A facile transformation of 2-aminochromone to 4-chlorocoumarin and its reaction with ethylenediamine

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2-Aminochromones **1a–c** and **8a–c** are converted into 4-chlorocoumarins **2a–c** and **9a–c**. On treatment with ethylenediamine, **2a–c** produce 2,3,4,5-tetrahydro-7-(2'-hydroxyphenyl)-1,4-diazepin-5-one **3a,b** and 4-(2-aminoethyl) aminocoumarin **4b,c** in ethanol; while in DMF **9a–c** give the bis[4-(2-formamidoethyl)aminocoumarins **10a–c**.

Keywords: 1, 4-diazepines, 2-aminochromones, coumarins, biscoumarins

Syntheses of benzodiazepines have attracted much attention because of their pharmaceutical importance as tranquilising, anticonvulsant, antianxiety, hypnotic[1] and antiinflammatory agents.[2] 1, 4-Diazepines are also important because of their utility in psychotherapy.[3] Syntheses of 1, 5-benzodiazepin-2-one and 1,4-diazepin-5-one have been accomplished by the reaction of 4-hydroxycoumarin with *o*-phenylenediamine[4] and ethylenediamine[5] respectively. 4-Chlorocoumarin **2** has been reported to react with C-nucleophiles,[6] P-nucleophiles,[7] and N-nucleophiles.[8] Although reactions of 4-chloro-3-nitrocoumarin with bisnucleophiles like 2-aminoethanol,[9] α, ω-alkanedithiols[10] and 2-sulfanylphenols[11] have been studied and spiro compounds found to form, reactions of **2** with diamino compounds have not been considered. In this paper, a new route to 4-chlorocoumarin **2** from 2-aminochromone **1**,[12] and the reactions of **2a–c** with ethylenediamine, are reported. Similar reactions with 2, 2'-diaminobischromones **8a–c**[12] are also studied.

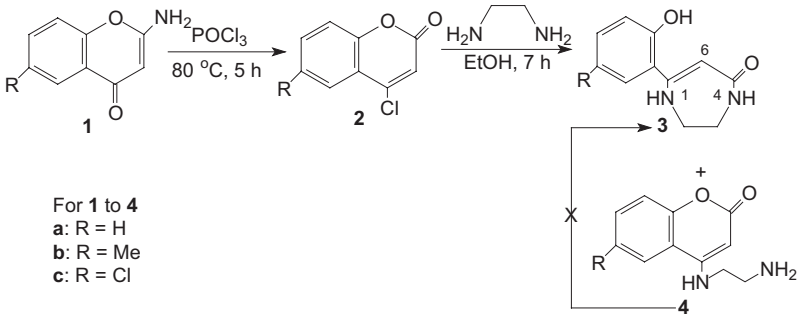
4-Chlorocoumarin **2** has been synthesised (i) by heating chromone-2-carboxylic acid with $SOCl_2$ or PCl_5 for 20 to 30 h or with PCl_5 in $POCl_3$ solution;[13] (ii) by treatment of $POCl_3$ on ethyl *N*-(2-chromonyl)carbamate,[14] or 4-hydroxycoumarin[15] (for the latter, formation of a tercoumarin is a wasteful side reaction); (iii) by treatment of Ph_3P and CCl_4 on 4-hydroxycoumarin.[16] An efficient method for the synthesis of 2-aminochromones **1** and 2,2'-diaminobischromones **8** has been reported from our laboratory.[12] Recently, the enamine moiety of 2-aminochromones **1** has been used for the synthesis of azaxanthones.[17] In this paper, the vinylogous amide functionality of **1** is utilised for the synthesis of 4-chlorocoumarins **2** by heating with $POCl_3$ at 80°C for 5 h (Scheme 1). This has advantages over the earlier reports by its easy work up, purer product and better yield.

In an endeavour to synthesise 1,4-diazepin-5-ones **3**, a mixture of 4-chlorocoumarin **2**, ethylenediamine and Et_3N in the ratio 1:1:1.2 was heated under reflux in ethanol. A white solid began to separate within half an hour. The heating was continued for 7 h with stirring. The deposited solid was filtered off. The filtrate afforded the desired 1,4-diazepinone **3** (see experimental) and the residue was stirred with water for 5 h. The solid, obtained by filtration from the water suspension, was washed thoroughly with water, dried in air and was digested with MeOH-ethyl acetate (1:1) for 3 h. A small portion (~ 10% of the deposited solid) remained insoluble and was filtered out. The filtrate (MeOH-EtOAc extract) on concentration provided compound **4** as a pure amorphous white solid. The white insoluble residue could not be characterised because of its poor solubility. This insoluble mass was stirred with saturated aqueous $NaHCO_3$ for 15 h, but no change in the solid was observed. Compounds **3** and **4** were isolated from the filtrate and the deposited solid, respectively, of the reaction mixture.

Use of pyridine in place of Et_3N does not show any change of the reaction; however, use of a mixture of **2** and ethylenediamine in the ratio 1: 2 showed a little improvement (5%) in the yield of **3**. Regarding the physical and analytical data of **3a**, some discrepancies are observed when compared with those of a previous report.[5] The melting point of **3a** we find to be 312–314°C, whereas the reported[5] value was 253–254°C. Again in the ^1H NMR spectrum, 6-H appears at δ 5.32 as a singlet, whereas the same proton was reported to appear at δ 4.25 as double doublet and having only one *J*-value of 1.8 Hz.

A possible mechanism for the formation of **3** and **4** may be as follows. Nucleophilic substitution takes place at the 4-position of the coumarin ring of **2** by ethylenediamine to form compound **4**, which subsequently cyclises slowly to produce **3**. In an attempt to obtain **3** in higher yield, compound **4** was heated under reflux in ethanol for 12 h, but surprisingly no change was observed. This observation is not in accordance with the above explanation.

In the previous report of the formation of 4-(2'-hydroxyphenyl)-1,5-benzodiazepin-2-one[4] or 7-(2'-hydroxyphenyl)-1,4-diazepin-5-one **3**,[5] from 4-hydroxycoumarin and *o*-phenylenediamine (**5**) or ethylenediamine respectively, by heating in xylene or toluene for 3–4 h, it was suggested that the initial attack of nucleophile takes place at the 4-position of



Scheme 1

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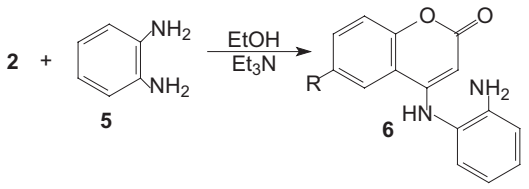


Scheme 2

the coumarin ring and then cyclisation occurs. However, the intermediate **6** or **4** was not isolated. To check the reality of this proposal, compound **6** was prepared by heating a mixture of **2, 5** and Et_3N in ethanol under reflux for 25 h in 20-30% yield (Scheme 2). However, this reaction did not occur when carried out in xylene in place of ethanol. Compound **6** was then heated under reflux in xylene for 25 h, but no change was observed. This observation firmly rules out the possibility of **6** as an intermediate *en route* to 4-(2'-hydroxyphenyl)-1,5-benzodiazepin-2-one.

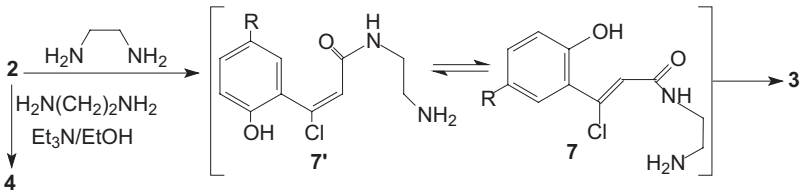
Competitive reactions at the C-2 and C-4 positions of 4-hydroxycoumarin by amines[18] and at those positions of 4-methoxycoumarin by C-nucleophiles[19] have been reported earlier. β-Chlorovinyl aldehydes are reported to form anils with *o*-phenylenediamine in ethanol; again, chlorovinylimines were shown to be intermediate in the formation of diazepines.[1d] In the present work, 4-chlorocoumarin (**2**), having a β-chloro-α,β-unsaturated lactone moiety, undergoes nucleophilic attack at both the C-2 and C-4 positions. To the best of our knowledge this is the first example in which an amine attacks the C-2 carbonyl competing with conjugate addition at the C-4 position of 4-chlorocoumarin.

Considering all the above facts, the formation of 1,4-diazepinone **3** may now be rationalised as follows (Scheme 3). Formation of compound **4** from **2** and ethylenediamine involves the initial attack of amine function at C-4 position of **2**, whereas compound **3** arises from the initial attack of ethylenediamine at C-2. *In situ* formation of 4-ethoxycoumarin followed by nucleophilic attack at the C-2 position of 4-ethoxycoumarin is ruled out as 4-chlorocoumarin failed to show any change when heated under reflux in ethanol in the presence of Et_3N for 15 h. So, the initial attack takes place at the C-2 position of **2** and the pyran ring then opens to form **7'**. This initially formed *E*-olefin **7′** isomerises to the *Z*-olefin **7**, possibly with the participation of the phenolic hydroxy group, and subsequently cyclises to **3**. The difficulty in following the other route **4** to **3** may be due to the strain developed in attaining a [4,3,1] bridged system in the transition state.

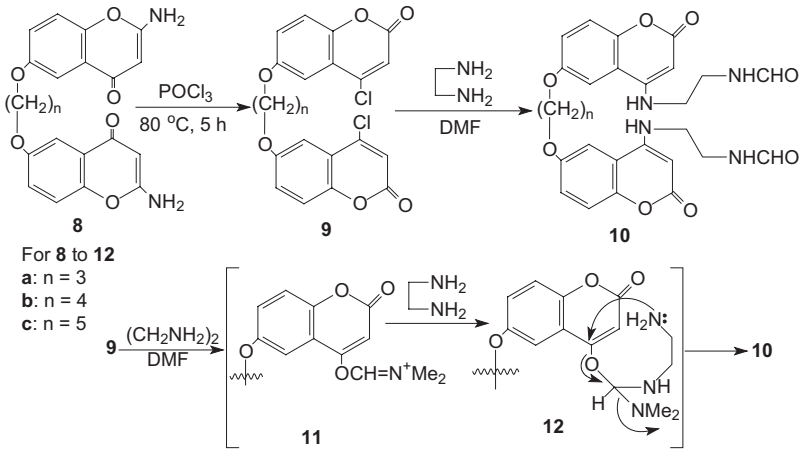
In an attempt to synthesise bis-(2,3,4,5-tetrahydro-1,4-diazepin-5-ones) from biscoumarins **9,** obtained from **8** by treatment with $POCl_3$, a mixture of **9**, ethylenediamine and Et_3N in 1:2:2.4 molar ratio was heated in DMF for 7 h. Because of the poor solubility of **9** in EtOH, the reaction was carried out in DMF. After isolation of the product, spectral analysis revealed it to be bis-[4-(2-formamidoethyl) aminocoumarin] **10** instead of the desired bis-(1,4-diazepin-5-one) (Scheme 4). Formation of **10** can be rationalised by considering the initial attack of DMF at the 4-position of **9** to produce **11**, which is then intercepted by ethylenediamine to form **12**. A rearrangement reaction initiated by the attack of terminal nitrogen on the 4-position of coumarin moiety and subsequent expulsion of Me_2N group would lead to the formation of **10** from **12**. However, treatment of **2** with ethylenediamine and Et_3N in DMF yielded **3** and **4** only. It has also been observed that DMF alone failed to carry out any change on 4-chlorocoumarin (**2**) or bis-(4-chlorocoumarin) (**9**), even after heating under reflux for 12 h. We have no explanation for the difference in behaviour of **2** and **9** towards ethylenediamine in DMF.

One noticeable thing in the ^1H NMR spectra of **9** and **10** is that the methylene protons $[O(CH_2)_nO]$ in compounds **9b** and **10b** (having a 4-carbon chain) appear as broad singlets, while those in compounds **9a,c** and **10a,c** appear with their usual multiplicities.[12]

In summary: we have developed a new method for the synthesis of 4-chlorocoumarins **2** and **9** and have studied their reactions with ethylenediamine, in which the formation of 7-(2′-hydroxyphenyl)-1,4-diazepin-5-ones **3** has been shown to occur by initial attack at the C-2 position of **2**.



Scheme 3



Scheme 4

Experimental

IR spectra were recorded on a Beckman IR 20A in KBr and ^{1}H NMR spectra on a Bruker 300 MHz spectrometer. Light petroleum refers to the fraction with distillation range 60–80°C.

General procedure for the synthesis of 4-chlorocoumarins (**2**): 2-Aminochromone **1**[12] (2 mmol) was heated in $POCl_3$ (10 ml) with stirring at 80°C for 5 h. The reaction mixture was cooled to room temperature and poured over crushed ice (100 g) and left overnight. The separated white solid was filtered, washed with water, dried in air and crystallised from ethyl acetate-light petroleum to produce **2.**

4-Chlorocoumarin (**2a**): White fine crystalline solid (260 mg, 72%); m.p. 90–92°C (lit.,[15a] m.p. 94°C). Compound **2a** had IR superimposable with that of an authentic sample prepared from 4-hydroxycoumarin.[15a]

4-Chloro-6-methylcoumarin (**2b**): White fine crystalline solid (290 mg, 75%); m.p. 118–120°C (lit.,[13] m.p. 117.5–118°C); IR: ν_{max}/cm^{-1} 3100, 1718, 1616, 1566; NMR: δ_H ($CDCl_3$) 2.46 (3 H, s, 6-Me), 6.59 (1 H, s, 3-H), 7.26 (1 H, d, J = 8.3 Hz, 8-H), 7.42 (1 H, dd, J = 8.3, 1.5 Hz, 7-H), 7.65 (1 H, d, J = 1.5 Hz, 5-H).

4, 6-Dichlorocoumarin (**2c**): White fine crystalline solid (365 mg, 85%); m.p. 162–164°C (lit.,[13] m.p. 165–166.5°C); IR: ν_{max}/cm^{-1} 3080, 1720, 1625, 1550; NMR: δ_H ($CDCl_3$) 6.66 (1 H, s, 3-H), 7.32 (1 H, d, J = 8.8 Hz, 8-H), 7.57 (1 H, dd, J = 8.8, 2.6 Hz, 7-H), 7.85 (1 H, d, J = 2.6 Hz, 5-H).

General procedure for the synthesis of 6,6′-(α,ω-polymethylenedioxy) di-(4-chlorocoumarins) (**9**): 2,2'-Diaminobischromone **8**[12] (2 mmol) was heated in $POCl_3$ (10 ml) with stirring at 80°C for 5 h. The reaction mixture was cooled to room temperature and was poured in crushed ice (100 gm) and left overnight. The separated white solid was filtered, washed with water, dried in air and crystallised from methanol to produce **9.**

6,6′-(1,3-Trimethylenedioxy)di-(4-chlorocoumarin) (**9a**): White fine crystalline solid (625 mg, 72%); m.p. 170–172°C; IR: ν_{max}/cm^{-1} 3050, 2840, 1730, 1610, 1580; NMR: δ_H (DMSO-d_6) 2.23–2.25 (2 H, m, CH_2), 4.20 (4 H, t, J = 5.9 Hz, 2 × OCH_2), 6.95 (2 H, s, 2 × 3-H), 7.29 (2 H, d, J = 2.4 Hz, 2 × 5-H), 7.38 (2 H, dd, J = 9.0, 2.4 Hz, 2 × 7-H), 7.46 (2 H, d, J = 9.0 Hz, 2 × 8-H); Anal. calcd. for $C_{21}H_{14}Cl_2O_6$: C, 58.22; H, 3.26. Found: C, 58.35; H, 3.15%.

6,6′-(1,4-Tetramethylenedioxy)di-(4-chlorocoumarin) (**9b**): White fine crystalline solid (750 mg, 84%); m.p. 170–172°C; IR: ν_{max}/cm^{-1} 3072, 2957, 2876, 1728, 1570, 1489; NMR: δ_H (DMSO-d_6) 1.91 [4 H, br s (splitting not observed),[12] 2 × CH_2], 4.15 [4 H, br s (splitting not observed),[12] 2 × OCH_2], 6.91 (2 H, s, 2 × 3-H), 7.23 (2 H, d, J = 2.6 Hz, 2 × 5-H), 7.32 (2 H, dd, J = 8.8, 2.6 Hz, 2 × 7-H), 7.42 (2 H, d, J = 8.8 Hz, 2 × 8-H); Anal. calcd. for $C_{22}H_{16}Cl_2O_6$: C, 59.08; H, 3.60. Found: C, 59.21; H, 3.48%.

6,6′-(1,5-Pentamethylenedioxy)di-(4-chlorocoumarin) (**9c**): White fine crystalline solid (630 mg, 68%); m.p. 160–162°C; IR: ν_{max}/cm^{-1} 3060, 3000, 2820, 1725, 1580, 1490; NMR: δ_H (DMSO-d_6) 1.62–1.64 (2 H, m, CH_2), 1.81–1.85 (4 H, m, 2 × CH_2), 4.09 (4 H, t, J = 6.0 Hz, 2 × OCH_2), 6.93 (2 H, s, 2 × 3-H), 7.29 (2 H, d, J = 1.9 Hz, 2 × 5-H), 7.34 (2 H, dd, J = 8.9, 1.9 Hz, 2 × 7-H), 7.44 (2 H, d, J = 8.9 Hz, 2 × 8-H); Anal. calcd. for $C_{23}H_{18}Cl_2O_6$: C, 59.89; H, 3.93. Found: C, 60.02; H, 4.08%.

General procedure for the reaction of 4-chlorocoumarin **2** *with ethylenediamine*

On heating a mixture of 4-chlorocoumarin **2** (2 mmol), ethylenediamine (2 mmol), triethylamine (2.4 mmol) in ethanol under reflux, a white solid began to separate within half an hour. The reaction mixture was heated under this condition for 7 h. The white solid was filtered off. The filtrate was concentrated and ice water was added to the concentrate to get a solid mass, which was filtered, dried and crystallised from MeOH-ethyl acetate (1 : 1) to produce 2,3,4,5-tetrahydro-7-(2'-hydroxyphenyl)-1,4-diazepin-5-one **3** in 35–40% yield. The residue (deposited solid in the reaction mixture) was stirred with water for 5 h, filtered, dried. It was then digested with methanol-ethyl acetate (1 : 1) and filtered hot. The filtrate (methanol-ethyl acetate extract) on concentration produced **4** in 30–35% yield, but the residue could not be characterised owing to poor solubility. Compounds **4a** and **3c** were not obtained from the reaction mixtures of **2a** and **2c**, respectively.

2,3,4,5-Tetrahydro-7-(2'-hydroxyphenyl)-1,4-diazepin-5-one (**3a**): White amorphous solid (165 mg, 40%); m.p. 312–314°C (lit.,[5] m.p. 253–254°C); IR: ν_{max}/cm^{-1} 3319, 2989, 1661, 1618, 1605, 1464; NMR: δ_H (DMSO-d_6) 3.05–3.08 (2 H, m, N–CH_2), 3.50–3.54 (2 H, m, N–CH_2), 5.32 (1 H, s, 6-H), 7.32–7.36 (2 H, m, 3'-H and 5'-H), 7.59–7.63 (1 H, m, 4'-H), 7.85 (1 H, t, J = 5.2 Hz exchangeable, N–H), 8.09–8.10 (2 H, m, exchangeable, O–H and N–H), 8.11 (1 H, dd, J = 8.0, 1.1 Hz, 6'-H); MS (positive ion electrospray): *m/z* 205 (M + H$^+$); Anal. calcd. for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.80; H, 6.08, N, 13.62%.

2, 3, 4, 5-Tetrahydro-7-(2'-hydroxy-5'-methylphenyl)-1, 4-diazepin-5-one (**3b**): White amorphous solid (150 mg, 35%); m.p. 320–322°C; IR: ν_{max}/cm^{-1} 3310, 3000, 1670, 1620, 1590 cm^{-1}; NMR: δ_H (DMSO-d_6) 2.37 (3 H, s, 5'-Me), 3.05–3.09 (2 H, m, N–CH_2), 3.49–3.53 (2 H, m, N–CH_2), 5.27 (1 H, s, 6-H), 7.21 (1 H, d, J = 8.3 Hz, 3'-H), 7.41 (1 H, dd, J = 8.3, 1.1 Hz, 4'-H), 7.86 (1 H, t, J = 5.2 Hz, exchangeable, N–H), 8.01 (1 H, d, J = 1.1 Hz, 6'-H), 8.13-8.17 (2 H, m, exchangeable, O–H and N–H); Anal. calcd. for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.46; N, 12.83. Found: C, 66.20; H, 6.28, N, 12.72%.

4-(2-Aminoethyl)amino-6-methylcoumarin (**4b**): White amorphous solid (140 mg, 32%); m.p. 192–194°C; IR: ν_{max}/cm^{-1} 3330, 3100, 1660, 1550, 1260 cm^{-1}; NMR: δ_H (DMSO-d_6) 1.85 (2 H, br s, exchangeable, NH_2), 2.37 (3 H, s, CH_3), 2.80-2.84 (2 H, m, N–CH_2), 3.24–3.28 (2 H, m, N–CH_2), 5.17 (1 H, s, 3-H), 7.19 (1 H, d, J = 8.3 Hz, 8-H), 7.39 (1 H, dd, J = 8.3, 0.9 Hz, 7-H), 7.64–7.70 (1 H, br s, exchangeable, N–H), 7.91 (1 H, d, J = 0.9 Hz, 5-H); MS (positive ion electrospray): *m/z* 219 (M + H$^+$); Anal. calcd. for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.46; N, 12.83. Found: C, 66.18; H, 6.56, N, 12.69%.

4-(2-Aminoethyl)amino-6-chlorocoumarin (**4c**): White amorphous solid (240 mg, 50%); m.p. 250–252°C; IR: ν_{max}/cm^{-1} 3317, 3100, 1659, 1549, 1265 cm^{-1}; NMR: δ_H (DMSO-d_6) 1.90 (2 H, br s, exchangeable, NH_2), 2.97–3.01 (2 H, m, N–CH_2), 3.48–3.51 (2 H, m, N–CH_2), 5.32 (1 H, s, 3-H), 7.37 (1 H, d, J = 8.7 Hz, 8-H), 7.65 (1 H, dd, J = 8.7, 1.4 Hz, 7-H), 7.77–7.92 (1 H, br s, exchangeable, NH), 8.23 (1 H, d, J = 1.4 Hz, 5-H); Anal. calcd. for $C_{11}H_{11}N_2ClO_2$: C, 55.35; H, 4.64; N, 11.74. Found: C, 55.48; H, 4.52, N, 11.55%.

General procedure for the synthesis of 4-(2′-aminophenyl)am inocoumarins (**6**): A mixture of 4-chlorocoumarin **2** (1 mmol), *o*-phenylenediamine **5** (1 mmol) and Et_3N (1.2 mmol) in ethanol was heated under reflux for 25 h. Solvent from the reaction mixture was removed under reduced pressure. Ice-water (50 gm) was added to the residue. The deposited solid was filtered, dried and purified by chromatography over silica gel (100–200). A white amorphous solid **6** was obtained using 20% ethyl acetate in benzene as eluent.

4-(2'-Aminophenyl)aminocoumarin (**6a**): White amorphous solid (75 mg, 30%), m.p. 228–230°C; IR: ν_{max}/cm^{-1} 3306, 3000, 1649, 1607, 1556, 1533; NMR: δ_H (DMSO-d_6) 4.66 (1 H, s, 3-H), 5.11 (2 H, br s, exchangeable, NH_2), 6.60–6.66 (1 H, m, 5'-H), 6.83 (1 H, dd, J = 8.0, 1.1 Hz, 3' -H), 7.03 (1 H, dd, J = 7.7, 1.1 Hz, 6′-H), 7.07–7.12 (1 H, m, 4'-H), 7.34–7.40 (2 H, m, 6-H and 8-H), 7.61–7.66 (1 H, m, 7-H), 8.25 (1 H, dd, J = 8.0, 0.9 Hz, 5-H), 8.95 (1 H, br s, exchangeable, NH); Anal. Calcd. for $C_{15}H_{12}N_2O_2$: C, 71.46; H, 4.79; N, 11.10. Found: C, 71.60; H, 4.90, N, 11.25%.

4-(2'-Aminophenyl)amino-6-methylcoumarin (**6b**): White amorphous solid (65 mg, 25%), m.p. 276–278°C; IR: ν_{max}/cm^{-1} 3317, 3000, 1647, 1625, 1562, 1533; NMR: δ_H (DMSO-d_6) 2.41 (3 H, s, CH_3), 4.64 (1 H, s, 3-H), 5.07 (2 H, br s, exchangeable, NH_2), 6.60–6.65 (1 H, m, 5'-H), 6.82 (1 H, dd, J = 8.0, 1.0 Hz, 3' -H), 7.00 (1 H, dd, J = 7.7, 1.5 Hz, 6'-H), 7.06–7.11 (1 H, m, 4'-H), 7.24 (1 H, d, J = 8.4 Hz, 8-H), 7.44 (1 H, dd, J = 8.4, 0.9 Hz, 7-H), 8.01 (1 H, d, J = 0.9 Hz, 5-H), 8.85 (1 H, br s, exchangeable, NH); Anal. Calcd. for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.30; H, 5.42, N, 10.30%.

General procedure for the synthesis of 6,6′-(α,ω-polymethylene-dioxy)di-[4-(2-formamidoethyl)aminocoumarins] (**10**): A mixture of biscoumarin **9** (1 mmol), ethylenediamine (2 mmol) and Et_3N (2.4 mmol) in DMF was heated under reflux at 100°C for 7 h. Solvent was removed under reduced pressure. Crushed ice (100 g) was added to the residue to afford a dirty brown solid. It was filtered, washed with water, dried and digested with $CHCl_3$–MeOH (1: 1) and filtered. The filtrate was chromatographed over silica gel (100–200) using ethyl acetate containing increasing amount of methanol as eluent. 10% Methanol in ethyl acetate afforded **10** as a yellow amorphous compound. No pure compound could be isolated from the residue obtained after digestion with $CHCl_3$–MeOH.

6,6′-(1,3-Trimethylenedioxy)di-[4-(2-formamidoethyl)amino-coumarin] (**10a**): Faintly yellow amorphous solid (110 mg, 20%); m.p. 252–254°C; IR: ν_{max}/cm^{-1} 3317, 3045, 1662, 1608, 1568; NMR: δ_H (DMSO-d_6) 2.25 (2 H, quintet, J = 5.4 Hz, CH_2), 3.30–3.40 (8 H, m, 4 × N–CH_2, partially merged with solvent peak), 4.21 (4 H, t, J = 5.4 Hz, 2 × OCH_2), 5.24 (2 H, s, 2 × 3-H), 7.20-7.28 [4 H, m, 2 × (7-H and 8-H)], 7.55 (2 H, d, J = 0.9 Hz, 2 × 5-H), 7.68 (2 H, br s, exchangeable, 2 × N–H), 8.08 (2 H, s, 2 × CHO), 8.18 (2 H, br s, exchangeable, 2 × N–H); MS (positive ion electrospray): *m/z* 559 (M + Na$^+$); Anal. calcd. for $C_{27}H_{28}N_4O_8$: C, 60.44; H, 5.26; N, 10.44. Found: C, 60.60; H, 5.40, N, 10.60%.

6, 6′-(1,4-Tetramethylenedioxy)di-[4-(2-formamidoethyl)aminocoumarin] (**10b**): Faintly yellow amorphous solid (140 mg, 25%); m.p. 266–268°C; IR: ν_{max}/cm^{-1} 3320, 3020, 1670, 1610, 1570; NMR: δ_H (DMSO-d_6) 1.93 [4 H, br s (splitting not observed),[12] 2 × CH_2], 3.35–3.40 (8 H, m, 4 × N–CH_2, partially merged with solvent peak), 4.11 [4 H, br s, (splitting not observed),[12] 2 × OCH_2], 5.24 (2 H, s, 2 × 3-H), 7.18–7.27 [4 H, m, 2 × (7-H and 8-H)], 7.53 (2 H, d, J = 1.0 Hz, 2 × 5-H), 7.67 (2 H, br s, exchangeable, 2 × N–H), 8.07 (2 H, s, 2 × CHO), 8.19 (2 H, br s, exchangeable, 2 × N–H); Anal. calcd. for $C_{28}H_{30}N_4O_8$: C, 61.08; H, 5.49; N, 10.18. Found: C, 61.20; H, 5.62, N, 10.09%.

6, 6′-(1,5-Pentamethylenedioxy)di[4-(2-formamidoethyl)aminocoumarin] (**10c**): Faint yellow amorphous solid (125 mg, 22%); m.p. 254–256°C; IR: ν_{max}/cm^{-1} 3310, 3050, 1650, 1615, 1540; NMR: δ_H (DMSO-d_6) 1.61–1.63 (2 H, m, CH_2), 1.80–1.82 (4 H, m, 2 × CH_2), 3.39–3.41 (8 H, m, 4 × N–CH_2, partially merged with solvent peak), 3.99–4.01 (4 H, m, 2 × OCH_2), 5.12 (2 H, s, 2 × 3-H), 7.00-7.03 (2 H, dd, J = 7.1, 1.0 Hz, 2 × 7-H), 7.09 (2 H, d, J = 7.1 Hz, 2 × 8-H), 7.36 (2 H, d, J = 1.0 Hz, 2 × 5-H), 7.43 (2 H, br s, exchangeable, 2 × N–H), 7.90 (2 H, s, 2 × CHO), 8.07 (2 H, br s, exchangeable, 2 × N–H); Anal. calcd. for $C_{29}H_{32}N_4O_8$: C, 61.69; H, 5.71; N, 9.92. Found: C, 61.82; H, 5.82, N, 9.75%.

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