

Synthesis of New 8-Formyl-4-methyl-7-hydroxy Coumarin Derivatives

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ABSTRACT. 8-Formyl-4-Methyl-7-Hydroxy Coumarin Derivatives were synthesized via Penchem condensation followed by Duff's reaction. Treatment of this with N,N-di substituted cyano acetamides in the presence of piperidine afforded New 8-Formyl-4-Methyl-7-Hydroxy Coumarin Derivatives (**7a-o**). Their structures were characterized by IR, ^1H and ^{13}C NMR and Mass spectral and elemental analysis data.

Key words: N,N-di substituted cyano acetamides, Piperidine, Coumarin derivatives

INTRODUCTION

Coumarin is a pleasantly fragrant benzopyrone compound, found in many plants, notably in high concentration in the tonka bean (*Dipteryx odorata*), vanilla grass (*Anthoxanthum odoratum*), sweet woodruff (*Galium odoratum*), mullein (*Verbascum* spp.), sweet grass (*Hierochloa odorata*), Cassia cinnamon (*Cinnamomum aromaticum*) and sweet clover. Natural products with coumarin moiety and have wide range of biological activity. They are used as drugs, intermediates and pesticides.¹ They are found to have anti-coagulant, inflammatory microbial,² oxidant,³ HIV, allergic, cancer,⁴ proliferative and viral⁵ properties. 4-methyl-7-hydroxy coumarin has similar structure of Scopoletin, an alkaloid which is isolated from medicinal plant (*Gelsemium Seperiven*) has an anti-cancer activity. Recently 4-methyl-7-hydroxy coumarin has been reported to have anti skin-cancer activity.⁶

Coumarin has clinical medical value by itself, as an edema modifier. Coumarin and other benzopyrones, such as 5,6 benzopyrone, 1,2 benzopyrone, diosmin and others stimulate macrophages and degrade extracellular albumen, allowing faster resorption of edematous fluids.

Coumarin itself has no anticoagulant activity but is transformed into the natural anticoagulant called dicoumarol by a number of fungi species. This occurs as the result of the production of 4-hydroxycoumarin, then further (in the presence of naturally occurring formaldehyde) into the actual anticoagulant dicoumarol, a fermentation product and mycotoxin. This substance was responsible for the bleeding disease known historically as "sweet clover disease" in cattle eating moldy sweet clover silage.

EXPERIMENTAL

Materials and Methods

Melting points were determined on Buchi-540 melting point apparatus and are un-corrected. FT-IR spectra were recorded as KBr pellet on Nicolet-380 FT-IR instrument (Model Thermo Electron corporation-Spectrum one), ^1H and ^{13}C NMR (proton decoupled) spectra were recorded on Varian 300 MHz spectrometer using DMSO- d_6 and CDCl_3 as solvent. Mass spectra were recorded on Agilent triple quadrupole mass spectrometer equipped with turbo ion spray interface at 360 °C.

Synthesis of 4-Methyl-7-hydroxy Coumarin of **2**⁷

Concentrated sulfuric acid (20 mL) was added to a 100 mL round bottom flask and cooled to 0-5 °C in an ice bath. A solution of resorcinol (0.001 mol) in ethyl acetate (0.0015 mol) was added to sulfuric acid under constant stirring at 0-5 °C. The reaction mass was stirred over night at room temperature and poured in to crushed ice under vigorous stirring. An off-white solid obtained was filtered and recrystallised in ethanol. m.p: 180-182 °C; ^1H NMR (300MHz, CDCl_3): δ 2.49 (s, 3H, C4-CH₃), 6.31 (s, 1H, C3-H), 6.92 (d, 1H, C6-H, $J=9.0$ Hz), 6.94 (s, 1H, C8-H), 7.57 (d, 1H, C5-H, $J=9.0$ Hz); IR (KBr, ν max): 3423 (-OH), 1733 (-CO), 1555 (-C=C-) cm^{-1} .

Synthesis of 4-Methyl-7-hydroxy-8-formyl Coumarin **3**⁸

7-hydroxy-4-methyl-coumarin (**2**) (0.001 mol) was dissolved in glacial acetic acid (20 mL) and hexamethylene tetramine (0.003 mol) was added to the reaction mixture. Heated to 80-85 °C in a water bath for 6.0 hr. A hot mix-

ture of 5 mL water and 30 mL hydrochloric acid was added, kept for 30 min. and cooled to room temperature. It was extracted with diethyl ether. And on evaporation of ether, a pale yellow solid was obtained. Yield: 22%; m.p. 176-178 °C; ^1H NMR (300 MHz, CDCl_3): δ 2.44 (s, 3H, C4-CH₃), 6.22 (s, 1H, C3-H), 6.90-6.93 (d, 1H, C6-H, $J=9$ Hz), 7.73-7.76 (d, 1H, C5-H, $J=9$ Hz), 10.63 (s, 1H, HCO), 12.28 (s, 1H, OH); IR (KBr, ν max): 3442(-OH), 1742 (-CO), 1644(-CHO), 1594(-C=C-) cm^{-1} .

Synthesis of N,N-di substituted cyano acetamide Derivatives (6 a-o)^{9,10}

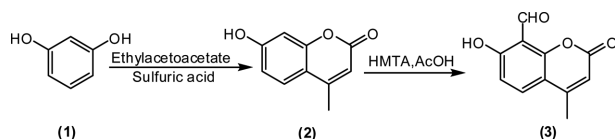
General procedure:

Amine (0.001 moles) was dissolved in 10 ml ethanol, 0.0012 moles of ethyl cyano acetate was added and stirred for 5.0 hr at reflux. Cooled the mass to 0-5 °C and filtered, which were used directly in the next step. Yields were varied from 60-70%.

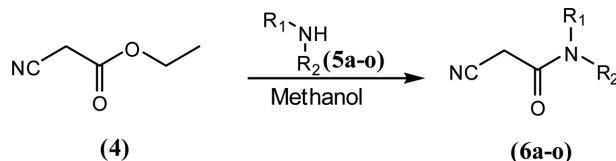
Synthesis of 7a-o by Knoevengel Condensation of 3 & 6a-o¹¹

General procedure:

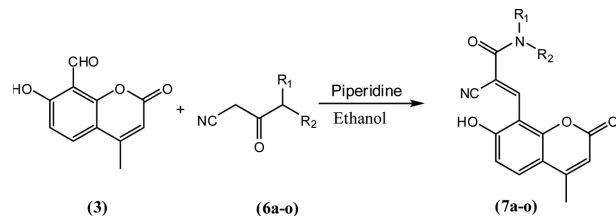
8-formyl-4-methyl-7-hydroxy Coumarin (3) (0.001 mol) was dissolved in 10mL ethanol containing N,N di substituted cyanoacetamide derivatives (6a-o) (0.001 mol) and catalytic amount of piperidine. Refluxed for 2.0 hr,



Scheme 1. Synthesis of 4-methyl-7-hydroxy-8-formyl coumarin.



Scheme 2. Synthesis of N,N-di substituted cyano acetamide derivatives (6 a-o).



Scheme 3. Synthesis of 7a-o by Knoevengel condensation of 3 & 6a-o.

cooled to 0-5 °C and filtered the solid. Pale yellow to orange red color solids were obtained. Yields varied from 50-60%.

SPECTRAL DATA

(E)-2-cyano-3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)-N-(1-(4-methoxyphenyl)ethyl) acryl amide (7a)

IR (KBr cm^{-1}): 3437 (-OH), 3275 (-NH), 2240 (-CN), 1729 (-CO, cyclic), 1624 (-CO), 1557 (-C=C-); ^1H NMR (DMSO- d_6): δ 11.8 (s, -OH), 8.9 (s, H, -NH), 8.5 (s, H, exocyclic CH=C), 6.9-7.2 (m, 4H, phenyl), 6.0-6.5 (m, 2H, coumarin ring), 5.0 (q, H, -CH-NH), 3.8 (s, 3H, -OCH₃), 2.45 (s, 3H, -CH₃), 1.5 (d, 3H, -CH₃); ^{13}C NMR (DMSO- d_6): δ 160.8 (C-2), 160 (C=O), 158.9 (C-1'), 155 (C-7), 153.4 (C-exocyclic), 153 (C-4), 146 (C-10), 133 (C-4'), 126.5 (C-3', C-5'), 125.2 (C-5), 118.2 (C-8), 115 (-CN), 114.0 (C-2', C-6', C-6), 112.5 (C-3), 112.0 (C-9), 103 (C-exocyclic), 56.1 (-OCH₃), 49.0 (C, -CH-NH), 21.5 (C, -CH₃), 19.5 (-CH₃ of C-4); MS: $m/z(M^++1)$ 405.4; Anal. Calcd for $\text{C}_{23}\text{H}_{20}\text{N}_2\text{O}_5$: C, 68.31; H, 4.98; N, 6.93; O, 19.78, Found: C, 68.29; H, 4.89; N, 6.91; O, 19.8.

(E)-2-cyano-3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)-N-(1-phenylethyl) acrylamide (7b)

IR (KBr, cm^{-1}): 3442 (-OH), 2257 (-CN), 3275 (-NH), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C); ^1H NMR (DMSO- d_6): δ 11.7 (s, H, -OH), 8.9 (s, H, -NH), 8.5 (s, H, exocyclic CH=C), 6.5-7.4 (m, 5H, phenyl), 6.0-6.4 (m, 2H, coumarin ring), 6.23 (d, 1H, endocyclic), 5.0 (q, H, -CH-NH), 2.5 (s, 3H, CH₃), 1.5 (d, 3H, CH₃); ^{13}C NMR (DMSO- d_6): δ 164.5 (C-4'), 160.7 (C-2), 159 (-CO), 155 (C-7), 153.5 (C, exocyclic ethylene), 152.5 (C-4), 146.8 (C-10), 128.7 (C-2', C-6'), 127 (C-3', C-5'), 126 (C-1'), 125 (C-5), 118 (C-8), 116 (-CN), 114.5 (C-6), 112.5 (C-3), 112 (C-9), 103 (C-exocyclic), 49 (-CH-NH-), 22 (-CH₃), 21.5 (-CH₃); MS: $m/z(M^++1)$ 375.0; Anal. Calcd for $\text{C}_{22}\text{H}_{18}\text{N}_2\text{O}_4$: C, 70.58; H, 4.85; N, 7.48; O, 17.09 Found C, 70.55; H, 4.80; N, 7.50; O, 17.0.

(E)-N-benzyl-2-cyano-3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)acrylamide (7c)

IR (KBr, cm^{-1}): 3430 (-OH), 3275 (-NH), 2230 (-CN), 1730.4 (-CO), 1674 (cyclic -CO), 1546 (-C=C) cm^{-1} ; ^1H NMR(DMSO- d_6): δ 11.7 (s, H, -OH), 8.9 (s, H, -NH), 8.5 (s, H, exocyclic CH=C), 7.5 (d, H, coumarin ring), 6.8 (d, H, coumarin ring), 7.2-7.4 (m, 5H, phenyl), 6.0 (s, H, endocyclic), 4.5 (s, 2H, -CH₂), 2.5 (s, 3H, CH₃); ^{13}C NMR (DMSO- d_6): δ 162.7 (C-2), 160 (-CO), 155 (C-7), 153.5 (C, ethylene), 152.5 (C-4), 146 (C-10), 134 (C-4'), 128.5

(C-2', C-6'), 126.5 (C-3', C-5'), 126 (C-1'), 125.2 (C-5), 118.2 (C-7), 115 (C, -CN), 114.5 (C-6), 112.5 (C-3), 112 (C-9), 103 (C-CN), 43.0 (C, -CH₂), 19.5 (C, -CH₃); MS: $m/z(M^++1)$ 361.9; Anal. Calcd for C₂₁H₁₆N₂O₄: C, 69.99; H, 4.48; N, 7.77; O, 17.76. Found C, 69.89; H, 4.44; N, 7.80; O, 17.66.

(E)-3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)-2-(piperidine-1-carbonyl) acrylonitrile (7d)

IR (KBr, cm⁻¹): 3442 (-OH), 2240.3 (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C); ¹H NMR (DMSO-*d*₆): δ 11.79 (s, -OH), 8.32 (s, H, exocyclic CH=C), 6.2-7.55 (m, 3H, coumarin ring), 3.7 (m, 4H, piperidine), 2.5 (s, 3H, CH₃), 1.6 (m, 2H piperidine), 1.53 (m, 4H, piperidine); ¹³C NMR (DMSO-*d*₆): δ 170.5 (CO), 160 (C-2), 155 (C-7), 153 (C, ethylene), 152.7 (C-4), 146 (C-10), 125.2 (C-5), 118.2 (C-8), 115 (CN), 114.0 (C-6), 112.5 (C-3), 112.0 (C-9), 106 (C, ethylene), 47.0 (2C, piperidine), 25.0 (2C, piperidine), 24.1 (C, piperidine), 19.5 (C, -CH₃); MS: $m/z(M^++1)$ 339.3; Anal. Calcd for C₁₉H₁₈N₂O₄: C, 67.44; H, 5.36; N, 8.28; O, 18.91. Found; C, 67.40; H, 5.39; N, 8.31; O, 18.20.

(E)-3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)-2-(pyrrolidine-1-carbonyl)acrylo nitrile (7e)

IR (KBr, cm⁻¹): 3442 (-OH), 2246 (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C); ¹H NMR (DMSO-*d*₆): δ 11.8 (s, -OH), 8.35 (s, H, exocyclic CH=C), 6.23-7.5 (3H, coumarin), 3.25 (t, 4H, pyrrolidine), 2.43 (s, 3H, -CH₃), 1.72 (t, 4H, pyrrolidine); ¹³C NMR (DMSO-*d*₆): δ 170.7 (-CO), 160, (C-2), 155 (C-7), 153 (C, exocyclic ethylene), 146 (C-10), 125.2 (C-5), 118.2 (C-8), 115 (-CN), 114.0 (C-6), 112.5 (C-3), 112.0 (C-9), 106 (C, ethylene), 45.7 (2C, pyrrolidine), 25.0 (2C, pyrrolidine), 19.5 (C, -CH₃); MS: $m/z(M^++1)$ 325.3; Anal. Calcd for C₁₈H₁₆N₂O₅: C, 66.66; H, 4.97; N, 8.64; O, 19.73. Found; C, 66.76; H, 5.02; N, 8.54; O, 19.80.

(E)-2-cyano-3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl) N-methylacrylamide (7f)

IR (KBr, cm⁻¹): 3442 (-OH), 3225 (-NH), 2248 (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C); ¹H NMR (DMSO-*d*₆): 11.8 (s, OH), 8.4 (s, H, exocyclic ethylene), 8.1 (m, -NH), 6.22-7.5 (m, 3H, coumarin ring), 2.72 (d, 3H, -HN-CH₃), 2.43 (s, 3H, -CH₃); ¹³C NMR (DMSO-*d*₆): δ 160.5 (CO), 159.7 (C-2), 155 (C-7), 153.8 (C, exocyclic ethylene), 153 (C-4), 146 (C-10), 125.2 (C-5), 118.2 (C-8), 115 (CN), 114.5 (C-6), 112.5 (C-3), 112.0 (C-9), 104 (C, ethylene), 25.5 (-NH-CH₃), 19.5 (C, -CH₃); MS: $m/z(M^++1)$: 285.3; Anal. Calcd for C₁₅H₁₂N₂O₄: C, 63.38; H, 4.25; N, 9.85; O, 22.51. Found; C, 63.80; H, 4.19; N, 9.65; O, 22.39.

(E)-2-cyano-3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-

8-yl) N,N-dimethylacrylamide (7g)

IR (KBr, cm⁻¹): 3442 (-OH), (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C); ¹H NMR (DMSO-*d*₆): 11.8 (s, -OH), 8.3 (s, H, -ethylene), 6.2-7.5 (m, 3H coumarin ring), 3.02 (d, 6H, -N(CH₃)₂), 2.43 (s, 3H, -CH₃); ¹³C NMR (DMSO-*d*₆): δ 160.5 (-CO), 159.7 (C-2), 155 (C-7), 153 (C, exocyclic ethylene), 152.5 (C-5), 146 (C-10), 125.2 (C-3), 118.2 (C-8), 115 (-CN), 114.0 (C-6), 112.5 (C-3), 112.0 (C-5), 107 (C, ethylene), 36.6 (2C, -N(CH₃)₂), 19.5 (C, -CH₃); MS: $m/z(M^++1)$: 300.0; Anal. Calcd for C₁₆H₁₄N₂O₄: C, 64.42; H, 4.73; N, 9.39; O, 21.45. Found; C, 64.24; H, 4.69; N, 9.55; O, 21.59.

(E)-2-cyanoN,N-diethyl-3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl) acrylamide (7h)

IR (KBr, cm⁻¹): 3442 (-OH), 2254 (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C); ¹H NMR(CDCl₃): δ 11.8 (s, -OH), 8.3 (s, H, ethylene), 6.24-7.55 (m, 3H coumarin ring), 3.72 (q, 4H, -H₂C-N-CH₂), 2.4 (s, 3H, -CH₃), 1.34 (t, 6H, - (CH₃)₂); ¹³C NMR (CDCl₃): δ 160.5 (CO), 159.7 (C-2), 155 (C-7), 153 (C-4), 146 (C-10), 125.2 (C-5), 118.2 (C-8), 115 (CN), 114.6 (C-6), 112.5 (C-3), 112.0 (C-9), 106 (C, ethylene), 40.8 (q, 2C, -CH₂), 19.5 (C, -CH₃), 12.5 (t, 2C, -(CH₃)₂); MS: $m/z(M^++1)$: 327.5; Anal. Calcd for C₁₈H₁₈N₂O₄: C, 66.25; H, 5.56; N, 8.58; O, 19.61. Found; C, 66.30; H, 5.64; N, 8.65; O, 19.16.

(E)-2-cyano-3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl) N,N-diisopropylacrylamide (7i)

IR (KBr, cm⁻¹): 3442 (-OH), 2244 (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C); ¹H NMR (CDCl₃): 11.8 (s, -OH), 8.35 (s, exocyclic ethylene), 6.23-7.55 (m, 3H, coumarin ring), 4.0 (m, 2H, -CH-), 2.45 (s, 3H, -CH₃), 1.27 (d, 12H, 4Me of isopropyl); ¹³C NMR (CDCl₃): δ 160.5 (CO), 159.7 (C-2), 155 (C-7), 153 (C, exocyclic ethylene), 152.7 (C-4), 146 (C-10), 125.2 (C-5), 118.2 (C-8), 115 (CN), 114.6 (C-6), 112.5 (C-3), 112.0 (C-9), 107 (C, ethylene), 47.0 (2C, -CH), 19.5 (C - CH₃), 21.5 (t, 4C, -4CH₃ of isopropyl); MS: $m/z(M^++1)$: 355.4; Anal. Calcd for C₂₀H₂₂N₂O₄: C, 67.78; H, 6.26; N, 7.90; O, 18.06. Found; C, 67.87; H, 6.30; N, 8.01; O, 18.14.

(E)-3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)-2-(1H-imidazole-1-carbonyl)acrylo nitrile (7j)

IR (KBr, cm⁻¹): 3442 (-OH), 2254 (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C), 1549 (-C=C, -C=N); ¹H NMR (DMSO-*d*₆): 11.8 (s, OH), 8.35 (s, H exocyclic ethylene), 6.23-7.55 (m, 3H coumarin ring), 8.14 (s, H, imidazole), 7.4 (d, H, imidazole), 7.14 (d, H, imidazole), 2.45 (s, 3H, -CH₃); ¹³C NMR(DMSO-*d*₆): δ 189.7 (C, -CO), 162 (C, exocyclic ethylene), 160.5 (C-2), 155 (C-7), 153 (C-4), 136.7 (C, imidazole), 130.0 (C, imidazole), 146 (C-

10), 125.2 (C-5), 117.5 (C, imidazole), 118.2 (C-8), 115 (-CN), 114.6 (C-6), 112.5 (C-3), 112.0 (C-9), 104 (C, ethylene), 19.5 (C, -CH₃); MS: $m/z(M^+ + 1)$: 322.3; Anal. Calcd for C₁₇H₁₁N₃O₄: C, 63.55; H, 3.45; N, 13.08; O, 19.92. Found; C, 63.45; H, 3.40; N, 13.11; O, 20.05.

(E)-2-cyano-3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)-N-(2-hydroxyethyl)acrylamide (7k)

IR (KBr, cm⁻¹): 3442 (-OH), 2254 (-CN), 1742 (-CO), 1594 (-C=C), 1549 (-C=C); ¹H NMR (DMSO-*d*₆): δ 11.8 (s, OH), 8.9 (t, -NH), 8.35 (s, H exocyclic ethylene), 6.23-7.55 (m, 3H coumarin ring), 4.8 (s, -OH, aliphatic), 3.6 (t, 2H, -CH₂-O), 3.4 (t, 2H, N-CH₂-), 2.45 (s, 3H, -CH₃); ¹³C NMR (DMSO-*d*₆): δ 161 (C-2), 159 (CO), 155 (C-7), 154 (C, exocyclic ethylene), 153 (C-4), 146.2 (C-10), 125.5 (C-5), 118.5 (C-8), 115 (-CN), 114.6 (C-6), 112.5 (C-3), 112.0 (C-9), 104 (C, ethylene), 61.0 (C-OH), 42 (-NH-C), 19.5 (C, -CH₃); MS: $m/z(M^+ + 1)$: 315.3; Anal. Calcd for C₁₆H₁₄N₂O₅: C, 61.14; H, 4.49; N, 8.91; O, 25.45. Found; C, 61.25; H, 4.50; N, 9.00; O, 25.55.

(E)-2-cyano-3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)acrylamide (7l)

IR (KBr, cm⁻¹): 3442 (-OH), 3225 (-NH), 2254 (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C), 1549 (-C=C); ¹H NMR (DMSO-*d*₆): 11.8 (s, OH), 8.35 (s, H exocyclic ethylene), 7.66 (s, 2H, -NH₂), 6.23-7.55 (m, 3H coumarin ring), 2.45 (s, 3H, -CH₃); ¹³C NMR (DMSO-*d*₆): δ 1647 (CO), 154 (C, exocyclic ethylene), 160.5 (C-2), 155 (C-7), 153 (C-4), 146 (C-10), 125.2 (C-5), 118.2 (C-8), 115 (-CN), 114.6 (C-6), 112.5 (C-3), 112.0 (C-9), 106 (C, ethylene), 19.5 (C, -CH₃); MS: $m/z(M^+ + 1)$: 271.24; Anal. Calcd for C₁₄H₁₀N₂O₄: C, 62.22; H, 3.73; N, 10.37; O, 23.68. Found; C, 62.45; H, 3.54; N, 10.27; O, 23.70.

(E)-N-benzhydryl-2-cyano-3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl)acrylamide (7m)

IR (KBr, cm⁻¹): 3442 (-OH), 2254 (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C), 1549 (-C=C); ¹H NMR (DMSO-*d*₆): 11.8 (s, OH), 8.35 (s, H exocyclic ethylene), 8.0 (s, H, -NH), 6.23-7.55 (m, 3H coumarin ring), 7.22-7.44 (m, 10H, benzhydryl), 6.16 (s, H, -CH), 2.45 (s, 3H, -CH₃); ¹³C NMR (DMSO-*d*₆): δ 161 (C-2), 160 (C, exocyclic ethylene), 159 (CO), 155 (C-7), 153 (C-4), 146 (C-10), 141.2 (C-4', C-4''), 128 (C-5', C-5'', C-3', C-3''), 129.2 (C-6', C-6'', C-2', C-2''), 126.2 (C-1', C-1''), 125.2 (C-5), 118.2 (C-8), 115 (-CN), 114.6 (C-6), 112.5 (C-3), 112.0 (C-9), 104 (C, ethylene), 52.5 (C, -CH of benzhydryl), 19.5 (C, -CH₃); MS: $m/z(M^+ + 1)$: 437.5; Anal. Calcd for C₂₇H₂₀N₂O₄: C, 74.30; H, 4.62; N, 6.42; O, 14.66. Found; C, 74.25; H, 4.66; N, 4.56; O, 14.56.

(E)-2-cyano-N-(2,4-dimethoxybenzyl)-3-(7-hydroxy-4-

methyl-2-oxo-2H-chromen-8-yl) acrylamide (7n)

IR (KBr, cm⁻¹): 3442 (-OH), 2254 (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C), 1549 (-C=C); ¹H NMR (DMSO-*d*₆): 11.8 (s, OH), 10.5 (s, -NH), 8.35 (s, H exocyclic ethylene), 8.1 (d, H of C-3'), 6.23-7.55 (m, 3H coumarin ring), 6.53-6.8 (2H, of C-2', C-6'), 3.8 (s, 6H of -OCH₃), 2.4 (s, 3H, -CH₃); ¹³C NMR (DMSO-*d*₆): δ 169 (C-1'), 64 (C, -CO), 160.5 (C-2), 155 (C-7), 153.6 (C, exocyclic ethylene), 154 (C-4, C-5'), 146 (C-10), 125.2 (C-5), 123 (C-3'), 118.2 (C-8), 117 (C-4'), 115 (-CN), 114.6 (C-6), 112.5 (C-3), 112.0 (C-9), 106 (C-2'), 104 (C, ethylene), 100 (C-6'), 56 (2C, -OCH₃), 19.5 (C, -CH₃); MS: $m/z(M^+ + 1)$: 407.4; Anal. Calcd for C₂₂H₁₈N₂O₆: C, 65.02; H, 4.46; N, 6.89; O, 23.62. Found; C, 65.07; H, 4.52; N, 6.79; O, 23.90.


(E)-2-cyano-N-(4,5-dihydrothiazol-2-yl)-3-(7-hydroxy-4-methyl-2-oxo-2H-chromen-8-yl) acrylamide (7o)

IR (KBr, cm⁻¹): 3442 (-OH), 2254 (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C), 1549 (-C=C), 750 (C-S); ¹H NMR (DMSO-*d*₆): 11.8 (s, OH), 8.45 (s, H exocyclic ethylene), 8.0 (s, H, -NH), 6.23-7.55 (m, 3H coumarin ring), 3.8 (t, 2H, -N-CH₂-), 3.25 (t, 2H, -S-CH₂), 2.45 (s, 3H, -CH₃); ¹³C NMR (DMSO-*d*₆): δ 169 (CO), 163.5 (-N-C=N), 162 (C, exocyclic ethylene), 160.5 (C-2), 155 (C-7), 153 (C-4), 146 (C-10), 125.2 (C-5), 118.2 (C-8), 115 (-CN), 114.6 (C-6), 112.5 (C-3), 112.0 (C-9), 106 (C, ethylene), 54 (=N-CH₂), 24 (-S-CH₂), 19.5 (C, -CH₃); MS: $m/z(M^+ + 1)$: 356.37; Anal. Calcd for C₁₇H₁₃N₃O₄S: C, 57.46; H, 3.69; N, 11.82; O, 18.01; S, 9.02. Found; C, 58.02; H, 3.70; N, 11.90; O, 18.20; S, 9.10.

RESULTS AND DISCUSSION

In this paper we reported that synthesis of some novel coumarin derivatives (**7a-o**) Resorcinol (**1**) reacts with ethyl acetoacetate in sulfuric acid and gives 7-hydroxy-4-methyl coumarin (**2**). The structure of **2** was established by IR, ¹H NMR and MS studies. It showed strong IR absorption bands at 3423, 1733, 1555 cm⁻¹ due to enol, coumarin carbonyl and alkene groups respectively. In its ¹H NMR spectrum three singlets at δ 2.49, 6.31 and 6.94 were assigned to a methyl group, olefinic proton and an aromatic proton respectively. Two aromatic protons of coumarin moiety appeared as doublets at 6.92, 7.57. Refluxing of (**2**) and hexamethylene tetramine in glacial acetic acid for 6 hours afforded 8-formyl-4-methyl-7-hydroxy Coumarin (**3**). The structure of (**3**) was established on the basis of IR, ¹H NMR and MS data. Presence of a singlet peak in its ¹H NMR spectrum at 10.63 confirms the formyl

Table 1. Synthesis of 7a-o

Compound	R ₁	R ₂
7a	H	(CH ₃ O)-C ₆ H ₅ -CH(CH ₃)-
7b	H	C ₆ H ₅ -CH(CH ₃)-
7c	H	C ₆ H ₅ -CH ₂
7d		-(CH ₂) ₅ -
7e		-(CH ₂) ₄ -
7f	H	CH ₃
7g	CH ₃	CH ₃
7h	C ₂ H ₅	C ₂ H ₅
7i	CH ₃ -CH-CH ₃	CH ₃ -CH-CH ₃
7j		-(CH=CH-N=CH)-
7k	H	CH ₂ CH ₂ OH
7l	H	H
7m	H	(C ₆ H ₅) ₂ CH
7n	H	2,4-OMe-C ₆ H ₃
7o	H	

group.

Refluxing of amines (**5a-o**) with ethyl cyano acetate (**4**) for 5 hours yielded N,N di substituted cyanoacetamide derivatives (**6a-o**). The condensation of (**3**) and (**6a-o**) in ethanol using catalytic amount of Piperidine for 2 hours gave corresponding coumarin derivatives (**7a-o**). The structures of (**7a-o**) were established on the basis of IR, ¹H NMR, ¹³C NMR, mass spectral data and elemental analysis.

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