Notes

Syntheses of 3-Pyrimidyl- and 3-Pyranyl-5,6-benzocoumarin Derivatives

Ibrahim M. El-Deen,* El-Sayed I. Al-Wakeel, and Ahmed G. El-Mawla

**Faculty of Education, Suez Canal University, Port-said, Egypt*
Faculty of Science, Suez Canal University, Ismailia, Egypt
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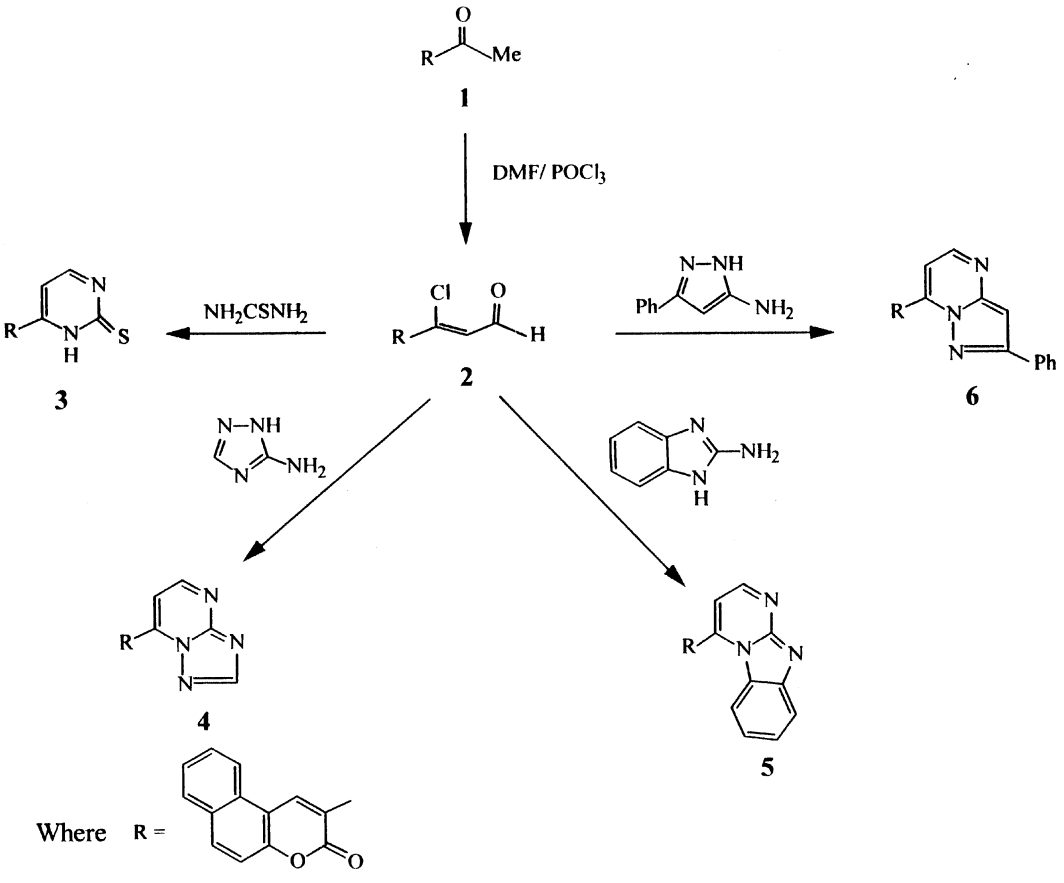
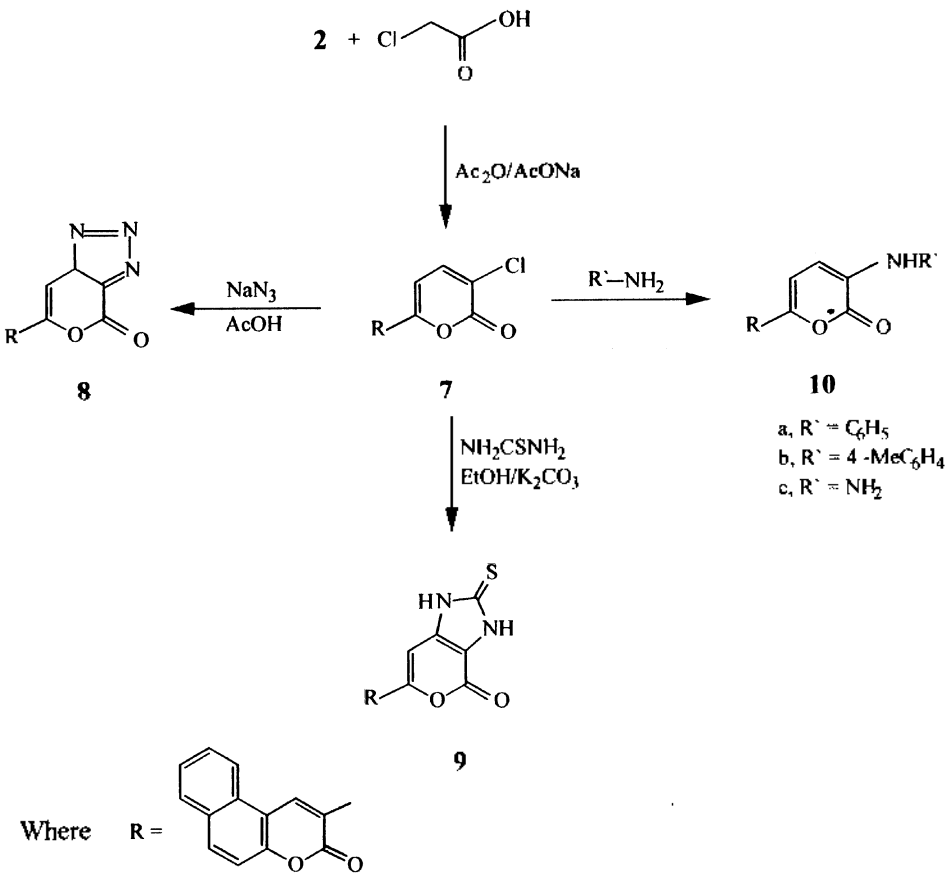
Sulpha drugs are well recognized for their various physiological activities,[1,2] likewise, many pyrimidine derivatives are used as therapeutic agents,[3-8] 5,6-Benzocoumarin derivatives show antimicrobial,[9] antiinflammatory[10] and anticancer[11] activities. The present work describes the syntheses of some new heterocyclyl-benzocoumarins, starting from 3-acetyl-5,6-benzocoumarin (**1**), which are depicted in Scheme 1 and 2.

3-(2'-Formyl-1'-chlorovinyl)-5,6-benzocoumarin (**2**) was prepared from 3-acetyl-5,6-benzocoumarin (**1**) and DMF-$POCl_3$, according to literature procedure.[12] Treatment of compound 2 with thiourea, 3-amino-1,2,4-triazole, 2-aminobenzimidazole and 3-amino-5-phenylpyrazole in dimethyl formamide gave the corresponding 3-(2'-mercapto or 1",2",4-triazolo[1',2'-b] or benzimidazole[1',2'-b] or 5"-phenylpyrazolo[1',2'-b]pyrimidin-6'-yl)-5,6-benzocoumarins (**3-6**).

It has been reported recently[13-16] that 3-(2'-formyl-1'-chlorovinyl)-5,6-benzocoumarin (**2**) reacts with chloroacetic acid in the presence of Ac_2O-AcONa to afford the corresponding 3-(3'-chloro-2'-oxo-2'H-pyran-6'-yl)-5,6-benzocoumarin (7).



Scheme 1



Scheme 2

Treatment of compound **7** with sodium azide in acetic acid gave 3-(1",2",3"-triazolo[3',4'-b]pyran-6'-yl]-5,6-benzocoumarin (**8**). Also, compound **7** reacted with thiourea, hydrazine monosulphate and aromatic amines (namely aniline and *p*-toludine) in ethanol to give 3-(2"-thioxo-2"H-imidazolo-[3',4'-b]pyran-6'-yl]-5,6-benzocoumarin (**9**) and 3-(substituent-2'-oxo-2H'-pyran-6'-yl)-5,6-benzocoumarins (**10a-c**).

Experimental Section

Melting points were determined on a Boetium Hostage apparatus and uncorreted. IR spectra were recorded on a Perkin-Elmer FTIR 1725 spectrometer. The H-NMR Sepctra were recorded on a General Electric QE 300, and chemical shifts were given with respect to TMS. Mass spectra were obtained on a VG Autspec CEI and FAB^+ and a Hewlett Packard MS-Engine thermospray. Microanalyses were conducted using an elemental analyzer 116.

General procedure for synthesis of 3-(substituentpyrimidayl)-5,6-benzocoumarins (3-6). A mixture of **2** (0.01 mol) and aminoheterocycles such as 3-aminotriazole, 2-aminobenzaimidazol and 3-amino-5-phenylpyrazole (0.01 mol) or thiourea (0.01 mol), and potassium carbonate (0.03 mol) in DMF (60 mL) was heated under reflux for 6 hr. The solid formed after cooling was filtered off, dried and recrystallized from ethanol to give corresponding product **4-6**. After the reaction with thiourea, the reaction mixture was cooled and acidified with diluted hydrochloric acid (2%). The product obtained was filtered, washed with water, dried and recrystallized from ethanol to give **3**.

3-(2'-Thioxo-2H-pyrimidin-6'-yl)-5,6-benzocoumarins (**3**), yield 64%; mp 205 °C; IR (cm^{-1}) 3253(NH), 1721 (lactone of coumarin); ^1H NMR (DMSO-d_6) δ 7.19-8.20 (m, 8H, ArH and H-5 of pyrimidine), 8.79 (d, 1H, H-3 of pyrimidine), 10.20 (s, 1H, NH); Mass (m/z) 306 (51) M^+; Found: C, 66.31; H, 3.13; N, 8.89; S, 10.21. $C_{17}H_{10}N_2O_2S$ requires: C, 66.66; H, 3.27; N, 9.15; S, 10.45.

3-(1",2",4-Triazolo[1,2'-b]pyrimidin-6'-yl)-5,6-benzocoumarin (**4**), yield 93%; mp 175 °C; IR (cm^{-1}) 1723 (lactone of coumarin), 1630 (C=N); Mass (m/z) 314 (38) M^+; Found: C, 68.62; H, 2.97; N, 17.47. $C_{18}H_{10}N_4O_2$ requires: C, 68.79; H, 3.18; N, 17.83.

3-(Benzimidazole[1',2'-b]pyrimidin-6'-yl)-5,6-benzocoumarin (**5**), yield 91%; mp 147 °C; IR (cm^{-1}) 1719 (lactone of coumarin), 1628 (C=N); ^1H NMR (DMSO-d_6) δ 7.01-8.21 (m, 12H, ArH and H-5 of pyrimidine), 8.78 (d, 1H, H-4 of pyrimidine); Mass (m/z) 363 (42) M^+; Found: C, 75.86; H, 3.37; N, 11.39. $C_{23}H_{13}N_2O_2$ requires: C, 76.05; H, 3.58; N, 11.57.

3-(5"-Phenylpyrazolo[1',2'-b]pyrimidin-6'-yl)-5,6-benzocoumarin (**6**), yield 64%; mp 184 °C; IR (cm^{-1}) 1721 (lactone of coumarin), 1629 (C=N); ^1H NMR (DMSO-d_6) δ 7.13-8.21 (m, 14H, ArH; pyrazol and H-5 of pyrimidine), 8.77 (d, H-4 of pyrimidine); Mass (m/z) 389 (82) M^+;

Found: C, 77.00; H, 3.49; N, 10.52. $C_{25}H_{15}N_3O_2$ requires: C, 77.12; H, 3.85; N, 10.79.

3-(3'-Chloro-2'-oxo-2'H-pyran-6'-yl)-5,6-benzocoumarin (7). A mixture of **2** (0.01 mol), chloroacetic acid (0.01 mol), acetic anhydride (0.01 mol) and fused sodium acetate (0.02 mol), was fused on a hot plate for 5-10 min. The reaction mixture was added to acetic acid (50 mL) and heated under reflux for 6 hr., then cooled and poured onto water. The resulting product was filtered off, washed with water, dried and recrystallized from ethanol to give **7**, yield 61%; mp 155-156 °C; IR (cm^{-1}) 1729-1719 (br, lactones of coumarin and pyrane); ^1H NMR (DMSO-d_6) δ 7.19-8.27 (m, 9H, ArH and pyrane ring); Mass (m/z) 325 (63) M^+; Found: C, 66.32; H, 2.49; Cl, 10.72. $C_{18}H_9ClO_4$ requires: C, 66.56; H, 2.77; Cl, 10.94.

3-(1'',2'',3''-Triazolo[3',4'-b]pyran-6'-yl]-5,6-benzocoumarin (8). A solution of 7 (0.01 mol) and sodium azide (0.01 mol) in acetic acid (50 mL) was heated in water-bath for 6 hr., then cooled and poured onto water. The resulting product was filtered off, washed with water, dried and recrystallized from ethanol to give **8**, yield 80%; mp 302 °C; IR (cm^{-1}) 1729-1721 (lactones of coumarin and pyrane ring); Mass (m/z) 331 (36) M^-; Found: C, 65.01; H, 2.48; N, 12.36. $C_{18}H_9N_3O_4$ requires: C, 65.25; H, 2.72; N, 12.69.

3-(2'-Thioxo-2H-imidazolo[3',4'-b]pyran-6'-yl]-5,6-benzocoumarin (9). A mixture of 7 (0.01 mol), thiourea (0.01 mol) and potassium carbonate (0.02 mol) in ethanol (50 mL) was heated under reflux for 6 hr. The reaction mixture was cooled and acidified with diluted HCl (2 mol/L). The deposited solid was filtered off, washed with water, dried and recrystallized from ethanol to give **9**, yield 55%; mp 210 °C; IR (cm^{-1}) 3185 (NH), 1732-1717 (lactones of coumarin and pyrane ring); ^1H NMR (DMSO-d_6) δ 7.20-9.19 (m, 8H, ArH and pyrane ring), 10.51-10.53 (br.s, 2H, NH); Mass (m/z) 362(73) M^-; Found: C, 62.63; H, 2.49; N, 7.51; S, 8.48. $C_{19}H_{10}N_2O_4S$ requires: C, 62.98; H, 2.76; N, 7.73; S, 8.84.

3-(3'-Substituent-2'-oxo-2'H-pyran-6'-yl)-5,6-benzocoumarins (10a-c). A solution of 7 (0.01 mol) and aromatic amines namely, aniline and p-toludine (0.01 mol) or hydrazine monosulphate (0.01 mol), and sodium acetate (0.02 mol) in ethanol (70 mL) was heated under reflux for 4 hr. The product formed after cooling was filtered off, washed with water and recrystallized from ethanol, to give **10a-c**.

3-(3'-Phenylamino-2'-oxo-2'H-pyran-6'-yl)-5,6-benzocoumarins (**10a**), yield 77%; mp 190 °C; IR (cm^{-1}) 3189 (NH), 1728-1717 (lactones of coumarin and pyrane ring); ^1H NMR (DMSO-d_6) δ 7.02-8.20 (m, 14H, ArH, and pyrane ring), 10.31 (s, 1H, NH); Mass (m/z) 381 (36) M^-; Found: C, 75.27; H, 3.66; N, 3.32. $C_{24}H_{15}NO_4$ requires: C, 75.59; H, 3.94; N, 3.67.

3-(3'-p-Methylphenylamino-2'-oxo-2'H-pyran-6'-yl)-5,6-benzocoumarins (**10b**), yield 61%; mp 183 °C; IR (cm^{-1}) 3186 (NH), 1726-1716 (lactones of coumarin and pyrane ring); ^1H NMR (DMSO-d_6) δ 2.32 (s, 3H, CH3), 7.10-8.19 (m, 13H, ArH and pyrane ring), 10.33 (s, 1H, NH); Mass (m/z) 395 (39) M^+; Found: C, 75.64; H, 4.03; N, 3.25. $C_{25}H_{17}NO_4$ requires: C, 75.95; H, 4.30; N, 3.54.

3-(3'-Hydrazino-2'-oxo-2'H-pyran-6'-yl)-5,6-benzocoumarins (**10c**), yield 53%; mp 240 °C; IR (cm^{-1}) 3340, 3251, 3180 (NH, NH2), 1729-1719 (lactones of coumarin and pyrane ring); ^1H NMR (DMSO-d_6) δ 9.23 (s, 1H, NH); Mass (m/z) 320 (42) M^-; Found: C, 67.29; H, 3.51; N, 8.44. $C_{18}H_{12}N_2O_4$ requires: C, 67.50; H, 3.75; N, 8.75.

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