Synthesis and fluorescent properties of coumarin–chalcone hybrids

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Four coumarin–chalcone hybrids were synthesised utilising condensation of acetylcoumarin with three benzaldehydes and cinnamaldehyde, respectively. Moreover, the absorption and fluorescence spectra of these synthesised compounds in dichloromethane were measured.

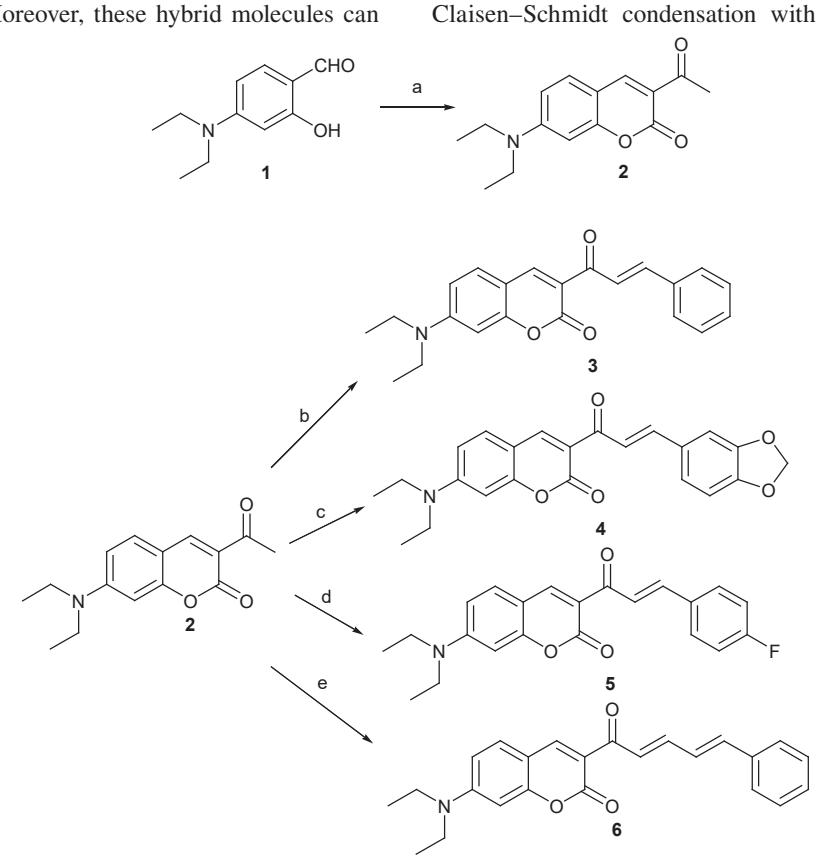
Keywords: coumarin, chalcone, hybrid, absorption spectra, fluorescence spectra

Coumarin and its derivatives have attracted much attention due to their various pharmacological activities, such as antiviral, anti-inflammatory and antitumour activity.[1] Furthermore, coumarins are widely used as laser dyes, nonlinear optical chromophores, fluorescent probes, fluorescent whiteners and solar energy collectors due to their outstanding optical properties, including superior photostability, large Stokes shifts and high quantum yields.[2,3]

Chalcones are one of the major classes of organic compounds and have been extensively investigated due to their variety of applications. They are reported to have antioxidant, antitumour and anti-inflammatory activities. Furthermore, chalcones exhibit excellent nonlinear optical properties and they can be used in organic light-emitting diodes.[4]

Therefore, incorporation of a coumarin nucleus with a chalcone moiety should likely to lead to a hybrid compound with significant properties. Indeed, coumarin–chalcone hybrids have been reported to have anti-inflammatory, antioxidant and antiviral activities.[5,6] They also show good thermal stability and fluorescent properties.[7] Moreover, these hybrid molecules can be used as chemosensors for cyanide anions, copper ions and biothiols.[8,9] Recently, our research group has been interested in preparing a diverse class of coumarin derivatives as well as investigating their fluorescent properties.[10–12] On the basis of the abovementioned observations, and as an extension of our study on fluorescent coumarins, we present herein the concise synthesis and fluorescent properties of several coumarin–chalcone hybrids.

As electron-withdrawing groups at the 3-position and electron-donating groups at the 7-position in the coumarin system have been shown to enhance the fluorescence of the molecules,[13] we employed the commercially available 4-(diethylamino)salicylaldehyde as the starting material for the synthesis of the title compounds. The synthetic strategy to achieve the target molecules is outlined in Scheme 1. Initially, 4-(diethylamino)salicylaldehyde (**1**) reacted with ethyl acetoacetate under solvent-free conditions in the presence of piperidine to afford 3-acetyl-7-(diethylamino)coumarin (**2**) in high yield. Next, the intermediate **2** was subjected to Claisen–Schmidt condensation with benzaldehyde catalysed



Scheme 1 Synthesis of compounds **3–6**. Regents and conditions: (a) ethyl acetoacetate, piperidine, solvent-free, r.t. 0.5 h, 91%; (b) benzaldehyde, piperidine, ethanol, reflux, 8 h, 56%; (c) piperonal, piperidine, ethanol, reflux, 10 h, 49%; (d) 4-fluorobenzaldehyde, piperidine, ethanol, reflux, 6 h, 66%; (e) cinnamaldehyde, piperidine, ethanol, reflux, 10 h, 51%.

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by piperidine in ethanol under reflux conditions to furnish the corresponding coumarin–chalcone hybrid **3** in moderate yield. The same condensation was also attempted in ethanol promoted by NaOH, but the expected product was obtained in very low yield along with appreciable quantities of byproducts. Compound **2** also underwent condensation with piperonal and 4-fluorobenzaldehyde in ethanol catalysed by piperidine to give the coumarin–chalcone hybrids **4** and **5**, respectively. Moreover, we also examined the condensation of intermediate **2** with cinnamaldehyde. Fortunately, the reaction proceeded well and the desired product **6** was obtained in moderate yield. As far as we know, the synthesis and photoluminescence properties of these four compounds **3**–**6** have not been reported in the literature. Then, the UV-Vis absorption and fluorescence spectra of the intermediate **2** and the four synthesised coumarin–chalcone hybrids **3**–**6** were measured in diluted dichloromethane solutions.

The UV-Vis absorption spectra are presented in Fig. 1. It can be seen that the linear absorption peak of intermediate **2** exists at 433 nm, which is very close to the reported value in chloroform solution.[14] The coumarin–chalcone hybrids **3**–**6** derived from **2** display obvious red-shift absorption maxima at 455, 458, 455 and 460 nm, respectively, due to their extended conjugation. In the cases of compounds **3**–**5**, although the molecular structures are modified in the terminal phenyl ring where different substituents are attached, they exhibit almost identical absorption spectra. Compared with **3**, compound **6** shows a slight bathochromic shift in the absorption maximum owing to its larger conjugation.

The fluorescence spectra of compounds **2**–**6** in dichloromethane are shown in Fig. 2. It is observed that intermediate **2** exhibits an emission peak at 465 nm, which is also similar to the reported value in chloroform solution.[14] Compounds **3**–**6** show emission maxima at 508, 506, 507 and 517 nm, respectively, which show a remarkable bathochromic shift compared with that of compound **2**. It also can be seen that the emission maxima of compounds **3**–**5** with different terminal phenyl moieties are very close to each other. However, compound **6** displays the highest emission peak among these compounds, obviously resulting from it having the largest conjugated system.

In conclusion, the facile synthesis of four coumarin–chalcone hybrids by Claisen–Schmidt condensation of 3-acetyl-7-(diethylamino)coumarin respectively with benzaldehyde, piperonal, 4-fluorobenzaldehyde and cinnamaldehyde has been described. The study also reveals that the absorption and emission maxima of these hybrids show a remarkable bathochromic shift compared with the acetylcoumarin precursor. In particular, the hybrid with the longest conjugation length exhibits the highest emission peak. The applicability of these coumarin–chalcone hybrids is yet to be established.

Experimental

Reagents and solvents were all from commercial sources and used without further purification. IR spectra were performed on a Digilab FTS-3000 FT-IR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Mercury Plus 400 MHz spectrometer. Melting points were measured on a Kofler apparatus and uncorrected. Column chromatography purifications were performed on 200–300 mesh silica gel. Analytical thin-layer chromatography (TLC) was performed on silica gel GF254 plates. High-resolution mass spectra (HRMS) were determined on a Bruker Daltonics APEX II 47e spectrometer. UV-Vis absorption and fluorescence spectra were recorded on a Hitachi U-3900H spectrometer and on a Hitachi F7000 FL spectrophotometer, respectively.

3-Acetyl-7-(diethylamino)coumarin (**2**)

4-(Diethylamino)salicylaldehyde (1.16 g, 6.0 mmol), ethyl acetoacetate (0.78 g, 6.0 mmol) and piperidine (0.5 mL) were added to a mortar successively. The mixture was ground well with a pestle at room temperature for 30 min. Then the mixture was dissolved in ethyl acetate (100 mL), neutralised with 3N HCl and extracted with brine (3 × 50 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was recrystallised in ethanol to afford **2** as: Yellow solid; yield 91%; m.p. 155–156 °C (lit.[15] 151–153 °C).

Synthesis of coumarin–chalcone hybrids (**3**–**6**)*; general procedure*

3-Acetyl-7-(diethylamino)coumarin (1.0 mmol) and the corresponding aldehyde (1.0 mmol) were dissolved in ethanol (30 mL) and piperidine (0.5 mL) was added. The mixture was stirred under reflux conditions and monitored by TLC. When the reaction was judged to be complete, the organic solvent was evaporated under reduced pressure. Then the mixture was dissolved in ethyl acetate (50 mL), neutralised with diluted aqueous hydrochloric acid and extracted with brine (3 × 50 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography using petroleum ether/ethyl acetate (v/v = 5:1) as eluent to afford the product.

7-(Diethylamino)-3-(3-phenylacryloyl)coumarin (**3**): Yellow solid; yield 56%; m.p. 161–163 °C; IR (KBr) (cm^{-1}): 2972, 1707, 1618, 1504, 1350, 1178, 1059, 780, 700; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (s,

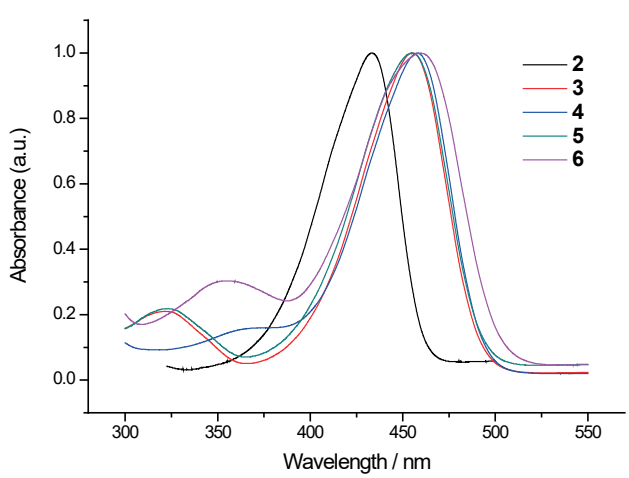

Fig. 1 Normalised absorption spectra of compounds **2**–**6** in dichloromethane (1 × 10^{-5} mol L^{-1}).

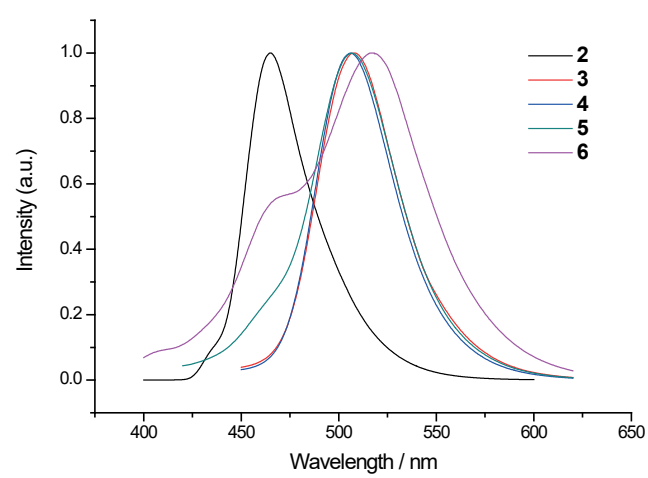

Fig. 2 Normalised emission spectra of compounds **2**–**6** in dichloromethane (1 × 10^{-5} mol L^{-1}).

1H), 8.16 (d, *J* = 15.6 Hz, 1H), 7.82 (d, *J* = 15.6 Hz, 1H), 7.69–7.67 (m, 2H), 7.42–7.38 (m, 4H), 6.61 (d, *J* = 8.8 Hz, 1H), 6.48 (s, 1H), 3.44 (q, *J* = 6.8 Hz, 4H), 1.24 (t, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.4, 160.8, 158.7, 152.9, 148.7, 143.2, 135.4, 131.8, 130.1, 128.7, 128.6, 124.9, 116.6, 109.8, 108.6, 96.6, 45.1, 12.4. HRMS calcd for $C_{22}H_{22}NO_3$ $[M + H]^+$: 348.1594; found: 348.1603.

7-(Diethylamino)-3-[3-(3,4-methylenedioxyphenyl)acryloyl] coumarin (**4**): Yellow solid; yield 49%; m.p. 222–224 °C; IR (KBr) (cm^{-1}): 2973, 1716, 1584, 1502, 1348, 1172, 1132, 814, 772, 679; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (s, 1H), 8.00 (d, *J* = 15.6 Hz, 1H), 7.75 (d, *J* = 15.6 Hz, 1H), 7.41 (d, *J* = 9.2 Hz, 1H), 7.22 (d, *J* = 1.2 Hz, 1H), 7.14 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.61 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.48 (d, *J* = 2.0 Hz, 1H), 6.01 (s, 2H), 3.45 (q, *J* = 7.2 Hz, 4H), 1.24 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.2, 160.8, 158.6, 152.9, 149.6, 148.5, 148.2, 143.1, 131.7, 129.9, 125.2, 123.0, 116.7, 109.8, 108.6, 108.4, 107.1, 101.5, 96.6, 45.1, 12.4. HRMS calcd for $C_{23}H_{22}NO_5$ $[M + H]^+$: 392.1492; found: 392.1486.

7-(Diethylamino)-3-[3-(4-fluorophenyl)acryloyl]coumarin (**5**): Yellow solid; yield 66%; m.p. 178–180 °C; IR (KBr) (cm^{-1}): 2971, 1702, 1619, 1508, 1502, 1353, 1178, 831, 671; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (s, 1H), 8.08 (d, *J* = 15.6 Hz, 1H), 7.78 (d, *J* = 15.6 Hz, 1H), 7.68–7.65 (m, 2H), 7.42 (d, *J* = 8.8 Hz, 1H), 7.10–7.05 (m, 2H), 6.62 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.49 (s, 1H), 3.46 (q, *J* = 7.2 Hz, 4H), 1.25 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.3, 163.9 (d, *J* = 250.0 Hz), 160.9, 158.7, 153.0, 148.8, 141.9, 131.8, 131.6 (d, *J* = 4.0 Hz), 130.6 (d, *J* = 8.0 Hz), 124.7 (d, *J* = 2.0 Hz), 116.5, 115.9 (d, *J* = 21.0 Hz), 109.9, 108.6, 96.6, 45.2, 12.5. HRMS calcd for $C_{22}H_{21}FNO_3$ $[M + H]^+$: 366.1500; found: 366.1512.

7-(Diethylamino)-3-(5-phenylpentadienoyl)coumarin (**6**): Yellow solid; yield 51%; m.p. 143–145 °C; IR (KBr) (cm^{-1}): 2927, 1708, 1622, 1513, 1418, 1284, 1033, 608; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (s, 1H), 7.69 (d, *J* = 15.2 Hz, 1H), 7.65–7.59 (m, 1H), 7.50–7.30 (m, 6H), 7.11–7.05 (m, 1H), 6.98 (d, *J* = 15.6 Hz, 1H), 6.62 (dd, *J* = 9.2, 2.4 Hz, 1H), 6.48 (d, *J* = 2.4 Hz, 1H), 3.46 (q, *J* = 7.2 Hz, 4H), 1.24 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.4, 160.8, 158.6, 152.9, 148.6, 143.4, 141.2, 136.4, 131.7, 128.9, 128.8, 128.5, 127.8, 127.2, 116.8, 109.8, 108.6, 96.6, 45.1, 12.5. HRMS calcd for $C_{24}H_{24}NO_3$ $[M + H]^+$: 374.1751; found: 374.1759.

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Electronic Supplementary Information

The ESI is available through: http://ingentaconnect.com/content/stl/jcr/2017/00000041/00000009

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