# SYNTHESIS AND STRUCTURE OF SOME 3,4-ANNELATED COUMARIN SYSTEMS

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**Abstract**

Refluxing of 4-chlorocoumarin-3-carbonitrile, heteroarylamines (3-aminopyrazole, 3-aminopyrazole-4-carbonitrile, 3-amino-1,2,4-triazole-5-thiol, 2-amino-6-fluorobenzothiazole, 2-amino-pyridin-3-ol, 1-aminoisoquinoline) and the catalytic amount of trimethylamine in acetonitrile gave the corresponding 3,4-annelated coumarins **1**-**6** in high yields. The spectral analysis showed that 7-amino-5-oxa-7a,8,11-triazacyclopenta[*b*]phenantren-6-one (**1**) existed as enamine, **2** as a mixture of enamine 7-amino-6-oxo-5-oxa-7a,8,11-triazacyclopenta[*b*]phenantren-10-carbonitrile (**2a**) and imine 7-imino-6-oxo-7*H*,8*H*-5-oxa-7a,8,11-triazacyclopenta[*b*]phenantren-10-carbonitrile (**2b**), whereas 10-fluoro-7-imino-7*H*-5-oxo-12-thia-7a,13-diazaindeno[1,2-*b*]phenantren-6-one (**4**), 11-hydroxy-7-imino-7*H*-7a,12-diazabenzo[*a*]anthracen-6-one (**5**) and 7-imino-7*H*-5-oxa-7a,14-diazadibenzo[*a,h*]anthracen-6-on (**6**) took imino forms.

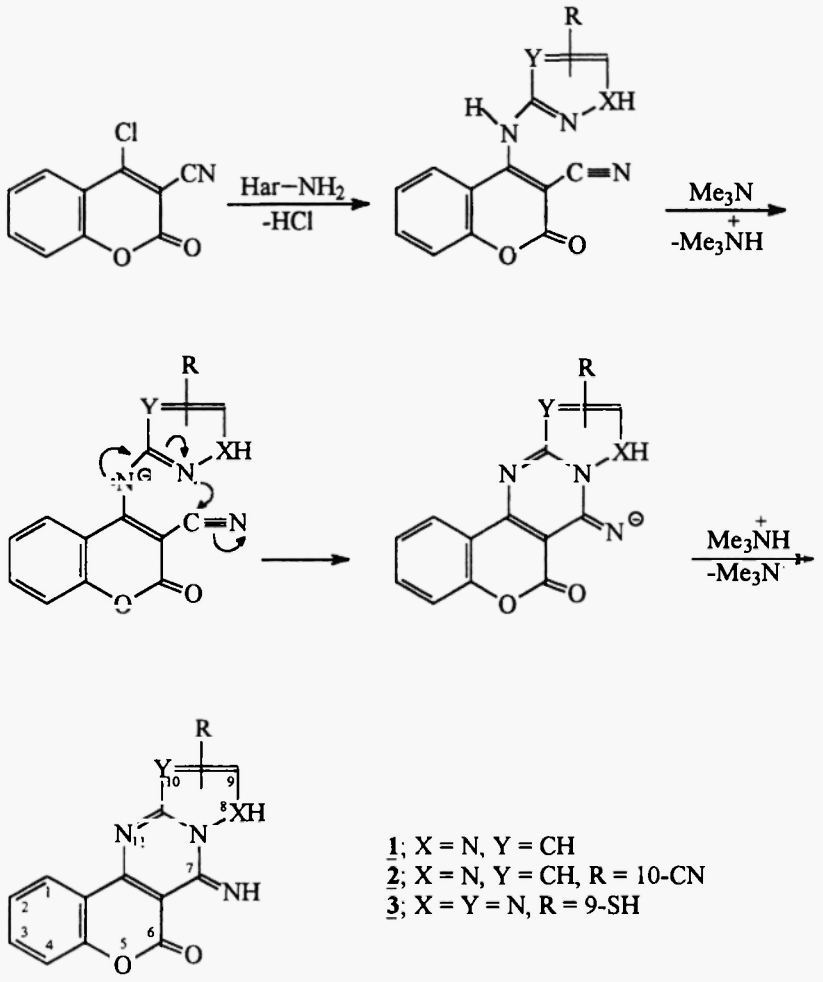
## Introduction

In our previous work (1, 2) on the chemistry of 3,4-disubstituted coumarins and the derived coumarins annelated in the 3,4-position we have prepared several fused systems starting from 4-chlorocoumarin-3-carbonitrile (3) and the appropriate heteroarylamine (2-amino-6-methylbenzothiazole, 2-aminobenzimidazole, 2-amino-5-chlorobenzoxazole, 3-amino-5-methylizoxazole and 2-amino-1,3,4-thiadiazole). It was shown that the obtained polycyclic imines underwent acidic hydrolysis giving the corresponding oxoderivatives (1, 2).

## Results and Discussion

The aim of the present paper is to prepare several similar coumarin-containing systems and to investigate their structure, having in mind the possible formation of enamino and/ or imino tautomeric forms.

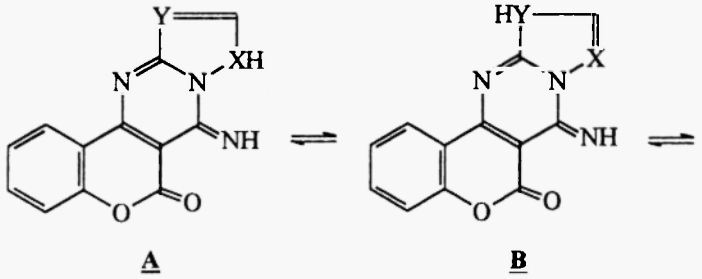
First we synthesized tetracyclic compounds **1**-**3** which could tautomerize in several ways. These preparations were performed by annelation of 4-chlorocoumarin-3-carbonitrile with 3-aminopyrazole, 3-aminopyrazole-4-carbonitrile or 3-amino-1,2,4-triazole-5-thiol in the presence of catalytic amount of trimethylamine. These conversions could succeed by the following mechanism (Scheme 1).



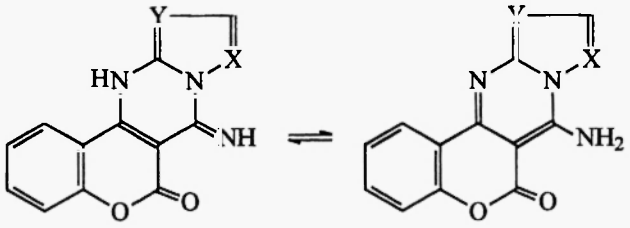

1; X = N, Y = CH
2; X = N, Y = CH, R = 10-CN
3; X = Y = N, R = 9-SH

**Scheme 1**

The products obtained can be presented either by imino forms **A**, **B** and **C** or by enamino form **D** (Scheme 2).



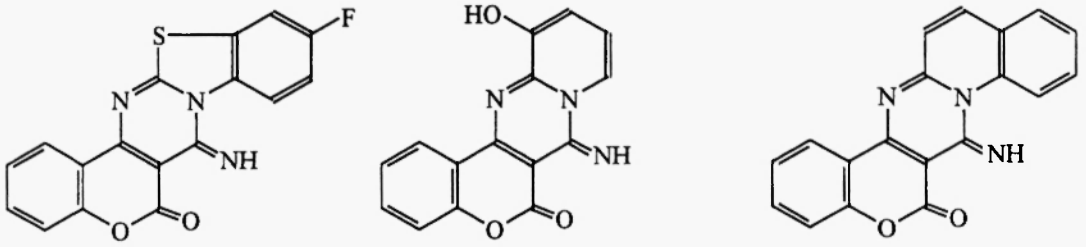

**A** **B**



C D

**Scheme 2**

Starting from the same coumarin substrate by the action of 2-amino-6-fluorobenzothiazole, 2-amino-pyridin-3-ol or 1-aminoisoquinoline under the similar conditions, the following compounds were synthesized (Scheme 3).



4 5 6

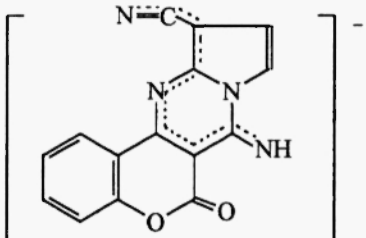
**Scheme 3**

It is obvious that compounds **4**-**6** existed only in the presented imino forms. Their structure was confirmed by spectral analysis: the corresponding molecular ions (intensity 16-21 %) were found in mass spectra, and IR spectra contained strong bonds at 1610-1650 $cm^{-1}$ corresponding to ν C=N. $^1H$ NMR spectra were taken in TFA showing the coumarin protons at the expected positions (δ):~ 8.25 ppm (H-1), ~ 7.42 and ~ 7.32 ppm (H-2 and H-4), and ~ 7.65 ppm (H-3). Hetero(aromatic) protons were registered at 7.36-8.41 ppm (**4**), 7.70-8.57 ppm (**5**), and 7.69-9.27 ppm (**6**). Unfortunately, it was impossible to identify imino group because it was converted by TFA into iminium and the corresponding protons probably coalesced with TFA proton, giving a broad signal at δ = 11.37 ppm. Due to low solubility of **4** and **6** in DMSO-$d_6$, only NMR spectra of **5** were recorded in this solvent. Beside of the coumarin and hetero(aromatic) protons which were found at the similar positions as above described, imino-protons were registered at 9.77 ppm. It is worth to mention that the spectra were temperature independent (r. t. and 80 °C), and the =NH peak disappeared by shaking with $D_2O$. $^{13}C$ spectrum corroborated imino structure by quaternary (APT) "amidine" carbon (C-7) registered at δ = 149.6 ppm. $^{13}C$ NMR spectrum of **6** taken in TFA contained a weak peak at 156.3 ppm which could be attributed to (C-7) bearing iminium group. Having in mind the spectral characteristics of imines **4**-**6** the structural analysis of the above described coumarins **1**-**3** should be more reliable.

$^1$H NMR spectra of **1** in DMSO-$d_6$ at r. t. and at 85 °C were identical. They contained signals of coumarin protons [8.29 (H-1), 7.60 (H-3) and 7.37-7.30 ppm (H-2, H-4)] and of heteroaromatic protons [8.32 (H-9) and 6.58 ppm (H-10)]; a broad singlet at 9.20 ppm (2H) was attributed to amino group. The chemical shift at 149.4 ppm in $^{13}$C spectrum belonging to quaternary atom C-7 bearing amino group, corroborated the enamino structure **D** also.

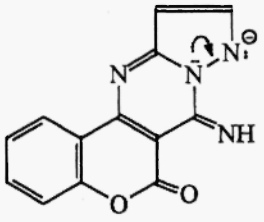
$^1$H NMR spectra of **2** taken in DMSO-$d_6$ showed, besides the coumarin and heteroaromatic protons signals found at expected positions, three types of nitrogen-protons: at ~9.2, ~9.7 and 8.44 ppm. By comparison with the above described data it can be concluded that the first belongs to enamino form **D**, the second to "amidine" proton (at C-6) and the third one has to be attributed to heteroaromatic nitrogen protons, either N-7 (form **A**), N-10 (form **B**) or N-11 (form **C**). It was demonstrated that this $^1$H spectrum is temperature dependent, and one can calculate that ratio of enamino and imino forms changed from 30 : 70 at r. t. to 60 : 40 at 85 °C. $^{13}$C NMR spectrum of **2** taken in DMSO-$d_6$ showed a signal at 9.73-9.70 ppm attributed to imino group (C-7). By shaking with $D_2O$ signals of nitrogen protons of **1** and **2** in DMSO-$d_6$ disappeared, and by recording spectrum in TFA coalesced with protons of solvent in a broad signal centered at 11.35 ppm.

Unfortunately, the sample **3** was quite insoluble in DMSO and the spectral analysis of imino-enamino tautomerism was impossible. But $^1$H NMR spectra of this compounds taken in TFA indicated presence of both forms by broadening and/ or multiplying the signals. On the basis of the above described data, it is obvious that the enamino form **D** of tautomerisable coumarin derivatives **1**-**3** is more (thermodynamically) stable than imine (**A**-**C**), and that compound **1** existed exclusively in this form. Electron-withdrawing cyano group of **2** initiated base catalysed tautomerization of enamine by stabilization of the intermediate "enamide" anion **E**:




**E**

By r. t. prevailed kinetic controlled imine, and by 85 °C the dominant product is equilibrium controlled enamine. Stability of enamine **D** is obvious from its structure: beside of the four conjugated double bonds in the annelated *N*-heterocyclic part of molecule, it contained a fused aromatic pyrazole ring. On the other hand, contribution of resonance structure **F** is probably minor because of destabilizing mesomeric electron-donating effect of tertiary N-7a on imide anion N-8, expliciting once again stability of enamine form.



**F**

It seems that structure **A** is the most stable one of all theoretically possible imino forms: it contained three conjugated endocyclic bonds and structures **B** and **C** are characterized by only two of them.

## Experimental

Melting points were determined with a Buechi apparatus. The IR spectra were recorded for KBr pellets with a Bomem MB 100 mid FT IR spectrophotometer. The $^{1}H$ and $^{13}C$ NMR spectra were recorded on a Varian EM 360 or Varian Gemini 300 spectrometer with tetramethylsilane as internal standard. Mass spectra were determined on a Shimadzu GCNS-QP 1000 spectrometer (70 eV). Elemental analyses were performed in Ruđer Boskovic Institute.

4-Chlorocoumarin-3-carbonitrile was prepared by the action of $POCl_3$ on 4-chloro-3-hydroxycoumarin in DMF according to reference (3).

### *General procedure for preparation of 3,4-annelated coumarins*

The solution of 4-chlorocoumarin-3-carbonitrile (1.0 g, 48 mmol) and of appropriate heteroarylamine, its hydrochloride or dihydrogensulfate (48 mmol) in acetonitrile (30 ml) in presence of catalytical amount of triethylamine was refluxed for 0.5-15 hours. After cooling, the precipitated solid was filtered off, washed with acetonitrile and crystallized from DMF.

### 7-Amino-5-oxa-7a,8,11-triazacyclopenta[*b*]phenantren-6-one (1)

Yield: 83 %, m. p. 248-250 °C from DMF. IR (KBr): 3350-3210 (N–H, O–H), 1710-1700 (C=O), 1660 (C=N), 1610 (C=C) $cm^{-1}$. $^{1}H$ NMR (DMSO-$d_6$): δ = 9.20 (b s, 2H, $NH_2$), 8.32 (d, 1H, H-9), 8.29 (s, 1H, H-1), 7.60 (t, 1H, H-3), 7.37-7.30 (dd, 2H, H-2, H-4), 6.58 (d, 1H, H-10) ppm. $^{13}C$ NMR (DMSO-$d_6$): δ = 161.5 (s, C=O), 152.2 (s, C-4a), 149.9 (s, C-10a), 149.4 (s, C-7), 148.8 (s, C-11a), 147.0 (d, C-9), 132.7 (d, C-3), 124.6 (d, C-1), 124.5 (d, C-2), 118.5 (s, C-6a), 116.8 (d, C-4), 96.9 (d, C-10), 85.2 (s, C-11b) ppm. $^{1}H$ NMR (TFA-$d_3$): δ = 7.98 (t, 2H, H-1, H-9), 7.64 (t, 1H, H-3), 7.30 (dd, 2H, H-2, H-4), 6.74 (s, 1H, H-10) ppm. MS(EI): m/z (%) = 252 (11.3), 251 (100), 210 (3.0), 185 (2.6), 126 (4.0), 93 (6.4), 84 (2.8), 53 (3.4), 41 (2.3), 37 (4.9), 31 (4.5). $C_{13}H_8N_4O_2$ (252.2): calcd. C 61.88, H 3.19, N 22.21; found C 61.71, H 3.37, N 22.15.

### 7-Amino-6-oxo-5-oxa-7a,8,11-triazacyclopenta[*b*]phenantren-10-carbonitrile (2a) and 7-imino-6-oxo-7*H*,8*H*-5-oxa-7a,8,11-triazacyclopenta[*b*]phenantren-10-carbonitrile (2b)

**2** Yield: 93 %, m. p. 291-293 °C from DMF. IR (KBr): 3360-3250 (N–H, O–H), 1740 (C=O), 1650 (C=N), 1600-1490 (C=C) $cm^{-1}$. $^{13}C$ NMR (DMSO-$d_6$): δ = 160.7 (s, C=O), 156.9 (s, C-7), 152.9 (s, C-4a), 150.1 (s, C-11a), 149.4 (s, C-10a), 148.5 (d, C-9), 133.8 (d, C-3), 125.0 (d, C-1), 124.8 (d, C-2), 117.7 (s, C-6a), 116.8 (d, C-4), 94.0 (s, C-11b) ppm. $^{1}H$ NMR (TFA-$d_3$): δ = 9.74 (m, 1H, H-9), 8.28 (m, 1H, H-1), 7.81 (t, 1H, H-3),

7.40 (t, 1H) and 7.45 (t, 1H) (H-2 and H-4) ppm. $C_{14}H_7N_5O_2$ (252.2): calcd. C 60.63, H 2.54, N 25.26; found C 60.72, H 2.57, N 25.36.

**2a** (imino form): $^1$H NMR (DMSO-$d_6$): δ = 9.73-9.70 (d, 1H, NH), 8.69 (s, 1H, H-1), 8.77-8.73 (m, 1H, H-9), 8.44 (s, 1H, NH), 7.89-7.84 (m, 1H, H-3), 7.57-7.51 (m, 2H, H-2, H-4) ppm.
**2b** (enamino form): $^1$H NMR (DMSO-$d_6$): δ = 9.20 (b s, 2H, $NH_2$), 8.35-8.33 (d, 2H, H-1, H-9), 7.69-7.67 (m, 1H, H-3), 7.44-7.39 (m, 2H, H-2, H-4) ppm.

**4-Amino(imino)-9-mercapto-(7*H*,8*H*)-5-oxa-7a,8,10,11-tetraazacyclopenta[*b*]phenantren-6-one (3)**

Yield: 77 %, m. p. 310-312 °C from DMF. IR (KBr): 3300-3200 (N–H, O–H), 1720-1700 (C=O), 1670 (C=N), 1625 (C=C) cm$^{-1}$. $^1$H NMR (TFA-$d_3$): δ = 8.05 (d, 1H, H-1), 7.80 (m, 1H, H-3), 7.60 (t, 1H) and 7.34 (t, 1H), (H-2 and H-4) ppm. $C_{12}H_7N_5O_2S$ (285.2): calcd. C 50.52, H 2.49, N 24.56; found C 50.38, H 2.82, N 24.34.

**10-Fluoro-7-imino-5-oxo-7*H*-12-thia-7a,13-diazaindeno[1,2-*b*]phenantren-6-one (4)**

Yield: 85 %, m. p. 321-323 °C from DMF. IR (KBr): 3300 (N–H, O–H), 1710 (C=O), 1610 (C=N), 1490 (C=C) cm$^{-1}$. $^1$H NMR (TFA-$d_3$): δ = 8.41 (d, 1H, H-8), 8.25 (d, 1H, H-1), 7.71 (t, 1H, H-11), 7.57 (m, 1H, H-3), 7.36 (m, 3H, H-2, H-4, H-9) ppm. MS(EI): m/z (%) = 337 (21.0), 336 (100), 216 (2.4), 168 (10.6), 112 (4.6). $C_{17}H_8N_3O_2SF$ (337.3): calcd. C 60.52, H 2.39, N 12.46; found C 60.64, H 2.32, N 12.46.

**11-Hydroxy-7-imino-7*H*-7a,12-diazabenzo[*a*]anthracen-6-one (5)**

Yield: 96 %, m. p. 295-297 °C from DMF. IR (KBr): 3300-3180 (N–H, O–H), 1660 (C=O), 1610 (C=N), 1500 (C=C) cm$^{-1}$. $^1$H NMR (DMSO-$d_6$): δ = ~10 (b s, 1H, OH), 9.77 (s, 1H, NH), 8.82-8.76 (dd, 2H, H-1, H-10), 7.61-7.56 (t, 1H, H-8), 7.39-7.36 (d, 1H, H-3), 7.32-7.25 (dd, 2H, H-2), H-4), 7.18 (t, 1H, H-9) ppm. $^{13}$C NMR (DMSO-$d_6$): δ = 160.9 (C=O), 152.7 (s, C-4a), 151.2 (s, C-11a), 149.6 (s, C-7), 133.2 (d, C-3), 127.8 (s, C-12a), 126.7 (d, C-1), 124.8 (s, C-11), 123.8 (d, C-2), 119.6 (d, C-8), 119.3 (d, C-10), 117.9 (s, C-6a), 116.3 (d, C-9), 115.9 (d, C-4), 93.6 (s, C-12b) ppm. $^1$H NMR (TFA-$d_3$): δ = 8.57 (d, 1H, H-8), 8.30 (d, 1H, H-1), 7.70 (t, 1H, H-9), 7.61 (d, 1H, H-3), 7.53 (t, 1H, H-10), 7.32 (d, 1H) and 7.41 (t, 1H) (H-2 and H-4) ppm. MS(EI): m/z (%) = 279 (15.5), 278 (100), 234 (6.0), 210 (7.5), 139 (4.0), 34 (12.7). $C_{15}H_9N_3O_3$ (279.2): calcd. C 64.40, H 3.25, N 15.04; found C 64.23, H 3.40, N 15.17.

**7-Imino-7*H*-5-oxa-7a,14-diazadibenzo[*a,h*]anthracen-6-on (6)**

Yield: 85 %, m. p. 330-332 °C from DMF. IR (KBr): 3300 (N–H, O–H), 1700 (C=O), 1650 (C=N), 1500 (C=C) cm$^{-1}$. $^1$H NMR (TFA-$d_3$): δ = 8.21 (m, 1H, H-1), 7.69 (s, 2H, H-3, H-10), 7.32 (m, 1H) and 7.44 (m, 1H) (H-2 and H-4), quinoline protons: 9.27 (d, 1H), 8.66 (m, 1H), 7.93 (s, 1H), and 7.81 (m, 2H) ppm. $^{13}$C NMR (TFA-$d_3$): δ = 165.6 (C=O), 159.97 (s, C-4a), 156.5 (s, C-13a), 156.3 (s, C-7), 153.9 (s, C-14a), 139.7 (d, C-13), 139.4 (d, C-12), 136.3 (s, C-7b), 133.9 (d, C-3), 131.4 (d, C-1), 129.7 (d, C-2), 129.1 (d, C-8), 128.8 (d, C-9), 127.8 (s, C-6a), 124.2 (d, C-4), 119.5 (d, C-11), 118.7 (d, C-10), 118.7 (s, C-11a), 96.2 (s, C-14b) ppm. MS(EI): m/z (%) = 313 (20.3), 312 (100), 286 (4.5), 285 (26.7), 192 (11.1), 156 (3.6), 66 (9.5). $C_{19}H_{11}N_3O_2$ (313.3): calcd. C 72.83, H 3.53, N 13.41; found C 71.60, H 3.39, N 15.22.

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