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Tetrahedron
Tetrahedron 61 (2005) 4957–4964

Substituted coumarin amidines: useful building blocks for the preparation of [1]benzopyrano[4,3-*b*]pyridin-5-one and [1]benzopyrano[4,3-*d*]pyrimidin-5-one derivatives

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Received 13 January 2005; revised 22 February 2005; accepted 10 March 2005

Available online 7 April 2005

Abstract—The synthesis of [1]benzopyrano[4,3-*b*]pyridin-5-ones **4a–f** and **4g–j** starting from 3-formylcoumarin and 3-cyanocoumarin *N*-functionalized amidines **3a–f** and **3g–j**, respectively, was reported. The ring-closure reaction mechanism, under basic or acidic media, was proposed. Furthermore, the reaction of 3-formylamidines **3a**,**c–f** with ammonium acetate gave good yields of 2-substituted [1]benzopyrano[4,3-*d*]pyrimidin-5-ones **7**.

1. Introduction

In recent years nitrogen polyheterocycles containing a coumarin nucleus have received increasing attention due to their potential biological properties, and considerable efforts have been undertaken to exploit synthetic routes to these compounds. In particular, the coumarin nucleus is present in compounds endowed with analgesic[1] and antiplatelet[2] properties, and in promising drugs useful as phosphodiesterase VII inhibitors[3] for the treatment of immunity-associated diseases.

The introduction of substituents in the C-3 position of the coumarin moiety is of great importance as this generates intermediates in the synthesis of heterocycles condensed with the benzopyran-2-one nucleus.

In the last few years we focused our attention on tertiary amidines bearing a 3-substituted coumarin group on N-1 as synthons to give nitrogen fused triheterocycles, through intramolecular cyclization reactions.

From acetamidines bearing a 3-nitrocoumarin group on N-1, we recently developed an easy method for the preparation of coumarin fused to imidazoles.[4]

In this context, we reported a preliminary communication[5] on acetamidines bearing the 3-formylcoumarin group on N-1 as a starting material to synthesize benzopyranopyridin-5-ones.

As a continuation of this study, we describe here, in full detail, the synthesis of substituted 2-amino- and 2,4-diaminobenzopyranopyridin-5-ones through acetamidines bearing a 3-formyl or 3-cyano coumarin group on N-1.

With the purpose to extend this strategy to different nitrogen polyheterocycle systems we report, for the first time, a new synthetic approach to 2-substituted benzopyranopyrimidin-5-ones. The key intermediates were again the acetamidines substituted at N-1 with the 3-formyl coumarin group.

2. Results and discussion

Amidines **3a–j** were prepared from azides **1a–b** and enamines **2a–f**. The new azide **1b** was achieved by reaction of sodium azide with the corresponding 4-chloro-2-oxo-2*H*-[1]benzopyran-3-carbonitrile.[6] We performed the reactions using equimolar amounts of 4-azido-3-formylcoumarin **1a**[7] or of 4-azido-3-cyanocoumarin **1b** and the appropriate enamine **2a–f**,[8–11] previously synthesized, in chilled dichloromethane solution. These reaction conditions allowed the isolation in good yields of the amidines **3a–f** and **3g–j**, respectively (Scheme 1).

Keywords: 3-Formylcoumarin amidines; 3-Cyanocoumarin amidines; Enediamino tautomers; Aldols; Intramolecular cyclization.
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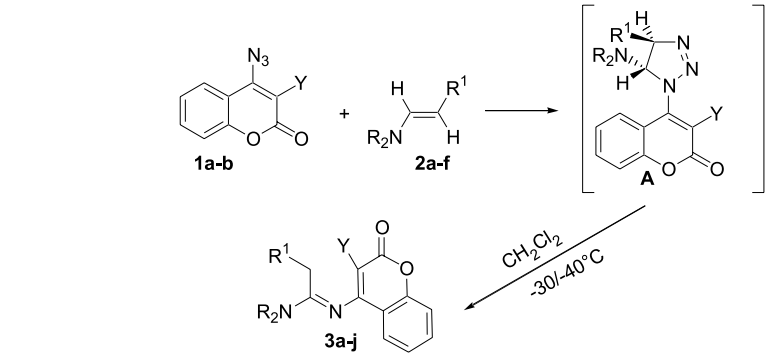
0040–4020/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2005.03.050



1a Y = CHO
1b Y = CN

2a $R^1 = C_6H_5$, NR_2 = morpholine
2b $R^1 = C_6H_5$, NR_2 = diethylamine
2c R^1= 4-BrC_6H_4, NR_2 = morpholine
2d R^1 = 4-$CH_3OC_6H_4$, NR_2 = morpholine
2e R^1 = *i*Pr, NR_2 = morpholine
2f $R^1 = CH_2C_6H_5$, NR_2 = morpholine

3a $R^1 = C_6H_5$, NR_2 = morpholine, Y = CHO
3b $R^1 = C_6H_5$, NR_2 = diethylamine, Y = CHO
3c R^1= 4-BrC_6H_4, NR_2 = morpholine, Y = CHO
3d R^1 = 4-$CH_3OC_6H_4$, NR_2 = morpholine, Y = CHO
3e R^1 = *i*Pr, NR_2 = morpholine, Y = CHO
3f $R^1 = CH_2C_6H_5$, NR_2 = morpholine, Y = CHO
3g $R^1 = C_6H_5$, NR_2 = morpholine, Y = CN
3h $R^1 = C_6H_5$, NR_2 = diethylamine, Y = CN
3i R^1 = *i*Pr, NR_2 = morpholine, Y = CN
3j $R^1 = CH_2C_6H_5$, NR_2 = morpholine, Y = CN

Scheme 1.

Despite the low reaction temperature, the 4,5-dihydrotriazole **A** could never be isolated, owing to its thermal instability as a result of the electron-withdrawing effect of the N-1 substituent[12] which facilitates the cleavage of the N1–N2 bond and promotes amidine rearrangement.

The proposed structures of amidines **3a–f** and **3g–j** were validated by spectral data, which were consistent with the available literature data for similar substitution patterns in coumarin derivatives.[13]

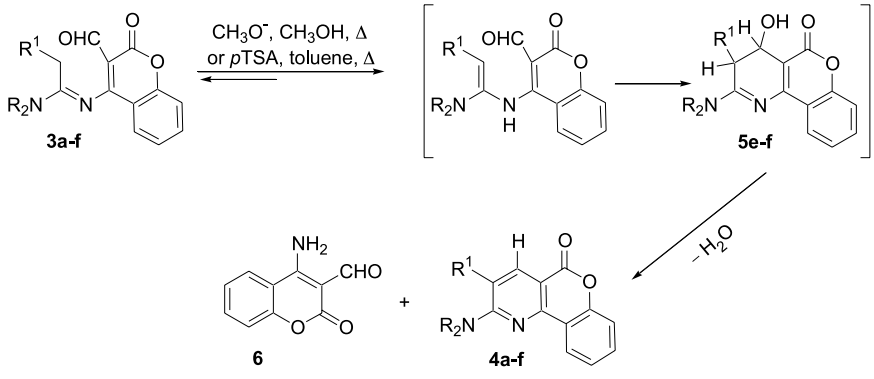
It is well known that the activation of the α-methylene group of amidines, with respect to condensation reaction, is attributed to the existence of amidine–enediamine tautomerism.[14]

Taking into account the structural features of amidines **3a–f** and **3g–j** we proposed, at first, to take advantage of the nucleophilic character of the α-methylene group of amidines,[14b,c] as well as the presence of formyl or cyano groups linked to C-3 of the coumarin ring, to plan an intramolecular condensation reaction.

The amidines **3a–d** were heated in methanol at reflux under basic conditions, and easily transformed into the expected 2-amino-benzopyranopyridinones **4a–d**. In the case of substrates **3e–f**, in addition to the desired products **4e–f**, the aldol intermediates **5e–f** and the side product **6**, arising from the hydrolytic reaction of amidine were also isolated (Scheme 2).

In aldol intermediate **5**, the subsequent water loss should be assisted by the substituent group bound to C-3.

To determine the best conditions to favour this process, and to enhance the yield of derivatives **4a–b**,**e–f**, we decided



3a, 4a, 5a $R^1 = C_6H_5$, NR_2 = morpholine
3b, 4b, 5b $R^1 = C_6H_5$, NR_2 = diethylamine
3c, 4c, 5c R^1= 4-BrC_6H_4, NR_2 = morpholine
3d, 4d, 5d R^1 = 4-$CH_3OC_6H_4$, NR_2 = morpholine
3e, 4e, 5e R^1 = *i*Pr, NR_2 = morpholine
3f, 4f, 5f $R^1 = CH_2C_6H_5$, NR_2 = morpholine

Scheme 2.

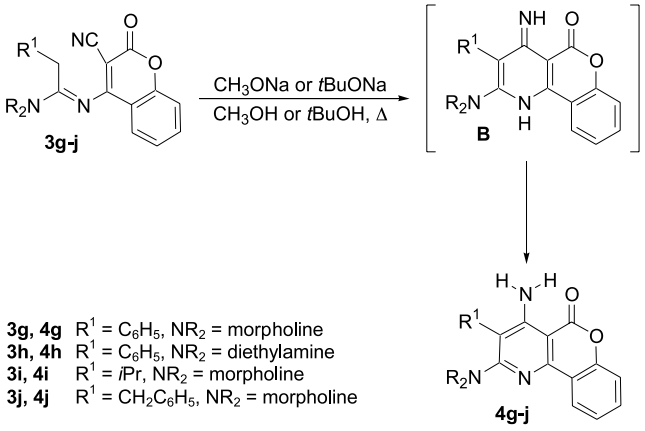
Table 1. Effect of experimental conditions on **4**,**5**,**6** ratio

Amidines **3**	Compd. **4** yield (%)		Compd. **5**[a] yield (%)	Compd. **6**[a] yield (%)
	Method A[b]	Method B[c]		
a	46	70	0	
b	58	88	0	
c	94	—	0	
d	85	—	0	
e	36[d]/18[e]	60	28[e]	35[e]
f	38[d]/22[e]	66	27[e]	33[e]

[a] Compound formed only with method A.
[b] CH_3ONa/CH_3OH: see Section 4.
[c] *p*-TSA/toluene: see Section 4.
[d] Total yield: see Section 4.
[e] Yields of **4**, **5**, **6** from chromatographic column: see Section 4.

to perform the reaction of related amidines in acidic medium.

The reaction of the amidines **3a**–**b**,**e**–**f** in toluene at reflux, containing a catalytic amount of *p*-toluensulfonic acid, afforded the expected benzopyranopyridin-5-ones **4a**–**b**,**e**–**f**. Table 1 shows the results obtained under basic and acidic media. Significant improvements in yields were achieved by acidic reaction conditions (Table 1, method B), thus confirming the hypothesis that the ring-closure reaction occurs through isomerization of the amidine **3** into its enediamino tautomer,[14] followed by an intramolecular condensation of the α-carbon with the formyl group. It is plausible to postulate, in basic medium, a similar mechanistic hypothesis.



Scheme 3.

We furthermore investigated the possibility to react 3-cyano substituted acetamidines **3g**–**j** with the aim to achieve 2,4-diaminobenzopyranopyridin-5-ones. By heating acetamidines **3g**–**j** in basic medium (methoxide for **3g**–**h** and *t*butoxide for **3i**–**j**, respectively), the expected tricyclic derivatives **4g**–**j** bearing an NH_2 group on C-4 were produced.

^{13}C NMR spectra of **4g**–**j** showed a quaternary carbon at about 150.6–151.7 ppm, as a diagnostic signal for C-4 linked to the amino group of the pyridine ring.[15] In the IR spectrum we also observed an absorption band in the range 1691–1698 cm^{-1}, assigned to the stretching of the coumarin carbonyl group, whose frequency is lowered[16] owing to the intramolecular hydrogen bonding, with the neighbouring amino function. The production of fused heterocycles **4g**–**j** can be rationalized as follows (Scheme 3).

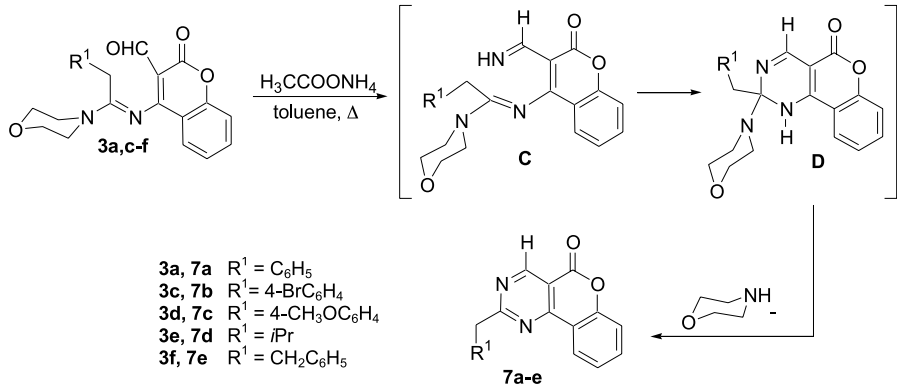
In a basic medium, the iminic intermediate **B** arising from the nucleophilic addition of the C-α amidinic carbon to the cyano group, through rapid isomerization gave the desired 4-amino group.

The described success to synthesize 2-aminobenzopyranopyridinones **4a**–**f** from the corresponding 3-formyl acetamidines **3a**–**f** prompted us to react the same compounds to obtain 2-substituted benzopyranopyrimidin-5-ones **7**. As a synthetic route, we considered a mixture of 3-formyl acetamidines **3a**,**c**–**f** with an excess of ammonium acetate in toluene at reflux. In a short reaction time, expected tricyclic derivatives **7a**–**e** were achieved in very good yield (Scheme 4).

The structural assignments of 2-alkyl-benzopyranopyrimidin-5-ones **7a**–**e** established by ^1H and ^{13}C NMR spectroscopy relating to the coumarin[13a] and pyrimidine[17] nuclei, were in agreement with the literature data.

In each case, we observed a typical pattern for the coumarin[13a] moiety. ^{13}C NMR spectra showed a first signal at about 160 ppm, corresponding to a singlet[17b] at about 9.5 δ related to CH-4 in HETCOR experiment, and a second signal at 174.3–176.2 ppm associated to the lactone carbonyl group, the latter validated also by IR (nujol) stretching at about 1720 cm^{-1}.

In the ^1H NMR spectra we noted a deshielding effect on the



Scheme 4.

methylene group linked to C-2 of the pyrimidine nucleus for the compounds **7a**–**e**, relative to the starting amidines **3a**,**c**–**f**, as a consequence of two nitrogen atoms in its *ortho* position.

The achievement of fused heterocycles **7** can be rationalized by the reaction path depicted in Scheme 4.

The reaction with ammonium acetate gave the imino intermediate **C**, which rapidly underwent ring-closure through addition to the C═N group of the amidine to give an unstable 2,2-disubstituted-benzopyranopyrimidone **D**. Morpholine elimination gave aromatic pyrimidine derivative **7**.

3. Conclusions

We have described new methods for the preparation of both substituted 5*H*[1]benzopyrano[4,3-*b*]pyridin-5-ones and 5*H*[1]benzopyrano[4,3-*d*]pyrimidin-5-ones in good yields. At the same time, these synthetic routes represent an expeditious access to polyheterocycles containing a coumarin moiety, adding further proof of the utility of substituted acetamidines as building blocks in organic synthesis. Although the synthesis of a limited number of derivatives is described in this paper, the flexibility of this methodology should provide access to many variously [1]benzopyrano[4,3-*b*]pyridin-5-ones and [1]benzopyrano-[4,3-*d*]pyrimidin-5-ones.

4. Experimental

4.1. General

Melting points were determined using a Buchi 510 (capillary) or an Electrothermal 9100 apparatus and are uncorrected. IR spectra were measured using Perkin–Elmer FT-IR 16 P.C. (Nujol), and Perkin–Elmer FT-IR Spectrum One (KBr) spectrometers. ^{1}H and ^{13}C NMR spectra were recorded on EM Varian Gemini 200 and on Bruker Avance 300 spectrometers in $CDCl_3$ solution unless otherwise stated. Chemical shifts are expressed in ppm from internal standard tetramethylsilane (δ), coupling constants (J) are given in Hz. Column chromatography was performed on Kieselgel 60 (Merck) 0.063–0.200 mm with eluents and ratios indicated in Section 4.

Materials. Azide **1a**,[7] enamines **2a**,**c**,**d**,[8] **2b**,[9] **2e**,[10] **2f** 11 and compounds **3a**,[5] **4a**,[5] **5e**[5] have already been described. 4-Chloro-2-oxo-2*H*-[1]benzopyran-3-carbonitrile[6] and 4-amino-3-formylcoumarin[7] **6** are known compounds.

4.1.1. 4-Azido-2-oxo-2*H*-[1]benzopyran-3-carbonitrile 1b. NaN_3 (1.092 g, 0.0168 mmol), protected from light, was suspended in dry DMF (30 mL) and chilled in an ice bath. A solution of 4-chloro-2-oxo-2*H*-[1]benzopyran-3-carbonitrile (3.3 g, 0.016 mmol) in dry DMF (50 mL) was added over 20 min. The mixture was then stirred a further 3 h at 0 °C before being poured onto ice. The red–orange precipitate was filtered and recrystallized from ethanol to give the azide **1b** (2.9 g, 85%) as orange crystals, mp 171 °C (decomp.); IR ν_{max} (KBr) 2228 (CN), 2148 and 2130 (N_3), 1722 (C═O) cm^{-1}; ^{1}H NMR δ 7.36–7.44 (2H, m, H-6, H-7); 7.71–7.79 (1H, m, H-5), 7.91 (1H, dd, J=8.4, 1.4 Hz, H-8); ^{13}C NMR ($DMSO_{d6}$): 90.5 (C-3), 112.8 (C-4a), 114.7 (CN), 118.1, 125.3, 126.3, 137.0 (CH), 153.5 (C-4), 157.7 (C-8a), 158.5 (C═O). Anal. Calcd for $C_{10}H_4N_4O_2$: C, 56.61; H, 1.90; N, 26.41; found: C, 56.49; H, 1.82; N, 26.59.

4.2. General procedure for the preparation of amidines 3a–f

The suitable enamine **2a**–**f** (10 mmol) was dissolved in CH_2Cl_2 (20 mL). With careful monitoring of the internal temperature (−40 °C, acetone–CO_2 bath), an equimolar amount of azide **1a**, dissolved in CH_2Cl_2 (30 mL), was slowly added dropwise with stirring. The mixture was kept at −30 °C until disappearance (TLC: cyclohexane/EtOAc, 3:2) of the starting azide **1a**. The stirring was continued until room temperature was reached. The solvent was then evaporated and the crude product purified by crystallization from *i*Pr_2O to give pure **3a**–**f**.

4.2.1. *N*,*N*-Diethyl-*N′*-(3-formyl-2-oxo-2*H*-[1]benzopyran-4yl)-2-phenyl-acetamidine 3b. Reaction time: 1.5 h. Yield 65%; pale yellow crystals, mp 127 °C; IR ν_{max} (Nujol) 1703 (C═O), 1668 (CHO) cm^{-1}; ^{1}H NMR: 1.24 (3H, t, J=7.3 Hz, CH_3), 1.29 (3H, t, J=7.3 Hz, CH_3), 3.30–4.11 (6H, m, CH_2NCH_2, CH_2), 7.10–7.30 (5 H+2 H, m, ArH, H-6, H-8), 7.53 (1H, td, J=7.3, 1.8 Hz, H-7), 8.05 (1H, dd, J=8.0, 1.8 Hz, H-5), 10.13 (1H, s, CHO); ^{13}C NMR: 11.8 (CH_3), 13.8 (CH_3), 38.0 (CH_2), 44.1 (CH_2N), 44.2 (CH_2N), 100.2 (C-3), 117.2, 123.9, 126.9, 133.3 (CH), 120.4 (C-4a), 127.3, 128.5, 129.2 (ArCH) 134.8 (ArC), 154.3 (C-4), 157.2 (C-8a), 165.4 (N═C–N), 165.6 (C═O), 189.1 (CHO). Anal. Calcd for $C_{22}H_{22}N_2O_3$: C, 72.91; H, 6.12; N, 7.73; found: C, 72.68; H, 5.94; N, 7.89.

4.2.2. 4-{[2-(4-Bromophenyl)-1-morpholin-4-ylethylidene]amino}-2-oxo-2*H*-[1]benzopyran-3-carbaldehyde 3c. Reaction time: 1 h. Yield 78%; pale yellow crystals, mp 153 °C; IR ν_{max} (Nujol) 1700 (C═O), 1660 (CHO) cm^{-1}; ^{1}H NMR: 3.59–4.03 (10H, m, morph., CH_2), 6.98 and 7.32 (4H, J=8.4 Hz, ArH), 7.21–7.35 (2 H, m, H-6, H-8), 7.57 (1H, td, J=8.4, 1.8 Hz, H-7), 7.97 (1H, dd, J=8.4, 1.8 Hz, H-5), 10.14 (1H, s, CHO); ^{13}C NMR: 37.3 (CH_2), 46.6 (CH_2NCH_2), 66.2 (CH_2OCH_2), 100.5 (C-3), 117.2, 124.1, 126.7, 133.2 (CH), 119.6 (C-4a), 121.5 (Ar*C*Br), 129.8, 132.3 (ArCH), 136.4 (ArC), 154.3 (C-4), 157.9 (C-8a), 164.6 (N═C–N), 165.0 (C═O), 189.2 (CHO). Anal. Calcd for $C_{22}H_{19}BrN_2O_4$: C, 58.04; H, 4.21; N, 6.15; found: C, 57.91; H, 4.02; N, 6.37.

4.2.3. 4-{[2-(4-Methoxyphenyl)-1-morpholin-4-ylethylidene]amino}-2-oxo-2*H*-[1]benzopyran-3-carbaldehyde 3d. Reaction time: 3 h. Yield 63%; yellow crystals, mp 138 °C; IR ν_{max} (Nujol) 1700 (C═O), 1658 (CHO) cm^{-1}; ^{1}H NMR: 3.54–4.01 (10H, m, morph., CH_2), 3.76 (3H, s, OCH_3), 6.76 and 7.00 (4H, J=8.4 Hz, ArH), 7.20–7.29 (2H, m, H-6, H-8), 7.55 (1H, td, J=7.3, 1.8 Hz, H-7), 7.98 (1H, dd, J=8.4, 1.8 Hz, H-5), 10.12 (1H, s, CHO); ^{13}C NMR: 37.2 (CH_2), 46.7 (CH_2NCH_2), 55.3 (OCH_3), 66.1(CH_2OCH_2), 100.7 (C-3), 117.1, 124.0, 127.0, 133.6 (CH), 120.1 (C-4a), 114.4, 130.0 (ArCH), 129.6 (ArC),

154.2 (C-4), 157.5 (C-8a), 158.6 (Ar*C*OCH$_3$) 164.7 (N=C–N), 165.4 (C=O), 189.3 (CHO). Anal. Calcd for $C_{23}H_{22}N_2O_5$: C, 67.97; H, 5.46; N, 6.89; found: C, 67.87; H, 5.74; N, 7.01.

4.2.4. 4-[(3-Methyl-1-morpholin-4-ylbutylidene)amino]-2-oxo-2*H*-[1]benzopyran-3-carbaldehyde 3e. Reaction time: 2 h. Yield 70%; yellow powder, mp 134 °C; IR ν_{max} (Nujol) 1699 (C=O), 1661 (CHO) cm^{-1}; ^{1}H NMR: 0.79 (3H, d, J=6.6 Hz, CH$_3$), 0.94 (3H, d, J=6.6 Hz, CH$_3$), 1.77–1.89 (1H, m, (CH$_3$)$_2$C*H*), 2.22–2.47 (2H, m, CH$_2$), 3.60–4.08, (8H, m, morph.), 7.18–7.31 (2H, m, H-6, H-8), 7.55 (1H, td, J=7.3, 1.8 Hz, H-7), 7.92 (1H, dd, J=8.0, 1.4 Hz, H-5), 10.07 (1H, s, CHO); ^{13}C NMR: 22.3 (CH$_3$), 23.3 (CH$_3$), 27.3 (*C*H), 39.6 (CH$_2$), 54.5 (CH$_2$NCH$_2$), 66.4 (CH$_2$OCH$_2$), 99.8 (C-3), 117.2, 123.9, 127.0, 133.5 (CH), 119.9 (C-4a), 154.3 (C-4), 157.7 (C-8a), 165.4 (N=C–N), 167.8 (C=O), 188.8 (CHO). Anal. Calcd for $C_{19}H_{22}N_2O_4$: C, 66.65; H, 6.48; N, 8.18; found: C, 66.78; H, 6.57; N, 7.97.

4.2.5. 4-[(1-Morpholin-4-yl-3-phenyl-propylidene)-amino]-2-oxo-2*H*-[1]benzopyran-3-carbaldehyde 3f. Reaction time: 2 h. Yield 69%; yellow powder, mp 108 °C; IR ν_{max} (Nujol) 1700 (C=O), 1653 (CHO) cm^{-1}; ^{1}H NMR: 2.60–2.99 (4H, m, CH$_2$–CH$_2$), 3.60–3.93 (8 H, m, morph.), 7.02–7.27 (5 H+2 H, m, ArH, H-6, H-8), 7.54 (1H, td, J=8.0, 1.8 Hz, H-7), 7.69 (1H, dd, J=8.0, 1.8 Hz, H-5), 10.08 (1H, s, CHO); ^{13}C NMR: 32.3 (CH$_2$), 33.3 (CH$_2$), 46.5 (CH$_2$NCH$_2$), 66.1 (CH$_2$OCH$_2$), 99.7 (C-3), 117.1, 124.0, 126.8, 133.5 (CH), 119.6 (C-4a), 127.1, 128.4, 128.9 (ArCH), 139.1 (ArC), 154.2 (C-4), 157.6 (C-8a), 165.2 (N=C–N), 167.3 (C=O), 188.9 (CHO). Anal. Calcd for $C_{23}H_{22}N_2O_4$: C, 70.75; H, 5.68; N, 7.17; found: C, 70.94; H, 5.54; N, 6.99.

4.3. General procedure for the preparation of amidines 3g–j

A solution of the appropriate enamine **2a**–**b**,**e**–**f** (10 mmol) in CH_2Cl_2 (20 mL) was added to a solution of an equimolar amount of azide **1b** dissolved in CH_2Cl_2 (30 mL), with careful monitoring of internal temperature (−30 °C, acetone–CO_2 bath). The resulting dark red solution was stirred at −30 °C until disappearance (TLC: cyclohexane/EtOAc, 1:1) of the starting azide **1b**. The stirring was continued until room temperature was reached. The solvent was then evaporated and the crude product purified by silica gel column, eluent EtOAc/cyclohexane (3:7). The crude oil crystallized from an appropriate solvent to give pure **3g**–**j**.

4.3.1. 4-[(1-Morpholin-4-yl-2-phenylethylidene)amino]-2-oxo-2*H*-[1]benzopyran-3-carbonitrile 3g. Reaction time: 2 h. Yield 60%; pale yellow crystals from AcOEt, mp 215 °C; IR ν_{max} (Nujol) 2206 (CN), 1700 (C=O) cm^{-1}; ^{1}H NMR: 3.55–4.10 (10H, m, morph., CH$_2$), 7.15–7.38 (5H+2 H, m, ArH, H-6, H-8), 7.61 (1H, td, J=8.0, 1.8 Hz, H-7), 7.89 (1H, dd, J=8.1, 1.8 Hz, H-5); ^{13}C NMR: 37.8 (CH$_2$), 46.2 (CH$_2$NCH$_2$), 66.4 (CH$_2$OCH$_2$), 81.4 (C-3), 116.9 (CN), 117.9 (C-4a), 117.5, 124.6, 126.0, 134.3 (CH), 127.8, 128.2, 129.5 (ArCH), 133.9 (ArC), 153.7 (C-4), 160.3 (C-8a), 162.1 (N=C–N), 164.1 (C=O). Anal. Calcd for $C_{22}H_{19}N_3O_3$: C, 70.76; H, 5.13; N, 11.25; found: C, 70.83; H, 5.34; N, 10.95.

4.3.2. *N*′-(3-Cyano-2oxo-2*H*-[1]benzopyran-4yl)-*N*,*N*-diethyl-2-phenyl-acetamidine 3h. Reaction time: 2 h. Yield 83%; apricot powder from AcOEt, mp 140 °C; IR ν_{max} (KBr) 2214 (CN), 1715 (C=O) cm^{-1}; ^{1}H NMR: 1.15 (3H, t, J=7.3 Hz, CH$_3$), 1.35 (3H, t, J=7.3 Hz, CH$_3$), 3.30–4.22 (6H, m, CH$_2$NCH$_2$ and CH$_2$), 7.12–7.33 (5 H+2 H, m, ArH, H-6, H-8), 7.58 (1H, td, J=6.9, 1.8 Hz, H-7), 7.90 (1H, dd, J=8.0, 1.8 Hz, H-5); ^{13}C NMR: 12.4 (CH$_3$), 13.8 (CH$_3$), 38.3 (CH$_2$), 44.4 (CH$_2$N), 44.6 (CH$_2$N), 79.7 (C-3), 117.4 (CN), 118.2 (C-4a), 117.4, 124.3, 126.0, 133.9 (CH), 127.6, 128.3, 129.3 (ArCH), 134.4 (ArC), 153.7 (C-4), 160.8 (C-8a), 162.9 (N=C–N), 163.0 (C=O). Anal. Calcd for $C_{22}H_{21}N_3O_2$: C, 73.52; H, 5.89; N, 11.69; found: C, 73.41; H, 5.66; N, 11.94.

4.3.3. 4-[(3-Methyl-1-morpholin-4-ylbutylidene)amino]-2-oxo-2*H*-[1]benzopyran-3-carbonitrile 3i. Reaction time: 3 h. Yield 70%; pink powder from *i*Pr$_2$O, mp 139 °C; IR ν_{max} (KBr) 2207 (CN), 1715 (C=O) cm^{-1}; ^{1}H NMR: 0.80 (3H, d, J=6.6 Hz, CH$_3$), 1.00 (3H, d, J=6.6 Hz, CH$_3$), 1.80–2.00 (1H, m, C*H*), 2.38–2.72 (2H, m, CH$_2$), 3.60–3.80 and 3.80–4.00 (8H, 2 m, morph.), 7.22–7.38 (2H, m, H-6, H-8), 7.59 (1H, td, J=8.4, 1.8 Hz, H-7), 7.79 (1H, dd, J=8.0, 1.8 Hz, H-5); ^{13}C NMR: 22.0 (CH$_3$), 23.3 (CH$_3$), 27.6 (*C*H), 39.9 (CH$_2$), 48.3 (CH$_2$NCH$_2$), 66.6 (CH$_2$OCH$_2$), 79.7 (C-3), 117.1 (CN), 117.9 (C-4a), 117.5, 124.4, 126.2, 134.2 (CH), 153.8 (C-4), 160.8 (C-8a), 163.7 (N=C–N), 164.6 (C=O). Anal. Calcd for $C_{19}H_{21}N_3O_3$: C, 67.24; H, 6.24; N, 12.38; found: C, 67.43; H, 6.52; N, 12.13.

4.3.4. 4-[(1-Morpholin-4-yl-3-phenylpropylidene)-amino]-2-oxo-2*H*-[1]benzopyran-3-carbonitrile 3j. Reaction time: 3 h. Yield 60%; pink powder from AcOEt, mp 105 °C; IR ν_{max} (KBr) 2210 (CN), 1716 (C=O) cm^{-1}; ^{1}H NMR: 2.75–3.12 (4H, m, CH$_2$–CH$_2$), 3.60–3.97 (8H, m, morph.), 7.02–7.36 (5 H+2 H, m, ArH, H-6, H-8), 7.45 (1H, dd, J=8.0, 1.7 Hz, H-5), 7.58 (1H, td, J=8.5, 1.7 Hz, H-7); ^{13}C NMR: 32.4 (CH$_2$), 33.8 (*C*H$_2$C$_6$H$_5$), 53.5 (CH$_2$NCH$_2$), 66.6 (CH$_2$OCH$_2$), 80.4 (C-3), 117.0 (CN), 117.7 (C-4a), 117.5, 124.6, 126.6, 134.3 (CH), 127.4, 128.6, 129.2 (ArCH), 138.7 (ArC), 153.8 (C-4), 160.7 (C-8a), 163.8 (N=C–N), 164.3 (C=O). Anal. Calcd for $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.46; N, 10.85; found: C, 71.08; H, 5.39; N, 11.04.

4.4. General procedure for the synthesis of [1]benzopyrano[4,3-*b*]pyridin-5-one derivatives 4a–f

Method A. A catalytic amount of sodium methoxide (0.5 ml, 30% solution) was added to a stirred suspension of the appropriate 3-formylamidine **3a**–**f** (4 mmol) in methanol (100 mL). The mixture was heated at reflux until the starting amidine disappeared. The solvent was evaporated under reduced pressure and the crude residue was crystallized from *i*Pr$_2$O to afford compounds **4a**–**d**. In the case of amidines **3e**–**f**, after disappearance of the starting compound (2 h) the crude reaction mixture was chromatographed on a silica gel column (EtOAc/cyclohexane, 1:4) affording a first fraction containing **4e**–**f**, a second fraction of 4-amino-3-formylcoumarin[7] **6** and finally the aldols **5e**–**f**, respectively. A catalytic amount of sodium methoxide (0.3 ml, 30% solution) was added to the previously obtained aldols **5e**–**f**. The mixture heated for an additional time (5 h), yielding a

second batch of benzopyranopyridin-5-one **4e–f** then crystallized from iPr$_2$O. The total yields of isolated and purified products **4a–f**,**5e–f** and **6** are listed in Table 1.

Method B. A suspension of the appropriate 3-formylamidine **3a–b**,**e–f** (4 mmol) in toluene (30 mL) containing a catalytic (0.02 g) amount of *p*-TSA was heated at reflux until disappearance of the starting amidine **3** (TLC: cyclohexane/EtOAc, 1:1, about 6 h), and then the solvent evaporated to dryness. The resulting solid residue was recrystallized from iPr$_2$O to give pure **4** derivatives. Analytical data are shown above. The yields of isolated and purified compounds **4a–b**,**e–f** are listed in Table 1.

4.4.1. 2-(Diethylamino)-3-phenyl-5*H*-[1]benzopyrano[4,3-*b*]pyridin-5-one 4b. Reaction time: 1 h. Cream crystals, mp 123 °C; IR ν_{max} (Nujol) 1711 (C=O) cm^{-1}; ^{1}H NMR: 1.12 (6H, t, J=7.3 Hz, 2×CH$_3$), 3.46 (4H, q, J=7.3 Hz, 2×CH$_2$), 7.35–7.59 (5H +3H, m, ArH, H-7, H-8, H-9), 8.14 (1H, s, H-4), 8.48 (1H, dd, J=8.4, 1.4 Hz, H-10); ^{13}C NMR: 13.0 (2×CH$_3$), 44.8 (2×CH$_2$N), 108.0 (C-4a), 117.3, 124.4, 124.7, 131.5 (CH), 120.1 (C-10a), 125.6 (C-3), 127.8, 128.0, 129.0 (ArCH), 140.3 (ArC), 141.3 (CH-4), 150.3 (C-6a), 153.5 (C-10b), 161.0 (C-2), 162.1 (C=O). Anal. Calcd for $C_{22}H_{20}N_2O_2$: C, 76.72; H, 5.85; N, 8.13; found: C, 76.81; H, 5.74; N, 7.95.

4.4.2. 3-(4-Bromophenyl)-2-morpholin-4-yl-5*H*-[1]benzopyrano[4,3-*b*]pyridin-5-one 4c. Reaction time: 0.5 h. White crystals, mp 141 °C; IR ν_{max} (KBr) 1725 (C=O) cm^{-1}; ^{1}H NMR: 3.44–3.52 (4H, m, CH$_2$NCH$_2$), 3.68–3.76 (4H, m, CH$_2$OCH$_2$), 7.33–7.60 (3H, m, H-7, H-8, H-9), 7.48 and 7.63 (4H, J=8.8 Hz, ArH), 8.26 (1H, s, H-4), 8.48 (1H, dd, J=8.4, 1.8 Hz, H-10); ^{13}C NMR: 48.9 (CH$_2$NCH$_2$), 66.4 (CH$_2$OCH$_2$), 110.1 (C-4a), 117.2, 124.4, 124.6, 131.8 (CH), 119.4 (C-10a), 122.3 (Ar*C*Br), 125.1 (C-3), 129.1, 132.4 (ArCH), 137.9 (ArC), 141.1 (CH-4), 150.3 (C-6a), 153.3 (C-10b), 161.3 (C-2), 162.7 (C=O). Anal. Calcd for $C_{22}H_{17}BrN_2O_3$: C, 60.43; H, 3.92; N, 6.41; found: C, 60.27; H, 3.76; N, 6.18.

4.4.3. 3-(4-Methoxyphenyl)-2-morpholin-4-yl-5*H*-[1]benzopyrano[4,3-*b*]pyridin-5-one 4d. Reaction time: 0.5 h. Cream crystals, mp 165 °C; IR ν_{max} (Nujol) 1708 (C=O) cm^{-1}; ^{1}H NMR: 3.43–3.50 (4H, m, CH$_2$NCH$_2$), 3.68–3.74 (4H, m, CH$_2$OCH$_2$), 3.88 (3H, s, OCH$_3$), 6.99 and 7.50 (4H, J=8.4 Hz, ArH), 7.27–7.58 (3H, m, H-7, H-8, H-9), 8.19 (1H, s, H-4), 8.42 (1H, d, J=8.4 Hz, H-10); ^{13}C NMR: 48.7 (CH$_2$NCH$_2$), 55.4 (OCH$_3$), 66.5 (CH$_2$OCH$_2$), 110.1 (C-4a), 117.1, 124.4, 124.5, 131.5 (CH), 119.6 (C-10a), 126.4 (C-3), 114.6, 128.7 (ArCH), 131.2 (ArC), 140.7 (CH-4), 149.7 (C-6a), 153.2 (C-10b), 159.6 (Ar*C*OCH$_3$), 161.5 (C-2), 162.0 (C=O). Anal. Calcd for $C_{23}H_{20}N_2O_4$: C, 71.12; H, 5.19; N, 7.21; found: C, 70.97; H, 5.06; N, 7.06.

4.4.4. 3-Isopropyl-2-morpholin-4-yl-5*H*-[1]benzopyrano[4,3-*b*]pyridin-5-one 4e. Reaction time: 7 h. Ivory powder, mp 175 °C; IR ν_{max} (Nujol) 1721 (C=O) cm^{-1}; ^{1}H NMR: 1.34 (6H, d, J=6.9 Hz, 2×CH$_3$), 3.20 (1H, quint, J=6.9 Hz, C*H*), 3.46–3.66 (4H, m, CH$_2$NCH$_2$), 3.90–3.98 (4H, m, CH$_2$OCH$_2$), 7.20–7.60 (3H, m, H-7, H-8, H-9), 8.37 (1H, s, H-4), 8.48 (1H, dd, J=8.0, 1.4 Hz, H-10); ^{13}C NMR: 24.3 (2×CH$_3$), 28.4 (CH), 51.2 (CH$_2$NCH$_2$), 67.0 (CH$_2$OCH$_2$), 112.1 (C-4a), 117.2, 124.61, 124.64, 131.5 (CH), 119.9 (C-10a), 136.6 (C-3), 137.0 (CH-4), 148.8 (C-6a), 153.0 (C-10b), 161.9 (C-2), 164.7 (C=O). Anal. Calcd for $C_{19}H_{20}N_2O_3$: C, 70.35; H, 6.21; N, 8.64; found: C, 70.23; H, 6.08; N, 8.79.

4.4.5. 3-Benzyl-2-morpholin-4-yl-5*H*-[1]benzopyrano[4,3-*b*]pyridin-5-one 4f. Reaction time: 7 h. White crystals, mp 174 °C; IR ν_{max} (Nujol) 1721 (C=O) cm^{-1}; ^{1}H NMR: 3.51–3.58 (4H, m, CH$_2$NCH$_2$), 3.81–3.88 (4H, m, CH$_2$OCH$_2$), 4.1 (2H, s, CH$_2$), 7.14–7.60 (5H +3H, m, ArH, H-7, H-8, H-9), 8.14 (1H, s, H-4), 8.48 (1H, dd, J=8.4, 1.4 Hz, H-10); ^{13}C NMR: 38.3 (CH$_2$), 50.1 (CH$_2$NCH$_2$), 66.9 (CH$_2$OCH$_2$), 111.2 (C-4a), 117.3, 124.6, 124.7, 131.7 (CH), 127.2, 129.0, 129.1 (ArCH), 119.8 (C-10a), 127.1 (C-3) 138.9 (ArC), 141.4 (CH-4), 149.5 (C-6a), 153.2 (C-10b), 161.6 (C-2), 164.5 (C=O). Anal. Calcd for $C_{23}H_{20}N_2O_3$: C, 74.18; H, 5.41; N, 7.52; found: C, 74.28; H, 5.45; N, 7.43.

4.4.6. 3-Benzyl-4-hydroxy-2-morpholin-4-yl-3,4-dihydro-5*H*-[1]benzopyrano[4,3-*b*]pyridin-5-one 5f. Reaction time: 2 h. Pale yellow oil, IR ν_{max} (Nujol) 3400 (OH), 1680 (C=O) cm^{-1}; ^{1}H NMR: 1.81 (1H, br s, OH), 2.40–2.52 (1H, m, CH-3), 2.65–3.00 (3H, m, C*H*NCH$_2$, CH$_2$Ph), 3.30–3.80 (4H+1H, m, CH$_2$OCH$_2$, C*H*NCH$_2$), 4.05–4.20 (2H, m, C*H*$_2$NCH$_2$), 4.92 (1H, s, CH-4), 7.10–7.60 (5H +3H, m, ArH, H-7, H-8, H-9), 8. 26 (1H, dd, J=8.4, 1.8 Hz, H-10); ^{13}C NMR: 37.0 (CH$_2$), 41.8 (CH-3), 45.0 and 46.9 (CH$_2$NCH$_2$), 65.9 and 67.1 (CH$_2$OCH$_2$), 68.7 (CH-4), 99.6 (C-4a), 117.1, 124.0, 125.8, 132.1 (CH), 120.0 (C-10a), 127.7, 129.2, 129.7 (ArCH), 137.6 (ArC), 154.6 (C-6a), 154.8 (C-10b), 164.2 (C-2), 168.2 (C=O). Anal. Calcd for $C_{23}H_{22}N_2O_4$: C, 70.75; H, 5.68; N, 7.17; found: C, 71.07; H, 5.84; N, 6.95.

4.5. General procedure for the synthesis of 4-amino-[1]-benzopyrano[4,3-*b*]pyridin-5-one derivatives 4g–h

A suspension of cyano amidine **3g** or **3h** (3.0 mmol) in methanol (40 mL) was added to a well-stirred solution of Na (0.076 g, 3.3 mmol) in methanol (15 mL). The reaction mixture was heated at reflux until disappearance (TLC: cyclohexane/EtOAc 2:3) of the starting amidine: 1 h for **4g** and 2 h for **4h**. The mixture was cooled to room temperature and afforded a solid product which was recrystallized from methanol to give **4g** or **4h**, respectively.

4.5.1. 4-Amino-2-morpholin-4-yl-3-phenyl-5*H*-[1]benzopyrano[4,3-*b*]pyridin-5-one 4g. Yield 92%, white crystals, mp 194 °C; IR ν_{max} (Nujol) 3429 and 3300 (NH$_2$), 1691 (C=O) cm^{-1}; ^{1}H NMR: 3.25–3.35 (4H, m, CH$_2$NCH$_2$), 3.52–3.59 (4H, m, CH$_2$OCH$_2$), 5.35 (2H, br s, NH$_2$), 7.31–7.60 (5H +3H, m, ArH, H-7, H-8, H-9), 8.47 (1H, dd, J=8.0, 1.8 Hz, H-10); ^{13}C NMR (DMSO$_{d6}$): 48.8 (CH$_2$NCH$_2$), 66.5 (CH$_2$OCH$_2$), 96.5 (C-4a), 106.4 (C-10a), 117.1, 125.1, 125.4, 132.6 (CH), 120.1 (C-3), 128.6, 130.5, 130.8 (ArCH), 135.6 (ArC), 151.5 (C-4), 152.8 (C-6a), 155.1 (C-10b), 161.3 (C-2), 162.7 (C=O). Anal. Calcd for $C_{22}H_{19}N_3O_3$: C, 70.76; H, 5.13; N, 11.25; found: C, 70.78; H, 5.24; N, 11.38.

4.5.2. 4-Amino-2-(diethylamino)-3-phenyl-5*H*-[1]benzopyrano[4,3-*b*]pyridin-5-one 4h. Yield 60%, white crystals, mp 180 °C; IR ν_{max} (KBr) 3487 and 3354 (NH_2), 1695 (C=O) cm^{-1}; ^1H NMR: 0.99 (6H, t, $J=6.9$ Hz, $2\times CH_3$), 3.46 (4H, q, $J=6.9$ Hz, $2\times CH_2$), 5.40 (2H, br s, NH_2), 7.30–7.46 (5H, m, ArH) 7.48–7.57 (3H, m, H-7, H-8, H-9), 8.46 (1H, dd, $J=8.0$, 1.4 Hz, H-10); ^{13}C NMR: 13.4 ($2\times CH_3$), 44.7 ($2\times CH_2N$), 96.5 (C-4a), 104.9 (C-10a), 116.8, 124.3, 125.2, 131.3 (CH), 120.7 (C-3), 128.1, 130.0, 130.9 (ArCH), 136.6 (ArC), 151.7 (C-4); 153.1 (C-6a), 154.9 (C-10b), 160.4 (C-2), 163.6 (C=O). Anal. Calcd for $C_{22}H_{21}N_3O_2$: C, 73.52; H, 5.89; N, 11.69; found: C, 73.77; H, 5.84; N, 11.56.

4.6. General procedure for the synthesis of 4-amino-[1]-benzopyrano[4,3-*b*]pyridin-5-one derivatives 4i–j

A suspension of cyano amidine **4i** or **4j** (3.0 mmol) in *t*butanol (40 mL) was added to a well-stirred solution of *t*BuOK (0.38 g, 3.3 mmol) in *t*butanol (10 mL). The reaction mixture was heated at reflux until disappearance (TLC: cyclohexane/EtOAc 2:3) of the starting amidine (about 2 h) and evaporated to dryness. The residue was poured into water and extracted with CH_2Cl_2 (3×40 mL). The combined organic layers were washed twice with water (2×40 mL) and dried over Na_2SO_4, filtered and evaporated to dryness. The crude product was recrystallized from methanol to give **4i** or **4j**, respectively.

4.6.1. 4-Amino-3-isopropyl-2-morpholin-4-yl-5*H*-[1]benzopyrano[4,3-*b*]pyridin-5-one 4i. Yield 56%, pale yellow crystals, mp > 300 °C; IR ν_{max} (KBr) 3465 (NH_2), 1698 (C=O) cm^{-1}; ^1H NMR: 1.44 (6H, d, $J=7.3$ Hz, $2\times CH_3$), 3.28–3.34 (4H, m, CH_2NCH_2), 3.57 (1H, quint, $J=7.3$ Hz, C*H*), 3.88–3.94 (4H, m, CH_2OCH_2), 5.90 (2H, br s, NH_2), 7.30–7.38 (2H, m, H-7, H-9), 7.52 (1H, td, $J=7.8$, 1.4 Hz, H-8), 8.47 (1H, dd, $J=7.8$, 1.4 Hz, H-10); ^{13}C NMR: 19.9 ($2\times CH_3$), 26.5 (CH), 51.8 (CH_2NCH_2), 67.4 (CH_2OCH_2), 99.4 (C-4a), 113.9 (C-10a), 116.9, 124.6, 125.3, 131.6 (CH), 120.6 (C-3), 150.6 (C-4), 152.7 (C-6a), 156.4 (C-10b), 164.1 (C-2), 165.1 (C=O). Anal. Calcd for $C_{19}H_{21}N_3O_3$: C, 67.24; H, 6.24; N, 12.38; found: C, 67.42; H, 6.25; N, 12.36.

4.6.2. 4-Amino-3-benzyl-2-morpholin-4-yl-5*H*-[1]benzopyrano[4,3-*b*]pyridin-5-one 4j. Yield 64%, pale yellow crystals, mp 135 °C; IR ν_{max} (KBr) 3435 and 3342 (NH_2), 1697 (C=O) cm^{-1}; ^1H NMR: 3.35–3.49 (4H, m, CH_2NCH_2), 3.75–3.85 (4H, m, CH_2OCH_2), 4.06 (2H, s, CH_2), 5.35 (2H, br s, NH_2), 7.20–7.40 (5H + 2H, m, ArH, H-7, H-9), 7.54 (1H, td, $J=8.0$, 1.4 Hz, H-8), 8.51 (1H, d, $J=8.0$ Hz, H-10); ^{13}C NMR: 33.0 (CH_2), 50.7 (CH_2NCH_2), 67.2 (CH_2OCH_2), 98.2 (C-4a), 104.9 (C-10a), 116.8, 124.5, 125.2, 131.6 (CH), 120.4 (C-3), 127.3, 127.8, 129.5 (ArCH), 137.0 (ArC), 151.3 (C-4), 152.7 (C-6a), 156.4 (C-10b), 163.6 (C-2), 165.1 (C=O). Anal. Calcd for $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.46; N, 10.85; found: C, 71.21; H, 5.47; N, 10.94.

4.7. General procedure for the synthesis of [1]benzopyrano[4,3-*d*]pyrimidin-5-one derivatives 7a–e

A solution of the amidine **3a**,**c**–**f** (20 mmol) in toluene (25 mL) was added to ammonium acetate (100 mmol). The resulting mixture was heated at reflux for the reported time (see after) until disappearance of the starting amidine **3** (TLC: cyclohexane/EtOAc, 4:1), then evaporated to dryness. The residue was poured into water and extracted with CH_2Cl_2 (3×40 mL). The combined organic layers were washed twice with water (2×40 mL) and dried over Na_2SO_4, filtered and evaporated to dryness. The resulting solid was recrystallized from iPr_2O to give pure **7** derivatives.

4.7.1. 2-Benzyl-5*H*-[1]benzopyrano[4,3-*d*]pyrimidin-5-one 7a. Reaction time: 1 h. Yield 63%, cream crystals, mp 131 °C; IR ν_{max} (Nujol) 1720 (C=O) cm^{-1}; ^1H NMR: 4.49 (2H, s, CH_2), 7.27–7.50 (5H + 2H, m, ArH, H-7, H-9), 7.71 (1H, td, $J=7.3$, 1.4 Hz, H-8), 8.63 (1H, dd, $J=7.7$, 1.4 Hz, H-10), 9.53 (1H, s, H-4); ^{13}C NMR ($DMSO_{d6}$): 46.4 (CH_2), 113.7 (C-4a), 118.2 (C-10a), 118.1, 125.3, 125.8, 135.3 (CH), 127.4, 129.2, 130.0 (ArCH), 138.2 (ArC), 154.8 (C-6a), 158.3 (C-10b), 159.8 (C-2), 160.7 (CH-4), 174.4 (C=O). Anal. Calcd for $C_{18}H_{12}N_2O_2$: C, 74.99; H, 4.20; N, 9.72; found: C, 74.87; H, 4.24; N, 9.76.

4.7.2. 2-(4-Bromobenzyl)-5*H*-[1]benzopyrano[4,3-*d*]pyrimidin-5-one 7b. Reaction time: 0.5 h. Yield 89%, cream crystals, mp 185 °C; IR ν_{max} (KBr) 1746 (C=O) cm^{-1}; ^1H NMR: 4.44 (2H, s, CH_2), 7.34 and 7.48 (4H, $J=8.4$ Hz, ArH), 7.39–7.49 (2H, m, H-7, H-9), 7.71 (1H, td, $J=7.7$, 1.8 Hz, H-8), 8.59 (1H, dd, $J=7.7$, 1.8 Hz, H-10), 9.53 (1H, s, H-4); ^{13}C NMR: 46.0 (CH_2), 112.5 (C-4a), 117.7 (C-10a), 121.1 (Ar*C*Br), 117.6, 125.2, 125.4, 134.6 (CH), 131.2, 131.8 (ArCH), 136.1 (ArC), 154.5 (C-6a), 158.5 (C-10b), 159.5 (C-2), 160.8 (CH-4), 174.3 (C=O). Anal. Calcd for $C_{18}H_{11}BrN_2O_2$: C, 58.88; H, 3.02; N, 7.63; found: C, 58.67; H, 3.00; N, 7.55.

4.7.3. 2-(4-Methoxybenzyl)-5*H*-[1]benzopyrano[4,3-*d*]-pyrimidin-5-one 7c. Reaction time: 1 h. Yield 82%, cream crystals, mp 110 °C; IR ν_{max} (Nujol) 1723 (C=O) cm^{-1}; ^1H NMR: 3.78 (3H, s, OCH_3), 4.39 (2H, s, CH_2), 6.87 and 7.37 (4H, $J=8.8$ Hz, ArH), 7.35–7.47 (2H, m, H-7, H-9), 7.65 (1H, td, $J=7.3$, 1.8 Hz, H-8), 8.58 (1H, dd, $J=7.8$, 1.8 Hz, H-10), 9.48 (1H, s, H-4); ^{13}C NMR: 45.8 (CH_2), 55.5 (OCH_3), 112.3 (C-4a), 117.8 (C-10a), 129.3 (ArC), 117.5, 125.2, 125.4, 134.4 (CH), 114.2, 130.4 (ArCH), 154.4 (C-6a), 158.3 (C-10b), 158.7 (Ar*C*OCH_3), 159.6 (C-2), 160.7 (CH-4), 175.2 (C=O). Anal. Calcd for $C_{19}H_{14}N_2O_3$: C, 71.69; H, 4.43; N, 8.80; found: C, 71.69; H, 4.41; N, 8.74.

4.7.4. 2-Isobutyl-5*H*-[1]benzopyrano[4,3-*d*]pyrimidin-5-one 7d. Reaction time: 1 h. Yield 85%, white crystals, mp 117 °C; IR ν_{max} (Nujol) 1723 (C=O) cm^{-1}; ^1H NMR: 1.05 (6H, d, $J=6.6$ Hz, $2\times CH_3$), 2.45 (1H, ept, $J=6.6$ Hz, C*H*), 3.05 (2H, d, $J=7.3$ Hz, CH_2), 7.39–7.50 (2H, m, H-7, H-9), 7.69 (1H, td, $J=7.7$, 1.8 Hz, H-8), 8.64 (1H, dd, $J=7.7$, 1.4 Hz, H-10), 9.53 (1H, s, H-4), ^{13}C NMR: 22.6 ($2\times CH_3$), 28.5 (CH), 49.1 (CH_2), 112.1 (C-4a), 117.9 (C-10a), 117.5, 125.1, 125.3, 134.3 (CH), 154.4 (C-6a), 157.9 (C-10b), 159.7 (C-2), 160.1 (CH-4), 176.2 (C=O). Anal. Calcd for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02; found: C, 70.77; H, 5.48; N, 10.98.

4.7.5. 2-(2-Phenylethyl)-5*H*-[1]benzopyrano [4,3-*d*]pyrimidin-5-one 7e. Reaction time: 3 h. Yield 94%, cream

crystals, mp 105 °C; IR ν_{max} (Nujol) 1720 (C=O) cm^{-1}; ^1H NMR: 3.31–3.35 and 3.45–3.46 (4H, 2×m, CH_2-CH_2), 7.18–7.53 (5H+2H, m, ArH, H-7, H-9), 7.70 (1H, td, J= 7.7, 1.8 Hz, H-8), 8.63 (1H, dd, J=7.7, 1.8 Hz, H-10), 9.53 (1H, s, H-4); ^{13}C NMR: 34.0 ($CH_2C_6H_5$), 41.6 (CH_2), 112.3 (C-4a), 117.8 (C-10a), 117.6, 125.2, 125.3, 134.5 (CH), 126.3, 128.4, 128.5, (ArCH), 140.9 (ArC), 154.4 (C-6a), 158.1 (C-10b), 159.8 (C-2), 160.3 (CH-4), 175.7 (C=O). Anal. Calcd for $C_{19}H_{14}N_2O_2$: C, 75.48; H, 4.67; N, 9.27; found: C, 75.40; H, 4.64; N, 9.25.

Acknowledgements

This work was supported by MIUR (Ministero dell'Istruzione e della Ricerca Universitaria). The authors thank Mrs. D. Nava for recording NMR spectra and HETCOR experiment as well as Dr. V. Bertacche for recording IR spectra.

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