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# Lewis acid promoted synthesis of methylene-bridged α-and γ-*bis*-benzopyrones

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The Lewis acid promoted Fries rearrangement of *O*-methoxyacetyl derivatives of hydroxy-chromanones, coumarins and chromones under solvent-free condition gives isomeric methylene-bridged bischromanones, biscoumarins and bischromones, respectively, in good yields. The benzopyrone precursors undergo intermolecular rearrangement wherein two benzopyrone moieties are joined through their benzene rings *via* an un-substituted methylene bridge.

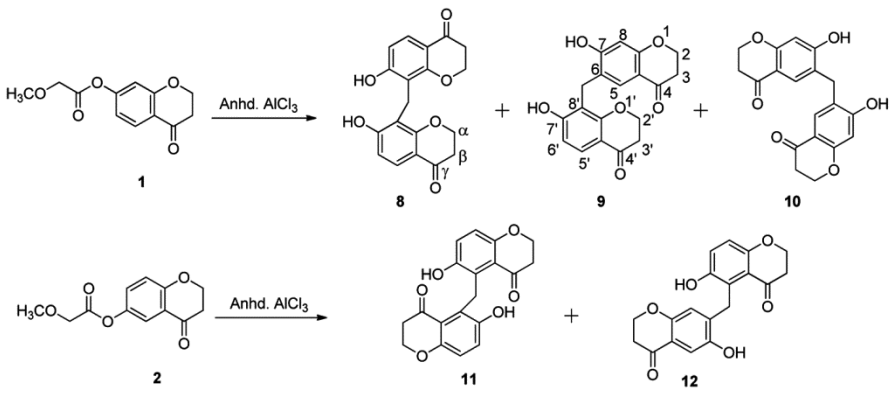
**Keywords**: *O*-Methoxyacetyl derivatives of hydroxyl-chromanones, coumarins and chromones, Lewis acid, methylene-bridged *bis*-benzopyrones, Fries rearrangement

The α-and the γ-methylene-*bis*-benzopyrones are known to have widespread biological activities[1] which include potent α-glucosidase inhibition[2], HIV integrase inhibition[3], efficacy in the inhibition of the activity of neurodegenerative enzyme acetylcholinesterase[4,5], anticancer activity with established structure activity relationship[6] and as ligands in rare-earth element complexes showing *in vitro* inhibitory activity for malignant cell proliferation[7]. Several procedures have been reported for their preparation[1,6-9]. However, just a few[10,11] link the two benzopyrone moieties through an unsubstituted methylene bridge *via* C-5 to C-8 carbons. The Fries reaction is one of the most convenient Lewis acid mediated reactions used for the preparation of hydroxy aryl ketones using phenolic esters. However, the Fries reaction of *O*-methoxyacetyl derivatives of chromanones (γ-dihydrobenzopyrones), coumarins (α-benzopyrones) and chromones (γ-benzopyrones) do not undergo the usual rearrangement. Instead, the reaction results in the formation of isomeric methylene *bis*-compounds. We now report herein a new general, solvent free, economical and efficient method for the synthesis of methylene α- and γ-*bis*-benzopyrones.

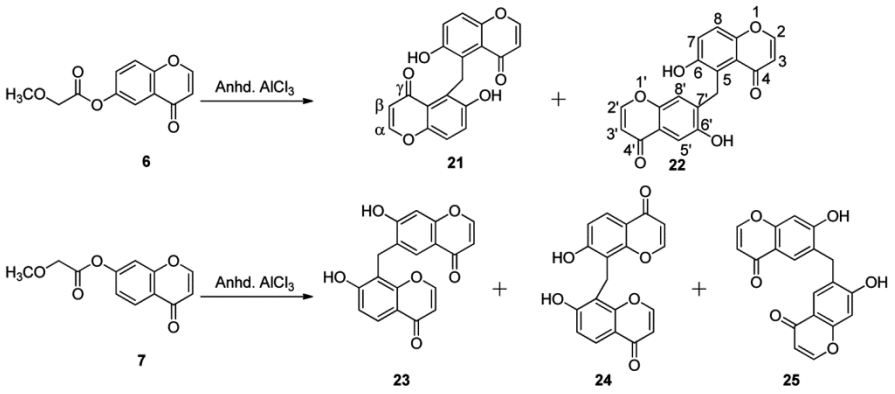
## Results and Discussion

*O*-Methoxyacetyl derivatives of hydroxy chromanones **1** and **2**, coumarins **3**-**5** and chromones **6** and **7** were subjected to Fries reaction using anhydrous $AlCl_3$ as the Lewis acid under dry conditions. Reactions were run with a 2:5 ratio of substrate to catalyst. The reaction time and temperature were 4 h and 170°C, respectively. In case of chromanones and chromones, the rearrangement afforded exclusively the corresponding isomeric methylene-*bis*-compounds containing the bridging methylene group at positions *ortho* to the hydroxyl group (Scheme I and Scheme II). Coumarins gave a mixture of isomeric methylene-*bis*-compounds **13-20** along with earlier reported furanocoumarins **13**, **15** and **18** (Scheme III)[12].

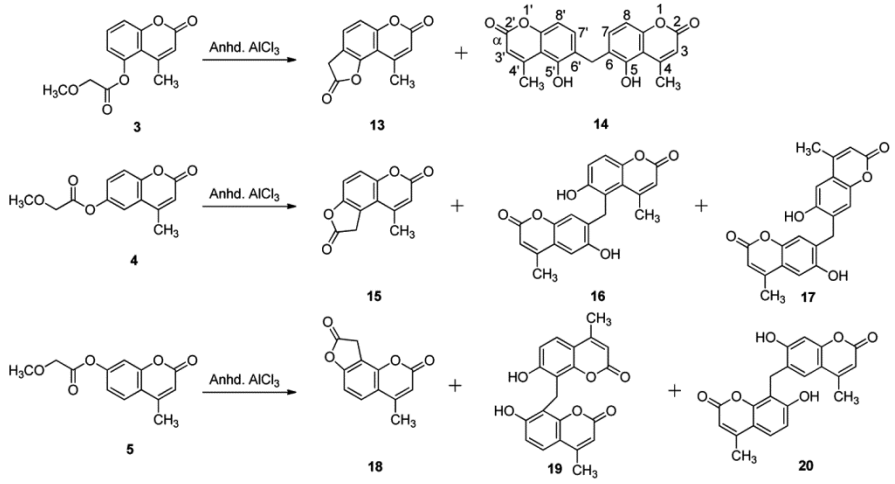
The reaction of **1** gave three isomeric products **8-10**. Compound **8** displayed a molecular ion peak at *m/z* 340 and was analysed for $C_{19}H_{16}O_6$, indicating a linkage between two reactant moieties along with a methylene group. Absorption maxima were observed at 319, 248 and 212 nm in its UV-Vis spectrum, typical for a 2,3-dihydrobenzopyrone system. Signals at δ 3.68 (s,2H) and at δ 17.2 in its $^1$H and $^{13}$C NMR spectrum, respectively, indicated the presence of a methylene group between the two aromatic moieties. A study of its $^1$H NMR spectrum clearly indicated substitution of the methylene group in the benzene ring of the γ-dihydrobenzopyrone because of the following reasons: Firstly, absorption at δ 2.50 and 4.27 (t, 4H each), showed that C-2 and C-3 carbons in both the moieties remained unsubstituted. Secondly, peak at δ 9.98 (brs, 2H) which disappeared when the sample was run in DMSO-$d_6$ containing $D_2O$,




Scheme I — Synthesis of methylene-*bis*-chromanones **8-12**




Scheme II — Synthesis of methylene-*bis*-chromones **21-25**




Scheme III — Synthesis of furanocoumarins **13**, **15** and **18** and methylene-*bis*-coumarins **14**, **16-17** and **19-20**

indicated the presence of two hydroxyl groups. This was supported by a band at 3279 $cm^{-1}$ (hydroxyl) in its IR spectrum. Thirdly, the presence of only one pair of *ortho*-coupled doublets (each integrating for two protons) at δ 6.49 and 7.35, indicated substitution at C-8 carbon of both chromanone moieties. Hence **8** was characterized as 8,8'-methylene *bis*-(7-hydroxychromanone). This was further confirmed by utilizing complimentary information from 2D-NMR experiments such as $^{1}H$-$^{1}H$ COSY, $^{1}H$-$^{13}C$ COSY and HMBC. Detailed spectral studies showed **9** to be an unsymmetrical isomer of **8**. Compound **9** showed a pair of *ortho*-coupled doublets at δ 6.65 and 7.65 (each integrating for one proton) indicating

substitution by the methylene group at C-8 carbon in one chromanone moiety along with two singlets at δ 6.42 and 7.90 (each integrating for one proton) indicating substitution by the methylene group at C-6 carbon of the other chromanone moiety. Hence, **9** was characterized as the unsymmetrical 6,8'-isomer. Comparison of the spectral data of **10** with that of **8** and **9** indicated it to be another of their symmetrical methylene *bis* isomer. Compound **10** formed as a minor product, displayed only two singlets at δ 6.43 and 7.85 (integrating for two protons each), in the aromatic region of its $^1$H NMR spectrum, assigned to H-8 and 8' and H-5 and 5' protons, respectively, thus confirming its structure.

*O*-Methoxyacetyl derivative **2** produced isomeric methylene-*bis*-compounds **11** (in minor amount) and **12**. These were identified by detailed spectral studies on a similar basis as for **8**, **9** and **10**. The $^1$H NMR spectrum of **11** showed the presence of only one pair of *ortho*-coupled doublets at δ 6.59 and 6.99 (each integrating for two protons) indicating substitution at C-5 carbon in both chromanone moieties and hence was identified as the symmetrical 5,5'-isomer. Comparison of spectral data of **12** with that of **11** indicated it to be its unsymmetrical isomer. In the aromatic region of its $^1$H NMR spectrum, the presence of a pair of *ortho*- coupled doublets at δ 6.87 and 7.15 (each integrating for one proton) indicated substitution at C-5 carbon in one chromanone moiety while two singlets at δ 7.01 and 7.34 (each integrating for one proton) indicated substitution at C-7 carbon in the other chromanone moiety, thereby confirming it to be the 5,7'-isomer (Scheme I).

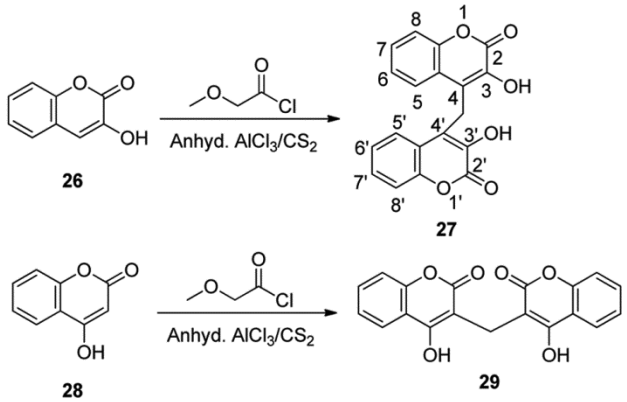
*O*-Methoxyacetyl derivative **3** upon standard condition treatment furnished furanocoumarin[12] **13** and methylene *bis* product **14** which was identified by detailed spectral analysis as the symmetrical 6,6'-isomer. Similarly, **4** and **5** produced furanocoumarins[12] **15** and **18** and isomeric methylene-*bis*-coumarins **16**, **17** and **19**, **20**, respectively, which were characterized by detailed spectral analysis on similar basis as discussed above (Scheme III).

*O*-Methoxyacetyl derivative **6** upon reaction gave **21** (in minor amount) and **22** while **7** gave **23** and **24** as the major products along with minor amount of **25** (Scheme II). These were also characterized by detailed spectral studies similar to the discussion above.

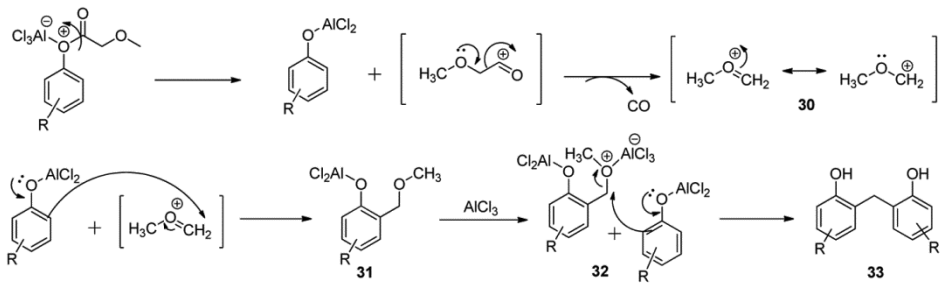
For the purpose of synthesising methylene *bis* compounds using Fries reaction starting from 3- and 4-hydroxycoumarins **26** and **28**, the corresponding *O*-methoxyacetyl derivatives were obtained in poor yields and hence, further reaction could not be done. However, when subjected to Friedel-Crafts reaction with methoxyacetyl chloride in presence of anhydrous $AlCl_3$ in $CS_2$ solvent, **26** and **28** afforded corresponding methylene *bis* coumarins **27** and **29**, respectively (Scheme IV). Their $^1$H NMR indicated no substitution in the benzene ring and absence of H attached directly to the pyrone ring. Detailed study of their spectral data was used to characterize them. The presence of methylene bridge in pyrone ring of **27** and **29** was at position *ortho* to the hydroxy group and was in agreement with the products formed in Scheme I, Scheme II and Scheme III.

To explain this novel product formation in the reaction, we propose a mechanism which involves generation of an unstable methoxyacyl cation that upon loss of CO generates a resonance stabilized methoxymethyl cation **30**, which subsequently undergoes electrophilic substitution on the phenolic nucleus of the benzopyrone moiety to form corresponding benzyl methyl ether **31**. Subsequent complexation with a Lewis acid generates the corresponding benzyl cation which on electrophilic substitution on another phenolic nucleus of the other benzopyrone moiety forms the methylene *bis* compound **33** (Scheme V).

The structures of all the synthesized compounds, *O*-methoxyacetyl derivatives (**1-7**), methylene-*bis*-compounds and furanocoumarins (**8-29**) were unambiguously established on the basis of their spectral (IR, $^1$H-, $^{13}$C-NMR, $^1$H-$^1$H COSY NMR, $^1$H-$^{13}$C HMBC NMR and HRMS) data analysis. The structure of known compounds **13**, **15** and **18** were further confirmed by the comparison of their physical and spectral data with those reported in literature[12].




Scheme IV — Synthesis of methylene-*bis*-coumarin **27** and **29**



Scheme V — Plausible mechanism for the synthesis of methylene-*bis*-compounds

**Experimental Section**

All chemicals were purchased from Sigma-Aldrich Chemicals Pvt. Limited India and from local commercial sources. Solvents were removed under reduced pressure using rotary evaporator, followed by further removal of the residual solvent under high vacuum. Column chromatography was performed over silica gel (60-120 mesh). Melting points were determined on Buchi M-560 instrument and are uncorrected. HRMS analysis was carried out using Agilent G6530AA LC Q-TOF mass spectrometer using ESI method. The IR spectra of compounds were recorded on Perkin-Elmer model 2000 FT-IR spectrometer and are expressed as wavenumber ($cm^{-1}$). The $^{1}H$- and the $^{13}C$- and other 2D NMR spectra were recorded on 250 or 300 MHz spectrometer using tetramethylsilane (TMS) as internal standard. The chemical shift values are on δ scale and the coupling constant (*J*) are in Hz.

**General procedure for the synthesis of *O*-methoxyacetyl derivatives, 1-7**

The corresponding hydroxyl compounds of **1-7** were prepared by earlier known procedures[13-15]. Dry pyridine was added drop-wise to a stirred solution of each of these hydroxy benzopyrones (10 mmol) followed by addition of methoxyacetyl chloride (15 mmol) under anhydrous conditions. The reaction mixture was warmed to 60-70°C on a water bath for 30 min and then left at room temperature for 24 h. The contents were then poured over an ice-water mixture and the precipitate thus formed was collected by filtration, washed with water, dried and crystallized from DCM-MeOH to afford compounds **1-7** in 90-98% yields.

**Note**: The hydroxy chromanones were prepared by catalytic hydrogenation of the corresponding chromones.

**7-*O*-Methoxyacetylchromanone, 1**: Colourless needles (94%); m.p. 117-118°C; IR $cm^{-1}$(KBr): 1765, 1653; $^{1}H$ NMR (300 MHz, $CDCl_3$): δ 2.71 (t, *J* = 6.4 Hz, 2H, H-3),3.55 (s, 3H, -$OCH_3$), 4.34 (s, 2H, -$OCH_2$-), 4.48 (t, *J* = 6.6 Hz, 2H, H-2), 6.35 (d, *J* = 2.3 Hz, 1H, H-8), 6.54 (dd, *J* = 2.3 and 8.7 Hz, 1H, H-6), 7.77 (d, *J* = 8.7 Hz, 1H, H-5); $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ 36.8, 60.1, 67.3,69.2, 101.1, 109.9, 115.2, 129.0, 163.8, 165.8, 168.8, 191.1; MS *m/z* 236 ($M^+$). Anal. Calcd for $C_{12}H_{12}O_5$: C, 60.99; H, 5.12. Found: C, 60.93; H, 5.11.

**6-*O*-Methoxyacetylchromanone, 2**: Colourless needles (95%); m.p.: 123°C; IR $cm^{-1}$(KBr): 1763, 1646; $^{1}H$ NMR (300 MHz, $CDCl_3$): δ 2.77 (t, *J* = 6.6 Hz, 2H, H-3),3.56 (s, 3H, -$OCH_3$), 4.34 (s, 2H, -$OCH_2$-), 4.48 (t, *J* = 6.6 Hz, 2H, H-2), 6.87 (d, *J* = 8.7 Hz, 1H, H-8), 7.02 (dd, *J* = 2.1 and 8.7 Hz, 1H, H-7), 7.28 (d, *J* = 2.2 Hz, 1H, H-5); $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ 37.5, 59.8, 67.2, 68.9, 108.1, 119.1, 120.9, 125.6, 150.3, 158.1, 168.7, 192.0; MS *m/z* 236 ($M^+$). Anal. Calcd for $C_{12}H_{12}O_5$: C, 60.99; H, 5.12. Found: C, 61.07; H, 5.16.

**5-*O*-Methoxyacetyl-4-methyl coumarin, 3**: Colourless needles (91%); m.p.: 125-127°C; UV nm (MeOH): 316, 268, 227; IR $cm^{-1}$(KBr): 1766, 1697; $^{1}H$ NMR (250 MHz, $CDCl_3$): δ 2.43 (d, *J* = 1.0 Hz, 3H, -$CH_3$ at C-4), 3.58 (s, 3H, -$OCH_3$), 4.34 (s, 2H, -$OCH_2$-), 6.35 (q, *J* = 1.0 Hz, 1H, H-3), 7.29-7.41 (m, 3H, H-6, 7 and 8); $^{13}C$ NMR (62.9 MHz, $CDCl_3$): δ 18.5, 59.6, 69.8, 115.9, 117.0, 118.1, 120.7, 125.0, 146.2, 151.2, 151.5, 160.2, 168.7; MS *m/z* 248 ($M^+$). Anal. Calcd for $C_{13}H_{12}O_5$: C, 62.88; H, 4.87. Foun d: C, 62.92; H, 4.86.

**6-*O*-Methoxyacetyl-4-methyl coumarin, 4**: Colourless needles (93%); m.p.: 117-118°C; UV nm (MeOH): 318, 269, 224; IR $cm^{-1}$(KBr): 1770, 1720; $^{1}H$ NMR (250 MHz, $CDCl_3$): δ 2.42 (d, *J* = 1.1 Hz, 3H, -$CH_3$ at C-4), 3.56 (s, 3H, -$OCH_3$), 4.33 (s, 2H, -$OCH_2$-), 6.33 (q, *J* = 1.1 Hz, 1H, H-3), 7.31 (d, *J* = 8.8 Hz, 1H, H-8), 7.34 (d, *J* = 1.9 Hz, 1H, H-5), 7.38 (dd, *J* = 1.9 and 8.8 Hz, 1H, H-7); $^{13}C$ NMR (62.9 MHz, $CDCl_3$): δ 18.6, 59.6, 69.7, 115.8, 117.1, 118.1, 125.0, 130.1, 146.1, 151.1, 151.7, 160.3, 168.8; MS

*m/z* 248 ($M^+$). Anal. Calcd for $C_{13}H_{12}O_5$: C, 62.88; H, 4.87. Found: C, 62.89; H, 4.89.

**7-*O*-Methoxyacetyl-4-methyl coumarin, 5**: Colourless needles (92%); m.p.: 136°C; UV nm (MeOH): 317, 270, 225; IR $cm^{-1}$(KBr): 1763, 1715; $^1H$ NMR (250 MHz, $CDCl_3$): δ 2.42 (d, *J* = 1.0 Hz, 3H, -$CH_3$ at C-4), 3.54 (s, 3H, -$OCH_3$), 4.32 (s, 2H, -$OCH_2$-), 6.26 (q, *J* = 1.0 Hz, 1H, H-3), 7.11 (dd, *J* = 2.1 and 8.8 Hz, 1H, H-6), 7.14 (d, *J* = 2.1 Hz, 1H, H-8), 7.64 (d, *J* = 8.8 Hz, 1H, H-7); $^{13}C$ NMR (62.9 MHz, $CDCl_3$): δ 18.6, 59.5, 69.4, 110.1, 114.5, 117.7, 117.9, 125.4, 151.7, 152.2, 153.9, 160.2, 168.05; MS *m/z* 248 ($M^+$). Anal. Calcd for $C_{13}H_{12}O_5$: C, 62.88; H, 4.87. Found: C, 62.78; H, 4.84.

**6-*O*-Methoxyacetylchromone, 6**: Colourless needles (94%); m.p.: 176°C; IR $cm^{-1}$(KBr): 1765, 1638; $^1H$ NMR (300 MHz, $CDCl_3$): δ 3.55 (s, 3H, -$OCH_3$), 4.31 (s, 2H, -$OCH_2$-), 6.35 (d, *J* = 6.0 Hz, 1H, H-3), 7.45 (dd, *J* = 2.6 and 9.0 Hz, 1H, H-7), 7.52 (d, *J* = 9.0 Hz, 1H, H-8), 7.87 (d, *J* = 6.0 Hz, 1H, H-2), 7.93 (d, *J* = 2.6 Hz, 1H, H-5);$^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ 59.6, 69.6, 112.6, 117.8, 119.8, 125.7, 127.8, 147.1, 154.2, 155.5, 168.7, 184.8; MS *m/z* 234 ($M^+$). Anal. Calcd for $C_{12}H_{10}O_5$: C, 61.52; H, 4.31. Found: C, 61.47; H, 4.29.

**7-*O*-Methoxyacetylchromone, 7**: Colourless needles (97%); m.p.: 187-188°C; IR $cm^{-1}$(KBr): 1762, 1635; $^1H$ NMR (300 MHz, $CDCl_3$): δ 3.61 (s, 3H, -$OCH_3$), 4.42 (s, 2H, -$OCH_2$-), 6.36 (d, *J* = 5.9 Hz, 1H, H-3), 6.80 (d, *J* = 2.4 Hz. 1H, H-8), 6.94 (dd, *J* = 2.4 and 8.8 Hz, 1H, H-6), 7.87 (d, *J* = 5.9 Hz, 1H, H-2), 7.98 (d, *J* = 8.8 Hz, 1H, H-5); $^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ 58.9, 68.8, 103.0, 111.1, 114.6, 116.1, 130.5, 155.2, 164.1, 166.9, 168.7, 169.1, 185.2; MS *m/z* 234 ($M^+$). Anal. Calcd for $C_{12}H_{10}O_5$: C, 61.52; H, 4.31. Found: C, 61.50; H, 4.27.

**General procedure for Lewis acid mediated rearrangement of O-methoxyacetyl derivatives, 1-7**

A mixture of *O*-methoxyacetyl derivative (**1-7**, 10 mmol) and anhydrous $AlCl_3$ (25 mmol) was heated slowly to 170°C over a period of 4 h. The complex formed was then decomposed by adding it to an ice-water mixture and acidifying the resulting solution with HCl (10 ml). The contents were heated on a water bath for 30 min, cooled and the solid product formed was collected, washed with water, dried and purified by column chromatography to afford methylene *bis*-compounds **8-25** in 60 to 80% yields.

**8,8'-Methylene-*bis*(7-hydroxychromanone), 8**: Elution with $CHCl_3$/MeOH (97:3) gave **8**(40%); m.p. > 300°C; UV nm (MeOH): 319, 278, 233; IR $cm^{-1}$(KBr): 3279, 1647; $^1H$ NMR (300 MHz, DMSO-$d_6$): δ 2.50 (t, *J* = 6.3 Hz, 4H, H-3 and 3'), 3.68 (s, 2H, -$CH_2$-), 4.27 (t, *J* = 6.3 Hz, 4H, H-2 and 2'), 6.49 (d, *J* = 8.6 Hz, 2H, H-6 and 6'), 7.35 (d, *J* = 8.6 Hz, 2H, H-5 and 5'), 9.98 (brs, 2H, 2×-OH); $^{13}C$ NMR (75.5 MHz, DMSO-$d_6$): δ 17.2, 37.3, 67.3, 109.9, 114.3, 114.5, 125.6, 162.1, 162.4, 190.8; MS *m/z* 340 ($M^+$). Anal. Calcd for $C_{19}H_{16}O_6$: C, 67.04; H, 4.74. Found: C, 67.10; H, 4.79.

**6,8'-Methylene-*bis*(7-hydroxychromanone), 9**: Elution with $CHCl_3$/MeOH (97:3) gave **8** in the earlier fractions followed by **9** in the later fractions (28%); m.p. > 300°C; UV nm (MeOH): 320, 247, 212; IR $cm^{-1}$(KBr): 3435, 1649; $^1H$ NMR (300 MHz, DMSO-$d_6$): δ 2.61 and 2.68 (t, *J* = 6.4 Hz, 2H each, H-3 and 3'), 3.29 (s, 2H, -$CH_2$-), 4.42 and 4.45 (t, *J* = 6.4 Hz, 2H each, H-2 and 2'), 6.42 (s, 1H, H-8), 6.65 (d, *J* = 8.6 Hz, 1H, H-6'), 7.65 (d, *J* = 8.6 Hz, 1H, H-5'), 7.90 (s, 1H, H-5), 10.04 (brs, 2H, 2×-OH); $^{13}C$ NMR (75.5 MHz, DMSO-$d_6$): δ 21.6, 37.0, 37.2, 66.9, 67.1, 102.1, 109.9, 113.1, 113.5, 121.7, 126.4, 161.8, 162.6, 190.3; MS *m/z* 340 ($M^+$). Anal. Calcd for $C_{19}H_{16}O_6$: C, 67.04; H, 4.74. Found: C, 67.02; H, 4.77.

**6,6'-Methylene-*bis*(7-hydroxychromanone), 10**: Elution with $CHCl_3$/MeOH (95:5) gave **10** (12%); m.p. > 300°C; UV nm (MeOH): 319, 247, 211; IR $cm^{-1}$(KBr): 3395, 1651; $^1H$ NMR (300 MHz, DMSO-$d_6$): δ 2.57 (t, *J* = 6.4 Hz, 4H, H-3 and 3'), 3.51 (s, 2H, -$CH_2$-), 4.31 (t, *J* = 6.4 Hz, 4H, H-2 and 2'), 6.43 (s, 2H, H-8 and 8'), 7.85 (s, 2H, H-5 and 5'), 10.87 (brs, 2H, 2×-OH); $^{13}C$ NMR (75.5 MHz, DMSO-$d_6$): δ 22.1, 37.3, 67.2, 102.7, 114.1, 120.9, 125.7, 161.9, 162.5, 190.7; MS *m/z* 340 ($M^+$). Anal. Calcd for $C_{19}H_{16}O_6$: C, 67.04; H, 4.74. Found: C, 67.09; H, 4.75.

**5,5'-Methylene-*bis*(6-hydroxychromanone), 11**: Elution with $CHCl_3$/MeOH (95:5) gave **11** (18%); m.p. > 300°C; UV nm (MeOH): 321, 249, 210; IR $cm^{-1}$(KBr): 3391, 1645; $^1H$ NMR (300 MHz, DMSO-$d_6$): δ 2.56 (t, *J* = 6.4 Hz, 4H, H-3 and 3'), 3.67 (s, 2H, -$CH_2$-), 4.24 (t, *J* = 6.4 Hz, 4H, H-2 and 2'), 6.59 (d, *J* = 8.6 Hz, 2H, H-8 and 8'), 6.99 (d, *J* = 8.6 Hz, 2H, H-7 and 7'), 10.03 (brs, 2H, 2×-OH); $^{13}C$ NMR (75.5 MHz, DMSO-$d_6$): δ 18.2, 37.6, 67.4, 105.7, 119.9, 120.1, 137.9, 147.1, 157.0, 191.9; MS *m/z* 340 ($M^+$). Anal. Calcd for $C_{19}H_{16}O_6$: C, 67.04; H, 4.74. Found: C, 67.08; H, 4.75.

**5,7'-Methylene-*bis*(6-hydroxychromanone), 12**: Elution with $CHCl_3$/MeOH (93:7) gave **12** (55%);

m.p. > 300°C; UV nm (MeOH): 321, 250, 211; IR $cm^{-1}$(KBr): 3382, 1637; $^1$H NMR (300 MHz, DMSO-$d_6$): δ 2.66 and 2.73 (t, *J* = 6.5 Hz, 2H each, H-3 and 3'), 3.34 (s, 2H, -$CH_2$-), 4.43 and 4.46 (t, *J* = 6.5 Hz, 2H each, H-2 and 2'), 6.87 (d, *J* = 8.6 Hz, 1H, H-8), 7.01 (s, 1H, H-8'), 7.15 (d, *J* = 8.6 Hz, 1H, H-7), 7.34 (s, 1H, H-5'), 9.95 (brs, 2H, 2×-OH); $^{13}$C NMR (75.5 MHz, DMSO-$d_6$): δ 21.1, 37.4, 37.5, 67.0, 67.1, 106.4, 118.7, 120.0, 127.7, 131.4, 137.5, 146.9, 156.7, 190.8, 191.4; MS *m/z* 340 ($M^+$). Anal. Calcd for $C_{19}H_{16}O_6$: C, 67.04; H, 4.74. Found: C, 66.98; H, 4.69.

**Furan-2(*3H*)-one[5,4-f]-4-methyl-*2H*-1-benzopyran-2-one, 13**: All spectral data are identical to the reported data[12].

**6,6'-Methylene-*bis*(5-hydroxy-4-methylcoumarin), 14**: Elution with $CHCl_3$/MeOH (92:8) gave **14** (62%); m.p.>300°C; UV nm (MeOH): 295, 255, 210; IR $cm^{-1}$(KBr): 3300, 1690; $^1$H NMR (250 MHz, DMSO-$d_6$): δ 2.46 (d, *J* = 1.1 Hz, 6H, 2×-$CH_3$),4.21 (s, 2H, -$CH_2$-), 6.32 (q, *J* = 1.1 Hz, 2H, H-3 and 3'), 6.93 (d, *J* = 8.6 Hz, 2H, H-8 and 8'), 7.45 (d, *J* = 8.6 Hz, 2H, H-7 and 7'), 9.79 (brs, 2H, 2×-OH);$^{13}$C NMR (62.9 MHz, DMSO-$d_6$): δ 18.4, 27.9, 113.8, 116.4, 117.5, 121.9, 126.7, 146.3, 151.4, 155.1, 159.4; MS *m/z* 364 ($M^+$). Anal. Calcd for $C_{21}H_{16}O_6$: C, 69.21; H, 4.44. Found: C, 69.15; H, 4.39.

**Furan-2(*3H*)-one[4,5-f]-4-methyl-*2H*-1-benzopyran-2-one, 15**: All spectral data are identical to the reported data[12].

**5,7'-Methylene-*bis*(6-hydroxy-4-methylcoumarin), 16**: Elution with $CHCl_3$/MeOH (95:5) gave **16** (18%); m.p.>300°C; UV nm (MeOH): 346, 280, 233; IR $cm^{-1}$(KBr): 3182, 1674; $^1$H NMR (250 MHz, DMSO-$d_6$): δ 2.35 (d, *J* = 1.0 Hz, 3H, -$CH_3$),2.36 (d, *J* = 1.0 Hz, 3H, -$CH_3$),4.33 (s, 2H, -$CH_2$-), 6.26 and 6.28 (s, 1H each, H-3 and 3'), 7.12 (s, 1H, H-8'), 7.15 (d, *J* = 8.8 Hz, 1H, H-8), 7.27 (d, *J* = 8.8 Hz, 1H, H-7),7.28 (s, 1H, H-5'),9.82 and 10.06 (brs, 1H each, 2×-OH); $^{13}$C NMR (62.9 MHz, DMSO-$d_6$): δ 17.9, 22.7, 26.9, 108.5, 109.4, 116.7, 17.8, 119.0, 119.6, 121.2, 130.0, 133.2, 140.6, 146.3, 147.8, 151.1, 152.5, 152.7, 153.6, 159.3, 159.8; MS *m/z* 364 ($M^+$). Anal. Calcd for $C_{21}H_{16}O_6$: C, 69.21; H, 4.44. Found: C, 69.22; H, 4.41.

**7,7'-Methylene-*bis*(6-hydroxy-4-methylcoumarin), 17**: Elution with $CHCl_3$/MeOH (90:10) gave **17** (42%); m.p.>300°C; UV nm (MeOH): 343, 280, 226; IR $cm^{-1}$(KBr): 3221, 1686; $^1$H NMR (250 MHz, DMSO-$d_6$): δ 2.50 (d, *J* = 1.5 Hz, 6H, 2×-$CH_3$), 3.97 (s, 2H, -$CH_2$-), 6.32 (m, 2H, H-3 and 3'), 7.04 (s, 2H, H-8 and 8'), 7.21 (s, 2H, H-5 and 5'),9.98 (brs, 2H each, 2×-OH); $^{13}$C NMR (62.89 MHz, DMSO-$d_6$): δ 18.4, 28.8, 110.4, 117.3, 119.7, 131.1, 133.1, 146.8, 151.9, 153.0, 160.5; MS *m/z* 364 ($M^+$). Anal. Calcd for $C_{21}H_{16}O_6$: C, 69.21; H, 4.44. Found: C, 69.25; H, 4.49.

**Furan-2(*3H*)-one[5,4-h]-4-methyl-*2H*-1-benzopyran-2-one, 18**: All spectral data are identical to the reported data[12].

**8,8'-Methylene-*bis*(7-hydroxy-4-methylcoumarin), 19**: Elution with $CHCl_3$/MeOH (96:4) gave **19** (48%); m.p.>300°C; UV nm (MeOH): 330, 230; IR $cm^{-1}$(KBr): 3320, 1690; $^1$H NMR (250 MHz, DMSO-$d_6$): δ 2.42 (s, 6H, 2×-$CH_3$),4.25 (s, 2H, -$CH_2$-), 6.15 (s, 2H, H-3 and 3'), 6.83 (d, *J*= 9 Hz, 2H, H-6 and 6'), 7.50 (d, *J*= 9 Hz, 2H, H-5 and 5'),10.31 (brs, 2H, 2×-OH); $^{13}$C NMR (62.89 MHz, DMSO-$d_6$): δ 17.3, 18.6, 110.2, 113.6, 123.9, 153.4, 154.2, 159.3, 160.9; MS *m/z* 364 ($M^+$). Anal. Calcd for $C_{21}H_{16}O_6$: C, 69.21; H, 4.44. Found: C, 70.17; H, 4.57.

**6,8'-Methylene-*bis*(7-hydroxy-4-methylcoumarin), 20**: Elution with $CHCl_3$/MeOH (92:8) gave **20** (22%); m.p.>300°C; UV nm (MeOH): 331, 232; IR $cm^{-1}$(KBr): 3330, 1700; $^1$H NMR (250 MHz, DMSO-$d_6$): δ 2.36 (s, 6H, 2×-$CH_3$),3.86 (s, 2H, -$CH_2$-), 6.09 (s, 2H, H-3 and 3'), 6.81 (d, *J*= 9 Hz, 1H, H-6'), 6.78 (s, 1H, H-8), 7.26 (s, 1H, H-5), 7.64 (d, *J*= 9 Hz, H-5') 10.45 and 10.79 (s, 1H each, 2×-OH); $^{13}$C NMR (62.9 MHz, DMSO-$d_6$): δ 18.1, 21.7, 26.4, 107.5, 108.3, 116.1, 117.2, 118.8, 119.1, 121.3, 130.1, 132.9, 141.1, 146.2, 147.6, 151.4, 152.5, 152.9, 153.6, 159.3, 159.7; MS *m/z* 364 ($M^+$). Anal. Calcd for $C_{21}H_{16}O_6$: C, 69.21; H, 4.44. Found: C, 68.92; H, 4.50.

**5,5'-Methylene-*bis*(6-hydroxychromone), 21**: Elution with $CHCl_3$/MeOH (95:5) gave **21** (15%); m.p.>300°C; UV nm (MeOH): 310, 248, 212 nm; IR $cm^{-1}$(KBr): 3089, 1631; $^1$H NMR (300 MHz, DMSO-$d_6$): δ 4.08 (s, 2H, -$CH_2$-),6.19 (d, *J*= 5.9 Hz, 2H, H-2and'), 7.10 (d, *J*= 9 Hz, 2H, H-8 and 8'), 7.21 (d, *J*= 9 Hz, 2H, H-7 and 7'), 7.79 (d, *J*= 5.9 Hz, 2H, H-2 and 2') 10.48 (brs, 2H each, 2×-OH); $^{13}$C NMR (75.5 MHz, DMSO-$d_6$): δ 18.3, 110.2, 117.5, 121.1, 129.5, 137.0, 146.2, 154.2, 154.4, 184.8; MS *m/z* 336 ($M^+$). Anal. Calcd for $C_{19}H_{12}O_6$: C, 67.84; H, 3.59. Found: C, 67.79; H, 3.57.

**5,7'-Methylene-*bis*(6-hydroxychromone), 22**: Elution with $CHCl_3$/MeOH (93:7) gave **22** (52%);

m.p.>300°C; UV nm (MeOH): 310, 247, 211 nm; IR $cm^{-1}$(KBr): 3098, 1629; $^1$H NMR (300 MHz, DMSO-$d_6$): δ 4.14 (s, 2H, -$CH_2$-),6.24 and 6.29 (d, *J*= 6.0 Hz, 1H each, H-3 and 3'), 7.28 (d, *J*= 9.1 Hz, 1H, H-7), 7.35 (d, *J*= 9.1 Hz, 1H, H-8), 7.45 (s, 1H, H-8'), 7.59 (s, 1H, H-5'), 7.85 and 7.92 (d, *J* = 6.0 Hz, 1H each, H-2 and 2'), 10.61 (brs, 2H each, 2×-OH); $^{13}$C NMR (75.5 MHz, DMSO-$d_6$): δ 17.9, 110.5, 117.3, 117.4, 121.5, 126.8, 129.5, 136.1, 138.9, 146.8, 154.2, 154.3, 154.5, 184.9; MS *m/z* 336 ($M^+$). Anal. Calcd for $C_{19}H_{12}O_6$: C, 67.84; H, 3.59. Found: C, 67.82; H, 3.60.

**6,8'-Methylene-*bis*(7-hydroxychromone), 23**: Elution with $CHCl_3$/MeOH (94:6) gave **23** (26%); m.p.>300°C; UV nm (MeOH): 306, 252, 211 nm; IR $cm^{-1}$(KBr): 3098, 1628; $^1$H NMR (300 MHz, DMSO-$d_6$): δ 4.12 (s, 2H, -$CH_2$-),6.10 and 6.17 (d, *J*= 5.9 Hz, 1H each, H-3 and 3'), 7.07 (d, *J* = 8.7 Hz, 1H, H-6'), 7.17 (s, 1H, H-8), 7.89 (d, *J* = 8.7 Hz, 1H, H-5'), 7.99 (s, 1H, H-5), 8.03 and 8.07 (d, *J*= 5.9 Hz, 1H each, H-2 and 2'), 10.62 (brs, 2H each, 2×-OH); $^{13}$C NMR (75.5 MHz, DMSO-$d_6$): δ 17.7, 103.2, 111.0, 114.1, 114.2, 115.2, 115.9, 123.1, 130.2, 155.4, 155.8, 163.0, 164.0, 185.1, 185.2; MS *m/z* 336 ($M^+$). Anal. Calcd for $C_{19}H_{12}O_6$: C, 67.84; H, 3.59. Found: C, 67.87; H, 3.64.

**8,8'-Methylene-*bis*(7-hydroxychromone), 24**: Elution with $CHCl_3$/MeOH (94:6) in the later fractions gave **24** (42%); m.p.>300°C; UV nm (MeOH): 307, 252, 211 nm; IR $cm^{-1}$(KBr): 3099, 1630; $^1$H NMR (300 MHz, DMSO-$d_6$): δ 4.27 (s, 2H, -$CH_2$-),6.09 (d, *J*= 5.8 Hz, 2H, H-3 and 3'), 6.83 (d, *J* = 8.7 Hz, 2H, H-6 and 6'), 7.70 (d, *J* = 8.7 Hz, 2H, H-5 and 5'), 7.98 (d, *J*= 5.8 Hz, 2H each, H-2 and 2'), 10.51 (brs, 2H each, 2×-OH); $^{13}$C NMR (75.5 MHz, DMSO-$d_6$): δ 17.5, 110.9, 114.1, 115.3, 116.1, 130.5, 155.6, 162.5, 163.9, 185.4; MS *m/z* 336 ($M^+$). Anal. Calcd for $C_{19}H_{12}O_6$: C, 67.84; H, 3.59. Found: C, 67.83; H, 3.62.

**6,6'-Methylene-*bis*(7-hydroxychromone), 25**: Elution with $CHCl_3$/MeOH (90:10) gave **25** (16%); m.p. > 300°C; UV nm (MeOH): 307, 252, 211; IR $cm^{-1}$(KBr): 3110, 1635; $^1$H NMR (300 MHz, DMSO-$d_6$): δ 4.17 (s, 2H, -$CH_2$-), 6.14 (d, *J* = 5.8 Hz, 2H, H-3 and 3'), 6.98 (s, 2H, H-8 and 8'), 7.92 (s, 2H, H-5 and 5'), 7.96 (d, *J* = 5.8 Hz, 2H, H-2 and 2'), 10.73 (brs, 2H, 2×-OH); $^{13}$C NMR (75.5 MHz, DMSO-$d_6$) δ 17.9, 103.2, 114.0, 115.9, 122.9, 130.3, 156.1, 162.8, 163.6, 184.9; MS *m/z* 336 ($M^+$). Anal. Calcd for $C_{19}H_{12}O_6$: C, 67.84; H, 3.59. Found: C, 67.80; H, 3.57.

**General procedure for the synthesis of methylene bis derivatives 27 and 29 from 3- and 4-hydroxycoumarin**

A mixture of 3- or 4-hydroxycoumarin (10 mmol), anhydrous $AlCl_3$ (25 mmol) and freshly distilled $CS_2$ (15 mL) was stirred for 30 min under an inert atmosphere and methoxyacetyl chloride (15 mmol) was added to it. The contents were stirred for another 30 min at RT and then refluxed for 2 h. The apparatus was assembled for downward distillation and $CS_2$ was removed completely. The remaining contents were added to ice-water mixture and the solid that precipitated was collected by filtration and crystallised from ethanol to give a white solid of compound **27** and **29** respectively.

**4,4'-Methylene-*bis*(3-hydroxycoumarin), 27**: Yield 53%; m.p. 265-266°C; IR $cm^{-1}$(KBr): 3450, 1680; $^1$H NMR (250 MHz, DMSO-$d_6$): δ 3.82 (s, 2H, -$CH_2$-), 6.56 (brs, 2H, 2×-OH), 7.30 (m, 2H), 7.32 (m, 2H), 7.35 (m, 4H); $^{13}$C NMR (62.9 MHz, DMSO-$d_6$): δ 20.6, 114.6, 116.6, 127.6, 129.7, 131.6, 135.3, 140.4, 142.1, 159.7; MS *m/z* 336 ($M^+$). Anal. Calcd for $C_{19}H_{12}O_6$: C, 67.84; H, 3.59. Found: C, 67.94; H, 3.63.

**3,3'-Methylene-*bis*(4-hydroxycoumarin), 29**: Yield 51%; m.p. 288°C; IR $cm^{-1}$(KBr): 3500, 1657; $^1$H NMR (250 MHz, DMSO-$d_6$): δ 3.85 (s, 2H, -$CH_2$), 7.37 (m, 2H), 7.39 (dd, 2H, *J* = 2.0, 8.1 Hz), m, 2H), 7.60 (m, 2H), 8.01 (dd, 2H, *J* = 1.5, 8.0 Hz), 11.33 (brs, 2H, 2×-OH); $^{13}$C NMR (62.9 MHz, DMSO-$d_6$): δ 20.1, 102.7, 116.8, 120.2, 124.1, 124.6, 132.4, 153.2, 166.1, 169.7; MS *m/z* 336 ($M^+$). Anal. Calcd for $C_{19}H_{12}O_6$: C, 67.84; H, 3.59. Found: C, 67.89; H, 3.62.

**Conclusion**

An efficient Lewis acid promoted synthesis of methylene α- and γ-*bis*-benzopyrones was achieved wherein the linking of two benzopyrone moieties was *via* a methylene bridge on their benzene ring. The reaction proceeded without any solvent system and produced isomeric methylene bis derivatives of chromanones, coumarin and chromones in good yields. Earlier reported formation of furanocoumarins in case of Fries rearrangement on 5-, 6- and 7-methoxyacetyl coumarins due to intramolecular rearrangement was not observed in case of corresponding reactions on chromanones and chromones, which gave only isomeric methylene-*bis*-derivatives by an intermolecular rearrangement in good yields. Friedel-Crafts reaction on 3- and 4-

hydroxycoumarins led to the formation of methylene *bis*-derivatives.

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