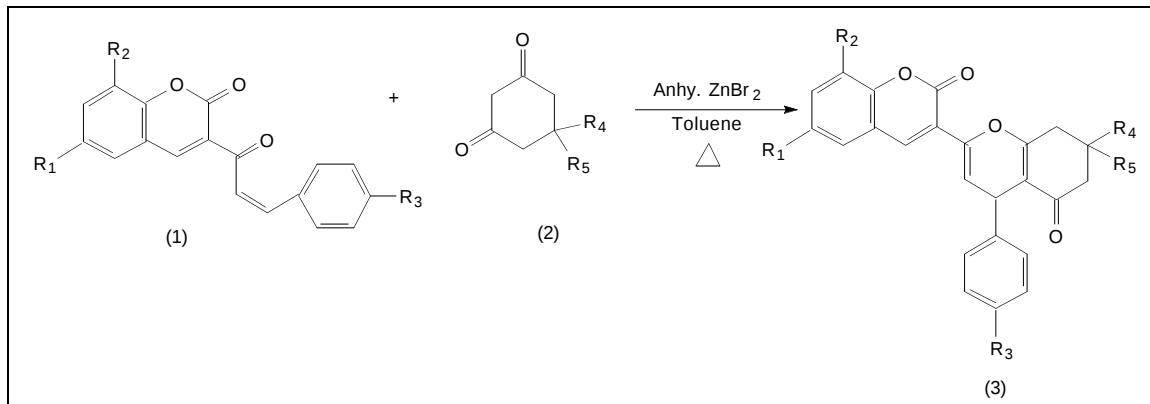


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Anhydrous zinc bromide catalysed reactions of arylidene-3-acetyl coumarins (**1a-c**) and 5,6-benzoanalogs of arylidene 3-acetyl coumarins (**4a,4b**) with 1,3-cyclohexanedione gives 3-(4-aryl-5-oxo-5,6,7,8-tetrahydro-4H-chromen-2-yl)-2H-chromen-2-ones (**3a, 3c**) and 5,6-benzoanalogs of 3-(4-aryl-5-oxo-5,6,7,8-tetrahydro-4H-chromen-2-yl)-2H-chromen-2-one (**5a,5b**). Under similar conditions arylidene-3-acetyl coumarins (**1a, 1b,1d, 1e, 1f**) and 5,6-benzoanalogs of arylidene 3-acetyl coumarin (**4b**) react with 5,5-dimethyl-1,3-cyclohexanedione (dimedone) yielding 3-(4-aryl-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromen-2-yl)-2H-chromen-2-ones (**3d-3h**) and the 5,6-benzoanalogs of 3-(4-aryl-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromen-2-yl)-2H-chromen-2-one (**5c**).

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INTRODUCTION

There is a continuous interest in the synthesis of benzopyrans, since they possess antijuvenile hormone activity [1], antianaphylactic activity in trachea [2] and are found to be antiallergic [3,4], antiinflammatory [5], and anticancer [6] agents and also helpful in diabetic complications [7]. In continuation of our earlier work [8-10] on the synthesis of benzopyrans, we report here a new one step efficient synthesis of 3-(4-aryl-5-oxo-5,6,7,8-tetrahydro-4H-chromen-2-yl)-2H-chromen-2-ones in good yields (65-78%).

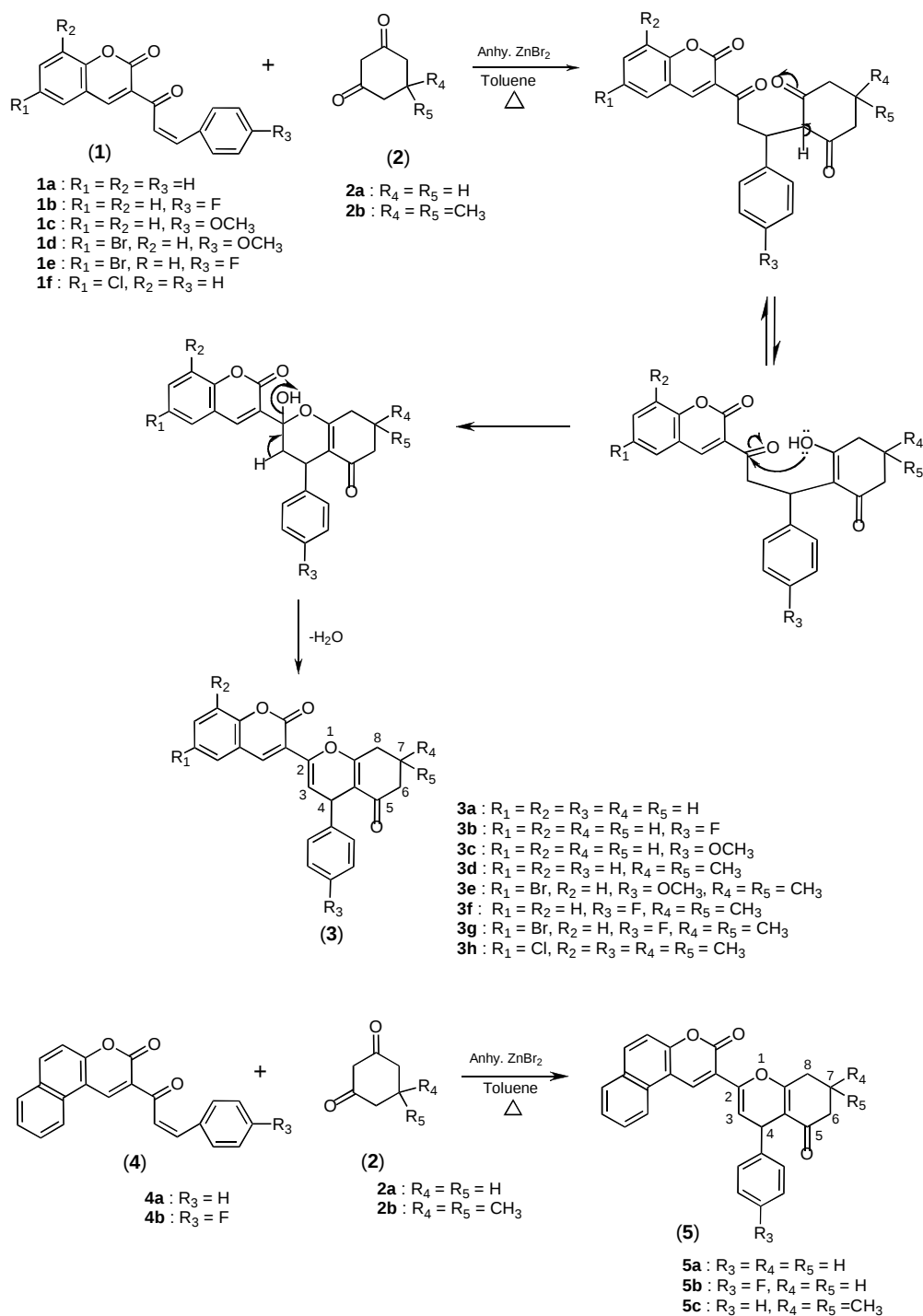
The synthesis utilizes the condensation of cyclohexane-1,3-dione and 5,5-dimethyl-1,3-cyclohexanedione with different chalcones (**1a-1f**) derived from 3-acetyl coumarins and the corresponding 5,6-benzo derivatives (**4a-c**) of 3-acetyl coumarins.

The formation of these compounds (**3-5**) may be explained by the initial formation of a 1:1 adduct which presumably underwent cyclisation in the presence of ZnBr_2 catalyst as shown in Scheme-1. The Lewis acid, zinc bromide will effectively polarize the carbon-oxygen double bond by coordinating the oxygen to the electron deficient Zn in ZnBr_2 . Due to

this carbonyl carbon will become more positively charged and is easily attacked by nucleophilic enolic hydroxy group to give the cyclised compound **3** and **5**. During the above reaction there is no formation of Michael adducts between cyclic 1,3-diketones and chalcones. This is confirmed from analytical and spectral data.

The infrared spectra of the newly prepared chromen derivatives (**3-5**) are consistent with their structures. They exhibit strong carbonyl bands at $1717\text{-}1741\text{ cm}^{-1}$ for lactone and $1656\text{-}1670\text{ cm}^{-1}$ for ketone respectively. The C-O stretching is observed at $1205\text{-}1213\text{ cm}^{-1}$. The ^1H nmr spectrum of **3a** exhibited besides the usual signals, two characteristic doublets at δ 4.47 (1H, $J = 6$ Hz, $\text{C}_4\text{-H}$) and at δ 6.66 (1H, $J = 3$ Hz, $\text{C}_3\text{-H}$). Its mass spectrum gave a peak at m/z 370 (M^+). The ^1H nmr spectrum of **3d** showed besides usual signals, the protons at C_6 as an AB quartet at δ 2.14 – 2.33. The appearance of AB quartet clearly showed that two methylene protons are non equivalent or not identical. The anisotropic effect of the adjacent carbonyl is responsible for their difference. The protons of C_4 and C_5 have appeared as doublets at δ 4.45 (d, 1H, $J = 6$ Hz, $\text{C}_4\text{-H}$) and 6.66 (d, 1H, $J = 6$ Hz, $\text{C}_5\text{-H}$).

Scheme-1



The ^{13}C nmr spectrum of **3d** showed two different signals for gemdimethyls at δ 28.0 and 29.4 respectively indicating that they are in different planes. Lactone carbonyl carbon appeared at δ 165.5 and the carbonyl carbon appeared at δ 197.2. The other carbon signals appeared in the usual region.

EXPERIMENTAL

General. Melting points were determined by POLMAN melting point apparatus (Model No. MP-96) and are uncorrected. The IR spectra (ν_{max} cm^{-1}) were recorded on Perkin-Elmer spectrophotometer. The 1H nmr, ^{13}C nmr spectra were recorded on 300 MHz Bruker-Avance instrument using

TMS as an internal standard. The mass spectra were scanned on Perkin-Elmer SCIEX API-2000 instrument. The purity of all compounds was established by TLC analysis using Merck precoated silica gel 60F₂₅₄ plates (0.2 mm thickness).

General Procedure for synthesis of 3-(4-aryl-5-oxo-5,6,7,8-tetrahydro-4H-chromen-2-yl)-2H-chromen-2-ones (3a-g and 5a-c). Compound **1** or **4** (0.01 mole) was dissolved in Toluene (30 ml) at 25°C, compound **2** (0.01 mole) and zinc bromide (0.003 mole) were added to the solution. The resulting suspension was heated to reflux (110 °C). The byproduct, water was removed azeotropically using Dean stark apparatus. The reflux was continued till the reaction gets completed (~3 hours). Toluene was removed by distillation under reduced pressure and recrystallised the product from isopropyl alcohol.

3-(5-Oxo-4-phenyl-5,6,7,8-tetrahydro-4H-chromen-2-yl)-2H-chromen-2-one (3a) was obtained by the reaction of **1a** with **2a** in 70% yield, mp 238-240 °C; ir (potassium bromide): 1730 (C=O, lactone), 1656 (C=O), 1208 cm⁻¹; ¹H nmr (DMSO-*d*₆): 2.05 (m, 2H, CH₂), 2.34 (m, 2H, CH₂), 2.78 (m, 2H, CH₂), 4.47 (d, 1H, J = 6 Hz, C₄-H, pyran), 6.66 (d, 1H, J = 6 Hz, C₃-H, pyran), 7.19-7.72 (m, 9H, Ar-H), 8.44 (s, 1H, C₄-H of coumarin); ms: (12.5 eV, ESI) m/z 370 (molecular ion); *Anal.* Calcd. for C₂₄H₁₈O₄ (370.4): C, 77.83; H, 4.90. Found: C, 77.78, H, 4.80.

3-(4-(4-Fluorophenyl)-5-oxo-5,6,7,8-tetrahydro-4H-chromen-2-yl)-2H-chromen-2-one (3b) was obtained by the reaction of **1b** with **2a** in 74% yield, mp 231-233 °C; ir (potassium bromide): 1717 (C=O, lactone), 1670 (C=O), 1208 cm⁻¹; ¹H nmr (DMSO-*d*₆): 2.02 (m, 2H, CH₂), 2.32 (m, 2H, CH₂), 2.77 (m, 2H, J = 6 Hz, CH₂), 4.49 (d, 1H, J = 6 Hz, Pyran), 6.64 (d, 1H, J = 6 Hz, Pyran), 7.08 – 7.69 (m, 7H, Ar-H), 7.88 (d, 1H, Ar-H), 8.43 (s, 1H, C₄-H of coumarin); *Anal.* Calcd. for C₂₄H₁₇FO₄ (388.39): C, 74.22; H, 4.41. Found: C, 74.15; H, 4.38.

3-(4-(4-Methoxyphenyl)-5-oxo-5,6,7,8-Tetrahydro-4H-chromen-2-yl)-2H-chromen-2-one (3c) was obtained by the reaction of **1c** with **2a** in 65% yield, mp 132-134 °C; ir (potassium bromide): 1732 (C=O, lactone), 1657 (C=O), 1280 cm⁻¹; ¹H nmr (CDCl₃): 2.07 (m, 2H, CH₂), 2.38 (m, 2H, CH₂), 2.71 (m, 2H, CH₂), 3.76 (s, 3H, CH₃), 4.52 (d, 1H, J = 6 Hz, pyran), 6.82 (d, 2H, J = 9 Hz, Ar-H), 6.89 (d, 1H, J = 5.14 Hz, pyran), 7.23 (d, m, 4H, Ar-H), 7.6 – 7.66 (m, 1H, Ar-H), 7.75 (s, 1H, Ar-H), 8.47 (s, 1H, C₄-H of coumarin); *Anal.* Calcd. for C₂₅H₂₀O₅ (400.42): C, 74.98; H, 5.03. Found: C, 75.12; H, 4.92.

3-(7,7-Dimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydro-4H-chromen-2-yl)-2H-chromen-2-one (3d) was obtained by the reaction of **1a** with **2b** in 75% yield, mp 140-142 °C; ir (potassium bromide): 1738.8 (C=O, lactone), 1656 (C=O), 1207 cm⁻¹; ¹H nmr (DMSO-*d*₆): 1.05 (s, 3H, CH₃), 1.10 (s, 3H, CH₃), 2.16 (ABq, 2H, -COCH₂), 2.69 (s, 2H, CH₂), 4.45 (d, 1H, J = 6 Hz, pyran), 6.66 (d, 1H, J = 6 Hz, pyran), 7.18 – 7.85 (m, 9H, Ar-H), 8.44 (s, 1H, C₄-H of coumarin); ¹³C nmr (DMSO-*d*₆) 28.0, 29.4, 32.7, 34.8, 41.2, 51.0, 111.9, 115.8, 116.1, 116.7, 118.7, 119.5, 125.7, 130.0, 130.3, 130.4, 133.4, 139.4, 141.4, 141.9, 153.4, 158.3, 160.1, 163.3, 165.5, 197.2; ms: m/z 398 (molecular ion); *Anal.* Calcd. for C₂₆H₂₂O₄ (398.45): C, 78.37; H, 5.56. Found: C, 78.28; H, 5.46.

6-Bromo-3-(4-(4-methoxyphenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromen-2-yl)-2H-chromen-2-one (3e) was obtained by the reaction of **1d** with **2b** in 72% yield, mp 178-180 °C; ir (potassium bromide): 1741 (C=O, lactone), 1656 (C=O), 1205 cm⁻¹; ¹H nmr (DMSO-*d*₆): 1.04 (s, 3H, CH₃), 1.09 (s, 3H, CH₃), 2.29 (ABq, 2H, J = 18 Hz, -COCH₂), 2.58 (s, 2H,

CH₂), 3.7 (s, 3H, OCH₃), 4.39 (d, 1H, J = 6 Hz, pyran), 6.64 (d, 1H, J = 6 Hz, Pyran), 6.85 (d, 2H, J = 6 Hz, Ar-H), 7.14 (d, 2H, J = 9Hz, Ar-H), 7.39 (d, 1H, J = 9Hz, Ar-H), 7.78 (d, 1H, J = 9 Hz, Ar-H), 8.12 (d, 1H, J = 2.1 Hz, Ar-H), 8.41 (s, 1H, C₄-H of coumarin); *Anal.* Calcd. for C₂₇H₂₃BrO₅ (507.37): C, 63.91; H, 4.56. Found: C, 63.69; H, 4.60.

3-(4-(4-Fluorophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromen-2-yl)-2H-chromen-2-one (3f) was obtained by the reaction of **1b** with **2b** in 72% yield, mp 196-198 °C. ir (potassium bromide): 1735 (C=O, lactone), 1666 (C=O), 1209 cm⁻¹. ¹H nmr (DMSO-*d*₆): 1.04 (s, 3H, CH₃), 1.09 (s, 3H, CH₃), 2.22 (ABq, 2H, J = 15 Hz, COCH₂), 2.68 (s, 2H, CH₂), 4.48 (d, 1H, J = 6 Hz, pyran), 6.64 (d, 1H, J = 3 Hz, pyran), 7.09 – 7.68 (m, 7H, Ar-H), 7.87 (d, 1H, J = 6 Hz, Ar-H), 8.45 (s, 1H, C₄-H of coumarin); *Anal.* Calcd. for C₂₆H₂₁FO₄ (416.44): C, 74.98; H, 5.08. Found: C, 75.11; H, 5.10.

6-Bromo-3-(4-(4-fluorophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromen-2-yl)-2H-chromen-2-one (3g) was obtained by the reaction of **1e** with **2b** in 76% yield, mp 175-177 °C; ir (potassium bromide): 1737 (C=O, lactone), 1661 (C=O), 1206 cm⁻¹. ¹H nmr (CDCl₃): 1.05 (s, 3H, CH₃), 1.08 (s, 3H, CH₃), 2.25 (ABq, 2H, J = 18 Hz, -COCH₂), 2.56 (s, 2H, CH₂), 4.53 (d, 1H, J = 6 Hz, pyran), 6.88 (d, 1H, J = 6 Hz, pyran), 7.19 – 7.29 (m, 4H, Ar-H), 7.59 – 7.68 (m, 3H, Ar-H), 8.41 (s, 1H, C₄-H of coumarin); *Anal.* Calcd. for C₂₆H₂₀BrFO₄ (495.35): C, 63.04; H, 4.07. Found: C, 63.09; H, 4.07.

6-Chloro-3-(7,7-dimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydro-4H-chromen-2-yl)-2H-chromen-2-one (3h) was obtained by the reaction of **1f** with **2b** in 70% yield, mp 190-192 °C; ir (potassium bromide): 1736 (C=O, lactone), 1205 cm⁻¹. ¹H nmr (CDCl₃): 1.09 (s, 3H, CH₃), 1.15 (s, 3H, CH₃), 2.26 (ABq, 2H, -COCH₂), 2.58 (s, 2H, CH₂), 4.54 (d, 1H, pyran), 6.9 (d, 1H, pyran), 7.28 – 7.64 (m, 7H, Ar-H), 8.04 (s, 1H, Ar-H), 8.42 (s, 1H, C₄-H of coumarin); *Anal.* Calcd. for C₂₆H₂₁ClO₄ (432.91): C, 72.14; H, 4.89. Found: C, 72.20; H, 4.81.

2-(5-Oxo-4-phenyl-5,6,7,8-tetrahydro-4H-chromen-2-yl)-3H-benzof[*f*]chromen-3-one (5a) was obtained by the reaction of **4a** with **2a** in 65% yield, mp 246-248 °C; ir (potassium bromide): 1730 (C=O, lactone), 1656 (C=O), 1209 cm⁻¹; ¹H nmr (CDCl₃): 2.05 (m, 2H, CH₂), 2.33 (m, 2H, CH₂), 2.90 (m, 2H, -COCH₂), 4.50 (d, 1H, J = 6 Hz, Pyran), 6.72 (d, 1H, J = 6 Hz, pyran), 7.16-7.29 (m, 5H, Ar-H), 7.59 – 7.83 (m, 3H, Ar-H), 8.09 (d, 1H, J = 9 Hz, Ar-H), 8.23 (d, 1H, J = 9 Hz, Ar-H), 8.66 (d, 1H, J = 8.7 Hz, Ar-H), 9.07 (s, 1H, C₄-H of coumarin); *Anal.* Calcd. for C₂₈H₂₀O₄ (420.46): C, 79.98; H, 4.79. Found: C, 79.92; H, 4.70.

2-(4-(4-Fluorophenyl)-5-oxo-5,6,7,8-tetrahydro-4H-chromen-2-yl)-3H-benzof[*f*]chromen-3-one (5b) was obtained by the reaction of **4b** with **2a** in 73% yield, mp 238-240 °C; ir (potassium bromide): 1730 (C=O, lactone), 1655 (C=O), 1217 cm⁻¹; ¹H nmr (CDCl₃): 2.12 (m, 2H, CH₂), 2.44 (m, 2H, CH₂), 2.84 (m, 2H, CH₂), 4.62 (d, 1H, J = 6 Hz, pyran), 6.94 (d, 1H, J = 6 Hz, pyran), 7.30 (m, 2H, Ar-H), 7.50-7.98 (m, 6H, Ar-H), 8.05 (d, 1H, Ar-H), 8.37 (d, 1H, Ar-H), 8.93 (s, 1H, C₄-H of coumarin); *Anal.* Calcd. for C₂₈H₁₉FO₄ (438.45): C, 76.70; H, 4.36. Found: C, 76.40, H, 4.27.

2-(7,7-Dimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydro-4H-chromen-2-yl)-3H-benzof[*f*]chromen-3-one (5c) was obtained by the reaction of **4a** with **2b** in 78% yield, mp 208-210°C; ir (potassium bromide): 1721 (C=O, lactone), 1655 (C=O), 1213 cm⁻¹. ¹H nmr (CDCl₃): 1.13 (s, 3H, CH₃), 1.19 (s, 3H, CH₃), 2.27 (ABq, 2H, -COCH₂), 2.56 (s, 2H, CH₂), 4.59 (d, 1H, J = 5.4 Hz, pyran), 6.96 (d, 1H, J = 5.4 Hz, pyran), 7.26 – 7.75 (m, 7H,

Ar-H), 7.93 – 8.02 (m, 3H, Ar-H), 8.35 (d, 1H, Ar-H), 8.9 (s, 1H, C₄-H of coumarin); *Anal.* Calcd. for C₃₀H₂₄O₄ (448.51): C, 80.33; H, 5.39. Found: C, 80.26, H, 5.30.

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