# Concise synthesis and fluorescent properties of coumarin-30 and its isomer 7-(diethylamino)-4-(1-methyl-1*H*-benzimidazol-2-yl)coumarin

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Coumarin-30 and its regioisomer 7-(diethylamino)-4-(1-methyl-1*H*-benzimidazol-2-yl)coumarin were synthesised utilising condensation of the corresponding formylcoumarin with *N*-methylphenylene-1,2-diamine as the key step. Furthermore, absorption and fluorescence emission spectra of the two coumarins were recorded.

**Keywords:** synthesis, formylcoumarin, *N*-methylphenylene-1,2-diamine, benzimidazol, fluorescence

Coumarins are an important class of organic compounds which exhibit a diverse array of pharmacological activities such as anti-inflammatory, antiviral and anticancer activity. Moreover, coumarin and its derivatives are extensively used as nonlinear optical chromophores, fluorescent whiteners, laser dyes, fluorescent probes and solar energy collectors due to their superior thermal stability and outstanding optical properties including large Stokes shifts, high quantum yields and superior photostability.[1] Therefore, coumarins have recently gained increasing attention because of their broad spectrum of properties and their relative ease of synthesis.

As one class of coumarin–benzimidazole hybrids, 3-benzimidazolylcoumarins also exhibit considerable biological activities and fluorescent properties. As a result, the synthesis and characterisation of these compounds have been well investigated. Traditionally, the 3-benzimidazolylcoumarins can be obtained by the condensation of coumarin-3-carboxylic acid or 3-(ethoxycarbonyl)coumarin with *o*-phenylenediamine catalysed by acid in moderate to good yield.[2,3] In addition, access to the 3-benzimidazolylcoumarins can also be conveniently achieved by Knoevenagel reaction of 2-cyanomethylbenzimidazole with substituted salicylaldehyde followed by hydrolysis in good yield.[4] Recently, it was reported that reaction of coumarin-3-carboxylic acid with *o*-phenylenediamine or *N*-alkylatedphenylene-1,2-diamine resulted an amide intermediate, which then underwent cyclisation by refluxing in acetic acid to afford the corresponding 3-benzimidazolylcoumarins in moderate to good yield in two steps.[5] However, to the best of our knowledge, the studies on the synthesis and property of 4-benzimidazolylcoumarins have not been previously reported by other researchers. Recently, we have been engaging in the synthesis of novel coumarin derivatives.[6,7] Specifically, we have synthesised coumarin-7 and its isomer 4-(2-benzimidazolyl)-7-(diethylamino)coumarin and found they exhibit obviously different UV-Vis absorption and fluorescence emission properties.[7] Since coumarin-30, namely 7-(diethylamino)-3-(1-methyl-1*H*-benzimidazol-2-yl) coumarin, is a well-known laser dye and has been investigated in many optical studies,[8] and as an extension of our study in the synthesis of benzimidazolylcoumarins, herein we present the expeditious synthesis and fluorescent properties of coumarin-30 (**1**) and its regioisomer 7-(diethylamino)-4-(1-methyl-1*H*-benzimidazol-2-yl)coumarin (**2**).

The synthetic strategy to obtain the target molecules is depicted in Scheme 1. Initially, the commercially available 4-(diethylamino)salicylaldehyde (**3**) was used as starting material for the synthesis of coumarin-30 (**1**). As we have reported in the synthesis of coumarin-7,[7] Wittig reaction of 4-(diethylamino)salicylaldehyde (**3**) with (ethoxycarbonylmethylene)triphenylphosphorane was smoothly performed in ethanol under reflux condition to furnish 7-(diethylamino)coumarin (**4**) in 75% yield. Thus, the Wittig protocol for such transformation has proven to be efficient and will offer an important complement to the existing procedure which often requires cumbersome steps.[9] Subsequently, the coumarin **4** was subjected to the Vilsmeier–Haack reaction with DMF and $POCl_3$ to provide 7-(diethylamino)-3-formylcoumarin (**5**) in 80% yield. Finally, condensation of intermediate **5** with *N*-methylphenylene-1,2-diamine was carried out in the presence of sodium bisulfite in methanol at reflux to give the desired product coumarin-30 (**1**) in 81% yield. In addition, we also examined the methylation of coumarin-7 with iodomethane promoted by a base such as $Et_3N$ with the objective to prepare coumarin-30 (**1**) directly. Unfortunately, the reaction proved futile and did not result in formation of any product even after a prolonged reaction time.

The synthesis of 7-(diethylamino)-4-(1-methyl-1*H*-benzimidazol-2-yl)coumarin (**2**) was accomplished by employing readily available *m*-diethylaminophenol (**6**) as starting material. The Pechmann reaction of *m*-diethylaminophenol (**6**) and ethyl acetoacetate was carried out under solvent-free conditions catalysed by $ZnCl_2$ to afford the 4-methylcoumarin **7** in 79% yield. Compound **7** was then converted into the 4-formylcoumarin **8** in moderate yield of 61% under treatment with $SeO_2$ in refluxing xylene. Ultimately, the formylcoumarin **8** reacted with *N*-methylphenylene-1,2-diamine in methanol promoted by sodium bisulfite to generate the expected 7-(diethylamino)-4-(1-methyl-1*H*-benzimidazol-2-yl)coumarin (**2**) in 76% yield. So, the approach described herein provides a succinct route to coumarin-30 or its analogues and will be a practical alternative to the reported methods.[5]

The UV-Vis absorption spectra of the two synthesised coumarins **1** and **2** in diluted dichloromethane solutions are given in Fig. 1. It is shown that the coumarin-30 (**1**) exhibits a sharp absorption peak at 413 nm, which is identical with that observed in methanol solution.[10] The absorption spectrum of **2** shows three sharp peaks located at 294, 339 and 405 nm, respectively. Compared with **1**, the absorption bands of **2** are clearly blue-shifted, suggesting that coumarin-30 **1** corresponds to a larger conjugated system than the isomer **2**. Figure 1 also shows the emission spectra of **1** (excited at 413 nm) and **2** (excited at 339 nm) in diluted dichloromethane solutions. It can be seen that the coumarin-30 **1** exhibits a bright blue emission peak at 476 nm, which is very close to the reported value in

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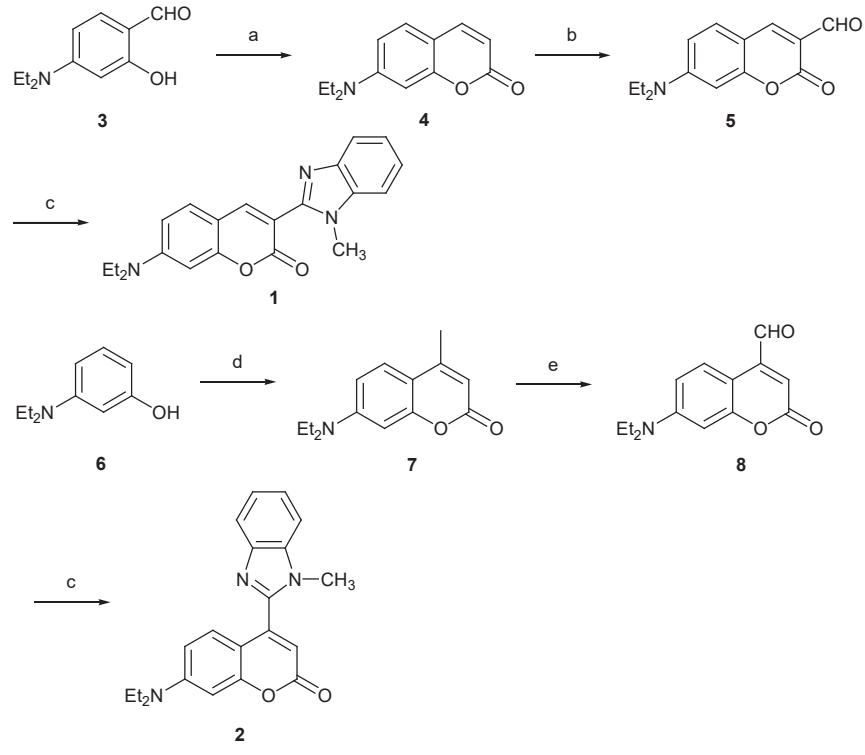


**Scheme 1** Regents and conditions: (a) $Ph_3P = CHCO_2Et$, ethanol, reflux, 6 h, 75%; (b) DMF, $POCl_3$, 60 °C, 7 h, 80%; (c) *N*-methylphenylene-1,2-diamine, $NaHSO_3$, MeOH, reflux, 1 h, **1**: 81%, **2**: 76%; (d) ethyl acetoacetate, $ZnCl_2$, solvent-free, r.t. to 50 °C, 0.5 h, 79%; (e) $SeO_2$, xylene, reflux, 8 h, 61%.

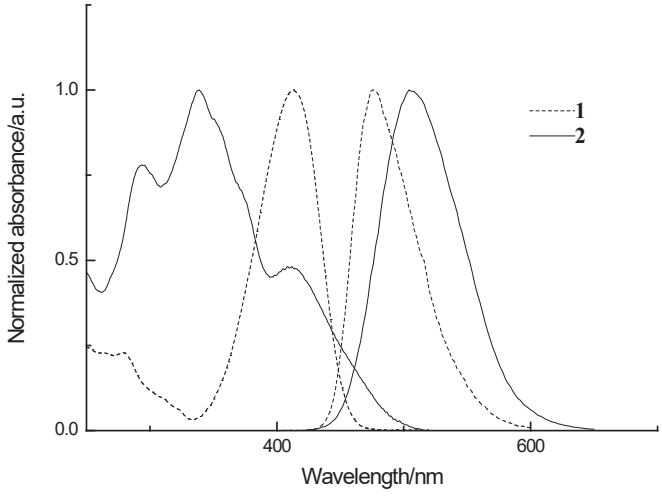


**Fig. 1** Normalised absorption and emission spectra of coumarin-30 (**1**) and its isomer (**2**) in dichloromethane ($1 \times 10^{-5}$ mol $L^{-1}$).

ethyl acetate solution.[10] Compound **2** shows bright green emission with a peak at 504 nm, obviously red-shifted by about 28 nm compared with that of **1**. As a consequence, the Stoke's shift of compound **2** is larger than that of coumarin-30 (**1**), indicating that the geometric change between the ground state and the first excited singlet state of **2** is likely larger than that of **1**.[11] Hence, the difference of the absorption-emission properties between coumarin-30 (**1**) and its regioisomer **2** is similar to that between coumarin-7 and its 4-substituted counterpart reported by us previously.[7]

In summary, the efficient and facile synthesis of 7-(diethylamino)-3-(1-methyl-1*H*-benzimidazol-2-yl)coumarin known as coumarin-30 and its isomer 7-(diethylamino)-4-(1-methyl-1*H*-benzimidazol-2-yl)coumarin employing the formylcoumarin as pivotal intermediate has been described. The study also reveals that these two coumarins, although possessing similar molecular structures, exhibit clearly dissimilar UV-Vis absorption and fluorescence emission properties. Applicability of these coumarins 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 FTIR 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 are 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 an Edinburgh Instruments FLS920 spectrometer, respectively.

*7-(Diethylamino)coumarin* (**4**): 4-(Diethylamino)salicylaldehyde (0.39 g, 2.0 mmol) and (ethoxycarbonylmethylene)triphenylphosphorane (0.83 g, 2.4 mmol) were dissolved in 20 mL of ethanol. The solution was stirred for 6 h under reflux conditions. Upon completion of the reaction (monitored by TLC), the ethanol was removed by rotary evaporation under reduced pressure. The resulting residue was purified by column chromatography using petroleum ether/ethyl acetate (v/v = 5:1) as eluent to afford **4** in 75% yield as yellow solid, m.p. 87–89 °C (lit.[12] 88–89 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 9.2 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 6.47 (d, *J* = 8.4 Hz, 1H), 6.36 (s, 1H), 5.92 (d, *J* = 9.2 Hz, 1H), 3.29 (q, *J* = 7.2 Hz, 4H), 1.10 (t, *J* = 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 161.8, 156.3, 150.3, 143.5, 128.5, 108.6, 108.4, 107.9, 97.0, 44.4, 12.1.

*7-(Diethylamino)-3-formylcoumarin* (**5**): Phosphorus oxychloride (1 mL) was added dropwise to anhydrous DMF (1 mL) at room temperature and stirred for 30 min to yield a red solution. This solution was combined with another solution of 7-(diethylamino)coumarin (0.33 g, 1.5 mmol) in DMF (2 mL), and the resulting mixture was

stirred at 60 °C for 7 h. When the reaction was judged to be complete (TLC monitoring), the mixture was poured into ice water (30 mL). The pH of the mixture was adjusted by adding NaOH aqueous solution (20%) to yield a large amount of precipitate. The crude product was filtered, washed thoroughly with water, dried and recrystallised in ethanol to give **5** as yellow solid in 80% yield, m.p. 165–166 °C (lit.[7] 166–167 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 10.07 (s, 1H), 8.19 (s, 1H), 7.37 (d, *J* = 9.2 Hz, 1H), 6.61 (dd, *J* = 9.2 and 2.4 Hz, 1H), 6.44 (s, 1H), 3.45 (q, *J* = 7.2 Hz, 4H), 1.23 (t, *J* = 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 187.7, 161.7, 158.8, 153.4, 145.2, 132.4, 114.1, 110.1, 108.1, 97.0, 45.2, 12.3.

*7-(Diethylamino)-4-methylcoumarin* (7): Ethyl acetoacetate (0.39 g, 3.0 mmol), *m*-diethylaminophenol (0.50 g, 3.0 mmol) and $ZnCl_2$ (0.40 g, 3.0 mmol) were added to a mortar successively. The mixture was ground thoroughly with a pestle at room temperature. Then, the mixture was heated at 50 °C and ground for 30 min. The resulting solid was dissolved in 50 mL of ethyl acetate, extracted with brine (3 × 50 mL). The organic phase was dried ($Na_2SO_4$), filtered and evaporated under vacuum. The resulting residue was purified by column chromatography using petroleum ether/ethyl acetate (v/v = 5:1) as eluent to afford **7** in 79% yield as colourless solid, m.p. 73–75 °C (lit.[13] 72–75 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.8 Hz, 1H), 6.59 (d, *J* = 8.8 Hz, 1H), 6.49 (s, 1H), 5.93 (s, 1H), 3.41 (q, *J* = 7.2 Hz, 4H), 2.34 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 162.2, 156.0, 152.9, 150.5, 125.5, 109.1, 108.7, 108.4, 97.7, 44.8, 18.4, 12.4.

*7-(Diethylamino)-4-formylcoumarin* (**8**): 7-(Diethylamino)-4-methylcoumarin (0.41 g, 1.8 mmol) and $SeO_2$ (0.31 g, 2.7 mmol) were dissolved in 10 mL of xylene. The resulting solution was stirred under reflux conditions for 12 h. The mixture was filtered whilst hot to remove selenium and the solvent was evaporated by rotary evaporation under vacuum. The resulting residue was purified by column chromatography using petroleum ether/ethyl acetate (v/v = 7:1) as eluent to afford **8** in 61% yield as red solid, m.p. 83–84 °C (lit.[14] 84–85 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 10.05 (s, 1H), 8.46 (d, *J* = 8.8 Hz, 1H), 7.05–6.97 (m, 2H), 6.63 (s, 1H), 3.47 (q, *J* = 7.2 Hz, 4H), 1.23 (t, *J* = 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 192.2, 161.3, 157.0, 149.3, 143.6, 127.3, 119.0, 111.2, 105.7, 100.0, 46.3, 12.1.

*7-(Diethylamino)-3-(1-methyl-1*H*-benzimidazol-2-yl)coumarin* (**1**): *N*-Methylphenylene-1,2-diamine (0.15 g, 1.2 mmol) was dissolved in 10 mL of methanol and sodium bisulfite (0.12 g, 1.2 mmol) was added. Then, a solution of 7-(diethylamino)-3-formylcoumarin (0.29 g, 1.2 mmol) in methanol (10 mL) was added dropwise with stirring. The mixture was stirred under reflux conditions for 6 h. The solvent was evaporated under reduced pressure and the resulting mixture was dissolved in dichloromethane (50 mL). The organic phase was washed successively with diluted aqueous hydrochloric acid (2 × 50 mL), saturated aqueous sodium bicarbonate (2 × 50 mL) and brine (3 × 50 mL). After dried over $Na_2SO_4$, the solvent was evaporated under vacuum. The resulting residue was purified by column chromatography using petroleum ether/ethyl acetate (v/v = 3:1) as eluent to afford **1** in 81% yield as yellow solid, m.p. 224–226 °C (lit.[13] 225–229 °C). IR (KBr) cm$^{-1}$: 2968, 1698, 1607, 1528, 1260, 1135, 812, 729. $^1$H NMR (400 MHz, $CDCl_3$): δ 8.20 (s, 1H), 7.78 (dd, *J* = 7.2 and 2.4 Hz, 1H), 7.41–7.28 (m, 4H), 6.63 (dd, *J* = 8.8 and 2.4 Hz, 1H), 6.55 (d, *J* = 2.4 Hz, 1H), 3.82 (s, 3H), 3.46 (q, *J* = 7.2 Hz, 4H), 1.25 (t, *J* = 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 160.2, 157.5, 151.8, 150.0, 147.2, 142.8, 136.6, 130.1, 122.8, 122.2, 119.5, 110.5, 109.6, 109.5, 108.4, 97.0, 45.0, 31.8, 12.4. HRMS for $C_{21}H_{22}N_3O_2$ $[M + H]^+$ calcd 348.1707; found: 348.1716.

*7-(Diethylamino)-4-(1-methyl-1*H*-benzimidazol-2-yl)coumarin* (**2**): Compound **2** was prepared from 7-(diethylamino)-4-formylcoumarin (0.29 g, 1.2 mmol) and *N*-methylphenylene-1,2-diamine (0.15 g, 1.2 mmol) by a method similar to that described for **1** in 76% yield as yellow solid, m.p. 225–227 °C. IR (KBr) cm$^{-1}$: 3412, 2972, 1693, 1615, 1455, 1413, 1031, 742. $^1$H NMR (400 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.78 (d, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.35–7.27 (m, 3H), 6.62 (dd, *J* = 8.8 and 2.0 Hz, 1H), 6.56 (d, *J* = 2.0 Hz, 1H), 4.03 (s, 3H), 3.41 (q, *J* = 7.2 Hz, 4H), 1.22 (t, *J* = 7.2 Hz, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 158.7, 155.4, 149.6, 148.9, 147.8, 142.8, 136.9, 124.6, 124.0, 123.6, 123.2, 120.0, 109.7, 108.8, 107.2, 98.3, 44.7, 31.9, 12.5. HRMS for $C_{21}H_{22}N_3O_2$ $[M + H]^+$ calcd 348.1707; found: 348.1711.

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