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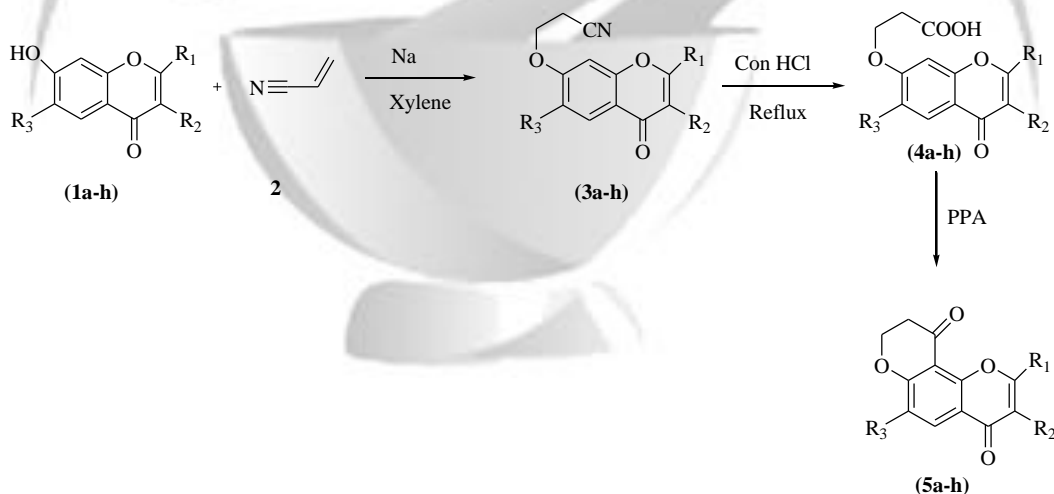
Synthesis of 8, 9 dihydro-7h-benzo [2, 3-h] chromene-4, 10-diones

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ABSTRACT

Michael reaction of 7-hydroxy chromone (1a-h) react with acrylonitrile a pinch of sodium gives 8, 9 dihydro-7H benzo [2, 3-h] chromene-4, 10-diones(5a-h) in good yields.



Keywords: Michael reaction, Acrylonitrile, Sodium, 7-Hydroxychromones.

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INTRODUCTION

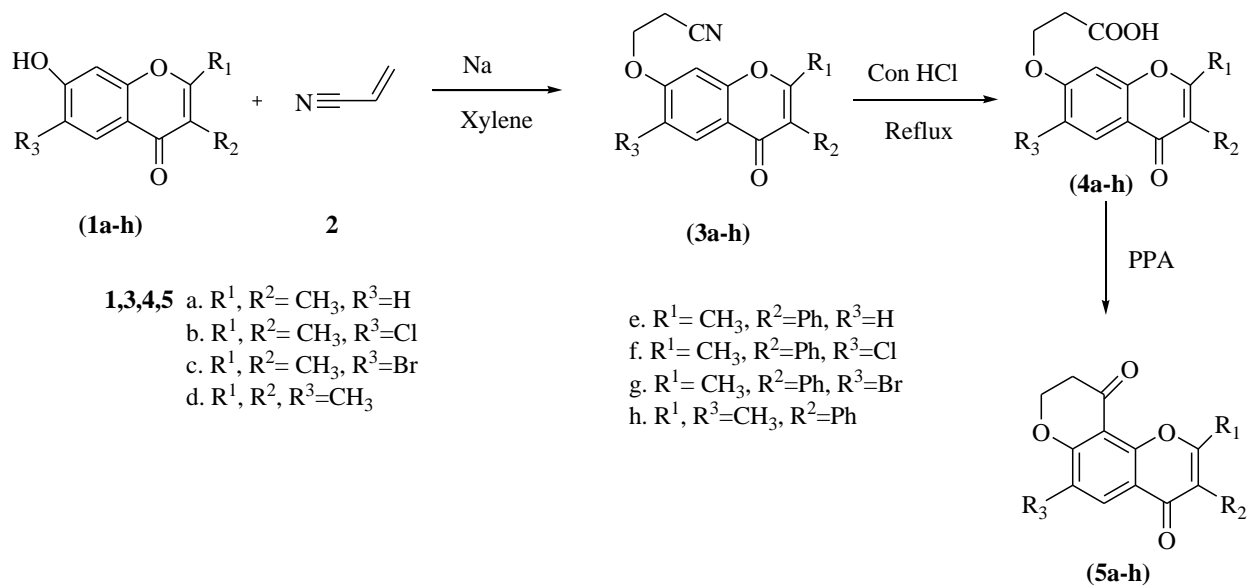
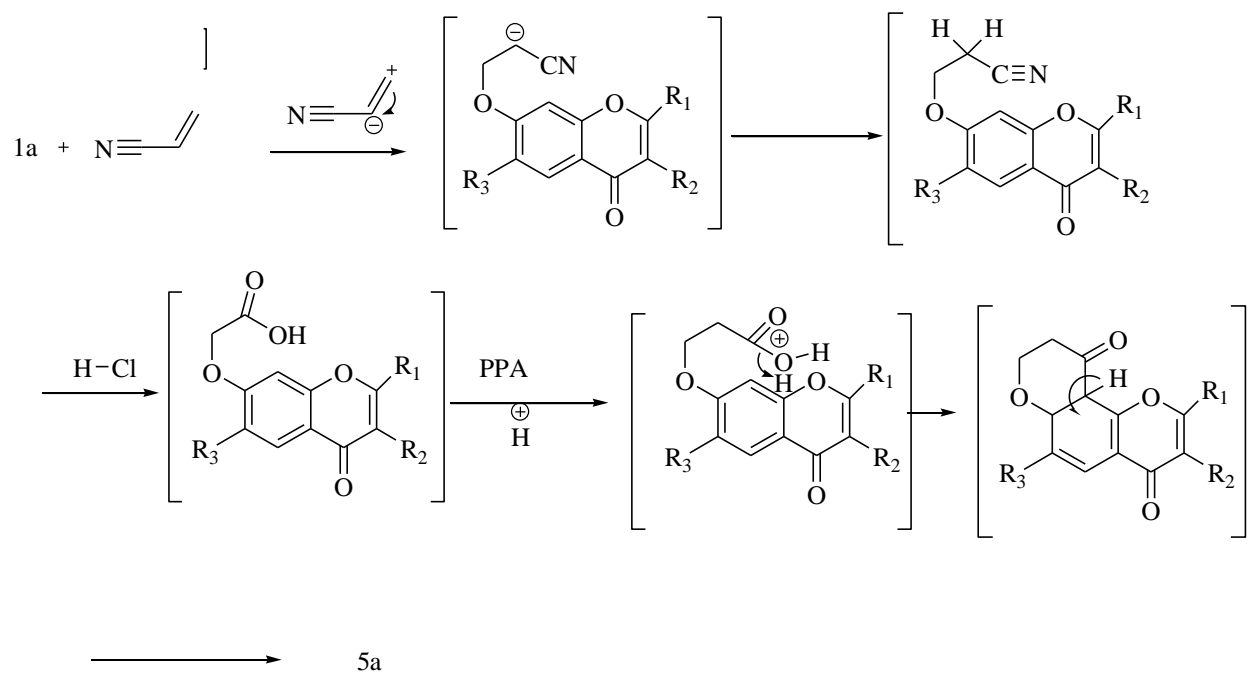
Natural and synthetic heterocyclic compounds play an important role in both drug discovery and chemical biology [1-5]. The heterocyclic are mainly of the classes of alkaloids, chromones, flavones, Isoflavones etc. The natural heterocyclics are plant secondary metabolites, which protect the plant from attack by pathogens, fungi, bacteria and insects. Several synthetic analogs of these heterocyclics show different bioactivity [6-8]. More than 50% of the drug used in the modern medicine is either derived from synthetic or natural heterocyclic systems.

Substituted chromanones and chromenes show a variety of biological activity, such as dopamine antihypertensive, ATP sensitive potassium channel openers antitumor and gastro protective agent [9,10]. In the present study new pyridyl fused chromenes are synthesized by the Michael reaction involves the reaction of a hydroxyl group and sodium metal in Acrylonitrile to give 8,9 dihydro-7H benzo [2, 3-h] chromene-4, 10-diones.

RESULTS AND DISCUSSIONS

Synthesis of 8,9 dihydro-7H-benzo [2,3-h] 2, 3 di methyl chromene-4, 10-diones (5a-h)
Michael reaction¹⁵⁻²⁰ of 7-hydroxychromones(**1a-h**),equimolar amount of 7-hydroxychromone (**1a**), and acrylonitrile, and a pinch of sodium was reflux at 95-105 °C for 30 hours by a Michael reaction to give a 8,9 di hydro-7H-benzo[2,3-h] 2,3 di methyl chromene-4, 10-diones(**5a**). Similarly (**5b-h**) were prepared. In its IR **5a** C=O of chromone appeared at 1620 cm⁻¹, C=O pyran ring appeared 1650 cm⁻¹ UV (MeOH) spectrum showed bands at recorded 302 nm (log ε 3.9), 289 nm (log ε 4.0), 245 nm (log ε 4.3). In the ¹H NMR (200 MHz CDCl₃) spectrum recorded in the 8-OCH₂ group of the new ring system appeared as doublet 5.15 (J=1.0 Hz) due to allylic coupling with C₁₀. These signals suggest are from the original 2, 3 dimethylchromone moiety. The C₂-CH₃, C₃-CH₃ protons appeared as a singlet at 2.5, 2.1 C₅-H appeared as doublet at 8.19 (J=9.0 Hz) and C₆-H appeared as a doublet at 6.92 (J=9.0 Hz). The structures (**5b-h**) were conformed by analytical and spectral data.

The mechanic pathway of (**1a-5a**) is shown in scheme 2. **1a** under the reflux condition of the Michael reaction generates, which react with the formyl group of the 2, 3 dimethyl chromone to give an Intermediate. The intra molecular nucleophilic cyclization of the 7-OH of 2,3 dimethyl chromone leads to cyclization of PPA and pyran ring formation the loss of water in presence of PPA gives rise to 8,9 dihydro-7H-benzo [2, 3-h] 2,3 dimethyl chromene-4, 10-diones (**5a**).

Scheme-1

Scheme-2


EXPERIMENTAL SECTION (5a-h):

General: - Melting points were determined in a sulfuric acid-bath and are uncorrected. IR spectra were recorded in KBr on a Shimadzu 435 spectrometer, ¹H NMR spectra on a Varian Gemini 200 MHz spectrometer with TMS as an internal standard and mass spectra on a Perkin Elmer Hitachi RDO-62 and MS-30 instrument.

General procedure for the synthesis of 8,9 dihydro-7H-benzo [2,3-h]2,3-dimethyl chromene-4,10-diones (5a-h). 7-hydroxychromones (**1a-h**) were synthesized by following literature methods.¹¹⁻¹⁵ 7-hydroxychromone (**1a**)(2 g), and acrylonitrile (**2**)(3ml), and a pinch of sodium was reflux at 95-105 °C for 30 hours by a Michael reaction. The resulting solution was poured into aq..Sodiumhydroxide solution (10%). The cooled reaction solution was when extracted with ethyl acetate and dried the pale yellow solid precipitates reflux with Con. Hydrochloric acid for 1 hour. The cooled reaction solution was extracted with ethyl acetate then ethyl acetate solution washed with sodium bicarbonate solution and water then dried and distilled the solvent pale yellow solid cyclization with PPA for 24 hours under stirring condition at room temperature then extract with ethyl acetate and washed with water dried and solvent removed by the distillation and product column chromatography and elution with petroleum ether ,ethyl acetate (9:1) to quantitatively 8,9 dihydro-7H-benzo[2,3-h] chromene-4, 10-diones(**5a**),(1.5 g), 65-75% yield mp 176 °C Similarly (**5b-h**) were prepared.

i) 8, 9 Dihydro-7H-benzo [2,3-h]2,3dimethylchromene-4,10-dione(5a):mp.176 °C, yield 75%. IR: (KBr); (C=O chromone) 1620cm⁻¹, (C=O pyran ring) 1650.2cm⁻¹; UV :(MeOH); 302 nm, (log ε 3.8) 289 nm. (log ε 4.0), 245 nm (log ε 4.2).¹H NMR: (200 MHz CDCl₃): δ 2.5 (H-2, s); δ 2.1 (H-3, s); δ 8.19 (H-5, d, J = 9Hz); δ 6.92 (H-6, d, J = 9Hz); δ 5.15 (OCH₂, s, J = 1.0 Hz); δ 7.77 (H-10, bs, J = 9 Hz).¹³C NMR: δ 65 (OCH₂); 132.31 (C-9); 196.9 (C-10); 174.91 (C-4); 158.55(C-6a); 153.21(C-10b); 151.5(C-2); 125.56(C-3); 121.1(C-4a); 122.8(C-5); 108(C-6); 115.01(C-10a); 21.5 C2-CH₃; 18.3 C-3-CH₃.
Mass (EIMS): M⁺ m/z 244, 243(M-1), 229,215,201,191.

ii) 8,9 Dihydro-7H-benzo [2,3-h] 6-chloro-2,3-dimethyl chromene-4, 10-dione (5b)
mp.175 °C, yield 75%. IR: (KBr); (C=O chromone) 1626cm⁻¹, (C=O pyran ring) 1655.8cm⁻¹
UV :(MeOH); 298nm, (log ε 5.2) 246nm (log ε 4.7)
¹H NMR: (200 MHz CDCl₃): δ 2.59 (H-2, s); δ 2.21 (H-3, s); δ 8.27 (H-5, d J = 9Hz); δ 5.05 (OCH₂, s, J = 1.0 Hz); δ 7.62 (H-10, bs, J = 9 Hz). ¹³C NMR: δ 65.55 (OCH₂); 133.7 (C-9); 196.9 (C-10); 175.4 (C-4); 157.5 (C-6a); 154.3 (C-10b); 152.1 (C-2); 126.5(C-3) 119.4 (C-4a); 135.55(C-5); 22.85 C2-CH₃; 18.9 C-3-CH₃.
Mass (EIMS): M⁺ m/z 278.5, 279.5 (M+1) 253, 229, 217, 205, 191

iii) 8,9 Dihydro-7H-benzo [2, 3-h] 6-bromo-2,3-dimethyl chromene-4, 10-dione (5c)
mp.179 °C, yield 76%. IR (KBr): (C=O of chromone) 1625 cm⁻¹, (C=O pyran ring) 1652.2 cm⁻¹
UV :(MeOH); 292nm, (log ε 5.2) 245nm (log ε 4.7)

^1H NMR: (200 MHz CDCl_3): δ 2.13 (H-2, CH_3); δ 2.15 (H-3, CH_3 , s); δ 8.32 (H-5, d); δ 2.22 (H-6, d, J = 9 Hz); δ 5.18 (OCH_2 , s, J = 1.0 Hz); δ 7.69 (H-10, bs, J = 9 Hz).

^{13}C NMR: δ 64.95 (OCH_2); 130.2 (C-9); 196.5 (C-10); 173.91 (C-4); 156.55 (C-6a); 152.1 (C-10b); 151.9 (C-2); 125.9(C-3) 118.6 (C-4a); 124.96(C-5); 107.8(C-6); 114.51(C-10a); 20.1 C2- CH_3 ; 18.55 C-3- CH_3 .

Mass (EIMS): $\text{M}^{\bullet++}$ m/z 323, 325 (M+2), 243, 229, 7 205, 191.

iv) 8,9 Dihydro-7H-benzo [2, 3-h] 2,3,6 trimethyl chromene-4, 10-dione (5d)

mp 180 $^\circ\text{C}$, yield 75%. IR (KBr); (C=O chromone) 1621.6 cm^{-1} , (C=O pyran ring) 1655.2 cm^{-1}

UV : (MeOH); 290 nm, (log ϵ 5.2) 241nm (log ϵ 4.7)

^1H NMR: (200 MHz CDCl_3): δ 2.44 (CH_3 , H-2 s); δ 2.21 (H-3, s); δ 7.98 (H-5, d, J = 9 Hz); δ 1.8 (CH_3 H-6, d, J = 9 Hz); δ 4.95 (OCH_2 , J = 1.0 Hz);

^{13}C NMR: δ 65.02 (OCH_2); 131.25(C-9); 130.19 (C-10); 173.49 (C-4); 157.55(C-6a); 153.41 (C-10b); 151.9 (C-2); 124.33(C-3) 119.7 (C-4a); 124.56(C-5); 107.85(C-6); 114.44(C-10a); 23.55 CH_3 -C-6; 22.22 CH_3 -C-2; 18.45 CH_3 -C-3;

Mass (EIMS): $\text{M}^{\bullet+}$ m/z 258, 257 (M-1), 244, 229, 217, 205, 191

v) 8,9 Dihydro-7H-benzo [2,3-h] 2-methyl-3-phenyl chromene-4, 10-dione (5e)

mp.64 $^\circ\text{C}$, yield 70%. IR: 1633.1 cm^{-1} (C=O chromone); 1750.8 cm^{-1} (C=O pyran ring);

UV: (MeOH): 338 nm, (log ϵ 3.8) 289 nm. (log ϵ 4.0), 252 nm (log ϵ 4.2)

^1H NMR: (200 MHz): δ 2.5 (CH_3 , H-2 s); δ 8.28 (H-5, d, J = 9 Hz); δ 6.95(H-6, d, J = 9 Hz); δ 5.00 (OCH_2 -8 s); δ 7.41 (H-2', 6', m); δ 7.28 (H-3', 4', 5', m)

^{13}C NMR: OCH_2 δ 65.55; 131.90, 129.26 (C-9 & C-10); 174 (C-4); 156.85 (C-6a); 151 (C-10b); 153.5 (C-2); 130.2 (C-1'); 129.62 (C-4'); 128.8 (C-2', 6'); 128.49 (C-3', 5'); 126 (C-3); 119 (C-4a); 126.2 (C-5); 112 (C-6); 114.85 (C-10a), 20.25 CH_3 -C-2.

Mass (EIMS): $\text{M}^{\bullet+}$ m/z-306, 305 (M-1), 291, 263.

vi) 8,9 Dihydro-7H-benzo [2,3-h] 6- chloro- 2-methyl-3-phenyl chromene-4, 10-dione (5f)

mp.65 $^\circ\text{C}$ yield 70%. IR: 1633.1 cm^{-1} (C=O chromone); 1755.2 cm^{-1} (C=O pyran ring);

UV : (MeOH): 223 nm, (log ϵ 5.7) 229 nm. (log ϵ 4.7)

^1H NMR: (200 MHz): δ 2.45 (CH_3 , H-2, s); δ 8.22 (H-5, d, J = 9 Hz); δ 5.21 (OCH_2 -8 s). δ 7.52 (H-2', 6', m); δ 7.40 (H-3', 4', 5', m); ^{13}C NMR: δ OCH_2 δ 65.87; 131.99, 129.22 (C-9& C-10); 172.44 (C-4); 145.8 (C-6a); 151.33 (C-10b); 153.19 (C-2); 130.29(C-1'); 129.92 (C-4'); 128.18 (C-2', 6'); 128.99(C-3', 5'); 126.11 (C-3); 119.88 (C-4a); 126.28 (C-5); 112.55 (C-6); 114.18 (C-10a); 20.6 CH_3 -C-2;

Mass (EIMS): $\text{M}^{\bullet+}$ m/z 340.5 341.5 (M+1), 305, 291, 214.191.

vii) 8,9 Dihydro-7H-benzo [2, 3-h] 6-bromo-2-methyl-3-phenyl chromene-4, 10-dione (5g)

mp.69 $^\circ\text{C}$, yield 68%. IR: 1633.1 cm^{-1} (C=O chromone); 1753.8 cm^{-1} (C=O pyran ring);

UV : (MeOH): 301 nm, (log ϵ 5.7) 250 nm. (log ϵ 4.7)

^1H NMR: (200 MHz): δ 2.58 (CH_3 -2 s); δ 7.94 (H-5, d, J = 9 Hz); δ 5.27 (OCH_2 -8 s); δ 7.47 (H-2', 6', m); δ 7.39 (H-3', 4', 5', m). ^{13}C NMR: δ OCH_2 at δ 65.77; 131.29,128.45 (C-9 & C-10); 173.4(C-4);

157.28 (C-6a); 154.81 (C-10b); 152.15 (C-2); 130.29 (C-1'); 129.65 (C-4'); 127.2 (C-2', 6'); 127.89 (C-3', 5'); 126.15 (C-3); 118.9 (C-4a); 126.52 (C-5); 111.2 (C-6); 122.85 (C-10a); 20.95 CH₃-C-2; Mass (EIMS): M⁺ m/z 385 387 (M +2), 305, 291, 214.190.

viii) 8,9 Dihydro-7H-benzo [2,3-h] 2,6-dimethyl-3-phenyl chromene-4, 10-dione (5h)

mp.66 °C, yield 65%. IR: 1634 cm⁻¹ (C=O chromone); 1755 cm⁻¹ (C=O pyran ring);

UV :(MeOH): 293 nm, (log ε 5.7), 242 nm. (log ε 4.7)

¹H NMR: (200 MHz): δ 2.55 (H-2, s); δ 7.57 (H-5, d, J = 9Hz); δ 2.15 (CH₃-6, S); δ 5.18 (OCH₂-8 s). δ 7.59 (H-2', 6', m); δ 7.48 (H-3', 4', 5', m); ¹³C NMR: δ OCH₂ at δ 65.29; 130.19, 129.77 (C-9 & C-10); 196.4 (C-4); 157.1 (C-6a); 150.2 (C-10b); 153.75 (C-2); 131.52 (C-1'); 175.9 (C-4'); 127.2 (C-2', 6'); 128.99 (C-3', 5'); 125.6 (C-3); 121.4 (C-4a); 126.5 (C-5); 135.75 (C-6); 113.85 (C-10a); 21.95 CH₃-C-2;

Mass (EIMS): M⁺ m/z 319, 320 (M+1), 289.262, 190.

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