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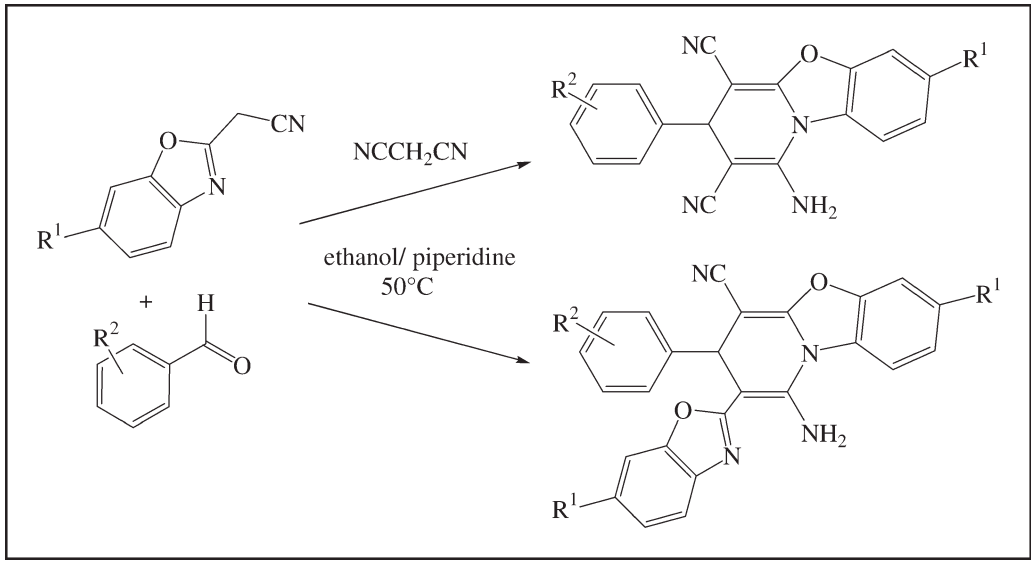

2-(Arylidene)cyanomethylbenzoxazoles have been prepared in water from benzoxazole-2-ylacetonitriles. Using multi-component reactions, a variety of heterocycles containing benzoxazole and nitrile functionality has been prepared.

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INTRODUCTION

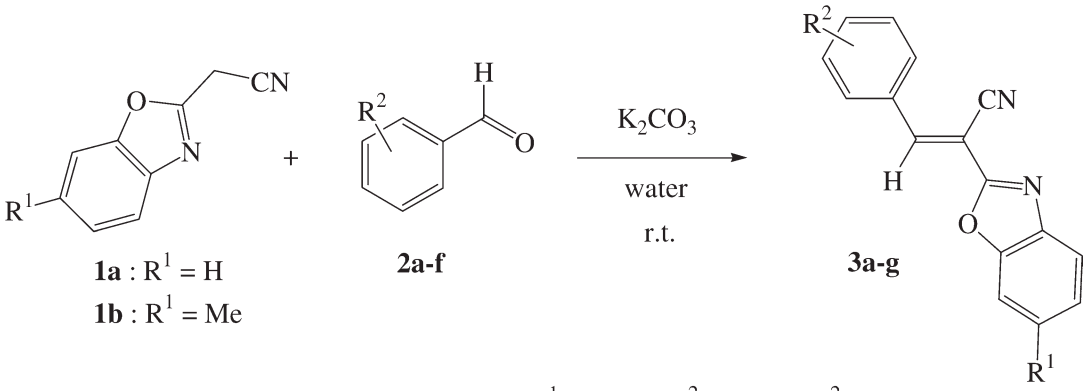
Molecules containing the benzoxazole moiety constitute a large family of heterocycles offering a range of biological and pharmacological activities [1–4] such as anti-tumoral [5,6], anticancer [7], antiviral [8,9], or antimicrobial [10,11] properties. They also lead to industrial applications in the field of textiles [12], dyes [13], and pigments [14]. Benzoxazoles offer a versatile reactivity and can be used as starting materials in heterocyclic compound syntheses, especially those containing an activated methylene group that can take part in condensation reactions [15]. In addition, the arylidene benzoxazoles containing an activated methylene linked to the reactive nitrile group, are frequently used in organic synthesis [16], as reactive precursors. They are currently used for their analgesic [17], insecticide, fungicide and nematicide [18] properties and as topo-isomerase I inhibitor [19,20].

Recently, new soluble metal catalysts have been revealed as powerful hydrogenation catalysts for the complete reduction of the nitrile groups into primary amines [21], thus these catalysts offer to nitrile containing heterocycles new applications as polydentate ligands with mixed coordinating-basic properties. These new catalytic transformations motivate that the benzoxazole syntheses can be revisited adopting greener processes.

The arylidene benzoxazole synthesis usually results from the classical Knoevenagel condensation which is currently performed in organic solvents, in the presence of a catalyst such as amines [22], Lewis acids [23], or even ionic liquids [24]. Recently, 2-benzoxazolyl acetonitrile was reacted with aromatic aldehydes in the presence of a catalytic amount of benzyldimethylamine to open an easy route to α,β-unsaturated α-oxazolines containing a nitrile function [16].

The interest, especially for environmental reasons and costs, of decreasing the use of organic solvents in synthesis and to develop new processes such as multi-component reactions (MCR) led us to adapt the previous synthesis of 2-benzoxazolyl acetonitrile for the

Scheme 1. Synthesis of benoxazoles **3a–g**.



1a : R^1 = H
1b : R^1 = Me

2a-f

3a-g

R^1 = H; R^2 = H (**3a**); R^2 = p-Cl (**3b**);
R^2 = *p*-OMe (**3c**); R^2 = *m*-Cl (**3d**);
R^2 = *m*-OMe (**3e**); R^2 = *m*-NO_2 (**3f**)
R^1 = Me; R^2 = H (**3g**)

production of α,β-unsaturated α-oxazolines in water for the production of polycyclic benzoxazole derivatives.

We now report the preparation of a variety benzoxazole containing heterocycles from α,β-unsaturated α-oxazolines and their one pot MCR synthesis directly from 2-benzoxazolyl acetonitrile, an aromatic aldehyde and an activated nitrile.

RESULTS AND DISCUSSION

The synthesis of 2-benzoxazolyl acetonitriles **1a** and **1b** has first been performed using the literature process [25]. These benzoxazoles are insoluble in water, but the addition of K_2CO_3 increases their water solubility and catalyses the condensation with a variety of aromatic aldehydes **2a–f**. The reaction was completed at room temperature for less than 10 minutes. The derivatives **3a–g** were obtained in good yields (81–95%) (Scheme 1). The ^{1}H-NMR spectrum showed the presence of only one stereoisomer with a singlet at 8.26–8.31 for the CH=C proton.

The X-ray diffraction study of compound **3g** confirmed the product structure. It showed that the flat benzoxazole and phenyl moieties are not coplanar to each other. It established that the cyano group and benzoxazole nitrogen are in the cisoid positions (Fig. 1).

These 2-arylidene cyanomethylbenzoxazoles **3** were used as starting materials for the access to new polycyclic heterocycles containing the benzoxazole moiety (Scheme 2). Heating of the derivatives **3** at 50°C for 30 min with malononitrile **4** in dry ethanol in the presence of piperidine, gave **5b**, **5e,** and **5f** in 45–53% (method A) [26,27]. Similarly, the 2-benzoxazolyl acetonitrile **1** on reaction with the benzoxazoles **3** led to heterocycles **6** in up to 63% yields. The structures of the compounds **5** and **6** were confirmed by infrared (IR), ^{1}H-NMR, ^{13}C-NMR, and high-resolution mass spectroscopy. ^{1}H-NMR spectra of **5a–g** present a characteristic singlet at δ 4.61–4.73 ppm (pyrido proton). For compounds **6a–g**, this typical pyrido proton was observed as a singlet at δ = 5.09–5.38 ppm in ^{1}H-NMR.

After the preparation of compounds **5** via heterocycles **3**, the synthesis of heterocycles **5** has been attempted by a one-pot three-components reaction directly from **1a** or **1b**, the arylaldehyde **2** and malononitrile **4** without the isolation of the intermediate **3** (method B) (Scheme 3). In each case, the heterocycles **5b** (68%), **5e** (63%), and **5f** (70%) were obtained in better yields than by the two step reaction (method A) for which 51, 45, 53% yields were obtained, respectively. Similarly, the benzoxazole **1** was reacted with half an equivalent of the arylaldehyde **2** in dry ethanol in the presence of $AcONH_4$ and piperidine at reflux for 2 h. The heterocycles **6** were directly obtained in better 52–75% yields than in the two step procedure (method A 30–63%). Thus, the direct three-component reaction has an obvious advantage with respect to the two steps reaction for the simplicity and yields.

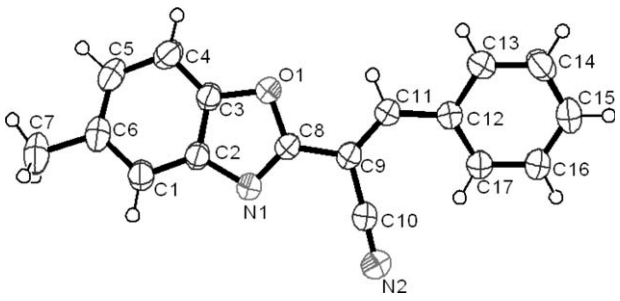
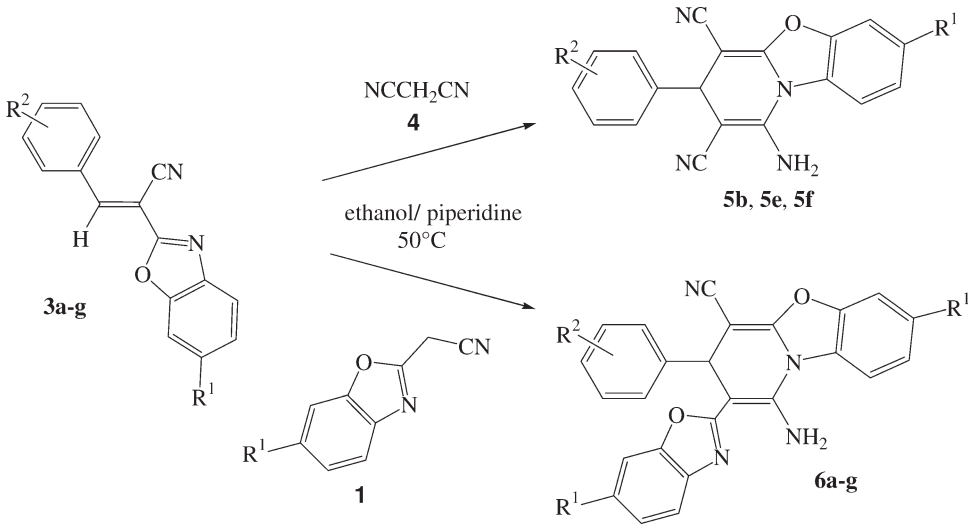


Figure 1. ORTEP of derivative **3g**.

Scheme 2. Synthesis of heterocycles **5** and **6** using method A.



CONCLUSION

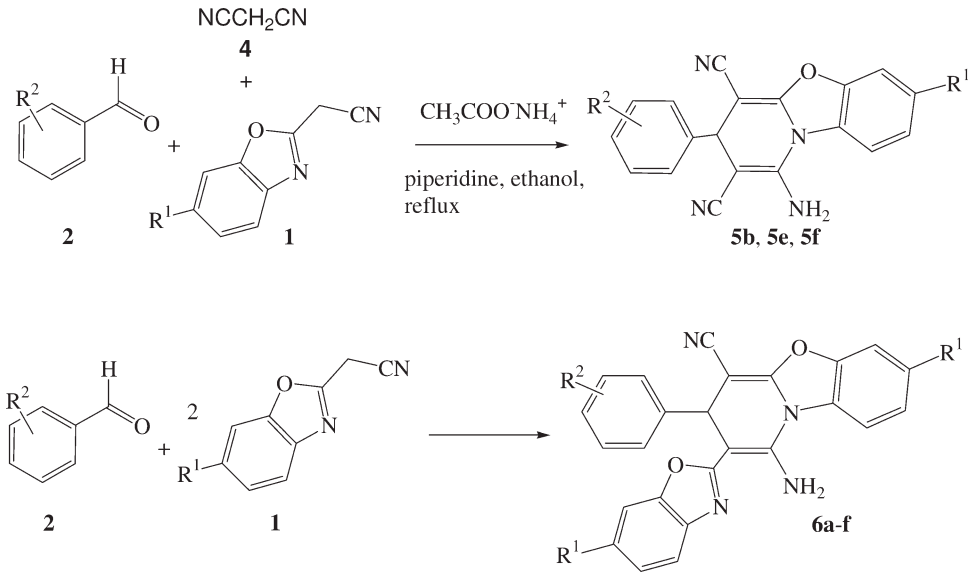
The above syntheses show a direct access to a variety of benzoxazole derivatives containing nitrile functionalities via reaction in water. Multicomponent reactions using aldehydes, benzoxazole acetonitriles and for some reactions malononitrile has been found to give good yields of heterocycles **5** and **6**. These substrates offer potential especially in catalytic hydrogenation of the nitrile functionalities for the preparation of amine derivatives that we are now exploring. The use of a chiral base, through organocatalysis, might also allow to control the stereogenic centre of these products [28].

EXPERIMENTAL

^{1}H and ^{13}C-NMR spectra were recorded on a AC 300 FT Bruker instrument (^{1}H: 300 MHz, ^{13}C: 75 MHz) and referenced internally to tetramethylsilane. IR spectra were recorded with a Perkin Elmer 298 spectrometer.

Preparation of 2-(arylidene)cyanomethylbenzoxazoles 3. To a stirred solution of 2-cyanomethylbenzoxazole **1a** (0.158 g, 1 mmol) and K_2CO_3 (0.069 g, 0.5 mmol) in water (10 mL), the appropriate aldehyde **2** (1 mmol) was added. The reaction mixture was stirred at room temperature for 2–10 min during which time yellow crystals appeared. The crystalline product was filtered, washed with ethanol, dried and recrystallized in the appropriate solvent. The crystals were filtrated and dried under vacuum to give the derivatives **3a–g** in 81–95% yields.

Scheme 3. Synthesis of heterocycles **5** and **6** using method B.



Spectroscopic data of products 3a–3g. The nucleus were numbered as in the X-ray structure (ORTEP) of **3g** (Fig 1).

IR of compounds 3. ν(cm^{-1}): 2230–2223 (CN), 1588–1574 (C=N), 1513–1502 (C=C).

(E)-2-(Benzoxazole-2-yl)-3-phenylacrylonitrile: 3a [29]. Yield: 85% Recrystallization in ethanol.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.36–7.41 (m, 2H, CH_{ar}), 7.43–7.60 (m, 4H, CH_{ar}), 7.77–7.82 (m, 1H, CH_{ar}), 8.03–8.06 (m, 2H, CH_{ar}), 8.32 (s, 1H, CH=C).

(E)-2-(Benzoxazole-2-yl)-3-(4-chlorophenyl)acrylonitrile: 3b [29]. Yield: 81% Recrystallization in ethanol.

^{1}H-NMR ($CDCl_3$, 300MHz): δ 7.37–7.45 (m, 2H, CH_{ar}), 7.49–7.52 (m, 2H, CH_{ar}), 7.55–7.62 (m, 1H, CH_{ar}), 7.78–7.83 (m, 1H, CH_{ar}), 7.98–8.01 (m, 2H, CH_{ar}), 8.26 (s, 1H, CH=C).

(E)-2-(Benzoxazole-2-yl)-3-(4-methoxyphenyl)acrylonitrile: 3c [29]. Yield: 92% Recrystallization in ethanol/dioxane.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 3.90 (s, 3H, OCH_3), 7.10–7.12 (m, 1H, CH_{ar}), 7.39–7.46 (m, 3H, CH_{ar}), 7.55–7.69 (m, 2H, CH_{ar}), 7.79–7.82 (m, 3H, CH_{ar}), 8.31 (s, 1H, CH=C).

(E)-2-(Benzoxazole-2-yl)-3-(3-chlorophenyl)acrylonitrile: 3d. Yield: 93% Recrystallization in ethanol/dioxane.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.36–7.49 (m, 5H, CH_{ar}), 7.51–7.63 (m, 1H, CH_{ar}), 7.79–7.85 (m, 1H, CH_{ar}), 8.29–8.34 (m, 1H, CH_{ar}), 8.69 (s, 1H, CH=C). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 102.5 (C_9), 114.4 (C_{10}), 110.8, 120.9, 125.4 and 126.6 (C_1, C_4, C_5 and C_6), 127.5, 129.6, 130.3 and 133.2 (C_{13}, C_{15}, C_{16} and C_{17}), 130.4 (C_{14}), 136.0 and 141.6 (C_5 and C_6) and 150.8 (C_{11}), 144.9 (C_{12}), 158.4 (C_8).

(E)-2-(Benzoxazole-2-yl)-3-(3-methoxyphenyl)acrylonitrile: 3e. Yield: 95% Recrystallization in ethanol/dioxane.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 3.90 (s, 3H, OCH_3), 7.09–7.12 (m, 1H, CH_{ar}), 7.37–7.46 (m, 3H, CH_{ar}), 7.55–7.60 (m, 2H, CH_{ar}), 7.68 (s, 1H, CH_{ar}), 7.79–7.82 (m, 1H, CH_{ar}), 8.29 (s, 1H, CH=C). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 55.5 (OCH_3), 99.4 (C_9), 115.0 (C_{10}), 110.7, 119.7, 125.3 and 126.3 (C_1, C_4, C_5 and C_6), 113.9; 120.7, 123.8 and 130.5 (C_{13}, C_{14}, C_{15} and C_{17}), 133.3, 141.6 and 149.4 (C_2, C_3, C_{12} and C_{16}), 150.7 (C_{11}), 160.0 (C_8).

(E)-2-(Benzoxazole-2-yl)-3-(3-nitrophenyl)acrylonitrile: 3f. Yield: 88% Recrystallization in ethanol.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ: 7.38–7.53 (m, 4H, CH_{ar}), 7.55–7.58 (m, 1H, CH_{ar}), 7.60–7.64 (m, 1H, CH_{ar}), 7.80–7.84 (m, 1H, CH_{ar}), 8.31–8.34 (m, 1H, CH_{ar}), 8.71 (s, 1H, CH=C). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ: 102.5 (C_9), 114.4 (C_{10}), 110.9, 120.9, 125.4 and 126.6 (C_1, C_4, C_5 and C_6), 127.6, 129.6, 130.4 and 133.3 (C_{13}, C_{15}, C_{16} and C_{17}), 130.4 (C_{14}), 136.0 and 141.6 (C_5 and C_6) and 150.8 (C_{11}), 145.0 (C_{12}), 158.4 (C_8).

(E)-2-(6-Methylbenzoxazol-2-yl)-3-phenylacrylonitrile: 3g. Yield: 85% Recrystallization in ethanol.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 2.43 (s, 3H, CH_3), 7.16 (d, 1H, J = 8.1 Hz, CH_{ar}), 7.39 (d, 1H, J = 8.4 Hz, CH_{ar}), 7.47–7.51 (m, 4H, CH_{ar}), 7.97–8.00 (m, 2H, CH_{ar}), 8.18 (s, 1H, CH=C).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 21.5 (C_7), 99.4 (C_9), 115.0 (C_{10}), 110.1, 120.4 and 127.4 (C_1, C_4 and C_5), 135.2 and 141.8 (C_2 and C_3), 129.4, 130.6, 132.8 (C_{13}, C_{14}, C_{15}, C_{16} and C_{17}), 132.1 and 148.5 (C_6 and C_{12}), 148.9 (C_{11}), 158.9 (C_8).

Synthesis of heterocycles 5 and 6 via method A (Scheme 2). To a solution of 2-cyanomethylbenzoxazole **1a** (0.158 g, 1 mmol) or malononitrile **4** (1 mmol) and piperidine (0.2 mL) in absolute ethanol (10 mL), the appropriate 2-arylidene cyanomethylbenzoxazole **3** (1 mmol) was added and the mixture was stirred at 50°C for 30 min. The formed crystalline product was filtered, washed with ethanol, and recrystallized from the appropriate solvent.

Synthesis of heterocycles 5 via method B (Scheme 3). To a solution of 2-cyanomethylbenzoxazole **1a** (0.158 g, 1 mmol), ammonium acetate (0.5 mmol) and piperidine (0.5 mL) in absolute ethanol (10 mL), the appropriate aldehyde **2** (1 mmol) and malononitrile **4** (0.066 g, 1 mmol) were added. The reaction was stirred under reflux for 2 h. The formed crystalline products **5** were filtered, washed with ethanol, and recrystallized from the appropriate solvent.

Synthesis of heterocycles 6 via method B (Scheme 3). To a solution of 2-cyanomethylbenzoxazole **1a** (0.316 g, 2 mmol), ammonium acetate (0.5 mmol) and piperidine (0.5 mL) in absolute ethanol (10 mL), the appropriate aldehyde **2** (1 mmol) was added. The reaction was stirred at reflux from 2 h. The formed crystals of heterocycles **6** were filtered, washed with ethanol and recrystallized from the appropriate solvent.

4-Amino-2-(4-chlorophenyl)-7-methyl-2H-9-oxa-4a-aza-fluorene-1,3-dicarbonitrile: 5b. Method A: Yield: 51%, Method B: Yield: 68%, Recrystallization in ethanol/dioxane.

^{1}H-NMR (DMSO, 300 MHz): δ 2.35 (s, 3H), 4.68 (s, 1H), 6.55 (s, 2H), 7.02 (d, J = 8.1 Hz, 1H), 7.33 (d, J = 8.1 Hz, 1H), 7.39 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.4 Hz, 2H), 7.57 (s, 1H). ^{13}C-NMR (DMSO, 75 MHz): δ 39.9, 60.1, 64.4, 110.4, 113.2, 116.6, 119.2, 124.3, 124.6, 127.4, 128.8, 129.5, 130.5, 132.3, 142.7, 146.3, 147.6, 156.6. MS (m/z) 383.0670 (M+Na).

4-Amino-2-(3-methoxyphenyl)-2H-9-oxa-4a-aza-fluorene-1,3-dicarbonitrile: 5e. Method A: Yield: 45%, Method B: Yield: 63%, Recrystallization in dioxane.

^{1}H-NMR (DMSO, 300 MHz): δ 3.75 (s, 3H, OMe), 4.63 (s, 1H, H-pyrido), 6.50–6.55 (m, 2H), 6.80–7.00 (m, 4H), 7.10–7.35 (m, 3H), 7.48 (d, J = 6.8 Hz, 1H), 7.70 (d, J = 6.8 Hz, 1H). ^{13}C-NMR (DMSO, 75 MHz): δ 55.1, 60.3, 64.7, 110.3, 112.5, 113.1, 113.4, 116.7, 119.2, 119.6, 124.2, 124.5, 125.3, 127.4, 129.9, 145.2, 146.2, 147.4, 156.4, 159.5. MS (m/z) 365.1006 (M+Na).

4-Amino-2-(3-nitrophenyl)-2H-9-oxa-4a-aza-fluorene-1,3-dicarbonitrile: 5f. Method A: Yield: 53%, Method B: Yield: 70%, Recrystallization in dioxane.

^{1}H-NMR (DMSO, 500 MHz): δ 5.00 (s, 1H), 6.67 (s, 2H), 7.20–7.30 (m, 2H), 7.49 (d, J = 7.3 Hz, 1H), 7.71 (t, J = 8.0 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 8.19 (d, J = 8.0 Hz, 1H), 8.30 (s, 1H). ^{13}C-NMR (DMSO, 125 MHz): δ 40.7, 59.9, 64.0, 110.8, 113.6, 117.0, 119.6, 122.6, 123.2, 124.8, 125.0, 127.9, 130.9, 135.0, 146.3, 146.8, 148.4, 148.6, 157.3. MS (m/z) 380.0756 (M+Na).

4-Amino-3-benzoxazol-2-yl-2-phenyl-2H-9-oxa-4a-aza-fluorene-1-carbonitrile: 6a. Method A: Yield: 30%, Method B: Yield: 52%, Recrystallization in dioxane.

^{1}H-NMR (DMSO, 300 MHz): δ 5.10 (s, 1H, H-pyrido), 7.21 (t, 2H, J = 7.8 Hz), 7.26–7.38 (m, 4H), 7.43 (d, 2H, J = 8.2 Hz), 7.53 (d, 1H, J = 8.2 Hz), 7.54 (d, 1H, J = 8.2 Hz), 7.59 (d, 1H, J = 8.2 Hz), 7.84 (d, 1H, J = 8.2 Hz), 7.90 (s, 2H). ^{13}C-NMR (DMSO, 75 MHz): δ 30.6, 61.7, 78.7, 109.8, 110.5, 113.1, 117.0, 117.4, 123.3, 124.4, 124.5, 124.6, 126.7, 127.1, 127.4, 128.7, 141.0, 144.7, 145.2, 146.5, 148.1, 156.1, 164.1. MS (m/z) 427.1165 (M+Na).

4-Amino-3-benzoxazol-2-yl-2-(4-methoxyphenyl)-2H-9-oxa-4a-aza-fluorene-1-carbonitrile: 6c. Method A: Yield: 45%, Method B: Yield: 65%, Recrystallization in DMF.

Table 1

X-ray data for **3g** [30].

Crystal data	
Formula: $C_{12}H_{17}N_2O$	F(000) = 544
Fw = 260.29	Calculated density: 1.306 g.cm^{-3}
Crystal system: monoclinic	Linear absorption factor: μ(MoKα) = 0.08 mm^{-1}
Space group: $P2_1/c$	Morphology: block
a = 11.0508(8) Å	Color: yellow
b = 12.0159(10) Å	Crystal size (mm^3): 0.32 × 0.22 × 0.15
c = 10.0074(9) Å	
β = 94.761(5)°	
V = 1324.25 (19) Å^3; Z = 4	
Data collection	
Temperature 296(2) K	Rint = 0.033
Diffractometer: Bruker APEX-II area detector	Absorption correction: multi-scan SADABS [33], T_{min} = 0.978, T_{max} = 0.988
Monochromator: graphite plate	Number of scanned reflections: 15413
Wavelength: MoKα = 0.71073 Å	Number of independent reflections: 4986
Scan mode: ω/θ	Number of observed reflections ($I > 2\sigma(I)$): 2755
θ range: 2.5–33.2°	Number of refined parameters: 181
Measurement area: $-16 \le h \le 16$; $-18 \le k \le 17$; $-15 \le l \le 14$	
Structure determination	
Structure determination: SHELXS97 [31]	
Structure refinement SHELXL97 [32]	
wR_2/R_1: 0.141/0.052	
Goodness-of-fit, S, on F^2: S = 1.02	
Final Fourier residual: min (−0.20 eÅ^{-3}), max (0.24 eÅ^{-3})	

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 3.68 (s, 3H, OCH_3), 5.09 (s, 1H, H-pyrido), 6.75–6.78 (m, 1H, CH_{ar}), 6.91–6.96 (m, 2H, CH_{ar}), 7.15–7.35 (m, 5H, CH_{ar}), 7.49–7.57 (m, 3H, CH_{ar}), 7.80–7.82 (m, 1H, CH_{ar}), 7.87 (brs, 2H, —NH_2). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 39.7, 54.8, 61.3, 78.4, 109.8, 110.49, 111.8, 112.9, 113.0, 117.9, 118.9, 123.2, 124.3, 124.5, 129.8, 116.9, 127.3, 140.6, 144.6, 146.7, 148.0, 156.3, 159.3, 164.0.

4-Amino-3-benzoxazol-2-yl-2-(3-chlorophenyl)-2H-9-oxa-4a-aza-fluorene-1-carbonitrile: 6d. Method A: Yield: 63%, Method B: Yield: 75%, Recrystallization in dioxane.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 5.16 (s, 1H, H-pyrido), 7.15–7.41 (m, 7H, CH_{ar}), 7.48–7.57 (m, 4H, CH_{ar}), 7.80 (d, 1H, J = 7.8 Hz, CH_{ar}), 7.89–7.94 (brs, 2H, —NH_2). ^{13}C-NMR (DMSO, 50 MHz): δ 39.9, 60.9, 77.9, 109.8, 110.5, 113.1, 116.9, 117.4, 123.3, 124.4, 124.5, 124.6, 125.8, 126.7, 127.2, 127.5, 130.5, 133.3, 140.9, 144.8, 146.6, 147.7, 148.0, 156.3, 163.9. MS (m/z) 461.0776 (M+Na).

4-Amino-3-benzoxazol-2-yl-2-(3-methoxyphenyl)-2H-9-oxa-4a-aza-fluorene-1-carbonitrile: 6e. Method A: Yield: 46%, Method B: Yield: 60%, Recrystallization in DMF.

^{1}H-NMR ($CDCl_3$, 300MHz): δ 3.68 (s, 3H, OCH_3), 5.10 (s, 1H, H-pyrido), 6.77 (d, 1H, J = 8.1 Hz, CH_{ar}), 6.91–6.97 (m, 2H, CH_{ar}), 7.19–7.33 (m, 5H, CH_{ar}), 7.50–7.58 (m, 3H, CH_{ar}), 7.81 (d, 1H, J = 7.8 Hz, CH_{ar}), 7.88 (brs, 2H, NH_2). ^{13}C-NMR ($CDCl_3$, 75 MHz) : δ : 39.7, 54.8, 61.3, 78.4, 109.8, 110.4, 111.8, 112.9, 113.0, 117.4, 118.8, 123.2, 124.4, 124.5, 129.8, 116.9, 127.3, 140.9, 144.7, 146.5, 146.6, 148.0, 156.1, 159.3, 164.0. MS (m/z) 457.1270 (M+Na).

4-Amino-3-benzoxazol-2-yl-2-(3-nitrophenyl)-2H-9-oxa-4a-aza-fluorene-1-carbonitrile: 6f. Method A: Yield: 57%, Method B: Yield: 72%, Recrystallization in dioxane.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 5.38 (s, 1H, H-pyrido), 7.16–7.37 (m, 4H, CH_{ar}), 7.46–7.64 (m, 4H, CH_{ar}), 7.84 (d, 1H, J = 7.8 Hz, CH_{ar}), 7.94–7.98 (m, 3H, —NH_2 and CHar), 8.06 (d, 1H, J = 8.10 Hz, CH_{ar}), 8.24 (s, 1H, CH_{ar8}). ^{13}C-NMR ($CDCl_3$, 75 MHz) : δ : 39.7, 61.3, 77.4, 109.7, 110.4, 111.8, 112.9, 113.0, 117.9, 118.9, 123.2, 124.3, 124.5, 130.2, 116.9, 127.3, 140.6, 144.6, 146.7, 148.0, 156.3, 159.3, 163.7. MS (m/z) 472.1018 (M+Na).

4-Amino-3-benzoxazol-2-yl-2-(3-methylphenyl)-2H-9-oxa-4a-aza-fluorene-1-carbonitrile : 6h. Method A: Yield: 57%, Method B: Yield: 71%, Recrystallization in dioxane.

^{1}H-NMR (DMSO, 300 MHz): δ 7.88 (s, 2H), 7.84 (d, 1H, J = 8.2 Hz), 7.56 (d, 1H, J = 8.2 Hz), 7.49 (d, 1H, J = 8.2 Hz), 7.46 (d, 1H, J = 8.2 Hz), 7.36–7.15 (m, 6H), 7.11 (t, 1H, J = 7.8 Hz), 7.06 (t, 1H, J = 7.8 Hz), 2.63 (s, 3H). ^{13}C-NMR (DMSO, 75 MHz): δ 18.5, 35.1, 61.7, 79.3, 109.7, 110.4, 112.9, 116.9, 117.4, 123.2, 124.2, 124.3, 124.5, 126.7, 126.9, 127.4, 127.9, 129.9, 133.8, 140.9, 144.4, 144.6, 146.4, 147.9, 155.7, 164.1. MS (m/z) 441.1325 (M+Na).

X-ray structure determination of benzoxazole 3g [30]. A single crystal of the compound **3g** with approximate dimensions 0.32 × 0.22 × 0.15 mm^3 was selected for lattice parameter determination and collection of intensity at 293(2) K, using a Bruker APEX-II area-detector diffractometer with graphite monochromated MoKα radiation (λ = 0.71073 Å). Intensities were collected by ω-2θ scan technique. The structure was solved by direct methods (SHELXS-97) [31] and refined with full-matrix least-squares technique (SHELXL-97) [32]. The positions of all remaining non-H atoms were obtained from successive Fourier syntheses. The positions of hydrogen atoms for aromatic rings were calculated using idealized geometry. The parameters of the crystal, data collection, and refinement are given in Table 1.

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