2930 (C-H, aliphatic), 1670 (C=O, δ-lactone), 1720 (C=O, indanone), 1621 (C=C, aromatic), 1055 (asymmetric and symmetric C-O-C stretching) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.20 (2H, m, C_{10}-H), 2.70 (2H, t, C_9-H, *J* 5.5 Hz), 2.96 (2H, t, C_{11}-H, *J* 5.5 Hz), 3.97 (3H, s, OCH_3), 7.28-7.67 (3H, m, Ar-H), 8.15 (1H, s, C_8-H), 11.40 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 23.3 (CH_2), 30.4 (CH_2), 34.9 (CH_2), 56.3 (OCH_3), 107.9 (C), 111.8 (C), 116.5 (CH), 121.2 (CH), 122.4 (CH), 125.3 (C), 128.7 (C), 136.2 (CH), 140.9 (C), 151.4 (C), 157.8 (C), 161.5 (C_7), 163.1 (C=O, δ-lactone), 197.8 (C=O, naphthalenone); Anal. Calcd. for $C_{18}H_{14}O_5$: C, 69.67; H, 4.55 %. Found: C, 69.55; H, 4.72 %.

7-Hydroxy-10,10-dimethyl-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione (2k). Yield 66%; mp 180-182 ºC; off-white solid; Selected IR frequencies (KBr): 3435 (broad, -OH), 3020 (C-H, aliphatic), 1660 (C=O, δ-lactone), 1715 (C=O, naphthalenone), 1605 (C=C, aromatic) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.11 (6H, s, 2 x CH_3), 2.70 (2H, s, C_9-H), 2.95 (2H, s, C_{11}-H), 7.30-7.59 (4H, m, Ar-H), 8.20 (1H, s, C_8-H), 11.44 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 28.2 (2 x CH_3), 33.6 (C), 44.7 (CH_2), 54.5 (CH_2), 108.6 (C), 112.4 (C), 117.5 (CH), 121.5 (CH), 123.6 (CH), 127.2 (C), 128.4 (CH), 137.3 (CH), 142.3 (C), 150.5 (C), 158.8 (C), 162.3 (C_7), 163.3 (C=O, δ-lactone), 200.9 (C=O, naphthalenone); Anal. Calcd. for $C_{19}H_{16}O_4$: C, 74.01; H, 5.23%. Found: C, 74.21; H, 5.33%. MS: 308.1 (M^+).

3,7-Dihydroxy-10,10-dimethyl-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione (2l). Yield 63%; mp 207-210 ºC; white solid; Selected IR frequencies (KBr): 3440 (broad, -OH), 3030 (C-H, aliphatic), 1650 (C=O, δ-lactone), 1710 (C=O, naphthalenone), 1615 (C=C, aromatic) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.11 (6H, s, 2 x CH_3), 2.73 (2H, s, C_9-H), 2.90 (2H, s, C_{11}-H), 7.34-7.61 (3H, m, Ar-H), 8.18 (1H, s, C_8-H), 11.39 (1H, s, -OH proton, D_2O exchangeable), 11.81 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 28.3 (2 x CH_3), 33.4 (C), 44.5 (CH_2), 54.2 (CH_2), 108.9 (C), 113.5 (C), 117.3 (CH), 121.7 (CH), 124.2 (C), 127.6 (CH), 128.9 (C), 137.6 (CH), 143.5 (C), 151.2 (C), 158.4 (C), 162.7 (C_7), 163.8 (C=O, δ-lactone), 200.7 (C=O, naphthalenone); Anal. Calcd. for $C_{19}H_{16}O_5$: C, 70.36; H, 4.97%. Found: C, 70.58; H, 5.20%.

7-Hydroxy-3-methoxy-10,10-dimethyl-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione (2m). Yield 59%; mp 182-186 ºC; white solid; Selected IR frequencies (KBr): 3435 (broad, -OH), 2990 (C-H, aliphatic), 1670 (C=O, δ-lactone), 1730 (C=O, naphthalenone), 1607 (C=C, aromatic), 1055 (asymmetric and symmetric C-O-C stretching) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.11 (6H, s, 2 x CH_3), 2.72 (2H, s, C_9-H), 2.96 (2H, s, C_{11}-H), 3.39 (3H, s, OCH_3), 7.35-7.69 (3H, m, Ar-H), 8.16 (1H, s, C_8-H), 11.40 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 28.4 (2 x CH_3), 33.4 (C), 44.3 (CH_2), 54.4 (CH_2), 56.4 (OCH_3), 109.4 (C), 113.3 (C), 116.7 (CH), 120.8 (CH), 124.3 (CH), 127.4 (C), 128.4 (C), 136.7 (CH), 143.2 (C), 151.3 (C),

158.8 (C), 162.9 (C_7), 163.5 (C=O, δ-lactone), 200.3 (C=O, naphthalenone); Anal. Calcd. for $C_{20}H_{18}O_5$: C, 70.99; H, 5.36%. Found: C, 70.87; H, 5.55%.

4,7-Dihydroxy-10,10-dimethyl-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione (2n). Yield 66%; mp 201-204 ^oC; white solid; Selected IR frequencies (KBr): 3440 (broad, -OH), 3033 (C-H, aliphatic), 1650 (C=O, δ-lactone), 1710 (C=O, naphthalenone), 1617 (C=C, aromatic) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.11 (6H, s, 2 x CH_3), 2.72 (2H, s, C_9-H), 2.92 (2H, s, C_{11}-H), 7.33-7.67 (3H, m, Ar-H), 8.15 (1H, s, C_8-H), 11.40 (1H, s, -OH proton, D_2O exchangeable), 11.82 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 28.2 (2 x CH_3), 33.7 (C), 44.7 (CH_2), 54.6 (CH_2), 109.2 (C), 113.2 (C), 117.8 (CH), 121.6 (CH), 123.8 (C), 127.9 (CH), 129.3 (C), 137.2 (CH), 143.2 (C), 151.7 (C), 158.8 (C), 162.3 (C_7), 163.6 (C=O, δ-lactone), 200.1 (C=O, naphthalenone); Anal. Calcd. for $C_{19}H_{16}O_5$: C, 70.36; H, 4.97%. Found: C, 70.20; H, 5.27%.

7-Hydroxy-4-methoxy-10,10-dimethyl-10,11-dihydro-6*H*-naphtho[2,1-*c*]chromene-6,12(9*H*)-dione (2o). Yield 55%; mp 193-197 ^oC; off-white solid; Selected IR frequencies (KBr): 3430 (broad, -OH), 3010 (C-H, aliphatic), 1665 (C=O, δ-lactone), 1730 (C=O, naphthalenone), 1615 (C=C, aromatic), 1045 (asymmetric and symmetric C-O-C stretching) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.11 (6H, s, 2 x CH_3), 2.70 (2H, s, C_9-H), 2.93 (2H, s, C_{11}-H), 3.40 (3H, s, OCH_3), 7.33-7.58 (3H, m, Ar-H), 8.19 (1H, s, C_8-H), 11.44 (1H, s, -OH proton, D_2O exchangeable); ^{13}C NMR: δ 28.5 (2 x CH_3), 33.4 (C), 44.7 (CH_2), 54.8 (CH_2), 56.9 (OCH_3), 108.0 (C), 113.5 (C), 116.6 (CH), 121.1 (CH), 124.5 (CH), 127.7 (C), 128.3 (C), 136.7 (CH), 143.4 (C), 151.5 (C), 158.8 (C), 162.8 (C_7), 163.4 (C=O, δ-lactone), 200.6 (C=O, naphthalenone); Anal. Calcd. for $C_{20}H_{18}O_5$: C, 70.99; H, 5.36%. Found: C, 70.66; H, 5.10%.

Acknowledgements

The author expresses his sincere thanks to the Department of Advanced Organic Chemistry, P. D. Patel Institute of Applied Sciences, Charotar University of Science & Technology (Charusat) for providing research facilities. Vaibhav Analytical Laboratory, Ahmedabad for IR spectral analysis as well as Oxygen Healthcare Research Pvt. Ltd., Ahmedabad for providing mass spectrometry facilities.

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