Synthesis of Some Oxazolyl - Pyrazolyl; 1,4-Dihydropyridinyl-pyrazolyl and 1,2,3,4-Tetrahydro pyrimidinyl-pyrazolyl coumarins

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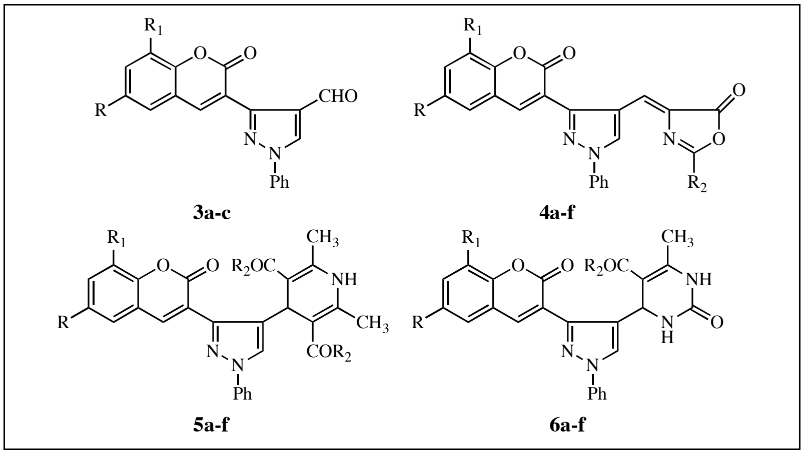

Various 3-[1-phenyl-4-(2-substituted-5-oxo-oxazol-4-ylidenemethyl) pyrazol-3-yl] coumarins **4a-f**; 3-[1-phenyl-4-(2,6-dimethyl-3,5-disubstituted-1,4-dihydropyridin-4-yl) pyrazol-3-yl] coumarins **5a-f** and 3-[1-phenyl-4-(6-methyl-5-substituted-2-oxo-1,2,3,4-tetrahydropyrimidin-4-yl) pyrazol-3-yl] coumarins **6a-f** have been synthesized utilizing Erlenmeyer-Plochl reaction, Hantzsch reaction and Biginelli reaction respectively using 3-(1-phenyl-4-formyl-pyrazol-3-yl) coumarins **3a-c** as a starting material.

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INTRODUCTION

Coumarins (2*H*-1-Benzopyran-2-ones) are well known aromatic lactones isolated from a variety of plant sources [1]. Owing to their diverse bioactivities *viz.* anticoagulant [2], antibacterial and antifungal [3] *etc.* many natural, semi synthetic and synthetic coumarins have become important class of molecules in drug research. A large number of coumarins having heterocyclic moieties like benzimidazole, triazole, diazole, diazine, thiadiazole *etc.* as a substituent group either in the lactone ring or in the benzene ring of coumarin are used as dyes or whitening agents [4]. Coumarins having nucleus like pyridine, indole, triazole, oxazine as a substituent group possess a variety of biological activities [5].

Pyrazole, oxazole, pyridine and pyrimidine are prominent heterocyclic moieties and their derivatives possess varied bioactivities. Certain pyrazole derivatives [6] are reported to have antioxidant, anti-inflammatory, antidepressant and antipyretic properties. Some oxazole derivatives [7] possess bactericidal, antitumor and antiarrhythmic properties. Certain 1,4-dihydropyridines [8] are well known for their antihypertensive and anti-inflammatory properties. Some pyrimidine derivatives [9] are reported for their antitumor, antiviral and analgesic properties.

Considering the importance of pyrazole, oxazole, 1,4-dihydropyridine and pyrimidine derivatives, it was thought worthwhile to synthesize coumarin derivatives having such nuclei as a substituent group and hence in the present work various 3-[1-phenyl-4-(2-substituted-5-oxo-oxazol-4-ylidenemethyl)pyrazol-3-yl] coumarins **4a-f**; 3-[1-phenyl-4-(2,6-dimethyl-3,5-disubstituted-1,4-dihydro-pyridin-4-yl) pyrazol-3-yl] coumarins **5a-f** and 3-[1-phenyl-4-(6-methyl-5-substituted-2-oxo-1,2,3,4-tetra-hydropyrimidin-4-yl) pyrazol-3-yl] coumarins **6a-f** have been synthesized utilizing Erlenmeyer-Plochl reaction, Hantzsch reaction and Biginelli reaction respectively (Scheme 1).

The coumarinyl pyrazole aldehyde **3** was used as a key aldehyde for the syntheses of compounds **4**, **5** and **6**. 3-Acetyl coumarins **1a-c** were converted into their corresponding phenyl hydrazones **2a-c**. The phenyl hydrazones **2a-c** upon Vilsmeier-Haack reaction gave the key aldehydes **3a-c**. The aldehydes **3a-c** on reaction with *N*-acetylglycine or *N*-benzoylglycine in the presence of sodium acetate and acetic anhydride gave 3-[1-phenyl-4-(2-substituted-5-oxo-oxazol-4-ylidenemethyl)-pyrazol-3-yl]coumarins **4a-f**. The reaction of aldehydes **3a-c** with acetyl acetone or ethyl acetoacetate under Hantzsch reaction condition gave 3-[1-phenyl-4-(2,6-dimethyl-3,5-disubstituted-1,4-dihydropyridin-4-yl)-

pyrazol-3-yl] coumarins **5a-f**. The Biginelli reaction of aldehydes **3a-c** using urea and acetyl acetone or ethyl acetoacetate gave 3-[1-phenyl-4-(6-methyl-5-substituted-2-oxo-1,2,3,4-tetrahydro pyrimidin-4-yl)pyrazol-3-yl] coumarins **6a-f**.

The structures of the compounds **4**, **5** and **6** were established on the bases of analytical and spectral data. The physical data of **4**, **5** and **6** are shown in Table 1.

EXPERIMENTAL

All the melting points reported are uncorrected. All ir spectra (KBr disc) were recorded on Shimadzu FT-IR 8400-S spectrometer. ^{1}H nmr and ^{13}C nmr spectra were recorded on a Brucker Avance 400 spectrometer operating at 400 MHz for ^{1}H nmr and 100 MHz for ^{13}C nmr. The chemical shift (δ) is reported in ppm using chloroform-d as a solvent and calibrated standard solvent signal. Elemental analyses were carried out with a Hareaus CHNO analyzer. 3-Acetyl coumarins **1a-c** were prepared according literature procedures [10].

Synthesis of coumarin phenyl hydrazones 2a-c. General Procedure. A mixture of appropriate 3-acetyl coumarin **1a-c** (0.01 mole), phenyl hydrazine (0.01 mole) and acetic acid (1.0 mL) in 50 mL of methanol was refluxed on water bath for 30 minutes. It was then allowed to come to room temperature. A solid product separated out was collected by filtration, washed with cold methanol, dried and recrystallized from ethanol.

Compound 2a. Yield 80%, mp 188 °C (lit [11] 188 °C).

Compound 2b. Yield 85%, mp 169 °C (lit [12] 170 °C).

Compound 2c. Yield 81%, mp 163 °C; ir: cm^{-1} 3330, 3035, 1723, 1603, 1245; ^{1}H nmr: δ 2.31 (3H, s, CH_3), 3.99 (3H, s, OCH_3), 7.06-7.39 (8H, m, Ar-H), 7.60 (1H, s, NH, D_2O exchangeable), 8.05 (1H, s, C_4-H of coumarin); ^{13}C nmr: δ 13.89(CH_3), 56.26(OCH_3), 113.29(CH), 113.34(CH), 119.82(CH), 120.21(C), 120.74(CH), 124.41(CH), 127.66(C), 129.33(CH), 139.05(C), 139.79(CH), 143.33(C), 144.53(C), 146.92(C), 160.02(CO). *Anal.* Calcd. for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 70.10; H, 5.25; N, 9.10.

Synthesis of 3-(1-phenyl-4-formyl-pyrazol-3-yl) coumarins 3a-c. General Procedure. To a well stirred and cooled (0°C) solution of coumarin phenyl hydrazones **2a-c** (0.06 mole) in anhydrous DMF (0.6 mole), $POCl_3$ (0.18 mole) was added dropwise during one hour. After complete addition of $POCl_3$, the reaction mixture was further stirred at 0 °C for one hour. After the reaction mixture was heated at 65-70 °C for 2 hours it was poured into crushed ice and left overnight in a refrigerator

Scheme 1

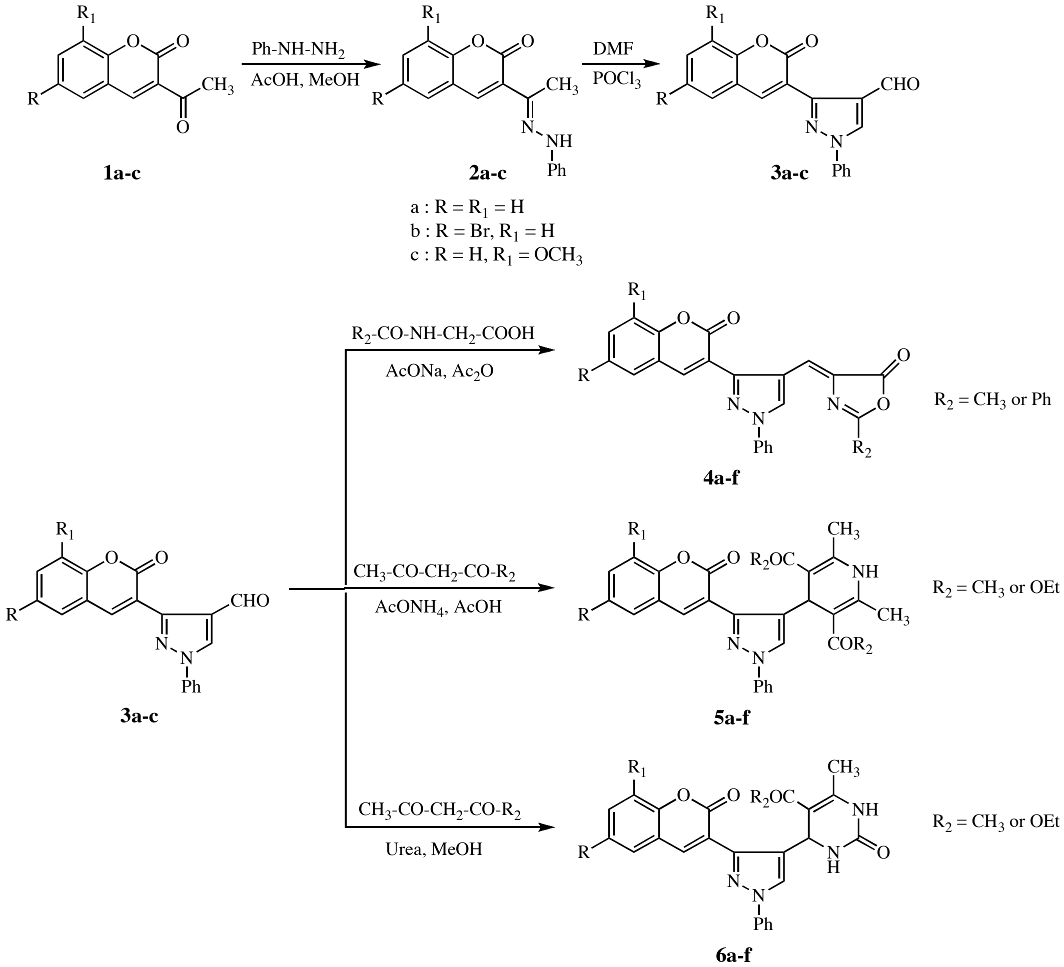

Table 1

Yield and melting point of **4a-f**, **5a-f** and **6a-f**.

Comp.	R	R$_1$	R$_2$	Yield (%)	mp (°C)	Comp.	R	R$_1$	R$_2$	Yield (%)	mp (°C)
4a	H	H	CH$_3$	55	281-83	**5d**	Br	H	OEt	60	179-81
4b	H	H	Ph	58	240-42	**5e**	H	OCH$_3$	CH$_3$	53	170-72
4c	Br	H	CH$_3$	56	278-79	**5f**	H	OCH$_3$	OEt	62	210-12
4d	Br	H	Ph	62	253-55	**6a**	H	H	CH$_3$	51	180-82
4e	H	OCH$_3$	CH$_3$	62	212-14	**6b**	H	H	OEt	60	172-74
4f	H	OCH$_3$	Ph	61	224-26	**6c**	Br	H	CH$_3$	58	198-99
5a	H	H	CH$_3$	53	281-82	**6d**	Br	H	OEt	59	242-44
5b	H	H	OEt	58	244-46	**6e**	H	OCH$_3$	CH$_3$	52	205-07
5c	Br	H	CH$_3$	54	214-15	**6f**	H	OCH$_3$	OEt	54	156-58

during which a solid product separated out, was collected by filtration, washed with Na_2CO_3 (5%, 3 x 30 mL) and water. It was then dried and recrystallized from ethanol.

Compound 3a. Yield 78%, mp 215-16 °C; ir: cm^{-1} 1723, 1689, 1603, 1407; ^{1}H nmr: δ 7.34-7.78 (9H, m, Ar-H), 8.24 (1H, s, C_4-H of coumarin), 8.54 (1H, s, $C_{5'}$-H of pyrazole), 10.07 (1H, s, CHO); ^{13}C nmr: δ 116.80(CH), 119.02(C), 119.89(CH), 120.22(C), 124.03 (C), 124.84(CH), 128.22(CH), 128.56(CH), 129.78(CH), 130.94 (CH), 132.51(CH), 138.92(C), 143.15(CH), 147.80(C), 154.19(C), 160.16(CO), 185.23(CHO). *Anal.* Calcd. for $C_{19}H_{12}N_2O_3$: C, 72.15; H, 3.82; N, 8.86. Found: C, 72.16; H, 3.85; N, 8.84.

Compound 3b. Yield 68%, mp 223-25 °C; ir: cm^{-1} 1730, 1680, 1600, 1410; ^{1}H nmr: δ 7.27-7.84 (8H, m, Ar-H), 8.15 (1H, s, C_4-H of coumarin), 8.55 (1H, s, $C_{5'}$-H of pyrazole), 10.06 (1H, s, CHO); ^{13}C nmr: δ 115.16(C), 117.40(C), 118.31(CH), 118.53(CH), 119.87(CH), 120.52(C), 121.46(C), 124.05(C), 128.34(CH), 129.83(CH), 130.69(CH), 131.25(C), 135.18 (CH), 138.82(C), 141.58(CH), 152.97(CO), 184.94(CHO). *Anal.*Calcd. for $C_{19}H_{11}N_2O_3Br$: C, 57.74; H, 2.81; N, 7.09. Found: C, 57.76; H, 2.80; N, 7.12.

Compound 3c. Yield 66%, mp 240-41 °C; ir: cm^{-1} 1726, 1683, 1608, 1395; ^{1}H nmr: δ 4.02 (3H, s, OCH_3), 7.16-7.67 (8H, m, Ar-H), 8.22 (1H, s, C_4-H of coumarin), 8.54 (1H, s, $C_{5'}$-H of pyrazole), 10.06 (1H, s, CHO); ^{13}C nmr: δ 56.33(OCH_3), 114.25 (CH), 119.64(C), 119.91(CH), 120.42(C), 124.06(C), 124.74 (CH), 128.22(CH), 129.79(CH), 130.81(CH), 138.93(CH), 141.60(CH), 143.34(C), 143.85(C), 147.18(C), 147.85(C), 159.68(CO), 185.39(CHO). *Anal.*Calcd. for $C_{20}H_{14}N_2O_4$: C, 69.36; H, 4.07; N, 8.09. Found: C, 69.38; H, 4.09; N, 8.08.

Synthesis of 3-[1-phenyl-4-(2-substituted-5-oxo-oxazol-4-ylidene methyl) pyrazol-3-yl] coumarins 4a-f. General Procedure. A mixture of appropriate 3-(1-phenyl-4-formyl-pyrazol-3-yl) coumarins **3a-c** (0.125 mole), *N*-acetylglycine or *N*-benzoylglycine (0.125 mole), acetic anhydride (0.75 mole) and fused sodium acetate (0.125 mole) was warmed in a water-bath till it became homogeneous solution (about 15-20 minutes) and then it was heated for two hours in a boiling water bath. After two hours heating, ethanol (30 mL) was added in the reaction mixture and left overnight. The crude solid obtained was extracted with chloroform (3 x 30 mL). The chloroform extract was washed with water (3 x 20 mL) and dried over anhydrous sodium sulfate. After removal of chloroform under reduced pressure, the remaining residue was purified by column chromatography using silica gel and ethyl acetate - pet ether (60-80) (2:8) as an eluent. It afforded **4a-f** as yellowish white solids, which were recrystallized from chloroform-hexane.

Compound 4a. ir: cm^{-1} 1725, 1720, 1600, 1430; ^{1}H nmr: δ 2.27 (3H, s, CH_3), 7.07 (1H, s, methylylidene proton), 7.22-7.70 (9H, m, Ar-H), 8.03 (1H, s, C_4-H of coumarin), 8.93 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 15.55(CH_3), 116.54(CH), 117.17(C), 118.89(C), 119.61(CH), 120.20(C), 122.36(CH), 124.82(CH), 127.72(CH), 128.53(CH), 129.56(CH), 130.74(C), 131.63 (CH), 132.47(CH), 139.01(C), 143.89(CH), 148.75(C), 154.03 (C), 159.94(C), 164.89(CO of coumarin), 166.90(CO of oxazolone). *Anal.*Calcd. for $C_{23}H_{15}N_3O_4$: C, 69.52; H, 3.80; N, 10.57. Found: C, 69.51; H, 3.81; N, 10.60.

Compound 4b. ir: cm^{-1} 1725, 1723, 1610, 1405; ^{1}H nmr: δ 7.19-8.17 (15H, m, Ar-H and methylylidene proton merged), 8.53 (1H, s, C_4-H of coumarin), 8.91 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 110.87(C), 114.25(CH), 119.61(C), 119.88(CH), 119.95(C), 120.41(C), 124.68(CH), 124.73(CH), 127.67(CH), 127.85(CH), 128.19(CH), 128.91(CH), 129.67(CH), 129.69(CH), 129.77(CH), 130.82(CH), 138.88(C), 143.34 (CH), 143.82(C), 143.87(C), 143.92(C), 148.28(C), 157.85(CO of coumarin), 164.73(CO of oxazolone). *Anal.* Calcd. for $C_{28}H_{17}N_3O_4$: C, 73.20; H, 3.73; N, 9.15. Found: C, 73.22; H, 3.75; N, 9.17.

Compound 4c. ir: cm^{-1} 1730, 1720, 1605, 1408; ^{1}H nmr: δ 2.31 (3H, s, CH_3), 6.97 (1H, s, methylylidene proton), 7.17-7.74 (8H, m, Ar-H), 8.40 (1H, s, C_4-H of coumarin), 8.89 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 14.32(CH_3), 114.61(CH), 119.41(CH), 119.88(CH), 119.95(C), 120.68(C), 124.37(CH), 124.67(CH), 127.15(CH), 127.89(C), 128.25(CH), 128.91(C), 129.69(CH), 129.77(C), 129.82(C), 130.88(CH), 138.34(C), 143.67(C), 143.82(C), 161.87(CO of coumarin), 167.32(CO of oxazolone). *Anal.* Calcd. for $C_{23}H_{14}N_3O_4Br$: C, 58.00; H, 2.96; N, 8.82. Found: C, 57.98; H, 3.00; N, 8.80.

Compound 4d. ir: cm^{-1} 1728, 1720, 1598, 1412; ^{1}H nmr: δ 7.17-8.05 (14H, m, Ar-H and methylylidene proton merged), 8.51 (1H, s, C_4-H of coumarin), 9.05 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 114.14(C), 116.50(CH), 117.16(C), 118.82(C), 119.62(C), 120.24(CH), 122.37(CH), 124.89(CH), 127.71 (CH), 128.53(CH), 129.56(CH), 130.74(CH), 131.69(CH), 132.43(C), 139.04(C), 143.89(CH), 148.75(C), 154.03(C), 159.97(C), 164.81(CO of coumarin), 165.90(CO of oxazolone). *Anal.* Calcd. for $C_{28}H_{16}N_3O_4Br$: C, 62.47; H, 3.00; N, 7.81. Found: C, 62.50; H, 2.98; N, 7.84.

Compound 4e. ir: cm^{-1} 1723, 1720, 1607, 1400; ^{1}H nmr: δ 2.51 (3H, s, CH_3), 3.93 (3H, s, OCH_3), 7.34-8.11 (9H, m, Ar-H and methylylidene proton merged), 8.40 (1H, s, C_4-H of coumarin), 9.30 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 15.55(CH_3), 56.20(OCH_3), 116.89(CH), 117.61(C), 118.20(C), 119.36(CH), 120.82(C), 122.72(CH), 124.53(CH), 127.56(C), 128.54(CH), 129.74(CH), 130.63(CH), 131.47(C), 132.01 (CH), 139.89(C), 143.75(CH), 148.03(C), 154.94(C), 159.90 (C), 164.89(CO of coumarin), 167.17 (CO of oxazolone). *Anal.* Calcd. for $C_{24}H_{17}N_3O_5$: C, 67.44; H, 4.01; N, 9.83. Found: C, 67.45; H, 3.99; N, 9.85.

Compound 4f. ir: cm^{-1} 1729, 1723, 1613, 1405; ^{1}H nmr: δ 4.01 (3H, s, OCH_3), 7.17-8.21 (14H, m, Ar-H and methylylidene proton merged), 8.53 (1H, s, C_4-H of coumarin), 9.16 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 56.32(OCH_3), 109.87(C), 114.25 (CH), 119.61(C), 119.88(CH), 119.95(C), 120.41(C), 124.68(C), 124.73(CH), 127.67(CH), 127.85(CH), 128.19 (CH), 128.91(CH), 129.67(C), 129.69(CH), 129.77(CH), 130.82(CH), 138.88(C), 143.34(CH), 143.82(C), 143.87(C), 143.92(C), 160.82(CO of coumarin), 167.92(CO of oxazolone). *Anal.* Calcd. for $C_{29}H_{19}N_3O_5$: C, 71.16; H, 3.91; N, 8.58. Found: C, 71.20; H, 3.95; N, 8.57.

In case of the compounds **4d** and **4f**, the numbers of carbon signals in ^{13}C NMR spectra were less than expected which may be due to identical chemical shift of certain carbons.

Synthesis of 3-[1-phenyl-4-(2,6-dimethyl-3,5-disubstituted-1,4-dihydropyridin-4-yl) pyrazol-3-yl] coumarins 5a-f. General Procedure. A mixture of appropriate 3-(1-phenyl-4-formyl-pyrazol-3-yl) coumarin **3a-c** (0.01 mole), acetyl acetone or ethyl acetoacetate (0.02 mole) and ammonium acetate (2.0 g) in 50 mL of acetic acid was stirred for 10 minutes at room temperature and then refluxed in an oil bath at 130 °C for 12 hours. It was allowed to come to room temperature and was left overnight. The reaction mixture was poured into ice-cold water. Then it was extracted with ethyl acetate (3 x 30 mL). The ethyl acetate extract was then washed with water (3 x 20 mL) and dried over anhydrous sodium sulfate. Removal of ethyl acetate under reduced pressure resulted in a crude solid which was further purified by column chromatography using silica gel and ethyl acetate - pet ether (60-80) (2:8) as an eluent to afford compounds **5a-f** as yellowish white solids, which were recrystallized from chloroform-hexane.

Compound 5a. ir: cm^{-1} 3305, 1723, 1680, 1605, 1440; ^{1}H nmr: δ 2.17 (6H, s, 2 x Ar-CH_3), 2.31 (6H, s, 2 x -COCH_3), 5.43 (1H, s, methine proton), 5.64 (1H, s, NH proton, D_2O exchangeable), 7.31-7.67 (9H, m, Ar-H), 7.73 (1H, s, C_4-H of coumarin), 7.80 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 19.43(2 x CH_3), 29.30(2 x -COCH_3), 30.62($C_{4''}$), 112.05(C), 116.63(CH), 118.51(C), 119.43 (CH), 122.90(CH), 125.04(CH), 126.60 (CH), 128.88(CH), 129.95(CH), 132.36(CH), 136.00(C), 139.71(C), 141.70(C), 142.71(CH), 143.50(C), 145.08(C), 160.07(CO of coumarin), 196.65(*C*OCH_3). (Here there was deficiency of one ^{13}C signal, which may be due to identical chemical shift of two carbon atoms.) *Anal.* Calcd. for $C_{29}H_{25}N_3O_4$: C, 72.64; H, 5.25; N, 8.76. Found: C, 72.66; H, 5.27; N, 8.79.

Compound 5b. ir: cm^{-1} 3310, 1760, 1728, 1600, 1445; ^{1}H nmr: δ 1.22 (6H, t, 2 x -COOCH$_2$$CH_3$), 2.15 (6H, s, 2 x Ar-$CH_3$), 4.08 (4H, q, 2 x -COO$CH_2CH_3$), 5.23 (1H, s, methine proton), 5.66 (1H, s, NH proton, D_2O exchangeable), 7.26-7.67 (9H, m, Ar-H), 7.81 (1H, s, C_4-H of coumarin), 7.89 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 14.37(CH_3), 19.55(-COOCH$_2$$CH_3$), 30.07 ($C_{4''}$), 59.92(-COO$CH_2CH_3$), 102.77(C), 116.48(CH), 119.09 (C), 119.38(CH), 122.96(CH), 124.46(CH), 126.33(CH), 126.64(CH), 128.02(C), 128.41(CH), 129.26(CH), 131.61(C), 139.92(C), 142.68(CH), 144.21(C), 145.52(C), 153.96(C), 160.23(CO of coumarin), 167.45 (*C*OOEt). *Anal.* Calcd. for $C_{31}H_{29}N_3O_6$: C, 69.00; H, 5.42; N, 7.79. Found: C, 69.03; H, 5.43; N, 7.80.

Compound 5c. ir: cm^{-1} 3300, 1725, 1680, 1605, 1435; ^{1}H nmr: δ 2.14 (6H, s, 2 x Ar-CH_3), 2.38 (6H, s, 2 x -COCH_3), 5.18 (1H, s, methine proton), 5.38 (1H, s, NH proton, D_2O exchangeable), 7.27-7.83 (8H, m, Ar-H), 7.92 (1H, s, C4-H of coumarin), 8.04 (1H, s, C5’-H of pyrazole); ^{13}C nmr: δ 18.93(CH_3), 30.09(-COCH_3), 30.99(C4”), 113.95(CH), 118.63(C), 120.18(CH), 121.93(CH), 125.40(CH), 126.04(CH), 128.60(CH), 130.88(C), 131.98(C), 132.36(CH), 138.60(C), 141.71(C), 142.70(CH), 143.71(C), 145.57(C), 147.80(C), 162.47(CO of coumarin), 195.95(*C*OCH_3). (Here there was deficiency of one ^{13}C signal, which may be due to identical chemical shift of two carbon atoms.) *Anal.* Calcd. for $C_{29}H_{24}N_3O_4Br$: C, 62.37; H, 4.33; N, 7.52. Found: C, 62.38; H, 4.31; N, 7.51.

Compound 5d. ir: cm^{-1} 3310, 1765, 1720, 1605, 1443; ^{1}H nmr: δ 1.16 (6H, t, 2 x -COO CH$_2$$CH_3$), 2.16 (6H, s, 2 x Ar-$CH_3$), 3.63 (4H, q, 2 x -COO$CH_2CH_3$), 5.29 (1H, s, methine proton), 5.72 (1H, s, NH proton, D_2O exchangeable), 7.32-7.78 (8H, m, Ar-H), 7.98 (1H, s, C_4-H of coumarin), 8.04 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 14.53(CH_3), 18.95(-COOCH$_2$$CH_3$), 30.29 ($C_{4''}$), 59.07(-COO$CH_2CH_3$), 106.37(CH), 118.48(C), 119.90(CH), 120.38(C), 121.96(CH), 123.99(C), 126.33(C), 126.64(CH), 127.02(CH), 128.26(C), 128.41(CH), 130.61(CH), 140.29(C), 141.68(C), 142.21(CH), 144.52(C), 152.96(C), 160.96(CO of coumarin), 168.23(*C*OOEt). *Anal.* Calcd. for $C_{31}H_{28}N_3O_6Br$: C, 60.20; H, 4.56; N, 6.79. Found: C, 60.23; H, 4.58; N, 6.80.

Compound 5e. ir: cm^{-1} 3301, 1729, 1675, 1615, 1448; ^{1}H nmr: δ 2.15 (6H, s, 2 x Ar-CH_3), 2.29 (6H, s, 2 x -COCH_3), 3.99 (3H, s, OCH_3), 5.41 (1H, s, methine proton), 5.96 (1H, s, NH proton, D_2O exchangeable), 7.10-7.65 (8H, m, Ar-H), 7.74 (1H, s, C_4-H of coumarin), 7.77 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 20.08(CH_3), 30.14(-COCH_3), 30.87($C_{4''}$), 56.21(OCH_3), 112.85(CH), 113.66(C), 119.14(CH), 119.69(CH), 119.87(C), 123.23(CH), 124.45(CH), 126.53(C), 126.95(CH), 127.29(C), 129.32(CH), 139.73(C), 142.91(C), 142.97(CH), 143.58(C), 145.47(C), 147.01(C), 160.11(CO of coumarin), 198.06 (*C*OCH_3). *Anal.* Calcd. for $C_{30}H_{27}N_3O_5$: C, 70.71; H, 5.34; N, 8.25. Found: C, 70.69; H, 5.36; N, 8.26.

Compound 5f. ir: cm^{-1} 3301, 1768, 1723, 1612, 1441; ^{1}H nmr: δ 1.23 (6H, t, 2 x –COO CH$_2$$CH_3$), 2.15 (6H, s, 2 x Ar-$CH_3$), 3.99 (3H, s, OCH_3), 4.07 (4H, q, 2 x -COOCH_2CH$_3$), 5.33 (1H, s, methine proton), 5.75 (1H, s, NH proton, D_2O exchangeable), 7.16-7.66 (8H, m, Ar-H), 7.79 (1H, s, C_4-H of coumarin), 7.89 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 15.07(CH_3), 19.85(-COOCH$_2$$CH_3$), 30.57($C_{4''}$), 56.62($OCH_3$), 60.92(-COO$CH_2CH_3$), 108.87(CH), 116.84(CH), 119.83 (CH), 120.06(C), 122.69(CH), 124.64(C), 126.33(C), 126.46 (CH), 128.19(C), 128.21(C), 129.92(CH), 131.61(CH), 140.02 (C), 142.89(CH), 144.21(C), 145.52(C), 155.06(C), 160.63(CO of coumarin), 166.95(*C*OOEt). *Anal.* Calcd. for $C_{32}H_{31}N_3O_7$: C, 67.48; H, 5.49; N, 7.38. Found: C, 67.50; H, 5.50; N, 7.40.

Synthesis of 3-[1-phenyl-4-(6-methyl-5-substituted-2-oxo-1,2,3,4-tetrahydropyrimidin-4-yl) pyrazol-3-yl] coumarins 6a-f. General Procedure. A mixture of appropriate 3-(1-phenyl-4-formyl-pyrazol-3-yl) coumarin **3a-c** (0.01 mole), acetyl acetone or ethyl acetoacetate (0.01 mole), urea (0.01

mole) and concentrated hydrochloric acid (0.5 mL) in 50 mL methanol was stirred for 10 minutes at room temperature and then refluxed on a water bath for 8 hours. On cooling, a crude solid product separated out which was collected by filtration, washed with water and purified by column chromatography using silica gel and ethyl acetate-pet ether (60-80) (2:8) as an eluent. It afforded **6a-f** as white solids, which were recrystallized from chloroform-hexane.

Compound 6a. ir: cm^{-1} 3308, 1725, 1683, 1610, 1443; ^{1}H nmr: δ 2.14 (3H, s, Ar-CH_3), 2.29 (3H, s, -COCH_3), 5.39(1H, s, methine proton), 7.09-7.64 (11H, m, nine Ar-H and two NH protons merged), 7.84 (1H, s, C_4-H of coumarin), 8.00 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 19.98(CH_3), 30.19(-COCH_3), 30.67($C_{4''}$), 113.83(CH), 114.66 (C), 118.94(CH), 119.97(CH), 123.35(C), 124.45(CH), 126.53(CH), 126.97(CH), 127.29(C), 129.37(CH), 139.73(CH), 142.91(CH), 142.99(C), 143.78(C), 145.49(C), 147.10(C), 158.17 (CO at $C_{2''}$), 160.11(CO of coumarin), 197.96 (-COCH$_3$). (Here there was deficiency of one ^{13}C signal, which may be due to identical chemical shift of two carbon atoms.) *Anal.* Calcd. for $C_{25}H_{20}N_4O_4$: C, 68.17; H, 4.58; N, 12.72. Found: C, 68.20; H, 4.60; N, 12.70.

Compound 6b: ir: cm^{-1} 3310, 1725, 1685, 1610, 1445; ^{1}H nmr: δ 1.21(3H, t, -COOCH$_2$ CH_3), 2.16 (3H, s, Ar-CH_3), 3.99 (2H, q, -COOCH_2CH$_3$), 5.40 (1H, s, methine proton), 7.08-7.55 (11H, m, nine Ar-H and two NH protons merged), 7.69 (1H, s, C_4-H of coumarin), 7.86 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 14.57(CH_3), 19.53(-COOCH$_2$$CH_3$), 30.37($C_{4''}$), 58.92(-COO$CH_2CH_3$), 108.67(C), 116.46(CH), 119.09(CH), 119.38 (CH), 122.96(C), 124.46(CH), 126.33(CH), 126.64(CH), 128.02(C), 128.49(C), 129.26(CH), 131.61(C), 139.99(CH), 142.69(C), 144.21(CH), 145.52(C), 153.96(C), 158.86(CO at $C_{2''}$), 160.20(CO of coumarin), 167.02(COOEt). *Anal.* Calcd. for $C_{26}H_{22}N_4O_5$: C, 66.37; H, 4.71; N, 11.91. Found: C, 66.39; H, 4.70; N, 11.92.

Compound 6c. ir: cm^{-1} 3315, 1720, 1690, 1615, 1435; ^{1}H nmr: δ 2.15 (3H, s, Ar-CH_3), 2.17 (3H, s, -COCH_3), 5.31 (1H, s, methine proton), 7.12-7.78 (10H, m, eight Ar-H and two NH protons merged), 7.80 (1H, s, C_4-H of coumarin), 7.89 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 20.84(CH_3), 29.04(-COCH$_3$), 30.94($C_{4''}$), 114.37(CH), 119.67(C), 119.77(CH), 119.90(CH), 120.40(C), 124.51(C), 124.75(CH), 127.43(C), 127.93(CH), 128.22(C), 129.59(CH), 129.79(CH), 130.86(C), 138.91(C), 142.75(CH), 143.37(C), 147.17(C), 158.36(CO at $C_{2''}$), 168.63 (CO of coumarin), 195.43(COCH$_3$). *Anal.* Calcd. for $C_{25}H_{19}N_4O_4Br$: C, 57.82; H, 3.69; N, 10.79. Found: C, 57.85; H, 3.70; N, 10.78.

Compound 6d. ir: cm^{-1} 3315, 1720, 1675, 1608, 1435; ^{1}H nmr: δ 1.17(3H, t, -COOCH$_2$ CH_3), 2.15 (3H, s, Ar-CH_3), 3.67 (2H, q, -COOCH_2CH$_3$), 5.30 (1H, s, methine proton), 7.12-7.80 (10H, m, eight Ar-H and two NH protons merged), 7.89 (1H, s, C_4-H of coumarin), 8.06 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 14.08(CH_3), 19.98(-COOCH$_2$$CH_3$), 29.02($C_{4''}$), 60.06(-COO$CH_2CH_3$), 109.80(C), 116.80(CH), 119.02(C), 119.89 (CH), 120.22(C), 124.23(C), 124.82(CH), 128.26(CH), 128.52 (CH), 129.78(CH), 130.98(C), 132.58(C), 138.82(CH), 143.18 (CH), 143.68(C), 147.80(C), 150.08(C), 156.69(CO at $C_{2''}$) 160.06(CO of coumarin), 164.10(COOEt). *Anal.* Calcd. for $C_{26}H_{21}N_4O_5Br$: C, 56.84; H, 3.85; N, 10.20. Found: C, 56.86; H, 3.87; N, 10.22.

Compound 6e. ir: cm^{-1} 3312, 1728, 1683, 1615, 1438; ^{1}H nmr: δ 2.13 (3H, s, Ar-CH_3), 2.39 (3H, s, -COCH_3), 4.09 (3H, s, OCH$_3$), 5.45 (1H, s, methine proton), 7.06-7.64 (10H, m, eight Ar-H and two NH protons merged), 7.75 (1H, s, C_4-H of coumarin), 7.78 (1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 19.99(CH_3), 29.93(-COCH$_3$), 30.03($C_{4''}$), 56.30(OCH$_3$), 113.28(CH), 118.84(CH), 118.98(CH), 120.42(C), 124.07(CH), 124.77(CH), 128.27(CH), 129.79(C), 130.87(C), 134.79(C), 136.81(C), 138.93(CH), 142.93(CH), 143.34(C), 143.85(C), 147.18(C), 147.85(C), 159.68(CO at $C_{2''}$), 160.05(CO of coumarin), 198.18(COCH$_3$). *Anal.* Calcd. for $C_{26}H_{22}N_4O_5$: C, 66.37; H, 4.71; N, 11.91. Found: C, 66.36; H, 4.70; N, 11.94.

Compound 6f. ir: cm^{-1} 3307, 1726, 1682, 1608, 1443; ^{1}H nmr: δ 1.22(3H, t, -COOCH$_2$ CH_3), 2.19(3H, s, Ar-CH_3), 3.89 (3H, s, OCH$_3$), 3.97(2H, q, -COOCH_2CH$_3$), 5.40(1H, s, methine proton), 7.09-7.65 (10H, m, eight Ar-H and two NH protons merged), 7.76 (1H, s, C_4-H of coumarin), 7.90(1H, s, $C_{5'}$-H of pyrazole); ^{13}C nmr: δ 19.87(CH_3), 30.18(-COO CH$_2$$CH_3$), 30.57($C_{4''}$), 56.21(OCH$_3$), 60.01(-COO$CH_2CH_3$), 112.88(CH), 113.68(C), 119.14 (CH), 119.69(CH), 119.87(C), 123.28(CH), 124.45(CH), 126.53(C), 127.15(C), 127.29(C), 129.32(CH), 139.72(CH), 142.92(CH), 142.97(C), 143.58(C), 145.47(C), 147.01(C), 157.81(CO at $C_{2''}$), 160.11(CO of coumarin), 168.18(COOEt). *Anal.* Calcd. for $C_{27}H_{24}N_4O_6$: C, 64.79; H, 4.83; N, 11.19. Found: C, 64.80; H, 4.82; N, 11.20.

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