Journal of the Korean Chemical Society
2012, *Vol. 56, No. 4*
Printed in the Republic of Korea
http://dx.doi.org/10.5012/jkcs.2012.56.4.459

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

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(Received January 13, 2012; Accepted June 13, 2012)

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

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

INTRODUCTION

Coumarin is a pleasanty 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 (Hierochloe 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 viral[5] properties. 4-methyl-7-hysroxy 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), ^{1}H 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 quadrapole mass spectrometer equipped with turbo ion spray interface at 360 ^{o}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 ^{o}C in an ice bath. A solution of resorcinol (0.001 mol) in ethyl acetoacetate (0.0015 mol) was added to sulfuric acid under constant stirring at 0-5 ^{o}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 ^{o}C; ^{1}H NMR (300MHz, $CDCl_3$): δ 2.49 (s, 3H, C4-CH_3), 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 ^{o}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; ^{1}H 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]

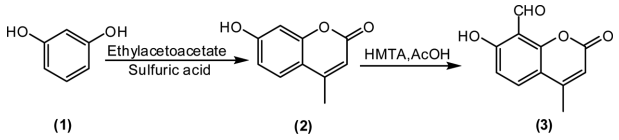
General procedure:

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%.

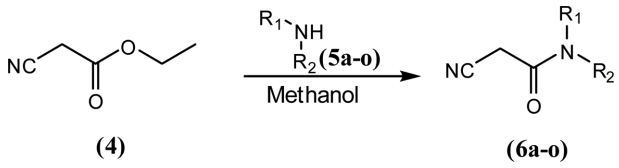
Synthesis of 7a-o by Knoevengel Condensation of 3 & 6a-o[11]

General procedure:

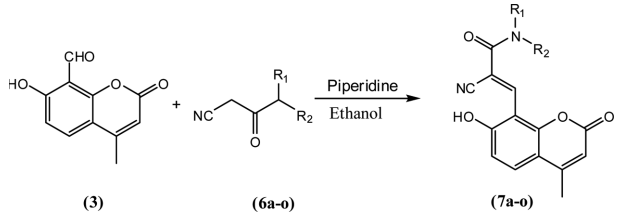
8-formyl-4-methyl-7-hydroxy Coumarin **(3)** (0.001 mol) was dissolved in 10mL ethanol containing N,N di substituted cyanoacetamide derivatives **(6a-o)** (0.001 mol) and catalytic amount of piperidine. Refluxed for 2.0 hr, cooled to 0-5 °C and filtered the solid. Pale yellow to orange red color solids were obtained. Yields varied from 50-60%.



***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.

SPECTRAL DATA

***(E)*-2-cyano-3-(7-hydroxy-4-methyl-2-oxo-2*H*-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-): ^{1}H 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, -OCH_3), 2.45 (s, 3H, -CH_3), 1.5 (d, 3H, -CH_3); ^{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 (-OCH_3), 49.0 (C, -CH-NH), 21.5 (C, -CH_3), 19.5 (-CH_3 of C-4); MS: m/z(M^++1) 405.4; Anal. Calcd for $C_{23}H_{20}N_2O_5$: 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-2*H*-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); ^{1}H 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, CH_3), 1.5 (d, 3H, CH_3); ^{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 (-CH_3), 21.5 (-CH_3); MS: m/z(M^++1) 375.0; Anal. Calcd for $C_{22}H_{18}N_2O_4$: 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-2*H*-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}; ^{1}H 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, -CH_2), 2.5 (s, 3H, CH_3); ^{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, $-CH_2$), 19.5 (C, $-CH_3$); MS: m/z(M^++1) 361.9; Anal. Calcd for $C_{21}H_{16}N_2O_4$: 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-2*H*-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); ^{1}H NMR (DMSO-d_6): δ 11.79 (s, -OH), 8.32 (s, H, exocyclic CH=C), 6.2-7.55 (m, 3H, coumarinring), 3.7 (m, 4H, piperidine), 2.5 (s, 3H, CH_3), 1.6 (m, 2H piperidine), 1.53 (m, 4H, piperidine); ^{13}C 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, $-CH_3$); MS: m/z (M^++1) 339.3; Anal. Calcd for $C_{19}H_{18}N_2O_4$: 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-2*H*-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); ^{1}H 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, $-CH_3$), 1.72 (t, 4H, pyrrolidine); ^{13}C NMR (DMSO-d_6): δ 170.7 (-CO), 160, (C-2), 155 (C-7), 153 (C, expcyclic 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, $-CH_3$); MS: m/z(M^++1) 325.3; Anal. Calcd for $C_{18}H_{16}N_2O_5$: 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-2*H*-chromen-8-yl) *N*-methylacrylamide (7f)**

IR (KBr, cm^{-1}): 3442 (-OH), 3225 (-NH), 2248 (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C); ^{1}H 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-CH_3), 2.43 (s, 3H, $-CH_3$); ^{13}C 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-CH_3), 19.5 (C, $-CH_3$); MS: m/z(M^++1): 285.3; Anal. Calcd for $C_{15}H_{12}N_2O_4$: 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-2*H*-chromen-8-yl) *N,N*-dimethylacrylamide (7g)**

IR (KBr, cm^{-1}): 3442 (-OH), (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C); ^{1}H 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, $-N(CH_3)_2$), 2.43 (s, 3H, $-CH_3$); ^{13}C 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, $-N(CH_3)_2$), 19.5 (C, $-CH_3$); MS: m/z(M^++1): 300.0; Anal. Calcd for $C_{16}H_{14}N_2O_4$: 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-cyano*N,N*-diethyl-3-(7-hydroxy-4-methyl-2-oxo-2*H*-chromen-8-yl) acrylamide (7h)**

IR (KBr, cm^{-1}): 3442 (-OH), 2254 (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C); ^{1}H NMR($CDCl_3$): δ 11.8 (s, -OH), 8.3 (s, H, ethylene), 6.24-7.55 (m, 3H coumarin ring), 3.72 (q, 4H, $-H_2C$-N-CH_2), 2.4 (s, 3H, $-CH_3$), 1.34 (t, 6H, -$(CH_3)_2$); ^{13}C NMR ($CDCl_3$): 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, $-CH_2$), 19.5 (C, $-CH_3$), 12.5 (t, 2C, -$(CH_3)_2$); MS: m/z(M^++1): 327.5; Anal. Calcd for $C_{18}H_{18}N_2O_4$: 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-2*H*-chromen-8-yl) *N,N*-diisopropylacrylamide (7i)**

IR (KBr, cm^{-1}): 3442 (-OH), 2244 (-CN), 1742 (-CO), 1644 (cyclic -CO), 1594 (-C=C); ^{1}H NMR ($CDCl_3$): 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, $-CH_3$), 1.27 (d, 12H, 4Me of isopropyl): ^{13}C NMR ($CDCl_3$): 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 - CH_3), 21.5 (t, 4C, -4CH_3 of isopropyl); MS: m/z(M^++1): 355.4; Anal. Calcd for $C_{20}H_{22}N_2O_4$: 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-2*H*-chromen-8-yl)-2-(1*H*-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); ^{1}H 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, $-CH_3$); ^{13}C 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, -CH_3); MS: m/z(M^++1): 322.3; Anal. Calcd for $C_{17}H_{11}N_3O_4$: 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); ^{1}H 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, -CH_2-O), 3.4 (t, 2H, N-CH_2-), 2.45 (s, 3H, -CH_3); ^{13}C 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, -CH_3); MS: m/z(M^++1): 315.3; Anal. Calcd for $C_{16}H_{14}N_2O_5$: 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); ^{1}H NMR(DMSO-d_6): 11.8 (s, OH), 8.35 (s, H exocyclic ethylene), 7.66 (s, 2H, -NH_2), 6.23-7.55 (m, 3H coumarin ring), 2.45 (s, 3H, -CH_3); ^{13}C 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, -CH_3); MS: m/z(M^++1): 271.24; Anal. Calcd for $C_{14}H_{10}N_2O_4$: 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); ^{1}H 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, benzhydril), 6.16 (s, H,-CH), 2.45 (s, 3H, -CH_3); ^{13}C 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 benzhydril), 19.5 (C, -CH_3); MS: m/z(M^++1): 437.5; Anal. Calcd for $C_{27}H_{20}N_2O_4$: 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); ^{1}H 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 -OCH_3), 2.4 (s, 3H, -CH_3); ^{13}C 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, -OCH_3), 19.5 (C, -CH_3); MS: m/z (M^++1): 407.4; Anal. Calcd for $C_{22}H_{18}N_2O_6$: 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); ^{1}H 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-CH_2-), 3.25 (t, 2H, -S-CH_2), 2.45 (s, 3H, -CH_3); ^{13}C 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-CH_2), 24 (-S- CH_2), 19.5 (C,-CH_3); MS: m/z(M^++1): 356.37; Anal. Calcd for $C_{17}H_{13}N_3O_4S$: 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, ^{1}H 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 ^{1}H 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, ^{1}H NMR and MS data. Presence of a singlet peak in its ^{1}H NMR spectrum at 10.63 confirms the formyl

***Table* 1.** Synthesis of 7a-o

Compound	R_1	R_2
7a	H	(CH_3O)-C_6H_5-$CH(CH_3)$-
7b	H	C_6H_5-$CH(CH_3)$-
7c	H	C_6H_5-CH_2
7d		-$(CH_2)_5$-
7e		-$(CH_2)_4$-
7f	H	CH_3
7g	CH_3	CH_3
7h	C_2H_5	C_2H_5
7i	CH_3-CH-CH_3	CH_3-CH-CH_3
7j		-(CH=CH-N=CH)-
7k	H	CH_2CH_2OH
7l	H	H
7m	H	$(C_6H_5)_2CH$
7n	H	2,4-OMe-C_6H_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, ^{1}H NMR, ^{13}C NMR, mass spectral data and elemental analysis.

Acknowledgments. The authors express their grateful thanks to Prof. C.D. Reddy, Department of Chemistry, Sri Venkateswara University, Tirupati, for his helpful discussions.

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