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The synthesis and optical properties of novel fluorescent iminocoumarins and bis-iminocoumarins: Investigations in the series of urea derivatives

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ABSTRACT

The condensation of 3-cyano-7-diethylamino-iminocoumarin with various isocyanates and diisocyanates as C-electrophiles gave a new series of N-substituted iminocoumarins and bis-iminocoumarins. The ten compounds obtained were characterized using IR, ^{1}H NMR, ^{13}C NMR, elemental analysis and mass spectrometry. Their optical properties, studied in dichloromethane by UV/vis absorption and fluorescence spectroscopy, were found to depend strongly upon the nature of the substituent borne by the imino group. For the sake of comparison, the optical properties of selected compounds were also analyzed in ethanol. Of the iminocoumarins studied, the alkylurea derivatives displayed the most interesting spectroscopic characteristics and may be of potential use as novel fluorescent probes in media of various polarity.

1. Introduction

It is well documented that coumarins are nowadays an important group of fluorescent organic compounds [1–7]. They are used as optical brightening agents and laser dyes, they provide enzyme substrates for fluorimetric titrations in biomedical analysis, and are at the basis of numerous fluorescent probes and advanced photophysical systems. In contrast, the 2-imino analogues have received little attention. They have been used for a long time as precursors of coumarins [8–15] and closely related structures [16]. It has also been shown that iminocoumarins functionalized at the 3-position can be used as starting materials to obtain novel heterocyclic compounds consisting of a benzopyrane moiety fused with pyrazole [17], naphthyridine [18], quinoline [18], quinazoline [19,20] and pyrimidine rings [21–25]. It also appeared more recently that, besides their obvious interest in heterocyclic synthesis, some iminocoumarins exhibit attractive optical properties [26,27], leading to nice applications in the field of fluorescent sensors [28,29] and dye-sensitized solar cells [30]. These compounds offer the distinct advantage to be easily modified by substitution on the imino group and they can be adapted for particular applications. Our group has been working for many years on the synthesis of various original structures incorporating a coumarinic or iminocoumarinic fragment in order to elaborate novel materials for applications based on their optical properties [31–37]. It rapidly appeared that 3-cyano-7-diethylamino-iminocoumarin (**1**, Scheme 1) was of particular interest owing to its excellent fluorescence properties, similar to those of the corresponding coumarin [35]. As it is important to know whether these properties are retained after substitution of the imino group, a systematic study was undertaken. It showed that the nature of the substituent introduced on the imino group is indeed of major importance for the spectroscopic behaviour of the compound obtained. This means that the type of coupling used to graft the fluorescent moiety **1** on a substrate is determinant for subsequent applications. For instance, the *N*-ethoxycarbonylated derivative obtained by reacting **1** with ethylchloroformate as C-electrophilic reagent, was highly fluorescent [34,35]. Similarly, among the various *N*-acylated analogues that were prepared using acid chlorides [36], those bearing an aryl group directly linked to the =N–CO– group showed good fluorescence efficiency in different solvents, and could thus be used as fluorescent tracers in different media. In contrast, the derivatives bearing an alkyl group on the imido function were strongly fluorescent in dichloromethane, but emitted very weakly in a polar and protic medium such as ethanol. Consequently, we proposed their use for the fluorescent staining of biological membranes.

As a continuation of this investigation, it was decided to explore the effect of other types of substitution of the imino group. To do so, a series of novel, 3-cyano-7-(diethylamino)-iminocoumarins were

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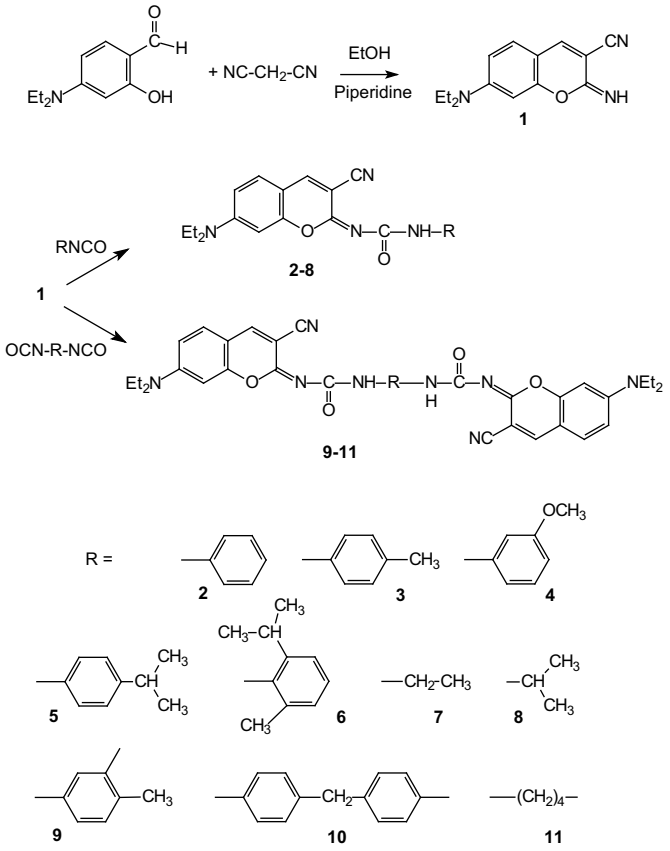

Scheme 1. Synthesis and chemical structure of compounds **1**–**11**.

prepared by condensation of **1** with C-electrophilic reagents such as isocyanates and diisocyanates. The urea derivatives of seven iminocoumarins and three bis-iminocoumarins were obtained, the urea group bearing various alkyl and aryl group. The optical properties of these compounds solubilised in dichloromethane were studied and compared.

2. Experimental

2.1. Apparatus

Melting points were determined by an Electrothermal 9100 apparatus. Infrared spectra were recorded on a Jasco FT-IR 420 spectrophotometer apparatus (in KBr pellets). ^{1}H and ^{13}C NMR spectra were obtained with a Bruker WP 200 spectrometer operating at 300 and 75 MHz, respectively, in $CDCl_3$ or DMSO-*d*6 with TMS as internal standard (chemical shifts in ppm). Elemental microanalyses were performed on an EA1112 analyser from CE Instruments. Mass spectrometry (CI) was performed on a DSQII ThermoFisher spectrometer using DCI/NH_3 as the ionization mode (positive mode).

All spectrophotometric measurements were conducted at 25 °C using a temperature-controlled cell holder. UV/vis absorption spectra were recorded on a Hewlett–Packard 8452A diode array spectrophotometer. The estimated experimental error was 2 nm on the band maximum. Steady state fluorescence work was performed on a Photon Technology International (PTI) Quanta Master 1 spectrofluorometer. All excitation and emission spectra were corrected. The fluorescence quantum yields (Φ) were determined using the classical formula: $\Phi_x = (A_s \times F_x \times n_x^2 \times \Phi_s)/(A_x \times F_s \times n_s^2)$ where A is the absorbance at the excitation wavelength, F the area under the fluorescence curve, and n is the refractive index of the solvents used. Subscripts s and x refer to the standard and to the sample of unknown quantum yield, respectively. Coumarin 6 in ethanol ($\Phi = 0.78$) was taken as the standard [38]. Fluorescence decay was measured with the stroboscopic technique using a Strobe Master fluorescence lifetime spectrophotometer from PTI. The excitation source was a flash lamp filled with a mixture of nitrogen and helium (30/70). Data were collected over 200 channels with a time-base of 0.1 ns per channel. Analysis of fluorescence decay was performed using the multiexponential method software from PTI.

2.2. Materials

For synthesis, acid chlorides, isocyanates and di-isocyanates were purchased from Aldrich. For spectroscopic measurements, analytical grade dichloromethane was from Prolabo and ethanol was from SDS.

2.3. General procedure for the synthesis of iminocoumarin and bis-iminocoumarin derivatives ***2*–*11***

3-Cyano-7-(diethylamino)-iminocoumarin **1** was synthesized as reported previously [33] using the Knoevenagel protocol. Subsequently, isocyanate (12 mmol) or diisocyanate (7 mmol)) diluted in 2 ml of chloroform was added dropwise, over 30 min, to a stirred solution of 10 mmol of **1** in 30 ml of chloroform at 0 °C. The basic medium was then allowed to reach room temperature. The mixture was kept under stirring at 20 °C during 30 min (compounds **2**, **4**, **9** and **10**), 45 min (**3**, **5**, **7** and **8**), 1 h (**11**) or 1 h30 (**6**). The products obtained were separated by filtration and then washed with methanol and dried before being characterized.

The compounds were examined by TLC on silica plates using chloroform as eluent. Most of them showed a single spot under excitation at 365 nm. A small amount of compound was systematically purified by TLC prior to spectroscopic work.

2.3.1. 1-[3-Cyano-7-(diethylamino)-2H-chromen-2-ylidene]-3-phenylurea (*2*)

Yield: 86%. m.p. 195 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.23$ (t, J = 7.0 Hz, 6H, $2 \times CH_3$), 3.43 (q, $J = 7.0$ Hz, 4H, $2 \times CH_2$), 6.49 (d, $J = 2.4$ Hz, 1H, H_8), 6.60 (dd, $J = 9.0$ Hz, $J = 2.4$ Hz, 1H, H_6), 7.08 (m, 1H, Ph), 7.13 (m, 2H, Ph), 7.23 (d, $J = 9.0$ Hz, 1H, H_5), 7.62 (m, 2H, Ph), 7.81 (s, 1H, H_4), 8.22 (s, 1H, NH). ^{13}C NMR (75 MHz, DMSO): $\delta = 12.62$ (CH_3), 44.67 (CH_2), 92.11 (C_3), 96.65 (C_8), 106.63 (C_6), 109.97 (C_{10}), 116.41 (C≡N), 118.95 (Ph), 122.98 (Ph), 129.05 (Ph), 131.52 (C_5), 139.92 (Ph), 148.73 (C_7), 149.90 (C_4), +153.06 (C_9), 156.23 (C_2), 157.47 (C═O). IR (KBr) cm^{-1}: $\nu = 1656$ (C═N), 1685 (C═O), 2225 (C≡N), 3344 (NH). Anal. Calcd. for $C_{21}H_{20}N_4O_2$: C, 69.98; H, 5.59; N, 15.54%. Found: C, 68.90; H, 5.33; N, 13.99%. MS: 361.1 ($M + H^+$).

2.3.2. 1-[3-Cyano-7-(diethylamino)-2H-chromen-2-ylidene]-3-p-tolylurea (*3*)

Yield: 82%. m.p. 188 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.23$ (t, $J = 7.2$ Hz, 6H, $2 \times CH_3$), 2.33 (s, 3H, $C\underline{H}_3$-Ph), 3.43 (q, $J = 7.2$ Hz, 4H, $2 \times CH_2$), 6.48 (d, $J = 2.4$ Hz, 1H, $\underline{H}_8$), 6.57 (dd, $J = 10.5$ Hz, $J = 2.4$ Hz, 1H, H_6), 7.14 (d, $J = 9.6$ Hz, 2H, Ph), 7.22 (d, $J = 10.5$ Hz, 1H, H_5), 7.49 (d, $J = 9.6$ Hz, 2H, Ph), 7.77 (s, 1H, H_4), 8.62 (s, 1H, NH). ^{13}C NMR (75 MHz,DMSO): $\delta = 12.22$ (CH_3), 20.91 ($\underline{C}H_3$-Ph), 44.82 (CH_2), 92.52 (C_3), 96.22 (C_8), 106.17 (C_6), 109.56 (C_{10}), 115.98 (C≡N), 128.98 (Ph), 129.59 (Ph), 131.11 (C_5), 131.37 (Ph)), 136.91 (Ph), 148.33 (C_7), 149.26 (C_4), 152.65 (C_9), 155.82 (C_2), 156.82 (CO). IR (KBr)

cm^{-1}: $\nu = 1660$ (C═N), 1695 (C═O), 2229 (C≡N) 3330 (NH). Anal. Calcd. for $C_{22}H_{22}N_4O_2$: C, 70.57; H, 5.92; N, 14.96%. Found: C, 69.90; H, 5.33; N, 13.99%. MS: 375.1 ($M + H^+$).

*2.3.3. 1-[3-Cyano-7-(diethylamino)-2*H*-chromen-2-ylidene]-3-(3-methoxyphenyl)urea (**4**)*

Yield: 90%. m.p. 126 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.07$ (t, $J = 6.9$ Hz, 6H, $2 \times CH_3$), 3.42 (q, $J = 6.9$ Hz, 4H, $2 \times CH_2$), 3.71 (s, 3H, OCH_3), 6.36 (d, $J = 1.2$ Hz, 1H, H_8), 6.58 (d, $J = 6.9$ Hz, 1H, Ph), 6.73 (dd, $J = 9.0$ Hz, $J = 1.2$ Hz, 1H, H_6), 7.16–7.21 (m, 2H, Ph), 7.31 (s, 1H, Ph), 7.42 (d, $J = 9.0$ Hz, 1H, H_5), 8.35 (s, 1H, H_4), 9.79 (s, 1H, NH). ^{13}C NMR (75 MHz, DMSO): $\delta = 12.82$ (CH_3), 44.82 (CH_2), 55.46 (OCH_3), 93.00 (C_3), 96.84 (C_8), 104.99 (C_6), 106.23 (Ph), 108.42 (Ph), 110.21 (C_{10}), 111.47 (Ph), 116.57 (C≡N), 130.01 (C_5), 131.73 (Ph), 141.23 (Ph), 149.04 (C_7), 150.01 (C_4), 153.28 (C_9), 156.41 (C_2), 157.50 (Ph), 160.08 (CO). IR (KBr) cm^{-1}: $\nu = 1652$ (C═N), 1690 (C═O), 2226 (C≡N), 3356 (NH). Anal. Calcd. for $C_{22}H_{22}N_4O_3$: C, 67.68; H, 5.68; N, 14.35%. Found: C, 66.90; H, 5.33; N, 13.99%. MS: 391.1 ($M + H^+$).

*2.3.4. 1-[3-Cyano-7-(diethylamino)-2*H*-chromen-2-ylidene]-3-(4-isopropylphenyl)urea (**5**)*

Yield: 80%. m.p. 195 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.05$ (d, $J = 6.9$ Hz, 6H, $2 \times CH_3$(iPr)), 1.14 (t, $J = 6.9$ Hz, 6H, $2 \times CH_3$), 2.81 (m, $J = 6.9$ Hz, 1H, CH(iPr)), 3.40 (q, $J = 6.9$ Hz, 4H, $2 \times CH_2$), 6.35 (s, 1H, H_8), 6.71 (d, $J = 9.0$ Hz, 1H, H_6), 7.14 (d, $J = 8.4$ Hz, 2H, Ph), 7.41 (d, $J = 9.0$ Hz, 1H, H_5), 7.52 (d, $J = 8.4$ Hz, 2H, Ph), 8.33 (s, 1H, H_4), 9.72 (s, 1H, NH). ^{13}C NMR (75 MHz, DMSO): $\delta = 12.81$ (CH_3), 24.52 (CH_3(iPr)), 33.37 (CH(iPr)), 44.82 (CH_2), 93.11 (C_3), 96.81 (C_8), 106.76 (C_6), 110.13 (C_{10}), 116.59 (C≡N), 119.18 (Ph), 126.91 (Ph), 131.71 (C_5), 137.77 (Ph), 143.21 (Ph), 148.90 (C_7), 149.79 (C_4), 153.23 (C_9), 156.42 (C_2), 157.47 (CO). IR (KBr) cm^{-1}: $\nu = 1650$ (C═N), 1680 (C═O), 2224 (C≡N) 3344 (NH). Anal. Calcd. for $C_{24}H_{26}N_4O_2$: C, 71.62; H, 6.51; N, 13.92%. Found: C, 70.90; H, 5.33; N, 13.99%. MS: 403.1 ($M + H^+$).

*2.3.5. 1-[3-Cyano-7-(diethylamino)-2*H*-chromen-2-ylidene]-3-(2-isopropyl-6-methylphenyl)urea (**6**)*

Yield: 40%. m.p 125 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.10$ (d, $J = 9.0$ Hz, 6H, $2 \times CH_3$(iPr)), 1.15 (t, $J = 6.9$ Hz, 6H, $2 \times CH_3$), 2.60 (m, 1H, CH(iPr)), 2.77 (s, 3H, C$\underline{H}_3$-Ph), 3.40 (q, $J = 6.9$ Hz, 4H, $2 \times CH_2$), 6.30 (d, $J = 2.4$ Hz, 1H, H_8), 6.70 (dd, $J = 8.7$ Hz, $J = 2.4$ Hz, 1H, H_6), 7.02 (dd, $J = 6.7$ Hz, $J = 6.9$ Hz, 1H, Ph), 7.35 (d, 6.7 Hz, 1H, Ph), 7.35 (d, $J = 8.7$ Hz, 1H, H_5), 7.77 (d, $J = 6.9$ Hz, 1H, Ph), 8.29 (s, 1H, H_4), 9.02 (s, 1H, NH). ^{13}C NMR (75 MHz, DMSO): $\delta = 12.83$ (CH_3), 20.88 (C$\underline{H}_3$-Ph), 25.62 (CH_3(iPr)), 33.40 (CH(iPr)), 44.95 (CH_2), 92.92 (C_3), 96.77 (C_8), 107.01 (C_6), 110.12 (Ph), 110.16 (C_{10}), 116.62 (C≡N), 123.23 (Ph), 125.65 (Ph), 127.32 (Ph), 130.90 (C_5), 132.05 (Ph), 144.62 (Ph), 149.00 (C_7), 149.77 (C_4), 153.13 (C_9), 155.22 (C_2), 156.40 (CO). IR (KBr) cm^{-1}: $\nu = 1649$ (C═N), 1688 (C═O), 2230 (C≡N) 3349 (NH). Anal. Calcd. for $C_{25}H_{28}N_4O_2$: C, 72.09; H, 6.78; N, 13.45%. Found: C, 70.90; H, 6.33; N, 13.99%. MS: 417.2 ($M + H^+$).

*2.3.6. 1-[3-Cyano-7-(diethylamino)-2*H*-chromen-2-ylidene]-3-ethylurea (**7**)*

Yield: 70%. m.p. 170 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.05$ (t, $J = 6.9$ Hz, 6H, $2 \times CH_3$), 1.05 (t, $J = 6.8$ Hz, 3H, CH_3(EtNH)), 3.11 (q, $J = 6.8$ Hz, 2H, CH_2(EtNH)), 3.42 (q, $J = 6.9$ Hz, 4H, $2 \times CH_2$), 6.28 (d, $J = 1.8$ Hz, 1H, H_8), 6.67 (dd, $J = 8.7$ Hz, $J = 1.8$ Hz, 1H, H_6), 7.37 (d, $J = 8.7$ Hz, 1H, H_5), 7.48 (s, 1H, NH), 8.24 (s, 1H, H_4). ^{13}C NMR (75 MHz, DMSO): $\delta = 12.80$ (CH_3), 25.40 (CH_3(EtNH)), 40.50 (CH_2(EtNH)), 44.80 (CH_2), 93.48 (C_3), 96.67 (C_8), 106.57 (C_6), 109.80 (C_{10}), 116.59 (C≡N), 131.56 (C_5), 148.34 (C_7), 148.84 (C_4), 153.01 (C_9), 156.35 (C_2), 159.57 (CO). IR (KBr) cm^{-1}: $\nu = 1671$ (C═N), 1699 (C═O), 2228 (C≡N), 3355 (NH). Anal. Calcd. for $C_{17}H_{20}N_4O_2$: C, 65.37; H, 6.45; N. 17,94%. Found: C, 66.10; H, 5.33; N, 16.99%. MS: 313.1 ($M + H^+$).

*2.3.7. 1-[3-Cyano-7-(diethylamino)-2*H*-chromen-2-ylidene]-3-isopropylurea (**8**)*

Yield: 71%. m.p. 192 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.09$ (t, $J = 6.9$ Hz, 6H, $2 \times CH_3$), 1.10 (d, $J = 6.6$ Hz, 6H, $2 \times CH_3$(iPr)), 3.40 (q, $J = 6.9$ Hz, 4H, $2 \times CH_2$), 3.81 (m, $J = 6.6$ Hz, 1H, CH(iPr)), 6.22 (s, 1H, H_8), 6.64 (d, $J = 8.4$ Hz, 1H, H_6), 7.37 (d, $J = 8.4$ Hz, 1H, H_5), 7.39 (s, 1H, NH), 8.21 (s, 1H, H_4). ^{13}C NMR (75 MHz, DMSO): $\delta = 12.74$ (CH_3), 23.42 (CH_3(iPr)), 41.80 (CH(iPr)), 44.85 (CH_2), 93.57 (C_3), 96.54 (C_8), 106.57 (C_6), 109.70 (C_{10}), 116.56 (C≡N), 131.51 (C_5), 148.18 (C_7), 148.87 (C_4), 152.91 (C_9), 156.33 (C_2), 159.03 (CO). IR (KBr) cm^{-1}: $\nu = 1654$ (C═N), 1691 (C═O), 2231 (C≡N) 3359 (NH). Anal. Calcd. for $C_{18}H_{22}N_4O_2$: C, 66.24; H, 6.79; N, 17.17%. Found: C, 66.90; H, 5.33; N, 15.99%. MS: 327.1 ($M + H^+$).

*2.3.8. 1-(4-Methyl-1,3-phenylene)bis[3-(3-cyano-7-(diethylamino)-2*H*-chromen-2-ylidene]urea) (9)*

Yield: 81%. m.p. 233 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.05$ (t, $J = 6.9$ Hz, 12H, $2 \times CH_3$), 2.24 (s, 3H, C$\underline{H}_3$-Ph), 3.39 (q, $J = 6.9$ Hz, 8H, $2 \times CH_2$), 6.32 (s, 2H, $2 \times H_8$), 6.66 (d, $J = 8.7$ Hz, 2H, $2 \times H_6$), 7.13 (d, $J = 8.4$ Hz, 1H, Ph), 7.24 (d, J = 8.4 Hz, 1H, Ph), 7.39 (d, $J = 8.7$ Hz, 2H, $2 \times H_5$), 7.89 (s, 1H, Ph), 8.26 (s, 2H, $2 \times H_4$), 9.12 (s, 2H, $2 \times$ NH). ^{13}C NMR (75 MHz, DMSO): $\delta = 12.72/12.77$ (CH_3), 17.78 (C$\underline{H}_3$-Ph), 44.88 (CH_2), 93.16/93.22 (C_3), 96.59/96.81 (C_8), 106.69/106.76 (C_6), 109.93/110.10 (C_{10}), 112.61 (Ph), 114.90 (Ph), 116.15/116.56 (C≡N), 126.91 (Ph), 130.71 (Ph), 131.67 (C_5), 136.96 (Ph), 138.15 (Ph), 148.51/148.78 (C_7), 156.38 (C_4), 153.09/153.19 (C_9), 156.38 (C_2), 158.73 (C═O). IR (KBr) cm^{-1}: $\nu = 1653$ (C═N), 1670 (C═O), 2231 (C≡N), 3344 (NH). Anal. Calcd. for $C_{37}H_{36}N_8O_4$: C, 67.67; H, 5.53; N, 17.06%. Found: C, 66.90; H, 5.33; N, 15.99%. MS: 657.3 ($M + H^+$).

*2.3.9. 1,1′-[4,4′-Methylenebis(4,1-phenylene)]bis{3-[3-cyano-7-(diethylamino)-2*H*-chromen-2-ylidene]urea} (**10**)*

Yield: 75%. m.p. 220 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1{,}09$ (t, $J = 6.9$ Hz, 12H, $4 \times CH_3$), 3.42 (q, $J = 6.9$ Hz, 8H, $4 \times CH_2$), 3.81 (s, 2H, Ph-C$\underline{H}_2$-Ph), 6.32 (s, 2H, $2 \times H_8$), 6.68 (d, $J = 8.7$ Hz, 2H, $2 \times H_6$), 7.13 (d, $J = 7.8$ Hz, 4H, Ph), 7.39 (d, $J = 9.0$ Hz, 2H, $2 \times H_5$), 7.53 (d, $J = 7.8$ Hz, 4H, Ph), 8.30 (s, 2H, $2 \times H_4$), 9.74 (s, 2H, $2 \times$ NH). ^{13}C NMR (75 MHz, DMSO): $\delta = 12.80$ (CH_3), 44.82 (CH_2), 79.68 (Ph-C$\underline{H}_2$-Ph), 93.11 (C_3), 96.82 (C_8), 106.77 (C_6), 110.13 (C_{10}), 116.57 (C≡N), 129.33 (Ph), 131.69 (C_5), 136.37 (Ph), 148.89 (C_7), 149.91 (C_4), 153.22 (C_9), 156.40 (C_2), 157.50 (C═O). IR (KBr) cm^{-1}: $\nu = 1650$ (C═N), 1691 (C═O), 2229 (C≡N) 3355 (NH). Anal. Calcd. for $C_{43}H_{40}N_8O_4$: C, 70.48; H, 5.50; N, 15.29%. Found: C, 69.90; H, 5.33; N, 13.99%. MS: 733.3 ($M + H^+$).

*2.3.10. 1,1′-(Butane-1,4-diyl)bis{3-[3-cyano-7-(diethylamino)-2*H*-chromen-2-ylidene]urea} (**11**)*

Yield: 88%. m.p. 265 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.09$ (t, $J = 6.9$ Hz, 12H, $4 \times CH_3$), 1.55 (t, $J = 8.6$ Hz, 4H, $2 \times CH_2$), 3.15 (t, $J = 8.9$ Hz, 4H, $2 \times CH_2$), 3.42 (q, $J = 6.9$ Hz, 8H, $2 \times CH_2$), 6.28 (s, 2H, $2 \times H_8$), 6.67 (d, $J = 9.0$ Hz, 2H, $2 \times H_6$), 7.37 (d, $J = 9.0$ Hz, 2H, $2 \times H_5$), 7.49 (s, 2H, $2 \times$ NH) 8.22 (s, 2H, $2 \times H_4$). ^{13}C NMR (75 MHz, DMSO): $\delta = 13.00$ (CH_3), 40.60 (CH_2), 44.90 (CH_2), 94.87 (C_3), 96.98 (C_8), 107.80 (C_6), 110.15 (C_{10}), 116.81 (C≡N), 132.02 (C_5), 148.88 (C_7), 150.14 (C_4), 154.13 (C_9), 155.23 (C_2), 157.55 (C═O). IR (KBr) cm^{-1}: $\nu = 1653$ (C═N), 1688 (C═O), 2228 (C≡N), 3350 (NH). Anal. Calcd. for $C_{34}H_{38}N_8O_4$: C, 65.58; H, 6.15; N, 17.99%. Found: C, 66.20; H, 5.33; N, 16.99%. MS: 623.3 ($M + H^+$).

3. Results and discussion

3.1. Synthesis

The synthetic procedure was accomplished in two steps (Scheme 1). Firstly, 3-cyano-7-(diethylamino)-iminocoumarin **1**

was prepared using the Knoevenagel condensation of 4-diethylamino-salicylaldehyde with an equimolecular amount of malononitrile. Secondly, its N-substitution was performed by reacting **1** with an isocyanate or diisocyanate derivative in chloroform. The ensuing products were isolated with good purity by simple filtration. Ten new iminocoumarin and bis-iminocoumarin derivatives were therefore prepared, all bearing one or two urea functions. Most of these compounds were obtained in good yields around 80%. It seems that, interestingly, the presence of the diethylamino group at the 7-position increased the reactivity of the imino group, due to the strong electron donating effect that is transmitted by charge transfer. Only for **6** was the yield quite small, probably because of the steric hindrance due to the substituted aryl group.

The FTIR spectra of compounds **2–11** showed the characteristic bands of the 3-cyanoimino moiety (C═N, C≡N), together with those specific to each N-substituent. Compared to the FTIR spectrum of **1** ($\nu_{C=N} = 1650\ cm^{-1}$, $\nu_{C\equiv N} = 2223\ cm^{-1}$) [33], we noted for N-substituted iminocoumarins that the C═N and C≡N bands were shifted toward high frequency, around 1660 and 2230 cm^{-1}, respectively. A new NH band appeared in the 3330–3360 cm^{-1} region for the substituted compounds, while the band associated to the free imino group NH in **1** (3317 cm^{-1}) disappeared. The ^1H NMR spectra of all compounds were in good agreement with the proposed structures. It can be noticed that the peak related to NH appeared around 7–10 ppm, while that related to the free NH group in **1** was at 8.25 ppm [**33**]. The structures of the compounds were also confirmed by ^{13}C NMR spectroscopy and mass spectrometry.

4. Optical properties

4.1. Optical properties of dyes *2–11* in dichloromethane

All compounds were first studied in dilute solution in dichloromethane, the data being gathered in Table 1.

4.1.1. UV/vis absorption spectra

For UV/vis absorption measurements, the dye concentration was between 1×10^{-5} and 2×10^{-5} M. The spectra of compounds **7** and **9** are given as an example in Fig. 1. All N-substituted iminocoumarin derivatives showed a maximum around 440 nm, with a shoulder more or less pronounced around 422 nm. The absorption spectra of bis-iminocoumarins **9–11** were very close to those of the monomers. It was checked with compounds **9** and **11** that the shape and position of these spectra, as well as the molar absorptivity, did not change with concentration between 5×10^{-4} M and 10^{-6} M. The effect of concentration was not studied on compound **10**, which is not very soluble in dichloromethane. If we refer to the unsubstituted iminocoumarin **1**, which exhibits two maxima of similar intensity at 414 and 428 nm [35], we notice that the introduction of the urea group has induced a significant shift towards long wavelengths.

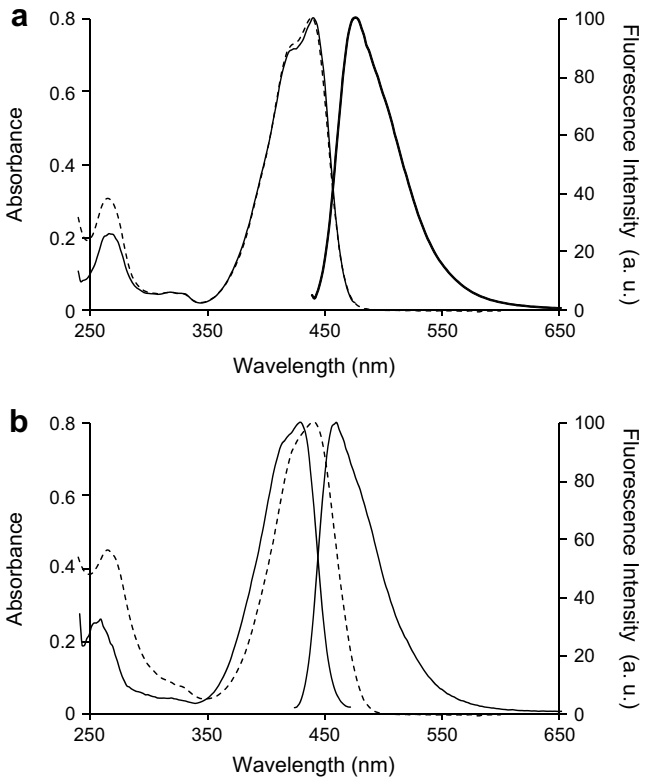

Fig. 1. UV/vis absorption spectra (dotted lines), normalized fluorescence excitation and emission spectra (plain lines) of compounds **7** (a) and **9** (b) in dichloromethane. Concentrations: 1.8×10^{-5} M and 1.0×10^{-5} M, respectively, for absorption and 1.1×10^{-6} M and 6.5×10^{-7} M, respectively, for fluorescence. $\lambda_{em} = 476$ nm, $\lambda_{ex} = 438$ nm.

4.1.2. Excitation spectra

For fluorescence spectroscopy, the dye concentration was in the 10^{-6} M range or below, so absorbance at the excitation wavelength was kept around 0.05. In these conditions, for all compounds, the excitation spectrum did not vary with the emission wavelength, indicating that there is only one emissive species in each sample. For compounds **2–8** and **11**, the excitation spectrum was superimposable to the absorption spectrum (see Fig. 1a for **7**), showing that the species visible on the absorption spectrum is actually responsible for fluorescence. In contrast, for **9** (Fig. 1b) and **10**, a discrepancy of 10 nm was noticed between the excitation and the absorption spectrum. Since the purity of the compounds was checked by TLC, this can be explained by the presence of aggregated molecules (although those were not detected by absorption spectroscopy for **9**), or most likely to the presence of conformers that are visible in the red part of the absorption spectrum, but not fluorescent.

Table 1
Maximum absorption wavelength (λ_{abs}), maximum excitation wavelength (λ_{ex}), maximum emission wavelength (λ_{em}), fluorescence quantum yield (Φ), fluorescence lifetime (τ), radiative (k_r) and non-radiative (k_{nr}) deactivation constants for compounds **2–11** in dichloromethane.

Compound	λ_{abs} (nm)	λ_{ex} (nm)	λ_{em} (nm)	Φ	τ (ns)	k_r ($10^8\ s^{-1}$)	k_{nr} ($10^8\ s^{-1}$)
2	443	443	488	$9.8\ (\pm 0.2) \times 10^{-2}$	0.3 ± 0.1	3.26	30.1
3	442	442	490	$1.1\ (\pm 0.2) \times 10^{-2}$	3.1 ± 0.4	0.35	3.19
4	443	442	486	$4.7\ (\pm 0.2) \times 10^{-2}$	0.5 ± 0.2	0.94	19.1
5	443	440	488	$1.1\ (\pm 0.2) \times 10^{-2}$	1.4 ± 0.4	0.79	7.06
6	439	442	480	0.40 ± 0.02	2.6 ± 0.4	1.54	2.31
7	439	440	476	0.85 ± 0.03	3.2 ± 0.2	2.66	0.47
8	439	440	476	0.74 ± 0.03	3.5 ± 0.4	2.11	0.74
9	440	430	460	0.11 ± 0.02	2.8 ± 0.6	0.39	3.18
10	440	430	460	$6.1\ (\pm\ 0.2) \times 10^{-2}$	2.7 ± 0.2	0.23	3.48
11	439	440	478	0.60 ± 0.03	2.6 ± 0.2	2.31	1.54

4.1.3. Steady-state emission spectra

The emission spectra of all compounds in dichloromethane displayed only one band, without any fine structure. It did not depend on the excitation wavelength. For compounds **2**–**5** bearing an aromatic group directly fixed to the =N–CO–NH– linker, the emission spectrum peaked at around 488 nm. In contrast, for compounds **7** and **8** that bear an aliphatic group, the emission maximum was situated at shorter wavelengths. The spectrum of **6**, which bears a bulky aromatic substituent, is intermediate between the formers.

Among bis-iminocoumarins, it can be noted that the spectrum of **11**, where the chromophores are linked by an aliphatic chain, was very close to that of **7** and **8**. Surprisingly, compounds **9** and **10**, where the chromophores are linked by an aromatic group, emit at lower wavelengths than the corresponding monomers.

If a comparison is drawn between compounds **2**–**11** and the unsubstituted iminocoumarin **1**, it can be seen that the emission spectra of the substituted compounds were shifted to the red, except those of **9** and **10** that peaked at exactly the same wavelength (460 nm).

4.1.4. Fluorescence quantum yields

Concerning the fluorescence quantum yields, the compounds can be obviously divided in two groups. The alkyl-substituted compounds **7** and **8** exhibited high fluorescence efficiency ($\Phi = 0.85$ and 0.74, respectively), while the aryl-substituted compounds **2**–**5** were less emissive by at least one order of magnitude.

Interestingly, compound **6** was much more emissive than the other compounds substituted by an aromatic group. This can be attributed to the strong steric hindrance that may force the compound in a given conformation or impede free rotation of the phenyl group.

For bis-iminocoumarin **11**, the quantum yield was weaker than for the monomeric homologues **7** and **8**. Regarding now the two other bis-iminocoumarins **9** and **10**, they just behave like the aryl-substituted homologues **2**–**5**.

4.1.5. Fluorescence lifetimes and deactivation constants

All fluorescence decays measured were monoexponential. The fluorescence lifetimes varied from several nanoseconds for most of the compounds to the sub-nanosecond range for **2** and **4**. Note that below 0.7 ns, the values given by our apparatus lack precision and must be considered with circumspection.

Having determined the fluorescence quantum yield and lifetime values, the radiative (k_r) and non-radiative (k_{nr}) deactivation constants were calculated from the classical formula: $k_r = \Phi/\tau$ and $k_{nr} = (1 - \Phi)/\tau$ (Table 1). Let us recall that, very schematically, a high value for k_r indicates that the energy levels of the molecule are compatible with high fluorescence efficiency, whereas a high value for k_{nr} suggests that molecular rotations or vibrations, or intermolecular interactions, open non-radiative deactivation channels that compete with fluorescence. In the present case, the analysis of the photophysical constants reveals that k_r decreases and k_{nr} increases markedly when passing from the alkyl-substituted compounds **7** and **8** to the aryl-substituted compounds **3**–**5** (The results obtained for **2** were discarded because of the large uncertainty on the lifetime measurement). This indicates that the loss of fluorescence efficiency observed with the aryl-substituted compounds can be attributed to both a disturbance of the energy levels and a rotation phenomenon that dissipates the excitation energy. It can be noted for compounds **2** and **4** that the k_{nr} value is particularly high, suggesting that rotation of the phenyl group actually plays a major role in deactivation of these compounds. Compound **6**, where rotation is probably impeded, is intermediate between the two groups. Concerning bis-iminocoumarins, the k_r and k_{nr} values found for **9** and **10** are very close to those found for the analogous monomer **3**, showing that in this case the bis-coumarin structure leads to no particular effect. But, it is noteworthy that the k_r value for **11** is similar to that found for **7** and **8**, while the k_{nr} value was increased. This indicates that new deactivation pathways are opened. This can be due to the overlapping of both chromophores, which is allowed by the flexibility of the linker, and leads to the formation of a non-fluorescent intramolecular excimer. This hypothesis is in line with different studies, which have shown that such an overlapping actually takes place in bis-coumarins where the chromophores are connected by aliphatic chains having 4–8 carbon atoms [39–42].

Table 2
Maximum absorption wavelength (λ_{abs}), maximum excitation wavelength (λ_{ex}), maximum emission wavelength (λ_{em}) and fluorescence quantum yield (Φ) for compounds **6-8** and **11** in ethanol.

Compound	λ_{abs} (nm)	λ_{ex} (nm)	λ_{em} (nm)	Φ
6	432	436	494	0.32 ± 0.02
7	433	436	490	0.36 ± 0.02
8	433	436	492	0.37 ± 0.02
11	430	436	492	$>0.24 \pm 0.02$

4.2. Optical properties of selected compounds in ethanol

The spectroscopic study in dichloromethane revealed that among the compounds investigated, iminocoumarins **6–8** and bis-iminocoumarin **11** displayed attractive fluorescence properties. Then, it seemed interesting to us to investigate rapidly the behaviour of these compounds in a protic and polar solvent such as ethanol. The data are gathered in Table 2.

It appears that absorption was slightly shifted to short wavelengths when passing from dichloromethane to ethanol. Meanwhile, emission was shifted to the red, as normally happens with this type of compounds, which are sensitive to solvent polarity [34]. Interestingly, all four dyes remain fluorescent in ethanol, meaning that they could be used as fluorescent tags in media of different polarity. Note that bis-iminocoumarin **11** was poorly soluble in ethanol and despite careful filtration, some aggregates may remain in suspension. Consequently, the actual quantum yield could be higher than the one indicated here.

5. Conclusions

It can be seen in this work that the Knoevenagel-type method used for synthesis is simple to implement. It allows substituted iminocoumarins to be obtained with good yields and high selectivity. From a spectroscopic point of view, it was interesting to see that the nature of the substituent borne by the =N–CO–NH- linker strongly governs the behaviour of the compound. This result is intriguing because the =N–CO–NH- group was not expected to transmit the effect of the substituent to the chromophore.

A comparison can be made with the results obtained in a previous work [36] about *N*-acyliminocoumarin derivatives, where the substituents were borne by a =N–CO- linker. Such a difference between aromatic and aliphatic substituents was not encountered in dichloromethane, differences only appearing in a protic solvent like ethanol. Besides, the *N*-acyl derivatives directly substituted by an aromatic group exhibited much better fluorescence efficiency than the alkyl derivatives, contrary to what was observed here. This comparison confirms that the nature of the modifications brought to the imino group is very important for

subsequent use of the compound, and justifies this type of investigations.

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