Journal of the Chinese Chemical Society, **2005**, *52*, 1191-1199

Synthesis and Some Reactions of Coumarin-3-yl Crotononitrile Derivatives

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Several new coumarinyl crotononitriles, **2a-i**, coumarinyl cinnamocoumarines **3a,b**, 4-amino-3-(substituted)-3,4-dihydrocoumarin **4a-c** and **9a-c**, nicotinic acid derivatives **10a,b** and 4-ethoxy-3-substituted-3,4-dihydrocoumarins **11**, were synthesized from 3-acetyl and/or 3-benzoyl coumarin. The behavior of coumarin-3-yl crotononitriles **2a,b** toward some electrophilic and nucleophilic reagents have been described with the aim of preparing some new heterocyclic compounds.

Keywords: Coumarin derivatives; Condensation; Addition; Coupling and cycloaddition reactions.

Several coumarin derivatives have attracted attention for their significant antibacterial,[1] coronaridilatory[2] and hypothermal[3,4] activities. Therefore, it is of interest to synthesize new coumarinic nitriles utilizing 3-acetyl and/or 3-benzoyl coumarins as starting material. The reaction of 3-acetyl and/or 3-benzoyl coumarin derivatives **1a-c** with nitrile compounds such as malononitrile, 3-iminobutyronitrile and ethyl cyanoacetate were studied in different conditions hoping to obtain 3-cyanovinyl coumarin derivatives **2a-i** for their application as building blocks for several heterocyclic compounds.

In previous studies, it was reported that[5-7] the condensation reaction of 3-acetyl coumarin with malononitrile in basic medium gives 2-cyano-3-(coumarin-3-yl) crotononitrile **2a**.

In the present investigation, 3-acetyl and/or 3-benzoyl coumarin derivatives **1a-c** condensed with malononitrile in boiling benzene containing a buffer mixture of ammonium acetate and acetic acid using a Dean-Stark water separator afforded the target compounds 1-(3-coumarinyl)ethylidine malononitrile derivatives **2a-c** as the sole product in the case of **1c** and contaminated with **3a,b** as by-products in case of **1a,b** (c.f. Scheme I). Formation of **2** is explained in terms of Knoevenagel condensation. The structures of **2a-c** have been confirmed from analytical and spectral data. The IR spectra of **2a-c** showed strong bands at 2220 equivalent to CN and 1725-1720 cm^{-1} equivalent to CO of δ-lacton. The ^{1}H-NMR (DMSO-d_6) spectrum of **2a** showed a singlet at δ 2.7 (s, 3H, CH_3), multiplet at 7.7-8.3 (m, 4H, Ar-H) and a singlet at 8.9 ppm (s, 1H, CH at C_4). The mass spectrum of **2a** showed a mass ion peak at (M^+ = 236) 100% equivalent to $C_{14}H_8N_2O_2$. Formation of **3a,b** as by-product are explained in terms of aldol-type self condensation of 3-acetyl coumarin derivatives. The structure of **3a,b** confirmed from its IR spectra showing strong bands at 1731-1725 cm^{-1} due to CO group of δ-lactone, 1662-1651 cm^{-1} due to CO group of unsaturated ketones and 1608-1606 cm^{-1} due to $\nu_{C=C}$. The mass spectrum of **3a** showed a mass ion peak at (M^+ = 358) equivalent to $C_{22}H_{14}O_5$.

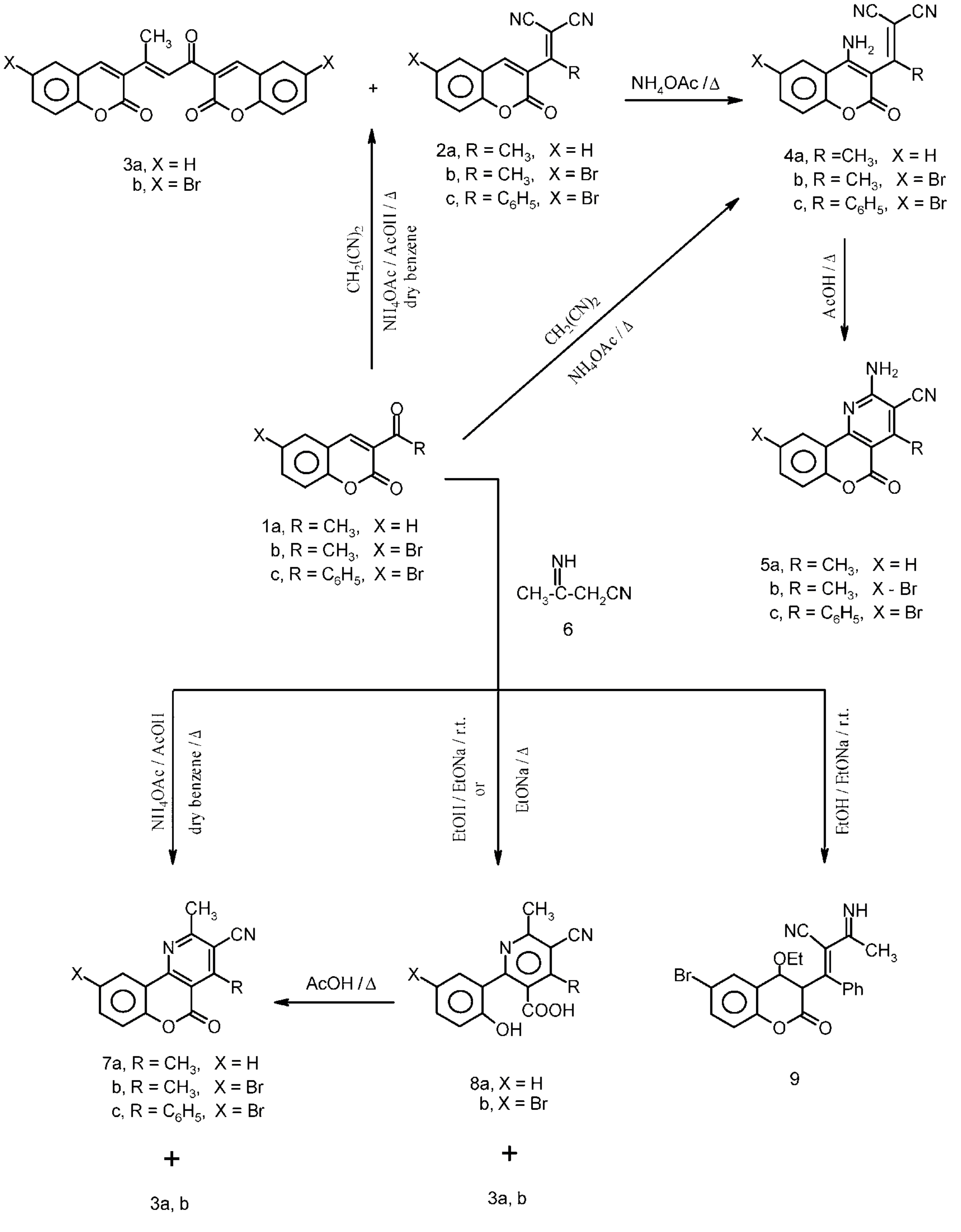
Conducting reactions of **1a-c** with malononitrile using ammonium acetate as catalyst yielded 4-amino-3(2,2-dicyano-1-substituted ethenyl)-3,4-dihydrocoumarins **4a-c** (c.f. Scheme I). Compounds **4a-c** were also obtained from refluxing **2a-c** with ammonium acetate.

The structures of **4a-c** were confirmed from their analytical and spectral data. The IR spectra of compounds **4a-c** showed strong absorption bands at 3430 cm^{-1} and 3395 cm^{-1} due to ν_{NH_2}, at 2221-2197.7 due to ν_{2CN} group and 1740-1734 cm^{-1} due to ν_{CO} of saturated δ-lactone. The ^{1}H-NMR spectrum of compound **4a** showed signals at δ 2.1 (d, 1H, at C-4), δ 2.5 (d, 1H, at C-3), δ 3.6 (s, 3H, CH_3), at 7.3-8.2 (m, 4H, Ar-H) and at δ 9.3 ppm (s, 2H, NH_2).

Compound **4a-c** when refluxed in acetic acid for 2 hrs., afforded the pyridocoumarin derivatives **5a-c** (c.f. Scheme I). The structures of **5a-c** were confirmed from their analytical and spectral data. The IR spectra of compound **5a-c** showed strong bands at 3394 and 3364 cm^{-1} due to ν_{NH_2}, 2216-2213 due to ν_{CN} and 1725-1720 cm^{-1} due to ν_{CO} of unsaturated δ-lactone. The mass spectrum of **5a** showed a parent peak at 251 (55%) corresponding to the molecular formula $C_{14}H_9N_3O_2$.

Similarly,[6,7] compounds **1a-c** reacted with 3-iminobutyronitrile **6** in different reaction conditions. Thus when **1a-c** reacted with **6** in the presence of ammonium acetate, acetic acid mixture in dry benzene furnished compound **7a-c**. The formation of **7a-c** via condensation of active methylene in **6**

Scheme I



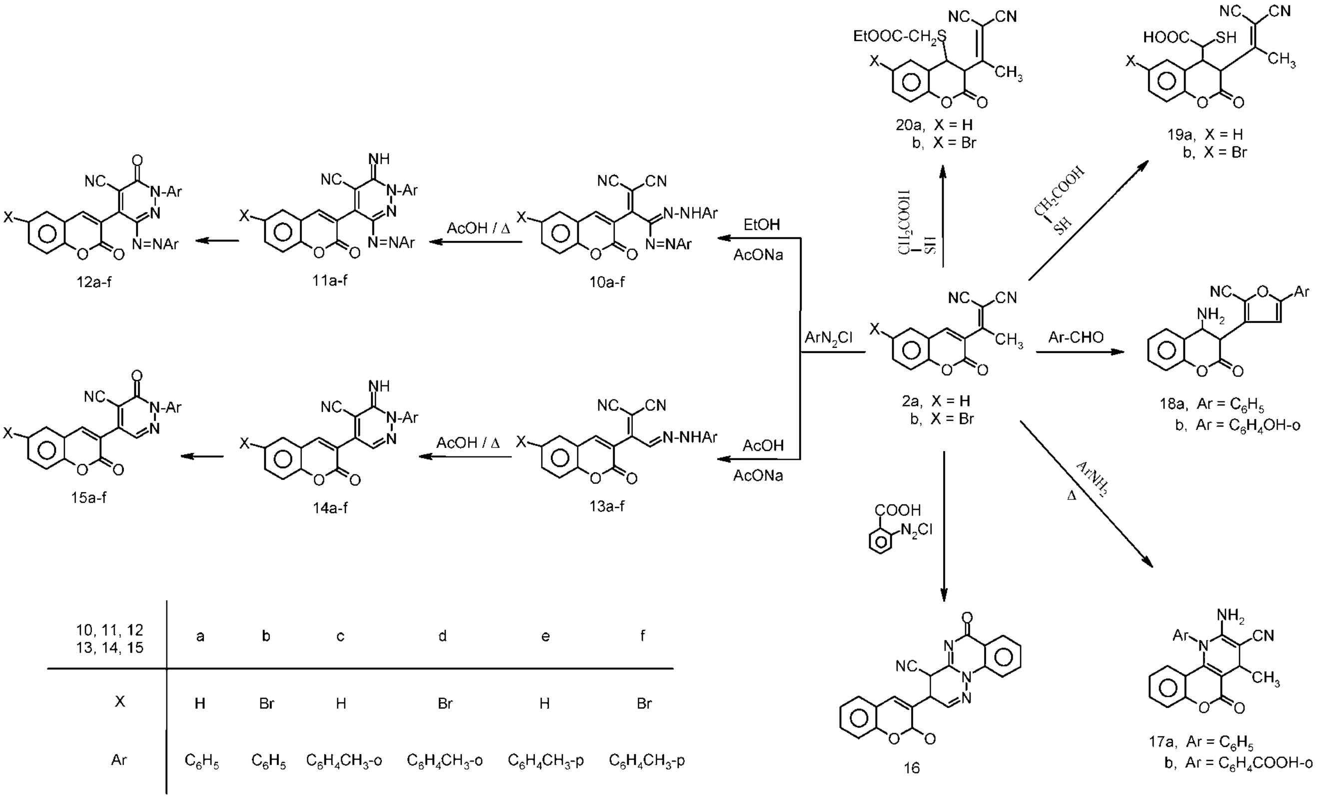
with the carbonyl group in **1a-c** to afford intermediate **7**, then addition of nucleophilic NH to the activated double bond C_3C_4 in pyran ring to afford the dihydropyridine derivative and then aromatized via loss of hydrogen to give the final isolable products **7a-c**. The structures of **7a-c** were established from the correct analytical data and their spectral data. The IR spectra of **9a-c** showed strong bands at 2220-2215 cm^{-1} due to ν_{CN} and at 1719-1710 cm^{-1} due to ν_{CO} of δ-lactone. The mass spectrum of **7b** showed the molecular ion peak at *m/e* = 328/330 (33%) corresponding to the molecular formula $C_{15}H_9N_2O_2Br$. Also, the mass spectrum of **7c** showed the molecular ion peak at *m/e* = 390/392 (100%) corresponding to the molecular formula $C_{20}H_{11}N_2O_2Br$.

The reaction of **1a,b** with **6** in the presence of ethanol and sodium ethoxide mixture at room temperature or fusion with sodium ethoxide, gives nicotinic acid derivatives **8a,b** as main products and **3a,b** as minor products. The structures of **8a,b** were confirmed from their analytical and spectral data. The IR spectra of **8a,b** showed strong absorption bands at 2219-2199 cm^{-1}, due to ν_{CN} groups and at 1650-1643 cm^{-1} due to ν_{CO} groups. ^1H-NMR (DMSO-d_6) spectrum of **8a** showed at δ 2.57 (s, 3H, CH_3), at δ 3.42 (s, 3H, CH_3), at δ 7.18-7.65 (m, 4H, Ar-H), at δ 8.81 (s, 1H, OH) and at δ 9.61 (s, 1H, COOH). The mass spectrum of **8a** showed a peak at *m/e* 250 (38%) due to splitting of water molecules (M^+-H_2O). Compound **8a,b** converted into **7a,b** when refluxed with acetic acid.

In contrast to the behaviour of **1a,b** toward **6**, compound **1c** reacted with **6** in the presence of ethanol and sodium ethoxide to give 4-ethoxy-3,4-dihydrocoumarin derivative **9**. The addition of ethanol to an activated double bond has been reported.[8] The structure of **9** was confirmed from analytical and spectral data. The IR spectrum of **9** showed bands at 3322 cm^{-1} due to ν_{NH}, at 2218 cm^{-1} due to ν_{CN} and 1740 cm^{-1} due to ν_{CO} of saturated δ-lactone the ^1H-NMR ($CDCl_3$) spectrum of **9** showed at δ 1.049 (t, 3H, $\underline{CH_3}CH_2O$), at 2.16 (s, 3H, CH_3 side chain), at δ 3.20 (d, 1H, at C_3), at δ 3.85 (d, 1H, at C_4), at δ 3.99 (q, 2H, $CH_3\underline{CH_2}O$), at δ 5.49 (s, 1H, NH) and at δ 7.2-7.61 ppm (m, 8H, Ar-H), and the mass spectrum of **9** showed the molecular ion at *m/e* = 438/440 (14.8%) corresponding to the molecular formula $C_{22}H_{19}N_2O_3Br$.

In continuation of our research program[6-15] for developing studies, the coupling of **2a,b** with aromatic diazonium salts and the coupling product were found to be dependent on the applied coupling reaction conditions. Thus, compounds **2a,b** coupled with aryl diazonium salts in ethanol containing sodium acetate gave acyclic azahydrazone **10a-f**. The supporting evidence for structures **10a-f** were provided by analytical and spectral data. The IR spectra of compounds **10a-f** showed strong bands at 4322-3236 cm^{-1} (NH) at 2235-2195 cm^{-1} (2CN) and at 1734-1722 cm^{-1} (CO groups). The ^1H-NMR (DMSO-d_6) spectrum of compound **10b** showed signals at δ 7.3-7.9 (m, 13H, Ar-H), 8.4 (s, 1H, H-4) and 12 ppm (s, 1H, NH). Further support for the structure **10a-f** was provided by the mass spectrum **10b** showing the molecular ion peak at *m/e* 522/524 equivalent to $C_{26}H_{15}N_6O_2Br$ and the mass spectrum of **10e** showing the mass ion peak at *m/e* 472 equivalent to $C_{28}H_{20}N_6O$. When compounds **10a-f** were refluxed in acetic

Scheme II



10, 11, 12 13, 14, 15	a	b	c	d	e	f
X	H	Br	H	Br	H	Br
Ar	C_6H_5	C_6H_5	$C_6H_4CH_3$-o	$C_6H_4CH_3$-o	$C_6H_4CH_3$-p	$C_6H_4CH_3$-p

acid, the pyridazin-6-ones **12a-f** were obtained. The formation of **12a-f** were assumed to proceed via **11a-f** which however could be isolated. The confirmatory evidence for structures **12a-f** were provided by analytical and spectral data. The IR spectra of **15a-f** showed strong absorption bands at 2231-2195 cm^{-1} (CN), at 1727-1721 cm^{-1} (CO) groups of unsaturated δ-lactone and at 1685-1665 cm^{-1} (CO) groups in pyridazine rings.

In contrast to the behaviour of **2a-c** towards aryl diazonium salts in ethanolic sodium acetate, the coupling with aryl diazonium salts in acetic acid containing sodium acetate yielded the mono coupling product **13a-f**. Supporting evidence for the structures **13a-f** were provided by analytical and spectral data. The IR spectra of **13a-f** showed strong absorption bands at 3416-3148 cm^{-1} due to (NH) group, at 2237-2189 cm^{-1} due to (2CN) groups and at 1732-1709 cm^{-1} due to (CO) groups of δ-lactone. Compounds **13a-f** could be cyclized on heating under reflux in acetic acid to yield **15a-f**. The formation of **15a-f** is assumed to proceed via intermediate **14a-f**. Supporting evidences for structure **15a-f** was provided by analytical and spectral data. The IR spectra of **15a-f** showed strong absorption bands at 2232-2180 cm^{-1} (CN) group, at 1729-1722 cm^{-1} due to (CO) groups of δ-lactone and at 1682-1656 cm^{-1} due to (CO) groups of pyridazine rings. The mass spectrum of compound **15a** showed the molecular ion peak at *m/e* = 341 equivalent to $C_{20}H_{11}N_3O_3$.

Compound **2a** coupled in ethanolic sodium acetate with diazotized anthranilic acid to give quinazotine derivative[9] structure of compound **16** was confirmed from its correct analytical data and spectral data. The IR spectrum of **16** showed strong absorption bands at 2237 cm^{-1} (CN), at 1720 due to ν_{CO} of δ-lactone and at 1671 cm^{-1} duet to ν_{CO} of pyrimidine ring. The ^{1}H-NMR (DMSO-d_6) spectrum of **16** showed signals at δ 7.03 (s, 1H, pyridazine), at 7.11 (m, 8H, Ar-H) and at 8.6 ppm (s, 1H, pyran C_4). The mass spectrum of **16** showed the molecular ion peak at *m/e* = 366 equivalent to $C_{21}H_{10}N_4O_3$.

The behaviour of compound **2a** towards primary aromatic amines, namely aniline and anthranilic acid, to give the pyridine derivatives **17a,b**. The structures of **17a,b** was inferred from corrected analytical data and their IR spectra of **17a,b** which showed strong absorption bands at 3423-3380 cm^{-1} due to ν_{NH_2} groups, at 2211-2193 cm^{-1} due to ν_{CN} groups and at 1724-1720 cm^{-1} due to ν_{CO} of δ-lactone. The mass spectrum of **17a** showed the molecular ion peak at *m/e* = 373 equivalent to $C_{20}H_{15}N_3O_2$ and the base peak at *m/e* 355 due to the splitting of H_2O molecule.

The reaction of pyridine derivative **2a** with aromatic aldehydes namely benzaldehyde and/or salicyaldehyde in the presence of ammonium acetate yielded furan derivatives **18a,b**. The structures of **18a,b** were supported by analytical and spectral data. The IR spectra of **18a,b** showed strong absorption bands at 3460-3371 cm^{-1} due to ν_{NH_2} gropus, 2208-2213 cm^{-1} due to ν_{CN} groups and at 1729-1731 cm^{-1} due to ν_{CO} of δ-lactone. The ^{1}H-NMR spectrum of **18a** showed signals at δ 3.2 (d, 1H, C_4 pyran) at 3.4 (d, 1H, C_3 pyran) at 7.4-8.4 (m, 10H, Ar-H) and at 9.1 ppm (s, 2H, NH_2). The mass spectrum of **18a** showed the molecular ion peak at *m/e* = 330 equivalent to $C_{20}H_{14}N_2O_3$.

Compound **2a,b** reacted with thioglycollic acid[10,11] in ethanol triethyl amine to give mercapto acetic acid derivatives **19a,b**. The structure of **19a,b** was provided by analytical and spectral data. The IR spectra of **19a,b** showed strong absorption bands at 3560-2668 cm^{-1} broad bands due to carboxylic OH groups, at 2226-2218 cm^{-1} due to ν_{CN} groups and 1745-1739 cm^{-1} due to ν_{CO} of δ-lactone groups. The ^{1}H-NMR spectrum (DMSO-d_6) of compound **19a** showed signals at δ 2.52 (t, 1H, C_4 pyran), at 3.35 (d, 1H, of thioglycollic acid), at 3.58 (s, 3H, CH_3), at 4.24 (s, 1H, -SH) and at 7.40-7.78 ppm (m, 4H, Ar-H). The mass spectrum of **19a** showed a molecular ion peak at *m/e* 328 equivalent to $C_{16}H_{12}N_2O_4S$.

Similarly[10,11] compound **2a-b** reacted with ethyl thioglycollate to yield 4-ethoxycarbonylmeththio-3,4-dihydrocoumarin derivatives **27a,b**. The structures of **27a,b** are provided by analytical and spectral data. The IR spectra of **20a,b** showed strong absorption bands at 2210 cm^{-1} due to ν_{CN} groups, 1737-1735 cm^{-1} due to ν_{CO} groups of saturated δ-lactone and at 1726-1722 cm^{-1} to ν_{CO} of ester groups. The ^{1}H-NMR spectrum ($CDCl_3$) of **20a** showed signals at δ 1.27 (t, 3H, $-CH_2\underline{CH_3}$), at 3.04 (s, 3H, CH_3), at 3.35 (d, 1H, C_4), at 3.73 (d, 1H, C_3), at 4.12 (s, 2H, CH_2- of thioglycollate), at 4.21 (q, 2H, $\underline{CH_2}CH_3$) and at 7.39-8.5 ppm (m, 4H, Ar-H). The mass spectrum of compound **20b** showed the molecular ion peak at *m/e* 434/436 (M^+/M^++2) equivalent to $C_{18}H_{15}N_2O_4BrS$.

EXPERIMENTAL

All melting points are uncorrected and were determined on a Stuart electric melting point apparatus. Elemental analysis was performed by the Microanalysis Center, Faculty of Science, Cairo University. Infrared spectra were recorded on Bruker or Satellite 2000 spectrometers using KBr discs. Mass spectra were determined on a GC-MS (QP/000 EX) Shimadzu spectrometer at an ionizing voltage of 70 eV. Nuclear magnetic resonance spectra were recorded on a Varian Mercury 300 MHz spectrometer using TMS as internal standard;

chemical shifts are reported in δ units.

Synthesis of 3-(substituted ethenyl) coumarin derivatives 2a-c and 3-[1-methyl-2-(3-coumarinoyl)ethenyl] coumarin derivatives 3a,b

A mixture of each of 6-substituted-3-acetyl and/or 3-benzoyl coumarin derivatives **1a-c** (0.01 mol.) and malononitrile (6.6 g, 0.1 mol.) was heated in glacial acetic acid (10 mL) and ammonium acetate (1 g) in dry benzene (75 mL) for 9 hrs. using a Dean-Stark water separator. The reaction mixture was filtered off on heat, the solids that separated were dried and recrystallized from the proper solvents to give α,β-unsaturated ketone derivatives **3a,b**. The solids that separated on cooling were filtered off, dried and recrystallized from the proper solvent to give compounds **2a-c**.

2a: recrystallized from ethanol to give yellow crystals in 57% yield, m.p. 163 °C. Anal. $C_{14}H_8N_2O_2$ (236.23), Calcd.: C, 71.18%; H, 3.41%; N, 11.85%; Found: C, 71.30%; H, 3.20%; N, 11.90%.

2b: recrystallized from ethanol to give yellow crystals in 60% yield, m.p. 204 °C. Anal. $C_{14}H_7N_2O_2Br$ (315.13), Calcd.: C, 53.36%; H, 2.24%; N, 8.88%; Br, 25.35%; Found: C, 53.25%; H, 2.30%; N, 8.85%; Br, 25.20%.

2c: recrystallized from dioxane to give colorless crystals in 80% yield, m.p. 185 °C. Anal. $C_{19}H_9N_2O_2Br$ (377.20), Calcd.: C, 60.50%; H, 2.41%; N, 7.42%; Br, 21.18%; Found: C, 60.45%; H, 2.40%; N, 7.40%; Br, 21.20%.

3a: recrystallized from acetic acid to give colorless crystals in 12% yield, m.p. 300 °C. Anal. $C_{22}H_{14}O_5$ (358.35), Calcd.: C, 73.74%; H, 3.94%; Found: C, 73.60%; H, 4.10%.

3b: recrystallized from acetic acid to give gray crystals in 11% yield, m.p. above 330 °C. Anal. $C_{22}H_{12}O_5Br_2$ (516.15), Calcd.: C, 51.20%; H, 2.34%; Br, 30.96%; Found: C, 51.30%; H, 2.20%; Br, 30.80%.

Synthesis of 4-amino-3-(2,2-dicyano-1-substituted ethenyl)-3,4-dihydrocoumarin derivatives 4a-c

Method (A)

A mixture of each of 3-acetyl and/or 3-benzoyl coumarin derivatives **1a-c** (0.01 mol.) and malononitrile (0.66 g, 0.01 mol.) in the presence of ammonium acetate (1.54 g, 0.02 mol.) was heated in an oil-bath at 150 °C for 30 min. The reaction mixture was poured onto ice/HCl. The solid that separated out was filtered, dried and recrystallized from the proper solvents to give compounds **4a-c**.

Method (B)

A mixture of each of 3-(substituted ethenyl) coumarin derivatives **2a-c** (0.01 mol.) and ammonium acetate (1.54 g, 0.02 mol.) was fused in an oil-bath at 150 °C for 2 hrs. The reaction mixture was treated by methanol. The formed precipitates were removed by filtration and recrystallized from the proper solvents to give compounds **4a-c**.

4a: recrystallized from methanol to give brown crystals in 65% yield, m.p. 218 °C. Anal. $C_{14}H_{11}N_3O_2$ (253.26), Calcd.: C, 66.40%; H, 4.38%; N, 16.59%; Found: C, 66.25%; H, 4.30%; N, 16.60%.

4b: recrystallized from methanol to give brown crystals in 55% yield, m.p. 226 °C. Anal. $C_{14}H_{10}N_3Br$ (332.16), Calcd.: C, 50.63%; H, 3.03%; N, 12.65%; Br, 24.05%; Found: C, 50.70%; H, 3.00%; N, 12.45%; Br, 23.90%.

4c: recrystallized from ethanol to give brown crystals in 43% yield, m.p. 241 °C. Anal. $C_{19}H_{12}N_3O_2Br$ (394.23), Calcd.: C, 57.89%; H, 3.07%; N, 10.65%; Br, 20.26%; Found: C, 58.00%; H, 2.95%; N, 10.50%; Br, 20.30%.

Synthesis of 4-amino-3-cyano-4-substituted-5H-benzopyrano[4,3-b]pyridine-5-one derivatives 5a-c

A solution of **4a-c** (0.01 mol.) in glacial acetic acid (30 mL) was refluxed for 3 hrs. The solids that separated on concentration and cooling were filtered off and recrystallized from the proper solvents as compounds **5a-c**.

5a: recrystallized from dioxane to give brown crystals in 66% yield, m.p. 271 °C. Anal. $C_{14}H_9N_3O_2$ (251.25), Calcd.: C, 66.93%; H, 3.61%; N, 16.72%; Found: C, 66.75%; H, 3.60%; N, 16.75%.

5b: recrystallized from dioxane to give yellow crystals in 39% yield, m.p. 285 °C. Anal. $C_{14}H_{10}N_3O_2Br$ (330.14), Calcd.: C, 50.93%; H, 2.44%; N, 12.72%; Br, 24.20%; Found: C, 51.00%; H, 2.30%; N, 12.65%; Br, 24.10%.

5c: recrystallized from dioxane to give brown crystals in 55% yield, m.p. 322 °C. Anal. $C_{19}H_{10}N_3O_2Br$ (392.21), Calcd.: C, 58.19%; H, 2.57%; N, 10.71%; Br, 20.37%; Found: C, 57.95%; H, 2.60%; N, 10.60%; Br, 20.40%.

Synthesis of 3-cyano-2-methyl-4-substituted-5H-benzopyrano[4,3-b]pyridine-5-one derivatives 7a-c

A mixture of each of 6-substituted-3-acetyl and/or 3-benzoyl coumarin derivatives **1a-c** (0.03 mol.) and 3-iminobutyronitrile **6** (2.46 g, 0.03 mol.) was heated in glacial acetic acid (10 mL) and ammonium acetate (1 g) in dry benzene (75 mL) for 11 hrs. using a Dean-Stark water separators compounds **3a,b** formed during the reflux were filtered off while the reaction mixture was hot and recrystallized from the proper solvents. The solid that separated on cooling was filtered off, dried and recrystallized from the proper solvents to give compounds **7a-c**.

7a: recrystallized from acetic acid to give orange crystals in 50% yield, m.p. 247 °C. Anal. $C_{15}H_{10}N_2O_2$ (250.26), Calcd.: C, 71.99%; H, 4.03%; N, 11.19%; Found: C, 72.20%; H, 3.85%; N, 11.30%.

7b: recrystallized from ethanol to give grey crystals in 55% yield, m.p. 205 °C. Anal. $C_{15}H_9N_2O_2Br$ (329.16), Calcd.: C, 54.74%; H, 2.76%; N, 8.51%; Br, 24.27%; Found: C, 54.50%; H, 2.90%; N, 8.40%; Br, 24.35%.

7c: recrystallized from dioxane to give yellow crystals in 75% yield, m.p. 243 °C. Anal. $C_{20}H_{11}N_2O_2Br$ (391.23), Calcd.: C, 61.40%; H, 2.83%; N, 7.16%; Br, 20.42%; Found: C, 61.30%; H, 2.90%; N, 7.00%; Br, 20.50%.

Synthesis of 5-cyano-4,6-dimethyl-2-(2′-hydroxyphenyl)-pyridine-3-caboxylic acid derivatives 8a,b

Method (A)

A mixture of each of 6-substituted-3-acetyl and/or 3-benzoyl coumarin derivatives **1a-c** (0.01 mol.) 3-iminobutyronitrile **6** (0.82 g 0.01 mol.) and sodium metal (0.23 g, 0.01 mol.) in the presence of 30 mL absolute ethanol were left for 5 days at room temperature. The reaction mixture was poured into crushed ice/HCl. The solid mixture that was obtained was fractionally crystallized from the proper solvents to yield compounds **8a-c**, and the residue crystallized from the proper solvents to give **3a-b**.

Method (B)

A mixture of each of 6-substituted-3-acetyl and/or 3-benzoyl coumarin derivatives **1a-c** (0.01 mol.) and 3-iminobutyronitrile **6** (0.82 g, 0,01 mol.) in the presence of sodium ethoxide (0.68 g, 0.01 mol.) was heated at 160 °C (bath temperature) for 30 min. The reaction mixture was poured into crushed ice/HCl to yield a solid mixture of **3a,b** and **8a,b**. The solid mixture that precipitated was triturated as in method (A) to give **8a,b** and **3a,b**.

8a: recrystallized from ethanol to give yellow crystals in 45% yield, m.p. 200 °C. Anal. $C_{15}H_{12}N_2O_3$ (268.27), Calcd.: C, 67.16%; H, 4.51%; N, 10.44%; Found: C, 66.95%; H, 4.60%; N, 10.30%.

8b: recrystallized from methanol to give yellow crystals in 50% yield, m.p. 181 °C. Anal. $C_{15}H_{11}N_2O_3Br$ (347.17), Calcd.: C, 51.90%; H, 3.19%; N, 8.06%; Br, 23.01%; Found: C, 51.70%; H, 3.30%; N, 7.90%; Br, 23.20%.

Synthesis of 4-ethoxy-3,4-dihydrocoumarin derivative 9

To a suspension of 6-bromo-3-benzoyl coumarin **1c** (3.2 g, 0.01 mol.) and 3-iminobutyronitrile **6** (0.8 g, 0.01 mol.) in 30 mL absolute ethanol were added 0.23 g (0.01 mol.) sodium metal. The reaction mixture was left for 7 days at room temperature, then poured into crushed ice/HCl. The solid that was obtained was filtered off and recrystallized from methanol to give compound **9** in 65% yield as pale yellow crystals, m.p. 148 °C. Anal. $C_{22}H_{19}N_2O_3Br$ (439.30), Calcd.: C, 60.14%; H, 4.35%; N, 6.37%; Br, 18.18%; Found: C, 60.40%; H, 4.20%; N, 6.45%; Br, 17.95%.

Synthesis of 3-(1,1-dicyano-3-arylazo-3-arylhydrazo propenyl) coumarin derivatives 10a-f

A solution of aryl diazonium chloride, namely phenyl, o-tolyl and p-tolyl diazonium chloride (0.02 mol.) (prepared from 0.02 mol. of the aromatic amine and the appropriate quantities of hydrochloric acid and sodium nitrite), was added gradually while stirring to a cold solution of each of **2a,b** (0.01 mol.) in ethanol (50 mL) containing sodium acetate (5 g). The reaction mixture was left for 30 min. The solid product so formed was collected by filtration and crystallized from the proper solvents to yield compounds **10a-f**.

10a: recrystallized from ethanol to give red crystals in 85% yield, m.p. 195 °C. Anal. $C_{26}H_{16}N_6O_2$ (444.44), Calcd.: C, 70.26%; H, 3.62%; N, 18.90%; Found: C, 69.95%; H, 3.70%; N, 18.80%.

10b: recrystallized from benzene to give red crystals in 88% yield, m.p. 182 °C. Anal. $C_{26}H_{15}H_6O_2Br$ (523.34), Calcd.: C, 59.67%; H, 2.88%; N, 16.05%; Br, 15.26%; Found: C, 59.45%; H, 2.90%; N, 16.10%; Br, 15.30%.

10c: recrystallized from methanol to give red crystals in 80% yield, m.p. 222 °C. Anal. $C_{28}H_{20}N_6O_2$ (472.49), Calcd.: C, 71.17%; H, 4.26%; N, 17.78%; Found: C, 71.10%; H, 4.00%; N, 17.65%.

10d: recrystallized from methanol to give red crystals in 80% yield, m.p. 190 °C. Anal. $C_{28}H_{19}N_6O_2Br$ (551.38), Calcd.: C, 60.99%; H, 3.47%; N, 15.24%; Br, 14.49%; Found: C, 61.10%; H, 3.30%; N, 15.30%; Br, 14.40%.

10e: recrystallized from dioxane to give red crystals in 80% yield, m.p. 235 °C. Anal. $C_{28}H_{20}N_6O_2$ (472.49), Calcd.: C, 71.17%; H, 4.26%; N, 17.78%; Found: C, 71.10%; H, 4.10%; N, 17.80%.

10f: recrystallized from benzene to give red crystals in 75% yield, m.p. 145 °C. Anal. $C_{28}H_{19}N_6O_2Br$ (551.38), Calcd.: C, 60.99%; H, 3.47%; N, 15.24%; Br, 14.49%; Found: C, 60.85%; H, 3.30%; N, 15.15%; Br, 14.55%.

Synthesis of 3-(1-aryl-3-arylazo-5-cyanopyridazin-6-one-4-yl) coumarin derivatives 12a-f

A solution of each of **13a-f** (0.01 mol.) in acetic acid (30 mL) was refluxed for 2 hr. The reaction mixture was poured into crushed ice. The solid products, so formed, were collected by filtration and crystallized from the proper solvents to give **15a-f**.

12a: recrystallized from acetic acid to give grey crystals in 70% yield. Anal. $C_{26}H_{15}N_5O_3$ (445.42), Calcd.: C, 70.10%; H, 3.39%; N, 15.72%; Found: C, 70.00%; H, 3.40%; N, 15.60%.

12b: recrystallized from ethanol to give brown crystals in 65% yield, m.p. 175 °C. Anal. $C_{26}H_{14}N_5O_3Br$ (524.31), Calcd.: C, 59.55%; H, 2.69%; N, 13.41%; Br, 15.23%. Anal. Found: C, 59.40%; H, 2.70%; N, 13.50%; Br, 15.20%.

12c: recrystallized from ethanol to give yellow crystals in 75% yield, m.p. 203 °C. Anal. $C_{28}H_{19}N_5O_3$ (473.47), Calcd.: C, 71.09%; H, 4.04%; N, 14.79%; Found: C, 70.90%; H, 4.10%; N, 14.85%.

12d: recrystallized from dioxane to give yellow crystals in 75% yield, m.p. 211 °C. Anal. $C_{28}H_{18}N_5O_3Br$ (552.37), Calcd.: C, 60.88%; H, 3.28%; N, 12.67%; Br, 14.46%; Found: C, 61.00%; H, 3.30%; N, 12.50%; Br, 14.55%.

12e: recrystallized from dioxane to give yellow crystals in 60% yield, m.p. 265 °C. Anal. $C_{28}H_{19}N_5O_3$ (473.47), Calcd.: C, 71.09%; H, 4.04%; N, 14.79%; Found: C, 71.20%; H, 3.80%; N, 14.85%.

12f: recrystallized from ethanol to give yellow crystals in 65% yield, m.p. 204 °C. $C_{28}H_{18}N_5O_3Br$ (552.37), Calcd.: C, 60.88%; H, 3.28%; N, 12.67%; Br, 14.46%; Found: C, 60.70%; H, 3.30%; N, 12.50%; Br, 14.60%.

Synthesis of 3-(1,1-dicyano-3-arylhydrazopropenyl) coumarin derivatives 13a-f

A solution of aryl diazonium chloride, namely phenyl, o-tolyl and p-tolyl diazonium chloride (0.01 mol.), was added gradually while stirring to a cold solution of **2a,b** (0.01 mol.) in acetic acid (50 mL) containing sodium acetate (5 g). The reaction mixture was left overnight in an ice-bath. The solid product that formed was collected by filtration and crystallized from the proper solvents to yield compounds **13a-f**.

13a: recrystallized from ethanol to give red crystals in 86% yield, m.p. 145 °C. Anal. $C_{20}H_{12}N_4O_2$ (340.43), Calcd.: C, 70.56%; H, 3.58%; N, 16.45%; Found: C, 70.70%; H, 3.40%; N, 16.55%.

13b: recrystallized from methanol to give red crystals in 81% yield, m.p. 143 °C. Anal. $C_{20}H_{11}N_4O_2Br$ (419.23), Calcd.: C, 57.29%; H, 2.64%; N, 13.36%; Br, 19.05%; Found: C, 57.40%; H, 2.50%; N, 13.50%; Br, 18.90%.

13c: recrystallized from methanol to give orange crystals in 85% yield, m.p. 171 °C. Anal. $C_{21}H_{14}N_4O_2$ (354.36), Calcd.: C, 71.17%; H, 3.98%; N, 15.87%; Found: C, 71.10%; H, 4.00%; N, 16.00%.

13d: recrystallized from methanol to give red crystals in 76% yield, m.p. 162 °C. Anal. $C_{21}H_{13}N_4O_2Br$ (433.25), Calcd.: C, 58.21%; H, 3.02%; N, 12.93%; Br, 18.44%; Found: C, 58.00%; H, 3.20%; N, 13.00%; Br, 18.50%.

13e: recrystallized from ethanol to give red crystals in 66% yield, m.p. 168% °C. Anal. $C_{21}H_{14}N_4O_2$ (354.36), Calcd.: C, 71.17%; H, 3.98%; N, 15.87%; Found: C, 70.90%; H, 4.10%; N, 15.95%.

13f: recrystallized from ethanol to give red crystals in 70% yield, m.p. 171 °C. Anal. $C_{21}H_{13}N_4O_2Br$ (433.25), Calcd.: C, 58.21%; H, 3.02%; N, 12.93%; Br, 18.44%; Found: C, 58.10%; H, 3.10%; N, 12.80%; Br, 18.55%.

Synthesis of 3-(1-aryl-5-cyanopyridazin-6-one-4-yl) coumarin derivatives 15a-f

A solution of each of **13a-f** (0.01 mol.) in acetic acid (30 mL) was refluxed for 2 hrs. The reaction mixture was poured into crushed ice. The solid products that separated out were crystallized from the proper solvents to give **15a-f**.

15a: recrystallized from acetic acid to give yellow crystals in 75% yield, m.p. 262 °C. Anal. $C_{20}H_{11}N_3O_3$ (341.31), Calcd.: C, 70.37%; H, 3.24%; N, 12.31%; Found: C, 70.25%; H, 3.40%; N, 12.20%.

15b: recrystallized from ethanol to give yellow crystals in 75% yield, m.p. 194 °C. Anal. $C_{20}H_{10}N_3O_3Br$ (420.20), Calcd.: C, 57.16%; H, 2.39%; N, 10.00%; Br, 19.01%; Found: C, 57.00%; H, 2.45%; N, 10.20%; Br, 18.90%.

15c: recrystallized from ethanol to give grey crystals in 76% yield, m.p. 193 °C. Anal. $C_{21}H_{13}N_3O_3$ (355.34), Calcd.: C, 70.97%; H, 3.68%; N, 11.82%; Found: C, 71.00%; H, 3.55%; N, 11.90%.

15d: recrystallized from methanol to give yellow crystals in 65% yield, m.p. 200 °C. Anal. $C_{21}H_{12}N_3O_3Br$ (434.22), Calcd.: C, 58.08%; H, 2.78%; N, 9.67%; Br, 18.40%; Found: C, 58.10%; H, 2.65%; N, 9.55%; Br, 18.50%.

15e: recrystallized from acetic acid to give yellow crystals in 60% yield, m.p. 208 °C. Anal. $C_{21}H_{13}N_3O_3$ (355.34), Calcd.: C, 70.97%; H, 3.68%; N, 11.82%; Found: C, 70.80%; H, 3.75%; N, 11.70%.

15f: recrystallized from ethanol to give yellow crystals in 75% yield, m.p. 192 °C. Anal. $C_{21}H_{12}N_3O_3Br$ (434.22), Calcd.: C, 58.08%; H, 2.78%; N, 9.67%; Br, 18.40%; Found: C, 58.20%; H, 2.75%; N, 9.80%; Br, 18.35%.

Synthesis of 4-cyano-3-(coumarin-3-yl)-6-oxo-pyridazino-[1,6-a]quinazoline 16

A solution of diazonium chloride of anthranilic acid (0.01 mol.) was added gradually while stirring to a cold solution of 3-(2,2-dicyano-1-methyl ethenyl) coumarin **2a** (2.36 g, 0.01 mol.) in ethanol (50 mL) containing sodium acetate (5 g). The reaction mixture was left for 30 min. The solid product so formed was collected by filtration and crystallized from ethanol to yield compound **16** in 75% yield, m.p. 218 °C. Anal. $C_{21}H_{10}N_4O_3$ (366.34), Calcd.: C, 68.85%; H, 2.75%; N, 15.29%; Found: C, 68.70%; H, 2.85%; N, 15.40%.

Synthesis of 2-amino-1-aryl-3-cyano-4-methyl-4,5-dihydrobenxopyrano[4,3-b]pyridine-5-one derivatives 17a,b

Method (A)

A solution of 3-(2,2-dicyano-1-methyl ethenyl) coumarin **2a** (2.36 g, 0.01 mol.) and primary aromatic amines, namely aniline and/or anthranilic acid (0.01 mol.) in n-butane (20 mL), was refluxed for 40 hrs. The solids that separated after concentration and cooling were filtered off to give compounds **17a,b**, respectively.

Method (B)

A solution of 3-(2,2-dicyano-1-methyl ethenyl) coumarin **2a** (2.36 g, 0.01 mol.) and primary aromatic amines, namely aniline and/or anthranilic acid (0.01 mol.), was heated in an oil-bath at about 150 °C for 2 hrs. The reaction mixture was poured into crushed ice; the solids that obtained were filtered off and crystallized from the proper solvents to give compounds **17a,b** respectively.

17a: recrystallized from ethanol to give brown crystals in 65% yield, m.p. 187 °C. Anal. $C_{20}H_{15}N_3O_2$ (329.35), Calcd.: C, 72.93%; H, 4.59%; N, 12.75%; Found: C, 72.85%; H, 4.70%; N, 12.60%.

17b: recrystallized from dioxane to give brown crystals in 85% yield, m.p. 222 °C. Anal. $C_{21}H_{15}N_3O_4$ (373.36), Calcd.: C, 67.55%; H, 4.04%; N, 11.25%; Found: C, 67.30%; H, 4.20%; N, 11.30%.

Synthesis of 4-amino-2-cyano-3,4-dihydro-3-(5-aryl furan-3-yl) coumarin derivatives 18a,b

A solution of 3-(2,2-dicyano-1-methyl ethenyl) coumarin **2a** (2.36 g, 0.01 mol.) and aromatic aldehydes, namely benzaldehyde and/or salicyaldehyde (0.01 mol.), in the presence of ammonium acetate (1.54 g, 0.02 mol.) were heated in an oil-bath at about 150 °C for 30 min. The reaction mixture was poured into an ice/HCl mixture; the solid that obtained was filtered off and crystallized from the proper solvents to give compounds **18a,b** respectively.

18a: recrystallized from methanol to give brown crystals in 65% yield, m.p. 166 °C. Anal. $C_{20}H_{14}N_2O_3$ (330.35), Calcd.: C, 72.72%; H, 4.27%; N, 8.47%; Found: C, 72.65%; H, 4.45%; N, 8.55%.

18b: recrystallized from ethanol to give green crystals in 60% yield, m.p. 234 °C. Anal. $C_{20}H_{14}N_2O_4$ (346.35), Calcd.: C, 69.36%; H, 4.07%; N, 8.08%; Found: C, 69.40%; H, 4.00%; N, 7.90%.

Synthesis of 2-[3-(2,2-dicyano-1-methyl ethenyl)-3,4-dihydrocoumarin-4-yl]mercapto acetic acid derivatives 19a,b

Method (A)

To a solution of either **2a** or **2b** (0.01 mol.) in 20 mL pyridine, were added (0.92 ≈ 1 mL; 0.01 mol.) thioglycollic acid. The reaction mixture was refluxed for 5 hrs. The solid products that were obtained after cooling were filtered off and recrystallized from dioxane as **19a,b**.

Method (B)

A mixture of each of **2a,b** (0.01 mol.), thioglycollic acid (0.92 g, ≈ 1 mL, 0.01 mol.) and few drops of triethylamine in 30 mL ethanol was refluxed for 5 hrs. The solid products that were obtained after concentration and cooling were filtered off and recrystallized from dioxane as **19a,b**.

19a: separated as yellow crystals in 80% yield, m.p. 275 °C. Anal. $C_{16}H_{12}N_2O_4S$ (328.35), Calcd.: C, 58.53%; H, 3.68%; N, 8.53%; S, 9.76%; Found: C, 58.50%; H, 3.65%; N, 8.45%; S, 9.85%.

19b: separated as yellow crystals in 75% yield, m.p. 280 °C. Anal. $C_{16}H_{11}N_2O_4Br$ (407.25), Calcd.: C, 47.19%; H, 2.72%; N, 6.87%; Br, 19.62%; S, 7.87%; Found: C, 47.20%; H, 2.65%; N, 6.75%; Br, 19.75%; S, 7.90%.

Synthesis of 3-(2,2-dicyano-1-methyl ethenyl)-4-(ethoxycarbonylmethylthio)-3,4-dihydrocoumarin derivatives 20a,b

Method (A)

A solution of either **2a** or **2b** (0.01 mol.) and ethyl thioglycollate (1.2 g ≈ 1.1 mL, 0.01 mol.) in 20 mL pyridine was refluxed for 5 hrs. The solids that were obtained after cooling were filtered off and recrystallized from the proper solvents to give **20a,b**.

Method (B)

A mixture of each of **2a,b** (0.01 mol.), ethyl thioglycollate (1.2 g ≈ 1.1 mL, 0.01 mol.) and few drops of triethylamine in 30 mL ethanol was refluxed for 5 hrs. The solids that were obtained after cooling were filtered off and recrystallized from the proper solvents as **20a,b**.

20a: recrystallized from ethanol to give yellow crystals in 75% yield, m.p. 177 °C. Anal. $C_{18}H_{16}N_2O_4S$ (356.37), Calcd.: C, 60.66%; H, 4.52%; N, 7.86%; S, 8.99%; Found: C, 60.65%; H, 4.55%; N, 7.75%; S, 8.80%.

20b: recrystallized from dioxane to give yellow crystals in 70% yield, m.p. 210 °C. Anal. $C_{18}H_{15}N_2O_4BrS$ (435.29), Calcd.: C, 49.66%; H, 3.47%; N, 6.43%; Br, 18.35%; S, 7.36%; Found: C, 49.50%; H, 3.65%; N, 6.50%; Br, 18.20%; S, 7.40%.

Received March 30, 2005.

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