Indian Journal of Chemistry
Vol. 59A, July 2020, pp. 895-903

Synthesis and spectral studies of coumarin derivatives as fluorescent probes towards Fe^{3+} and Cu^{2+}

Jun Zhang*, Zongwen Pang & Chuan Dong

Institute of Environmental Science, Shanxi University, Taiyuan 030006, PR China

E-mail: dc104@sxu.edu.cn

Received 28 December 2019; revised and accepted 27 April 2020

Three novel coumarin derivatives have been designed and facilely synthesized, namely 6-[bis-(2-acetoxyethyl)aminomethyl]-4-methyl coumarin (BAMC), 4-(trans-4-methylformate-styryl)-6-[bis-(2-acetoxyethyl) aminomethyl]-coumarin (TSAC) and Trans-4-[2-(benzimidazole-2-substituted)vinyl]-6-methyl coumarin (TBVC). The synthesis route of the coumarin derivatives via various reactions including Pechmann, Wittig and substitution, three strategies are applied in the construction of the coumarin-based fluorescent probes, in view of the impact of the electronic push-pull effect, extended electronic conjugated system, and the strong fluorescence emission group, respectively. The compounds BAMC and TSAC are proved to be selective fluorescent probes to Fe^{3+} and Cu^{2+} based on the intramolecular charge transfer mechanism. TBVC exhibits enhanced fluorescent emission in tetrahydrofuran offers the potential for the high-performance fluorescent probe. The relationship between the structure and the fluorescence mechanism of coumarin probes is explored.

Keywords: Synthesis, Fluorescent probe coumarin, ICT, Benzimidazole

Iron is one of the necessary ions in living organisms. Fe^{3+} participates in many biochemical processes such as cellular metabolism and enzyme catalysis[1]. Copper plays a key role in maintaining the health and normal operation of organs. The lack of copper leads to serious illnesses, while excess copper may cause many kinds of physiology disorders[2]. The highly specific and sensitive detection of $Fe^{3+}$and Cu^{2+} has been a big challenge in life and environmental science[3,4]. Currently, the detection of Fe^{3+} and Cu^{2+} are generally discrete and need expensive instruments, or large sample volumes, or special skills, or complicated procedures[5]. Given this, it offers extraordinary advantages to develop chemosensor with dual recognition of Fe^{3+} and Cu^{2+}.

Coumarins and its derivatives are widely distributed in nature. They are important heterocyclic compounds with a variety of biological and pharmacological actives[6]. Many coumarin compounds are beneficially used as anti-aging and anti-oxidation agents. They are an effective treatment against chronic diseases including cardiovascular disease[7], AIDS[8,9], and cancer[10]. The fluorescent probe offers high sensitivity, selectivity, and applicability in separation-free detection and situ monitoring of metal ions[11-13]. When used as fluorescent probes, coumarin and its derivatives have many special advantages, for example, high fluorescence quantum yield, large stokes shift, excellent light stability, and less toxicity. Coumarin is also an excellent precursor for the synthesis of the fluorescent probe. Many coumarin derivatives are available for the design and synthesis of Fe^{3+} and Cu^{2+} fluorescent probes[14-16].

The coumarin-based fluorescence probes are normally constructed in consideration of the electron withdrawing-donating group. In the coumarin molecule, the lactone rings afford a relatively low electron density at the 3- or 4- position The intramolecular charge intends to transfer from position 6- or 7- to position 3- or 4-. The electron-withdrawing group is commonly introduced to the position 3- or 4-, while the electron-donating group is introduced to the position 6- or 7-. In this way, the intramolecular charge transfer (ICT) is enhanced, and a push-pull electronic system is formed. This is a commonly used method to improve the fluorescence efficiency of coumarin compounds[17,18]. The fluorescent probes based on ICT or photoinduced electron transfer (PET) mechanism are popular for the detection of various cations[19-21]. Amino-substituted coumarins are the classical fluorophores with a large conjugated system and a rigid structure. The amino

group has a strong electron-donating ability, while the carbonyl group has a strong electron-withdrawing ability. These two kinds of groups are distributed in the two sides of the coumarin molecule. Thereupon a push-pull electron system is well organized. In general, amino-substituted coumarins are highly fluorescent based on ICT mechanism[22].

Currently, the development of coumarin probes is propelled forward by the growing demand for high-performance fluorescent probes. The coumarin probes have not been confined to a simple structure. Also, in the synthesis of probes from coumarin precursors, the groups' effect on fluorescence is not the only concern in many cases. To get a fluorescent probe with excellent properties, not only the push-pull electronic groups but also the conjugated system is often considered[23]. Besides adjusting the push-pull electronic system, there are other effective methods for designing coumarin-based fluorescent probes. For example, the coumarin parent molecule is modified by groups with strong emissions, such as benzimidazole. In this way, the fluorescence intensity of the product is enhanced substantially, and the fluorescence emission is red-shifted regarding the parent coumarin[24, 25].

In this research, three strategies were applied to the synthesis of three coumarin derivatives for fluorescent probes. Three novel coumarin derivatives were synthesized, namely 6-[bis-(2-acetoxyethyl)aminomethyl]-4-methyl coumarin (BAMC), 4-(trans-4-methylformate-styryl)-6-[bis-(2-acetoxyethyl)aminomethyl]-coumarin (TSAC) and Trans-4-[2-(benzimidazole-2-substituted)vinyl]-6-methyl coumarin (TBVC). The first BAMC was conveniently synthesized in the view of the impact of the electron withdrawing-donating group. The second TSAC possesses an extended electronic-conjugated system by attaching a methyl benzoate to the position 4- of BAMC. The third TBVC was designed by introducing a benzimidazole with strong fluorescence emission to the position 4- of coumarin molecule. Promising results were obtained by using Pechmann and Wittig reactions to shorten the synthesis route of coumarin derivatives. BAMC and TBVC were discussed in terms of selectivity and viability as the fluorescent probes for Fe^{3+} and Cu^{2+}.

Materials and Methods

Melting points were determined on the x-5 melting point detector. IR spectra were recorded with an FTIR-8300 (Shimadzu). ^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker DLX 300 MHz instrument. ESI was measured with an LTQ-MS (Thermo) instrument. The absorption spectra were obtained on a TU-1901 dual-beam UV-Visible spectrophotometer (Beijing Purkinje General Instrument Co., Ltd., Beijing, China). Fluorescence spectra were recorded with an F-4500 spectrofluorometer (Hitachi). All the reagents were purchased from Beijing Chemical Plant without further purification before use.

Synthesis of 4, 6-Dimethyl coumarin (1)

To a flask containing p-cresol (7.02 g, 65 mmol) and ethyl acetoacetate (8.5 g, 65 mmol), 75% H_2SO_4 (16.5 mL) solution was slowly dripped in. After being stirred at 60-62 °C for 12 h, the mixture was poured into ice-water and stir-washed thoroughly with a 5% NaOH solution. The product was recrystallized with hot ethanol to give 3.7 g white needle crystals in 33 % Yield, m.p. 152-154 °C. These data are consistent with the literature[26].

Synthesis of 6-Bromomethyl-4-methyl coumarin (2)

To a flask containing compound **1** (2 g, 11.5 mmol), bromosuccinimide (NBS) (2.05 g, 11.5 mmol) and benzoyl peroxide (0.04 g) were added, and then sodium-dried benzene (30 mL) was dripped in. The mixture was stirred under reflux for 6 h. Then the solvent was evaporated. The solid was washed with hot water and recrystallized with acetic acid to give white needle crystals 1.2 g in 40% yield.

Synthesis of 6-Diethanolaminomethyl-4-methyl coumarin (DMC)

To a flask containing compound **2** (0.88 g, 3.47 mmol), diethanolamine (0.37 g, 3.53 mmol) and K_2CO_3 (0.97 g, 6.79 mmol) were added, and then acetonitrile (30 mL) was added. The mixture was stirred at reflux under N_2 for 4 h. After that, the excess K_2CO_3 was removed by filtration, and the solvent was removed by rotary evaporation. The solid residue was purified by column chromatography (dichloromethane: methanol = 9:1) to give a white solid 0.86 g in 90% yield, m.p.132-134 °C.

Synthesis of 6-[Bis-(2-acetoxyethyl)-aminomethyl]-4-methyl-coumarin (BAMC)

DMC (0.7 g, 2.5 mmol) and triethylamine (TEA) (7.56 g, 75 mmol) were dissolved in tetrahydrofuran (THF) (15 mL). Acetyl chloride (3.94 g, 50.5 mmol) was dissolved in THF (15 mL). The latter solution was added dropwise with stirring into the former. The

mixture was stirred at room temperature for 1.5 h. After that, a saturated NaCl solution (50 mL) was added and the mixture was extracted three times with diethyl ether. The solvent was removed by rotary evaporation and the residue was subjected to column chromatography (ethyl acetate: cyclohexane = 5:4) to give a yellow viscous liquid 0.55 g in 60 % yield. ^{1}H NMR ($CDCl_3$, 300 MHz), δ:2.05-2.18(6H,-CH_3), 2.36(3H,-CH_3), 4.18-4.14(4H,-CH_2), 3.77(2H,-CH_2), 2.83-2.80(4H,-CH_2), 7.56(1H, Ph-H), 7.54-7.30(2H, Ph-H), 7.28(1H, Ph-H), (Fig. S1).^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS) δ = 20.8, 111.4, 161.0, 112.3, 61.7, 116.8, 127.7, 60.9, 153.3, 152.6, 170.8, 138.3, 127.6, 19.1, 53.8 ppm; HRMS (ESI) $[M+H]^+$calcd for $C_{19}H_{23}NO_6$, 362.16, found, 362.15. Elemental analysis: found C, 63.14; H, 6.42; N, 3.88; O, 26.53.

Synthesis of 4-Formyl-6-methyl coumarin (5)

Compound **1** (4g, 22.9 mmol) and SeO_2 (4 g, 35.9 mmol) were added into xylene (150 mL). After refluxing for 20 h, the mixture was filtered to remove the black selenium, and the filtrate was concentrated, cooled, filtered and dried to give 2.75 g of yellow needles in 65% yield, m.p.170-172 °C. This data is consistent with the literature[27].

Synthesis of phosphine salt (6)

Methyl benzoate (12.08 g, 0.08 mol) was dissolved in cyclohexane (80 mL), and then NBS (14.24 g, 0.08 mol) and benzoyl peroxide (30 mg) were added. The mixture was stirred under reflux with normal lighting for 3 h. After filtration, the filtrate was concentrated and dried to give a yellow oily benzyl bromide. Then the benzyl bromide was dissolved in anhydrous acetone (40 mL), and triphenylphosphine (20.96 g, 0.08 mol) was added. After stirred under reflux for 1 h, the mixture was cooled and filtered to give a white phosphine salt. The filter cake was washed with a small amount of anhydrous acetone to give phosphine salt product 25.6 g in 65% yield.

Synthesis of 4-[Trans-4-(methylformate)-styryl]-6-methyl coumarin (7)

Compound **5** (0.376 g, 2 mmol) was dissolved in THF (50 mL), and then compound **6** (1.08 g, 2.2 mmol) and K_2CO_3 (1.38 g, 1 0 mmol) were added. The suspension was stirred at room temperature for 8 h. After filtration, the filtrate was evaporated and dried. The residue was recrystallized with ethanol to give a yellow solid 0.31 g in 48% yield, m.p.133-135 °C.

Synthesis of 4-[Trans-4-(methylformate)-styryl]-6-bromomethylcoumarin (8)

Compound **7** (1.2 g, 3.75 mmol), NBS (0.67 g, 3.75 mmol) and benzoyl peroxide (0.04 g) were added into a flask, and then dry benzene (50 mL) was added. The mixture was stirred under reflux for 9 h. After the solvent was concentrated, the precipitated solid was successively cooled, filtered and washed with water, recrystallized with acetic acid to give a pale yellow solid 0.72 g in 48% yield.

Synthesis of 4-[Trans-4-(methylformate)-styryl]-6-methyldiethanolamine coumarin (TSC)

Diethanolamine (0.37 g, 3.53 mmol), compound **8** (0.88 g, 3.47 mmol), and K_2CO_3 (0.97 g, 6.79 mmol) were added into a three-necked flask, and then acetonitrile (30 mL) was added. The mixture was stirred at reflux under N_2 for 4 h. After that, the excess K_2CO_3 was filtrated out, the solvent was removed by rotary evaporation. The solid residue was purified by column chromatography (dichloromethane: methanol = 9:1) to give a white solid 0.86 g in 90% yield, m.p.171-172 °C.

Synthesis of 4-[Trans-4-(methylformate)-styryl]-6-[bis-(2-acetoxyethyl)-aminomethyl]-coumarin (TSAC)

TEA (4.4 g, 43.75 mmol) was dissolved in THF (15 mL), and then TSC (0.74 g, 1.75 mmol) was added. The THF (15 mL) containing acetyl chloride (2.76 g, 35.4 mmol) was dripped in the former solution with stirring. The mixture was stirred at room temperature for 1.5 h, and then brine (30 mL) was added. With the addition of ether, insoluble floc was precipitated. After washed twice with diethyl ether, the residue was subjected to column chromatography (dichloromethane: methanol = 10:1) to give a yellow solid 0.49 g in 55% yield, m.p.196-198 °C. ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 3.97 (3H,-CH_3), 2.00-2.05(6H,-CH_3), 4.16-4.20(4H,-CH_2-), 2.79-2.83 (4H,-CH_2-), 3.78(2H,-CH_2-), 6.65(1H, Ph-H), 7.28-7.37(2H, Ph-H), 7.40-7.56(2H, =CH-), 7.61-7.73(2H, Ph-H), 7.76(1H, Ph-H), 8.11-8.14(2H, Ph-H), (Fig. S2).^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS) δ = 126.27,116.8, 53.8, 130.2, 1.7, 112.3, 133.5, 60.9, 114.7, 166.1, 127.6, 147.2, 128.7, 153.5, 138.3, 132.2, 20.8, 159.7, 130.7, 52.3, 170.8, 127.7 ppm; HRMS (ESI) $[M+H]^+$calcd for $C_{28}H_{29}NO_8$, 508.19, found, 508.18. Elemental analysis: found C, 66.23; H, 5.77; N, 2.76; O, 25.24.

Synthesis of 2-Methylbenzimidazole (11)

o-phenylenediamine (20 g, 185 mmol) was added into acetic acid (38 mL). The mixture was stirred

under reflux for 4 h and then cooled to room temperature. The pH of the solution was adjusted to be 7-8 with a 5% NaOH solution, and a pink solid was precipitated. The solid was filtered and recrystallized several times with water to give a white crystal 12.2 g in 50% yield, m.p.177-180 °C. This data is consistent with the literature[28].

Synthesis of Trans-4-[2-(benzimidazole-2-substituted)-vinyl]-6-methyl coumarin (TBVC)

Compounds **11** (0.8 g, 6 mmol) and **5** (1.13 g, 6 mmol) were added into acetic acid (7.5 mL) mixed with acetic anhydride (2.3 mL). The mixture was stirred under reflux for 6 h. Then it was cooled to room temperature and ice-cold water was added to precipitate solid. Afterword, the pH of the solution was adjusted to be 7-8 with a 5% NaOH solution. The residue was filtered, dried, and purified by column chromatography to give a yellow solid 0.54 g in 30% yield, m.p. 195-197 °C. ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 2.41(3H,-CH_3), 7.17-7.39(2H, -CH=CH-), 7.53-7.76(3H,Ph-H), 6.96(1H, =CH-), 8.14-8.27(2H, Ph-H), 8.65-8.72(2H, Ph-H), 10.15(1H,-NH), (Fig. S3). IR (KBr/cm^{-1}):3420(N-H), 3065(Ar-H), 2924, 2854(-CH_3), 1727(-CO-), 1621(C=C), 1657(C=N-), 935(C-O), 1375(C-H), 740(C-H), (Fig. S4).^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS) δ = 121.3, 153.5, 122.5, 137.3, 115.9, 152.9, 137.9, 114.8, 159.7, 114.7, 134.9, 112.3, 147.2, 116.8, 122.5, 120.4, 132.2, 20.9, 133.9 ppm; HRMS (ESI) $[M+H]^+$calcd for $C_{19}H_{14}N_2O_2$, 303.11, found, 303.12. Elemental analysis: found C, 75.44; H, 4.68; N, 9.25; O, 10.53.

UV-visible spectra of BAMC, TSAC and TBVC

The stock solution of BAMC and TSAC (1.6×10^{-4} mol/L), TBVC (1.5×10^{-4} mol/L) were prepared by dissolving the compounds in CH_2Cl_2. Each stock solution (0.5 mL) was added into a 10 mL colorimetric tube, and the solvent was blown off with N_2. After the sample's volume was diluted to be 5 mL using CH_2Cl_2, $(Et)_2O$, EtOAc, MeCN, EtOH, and MeOH, respectively, the solution of BAMC and TSAC (1.6×10^{-5} mol/L) and TBVC (1.5×10^{-5} mol/L) were obtained and measured by UV-visible spectroscopy.

Fluorescence spectrum of BAMC, TSAC, and TBVC

TheMeCN solution of Ag^+, Na^+, Cu^{2+}, K^+, Zn^{2+}, Fe^{3+}, Co^{2+}, Sn^{2+}, Hg^{2+} and Pb^{2+} were set at the concentration of 1.0×10^{-4} mol/L. A stock solution of BAMC and TSAC (0.5 mL, 1.6×10^{-4} mol/L) was added into a 10 mL colorimetric tube, and the solvent was blown off with N_2. After the volume of samples were diluted to be 5 mL using the MeCN solution of metal ions, respectively, the solution of BAMC and TSAC (1.6×10^{-5} mol/L) was obtained. The TBVC solution of cyclohexane, CH_2Cl_2, $(Et)_2O$, THF, Me_2CO, and MeOH were set at the concentration of 3.12×10^{-7} mol/L. All the fluorescence spectra were recorded at room temperature. Excitation and emission slit-widths were both set at 10 nm.

Result and Discussion

Optimization of synthesis conditions

In the presence of TEA, DMC reacts with acetyl chloride to form BAMC. The molar ratio of starting material, the amount of alkali, temperature and time were optimized as shown in Table 1 and Table 2. The optimum molar ratio of DMC, acetyl chloride and TEA is 1:20:30. The reaction time is 1 h and the reaction temperature is 20 °C. Similarly, in the presence of TEA, TSC reacts with acetyl chloride to form TSAC. The optimum reaction conditions were determined as that the molar ratio of TSC, acetyl chloride, and TEA is 1:20:25, the reaction time is 0.75 h and the reaction temperature is 20 °C.

Synthetic route of BAMC, TSAC and TBVC

To introduce Bis-(2-acetoxyethyl)-amino into position 6- of coumarin, the conventional synthesis methods have disadvantages of the long route and high costs[29]. In our method, the cheap p-cresol was used as a starting material. Coumarin is synthesized

Table 1 — Effect of temperature and reaction time on the yield of BAMC and TSAC

T (°C)	BAMC		TSAC	
	Time (h)	Yield (%)	Time (h)	Yield (%)
20	1.0	60	0.75	55
30	1.0	58	0.75	52
40	1.0	54	0.75	50
20	0.6	52	0.50	49
20	1.4	61	1.00	56

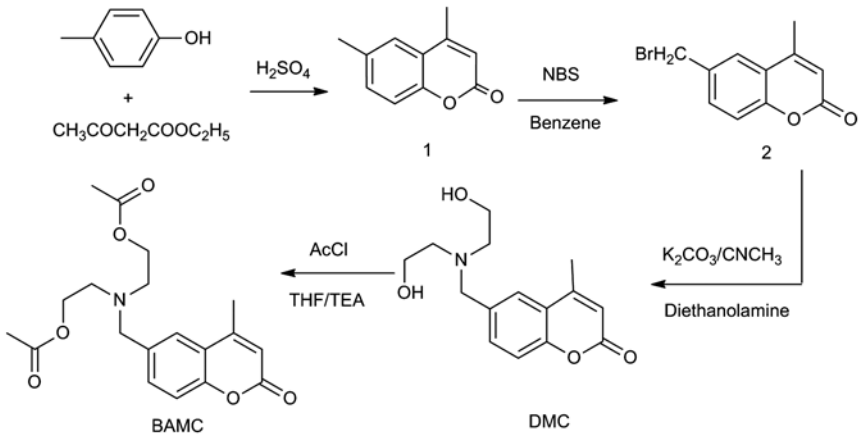
Table 2 — Effect of ratio of material on the yield of BAMC and TSAC

Acetyl chloride	BAMC			TSAC		
	TEA	DMC	Yield (%)	TEA	TSC	Yield (%)
15	30	1	51	25	1	48
20	30	1	60	25	1	55
25	30	1	57	25	1	54
20	25	1	53	20	1	51
20	35	1	59	30	1	53

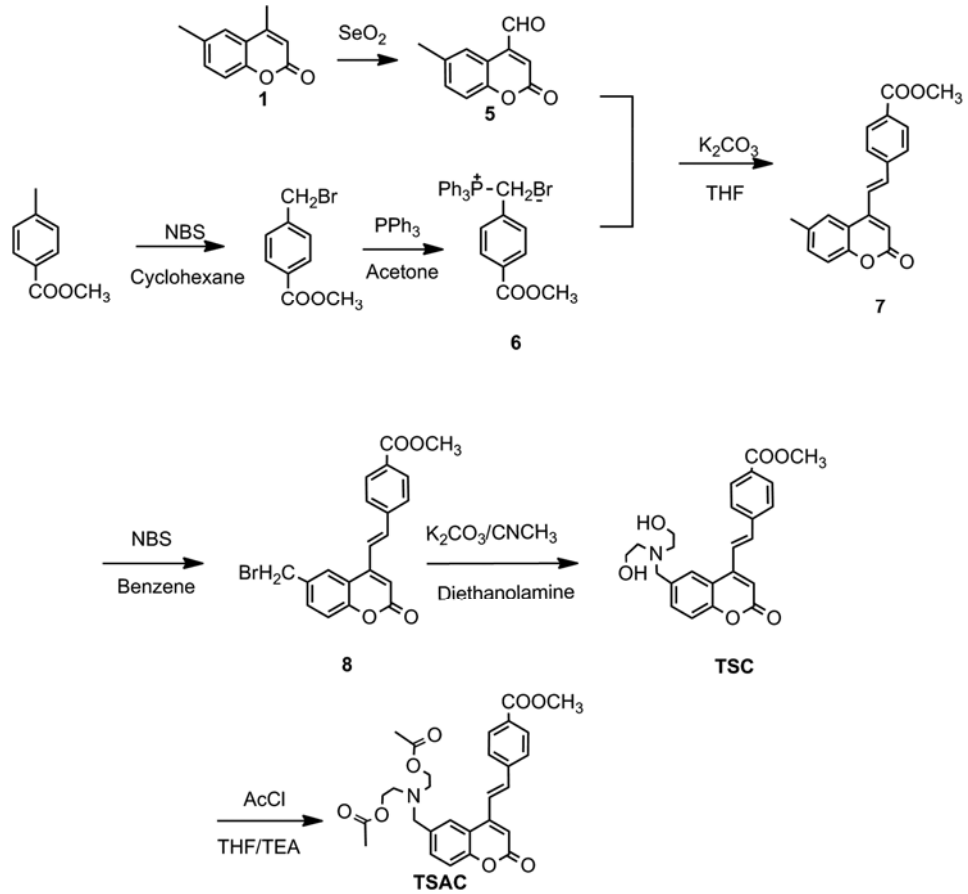
via Pechmann condensation. BAMC was conveniently synthesized in the view of the electron withdraw-donating group. The synthetic route of BAMC is presented in Scheme 1.

To improve the fluorescence properties of BAMC, a new conjugated system was designed via Wittig reaction. Methyl benzoate was attached to the position 4- of coumarin molecule BAMC by a double bond. An extended electronic conjugated system was successfully fabricated. The synthetic route of TSAC is presented in Scheme 2.

A benzimidazole with strong fluorescence emission was introduced to the position 4- of 4-formyl-6-methyl coumarin. The fluorescent coumarin of TBVC



Scheme 1 — Schematic representation for the synthesis of BAMC.



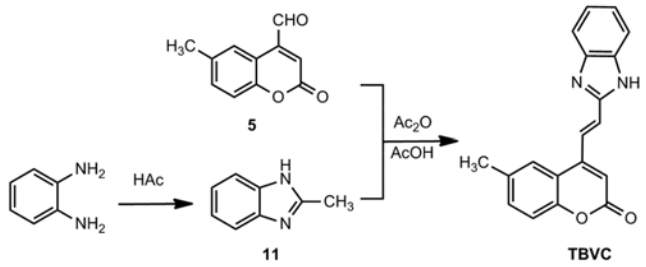
Scheme 2 — Schematic representation for the synthesis of of TSAC.

was consequently synthesized. The addition of benzimidazole is aimed to improve the fluorescence of coumarin. It is the sole way to extend the π-conjugated system. The synthesis route of TBVC is presented in Scheme 3.

Spectral characteristics of BAMC, TSAC, and TBVC

The solvent effect refers to the change of wavelength, intensity and the shape of solute absorption peak in different degrees due to the influence of polarity or acid-base of solvent[30,31]. The UV absorption of BAMC, TSAC, and TBVC were investigated in different organic solvents (Fig. S5). The spectroscopy data were collected in Table 3. It is shown that the solvent effects on the absorption spectra of BAMC and TSAC were not obvious, while that of TBVC is somewhat significant. The shape of the absorption peak of TBVC is basically the same in different solvents. With the increase in the solvent polarity, the maximum absorption of TBVC is bathochromically shifted about 16 nm. It was noted that the solvent's polarity had a great impact on the absorption intensity of TBVC. For example, the maximum absorbance value of TBVC was determined to be 0.34 in ether regarding the 0.10 in dichloromethane.

The fluorescence spectra of BAMC, TSAC, and TBVC were measured (Fig. S6). The fluorescence response of BAMC and TSAC to 10 kinds of metal ions including Ag^{+}, Na^{+}, Cu^{2+}, K^{+}, Zn^{2+}, Fe^{3+}, Co^{2+}, Sn^{2+}, Hg^{2+}, and Pb^{2+} were investigated at room temperature (Fig. 1a, 1b). The concentration of BAMC and TSAC is 1.6×10^{-5} mol/L. The high sensitivity of probes BAMC and TSAC toward Fe^{3+} and Cu^{2+} was identified in this screening experiments. Based on the ion screening experiments, the effect of Fe^{3+} and Cu^{2+} on the fluorescence spectra of BAMC and TSAC was evaluated (Fig. 1c, 1d). BAMC displays a sensitive response to Fe^{3+}. With the increase in the concentration of Fe^{3+}, the fluorescence of BAMC is gradually weakened. When about sixty equivalents of Fe^{3+} was added, the fluorescence of BAMC was almost completely quenched. These results support that BAMC belongs to the ICT type other than the PET type probe. The electronic distribution plays a dominant role in the fluorescence of the coumarin molecule. The ICT processesof BAMC is inhabited by the complexation with paramagnetic Fe^{3+} and Cu^{2+}, which results in the fluorescence quench of BAMC in acetonitrile[32-34].



Scheme 3 — Schematic representation for the synthesis of TBVC.

TSAC exhibits an excellent selectivity towards Fe^{3+} and Cu^{2+}over other metal ions. Fig. 2 shows a comparison of fluorescence intensity upon 10 kinds of metal ions (1×10^{-4} M) injecting into the acetonitrile solution of TSAC (1.6×10^{-5} M). When about six equivalent concentration of Fe^{3+} was added, the fluorescence intensity of TSAC was quenched to be 12.1% of the original. For Cu^{2+} in the same concentration, the fluorescence intensity remains a third of the original. Like BAMC, the donor groups in TSAC are also attached to the position 6- of coumarin molecule. So, the fluorescence mechanism of probe TSAC is still subject to ICT. Probe TSAC has a larger conjugated system than BAMC, which brings out an enhanced ICT with a redshift of 5 nm in fluorescence emission. TSAC sensitively and fleetly gives instant fluorescence response to the complexation with Fe^{3+}. It is obvious that the selectivity of the probe TSAC to $Fe^{3+}$is greater than that of Cu^{2+}.

According to Stern-Volmer plot[35] (Fig. S7), the quenching constant was calculated and collected in Table 4. Analysis of the Job plot suggests both Cu^{2+}

Table 3 — UV-spectral data of BAMC (1.6×10^{-5} mol/L), TSAC (1.6×10^{-5} mol/L) and TBVC (1.5×10^{-5} mol/L) in different solvents

Solvent	BAMC		TSAC		TBVC	
	λ_{max} (nm)	Abs	λ_{max}(nm)	Abs	λ_{max} (nm)	Abs
CH_2Cl_2	322	0.10	320,276	0.38,0.28	320	0.10
$(Et)_2O$	320	0.09	322,275	0.36,0.30	322	0.34
EtOAc	318	0.10	318,276	0.35,0.27	333	0.18
MeCN	316	0.09	320,276	0.35,0.26	333	0.17
EtOH	319	0.09	322,275	0.34,0.25	336	0.17
MeOH	320	0.09	322,275	0.31,0.23	332	0.16

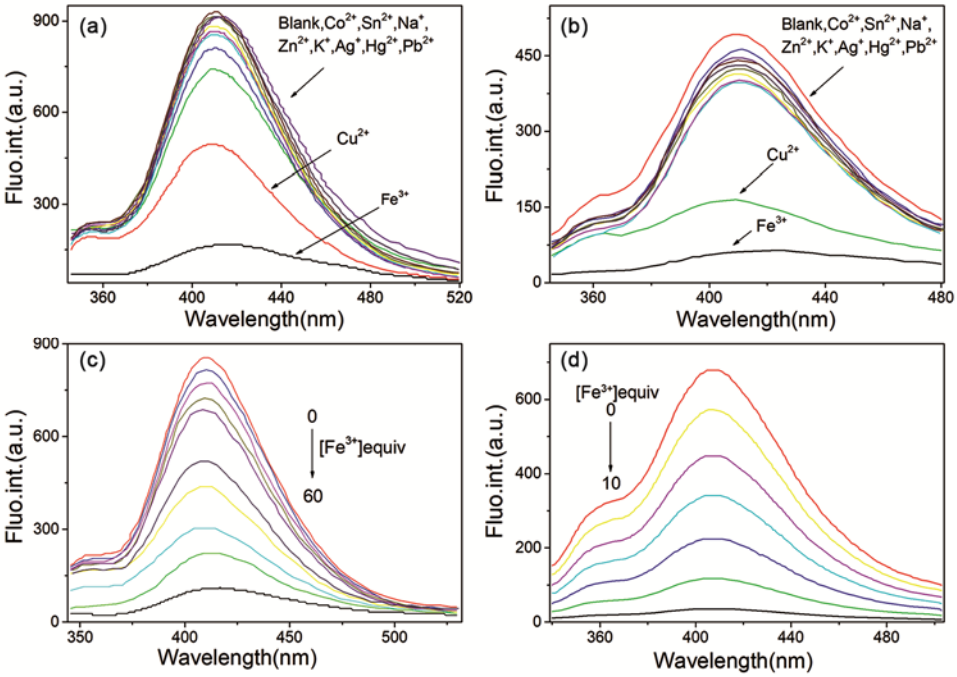


Fig. 1 — Fluorescence spectra of (a) BAMC, (b) TSAC in the presence of 10 equiv metal ions in acetonitrile. Fluorescence changes of (c) BAMC (excited at 315 nm) and (d) TSAC (excited at 320 nm) with the addition of Fe^{3+} in acetonitrile.

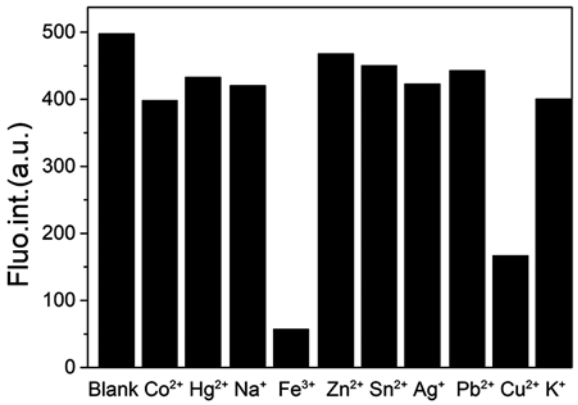


Fig. 2 — Comparison of fluorescence intensity with metal ions injecting to TSAC.

and Fe^{3+} form a 1:1 complex with the sensor (Fig. S8). The binding constants (log K) of the fluorescent probes with metal ions in acetonitrile derived from the Benesi-Hildebrand equation based on a 1:1 binding mode were calculated and collected in Table 4[36].

Di-(2-hydroxyethyl)amino group, di-(2-acetoxyethyl)amino group or bis(N-diethylamino-sulfurthiocarbamoylethyl) amino group isnormal recognition groups in coumarin-based fluorescent probes. If these groups are at the position 6- or 7- of coumarin molecule, generally an ICT type probe is formed. If they are at the position 4- of coumarin molecule, it is usually given a PET type probe[37]. It is known that the electron density in position 6- or 7- is higher than that of position 3- or 4- in coumarin molecule. The charge is more likely transferred from position 6- or 7- to position 3- or 4-. In this regard, the charge transfer is enhanced by the recognition groups at the position 6- or 7-, or inhibited by that at the position 3- or 4- in different degrees. The observations in this research also support the above supposition. It provides a beneficial reference for the design and synthesis of coumarin fluorescent probes.

TBVC exhibits unique spectral properties. In the fluorescent spectra of TBVC, two strong fluorescence emission peaks at 420 nm and 500 nm were observed in different solvents except for cyclohexane. The solvent polarity has a greater impact on the fluorescence intensity of TBVC than that of BAMC or TSAC. As showing in Fig. 3, the fluorescence intensity of TBVC is increased with the increase of solvent polarity from cyclohexane to THF as the dipole moment of the molecule in the excited state was closely related to solvent polarity. The decay probability of exciting molecules increases correspondingly. Therefore, the fluorescence intensity of excited molecules is increased. However, the fluorescence intensity is weakened with a further increase in solvent polarity from acetonitrile to ethanol. Because the strong ICT will be converted to

Table 4 — The analysis for fluorescence quenching of BAMC and TSAC (1.6×10^{-5} mol/L) by Fe^{3+} and Cu^{2+} (1.0×10^{-4} mol/L) in acetonitrile

	Binding constants (log K)		Quenching constant (M^{-1})	
	Fe^{3+}	Cu^{2+}	Fe^{3+}	Cu^{2+}
BAMC	3.13	2.52	5.18×10^{5}	2.01×10^{4}
TSAC	4.94	3.84	6.80×10^{5}	5.83×10^{4}

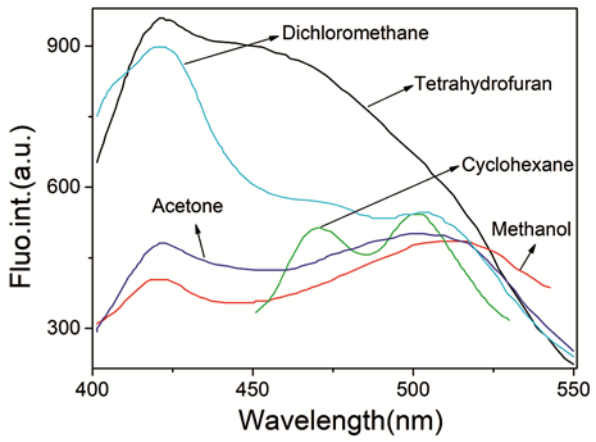


Fig. 3 — The fluorescent emission spectra of TBVC (3.12×10^{-7} M) in different solvents. Excitation wavelength: 370 nm. Slitwidth (Ex): 10 nm.

the twisted intramolecular charge transfer (TICT), for which the non-radiation decay rate is increased and a fluorescence quenching is resulted[38,39].

Compared with the parent coumarin, the π-electron conjugation in TBVC is fairly increased by the introduction of benzimidazole. Consequently, the fluorescence intensity of TBVC is significantly enhanced. The emission peak of TBVC is red-shifted to the visible-light region regarding parent coumarin or benzimidazole molecule. Based on these facts, TBVC is proved to be an excellent polar fluorescent probe for microenvironment. Thus, TBVC may find potential applications in the development of novel fluorescent dyes, sensitive fluorescent probes, and new photoelectric material.

Conclusions

Two selective fluorescent probes toward Fe^{3+} and Cu^{2+}, namely BAMC, TSAC and a fluorescent dye TBVC with strong fluorescent emission were synthesized from 4, 6-Dimethyl coumarin. The synthetic routes are via a series of reactions including Pechmann, Wittig, and substitution. The short synthetic routes are developed with high yield. Three coumarin derivatives all have stable fluorescence properties. They emit strong fluorescence at room temperature with a large red-shift in emission maxima regarding the parent coumarin. In addition, advantageous results were obtained in the design and synthesis of fluorescent probes for Fe^{3+} and Cu^{2+}. Three methods for the construction of coumarin-based fluorescent probes are summarized, reviewed and applied. These results are also contributed to understanding the relationship between synthesis strategies and the structure-property of coumarin compounds.

Supplementary Data

Supplementary data associated with this article are available in the electronic form at http://www.niscair.res.in/jinfo/ijca/IJCA_56A (07) 895-903_SupplData.pdf.

Acknowledgment

This work was supported by grants from the National Natural Science Foundation of China (No.21575084), the open funds of Guangxi Key Laboratory of Electrochemical Energy Materials (No. 2019-006).

References

1 Pivetta T, Masuri S, Cabiddu M G, Caltagirone C, Pintus A, Massa M, Isaia F & Cadoni E, New J Chem, 43 (2019) 12032.
2 Verwilst P, Sunwoo K & Kim J S, *Chem Commun*, 51 (2015) 5556.
3 Zhan S, Xu H, Zhang W, Zhan X, Wu Y, Wang L & Zhou P, *Talanta*, 142 (2015) 176.
4 Roy N, Dutta A, Mondal P, Paul P C & Singh T S, *J Fluoresc*, 27 (2017) 1307.
5 Lin X M, Gao G M, Zheng L Y, Chi Y W & Chen G N, *Anal. Chem*, 86 (2014) 1223.
6 Riveiro M E, De Kimpe N, Moglioni A, Vazquez R, Monczor F, Shayo C & Davio C, *Curr Med Chem*, 17 (2010) 1325.
7 Lee A Y, Levine M N, Baker R I, Bowden C, Kakkar A K, Prins M, Rickles F R, Julian J A, Haley S, Kovacs M J & Gent M, *New Engl J Med*, 349 (2003) 146.
8 Kashman Y, Gustafson K R, Fuller, R W, Cardellina 2nd J H, McMahon J B, Currens M J, Buckheit Jr R W, Hughes S H, Cragg G M & Boyd M R, *J Med Chem*, 35 (1992) 2735.
9 Pengsuparp T, Serit M, Hughes S H, Soejarto D D & Pezzuto J M, *J Nat Prod*, 59 (1996) 839.
10 Hung C M, Kuo D H, Chou C H, Su Y C, Ho C T & Way T D, *J Agric Food Chem*, 59 (2011) 9683.
11 Li X, Gao X, Shi W & Ma H, *Chem Rev*, 114 (2014) 590.

12 Fallah A, Gülcan H O & Gazi M, *J Fluoresc*, 28 (2018) 1255.
13 Jeong Y & Yoon J, *InorgChim Acta*, 381 (2012) 2.
14 Kaya E N, Yuksel F, Özpınar G A,Bulut M & Durmuş M, *Sensor Actuat B*, 194 (2014) 377.
15 Wang W, Wu J, Liu Q, Gao Y, Liu H & Zhao B, *Tetrahedron Lett*, 59 (2018) 1860.
16 Ge F, Ye H, Zhang H & Zhao BX, *Dyes Pigm*, 99 (2013) 661.
17 Dakanali M, Roussakis E, Kay A R & Katerinopoulos H E, *Tetrahedron Lett*, 46 (2005) 4193.
18 Lim N C &Brückner C, *Chem Commun*, 9 (2004) 1094.
19 Zhang J, Cui H, Hojo M, Shuang S & Dong C, *Bioorg Med Chem Lett*, 22 (2012) 343.
20 Panchenko P A, Fedorov Y V, Fedorova O A & Jonusauskas G, *Dyes Pigm,* 98 (2013) 347.
21 Lin W, Yuan L, Cao Z, Feng Y & Long L, *Chem Eur J*, 15 (2009) 5096.
22 Gustavsson T, Cassara L, Gulbinas V, Gurzadyan G, Mialocq J C, Pommeret S, Sorgius M & Van der Meulen P, *J Phys Chem A,* 102 (1998) 4229.
23 Shi W & Ma H, *Chem Commun*, 48 (2012) 8732.
24 Tsay S C, Hwu J R, Singha R, Huang W C, Chang Y H, Hsu M H, Shieh F K, Lin C C, Hwang K C, Horng J C & De Clercq E, *Eur J Med Chem*, 63 (2013) 290.
25 Paul K, Bindal S & Luxami V, *Bioorg Med Chem Lett*, 23 (2013) 3667.
26 De S K & Gibbs R A, *Synthesis*, 8 (2005) 1231.
27 Joshi S D & Usgaonkar R N, *Indian J Chem*, 21B (1982) 399.
28 Gazit A, Yee K, Uecker A, Böhmer F D, Sjöblom T, Östman A, Waltenberger J, Golomb G, Banai S, Heinrich M C & Levitzki A, *Bioorg Med Chem*, 11 (2003) 2007.
29 KirpichËnok M A, Gorozhankin S K & GrandbergI I, *ChemInform*, 21 (1990) 1.
30 Raju B B&Varadarajan T S, *J Phys Chem*, 98 (1994) 8903.
31 Tasior M, Kim D, Singha S, Krzeszewski M, Ahn K H & Gryko D T, *J Mater Chem C*, 3 (2015) 1421.
32 Ouyang H, Gao Y & Yuan Y, *Tetrahedron Lett*, 54 (2013) 2964.
33 Hua J & Wang Y G, *Chem Lett*, 34 (2005) 98.
34 Tang L, Li F, Liu M & Nandhakumar R, *Bull Korean Chem Soc*, 32 (2011) 3401.
35 Saxena A, Fujiki M, Rai R & Kwak G, *Chem Mater*, 17 (2005) 2181.
36 Ho I T, Lee G H & Chung W S, *J Org Chem*, 72 (2007) 2434.
37 Kulatilleke C P, De Silva S A & Eliav Y, *Polyhedron*, 25 (2006) 2593.
38 Sobolewski A L & Domcke W, *Chem Phys Lett*, 259 (1996) 119.
39 Turecek F & Syrstad E A, *J Am Chem Soc*, 125 (2003) 3353.