

A new anthracene derivative of calix[4]arene as a fluorescent chemosensor

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Abstract: A new anthracene derivative of calix[4]arene was synthesized as a highly fluorescent compound. This compound was examined for its fluorescent properties towards different metal ions (Li^+ , Na^+ , Mg^{2+} , Ca^{2+} , Ba^{2+} , Ni^{2+} , Cu^{2+} , Zn^{2+} , Pb^{2+}) by UV and fluorescence spectroscopy. On complexation by alkaline earth metal cations and transition metal cations, the fluorescence spectrum was quenched. In particular, Ca^{2+} caused greater than 98% quenching of the anthracene derivative of calix[4]arene.

Key words: Calix[4]arene, anthracene, fluorescent chemosensor, Schiff base

1. Introduction

Fluorescent chemosensors for metal ion analysis are of great importance due to their potential applications in a wide range of areas such as cell biology, biochemical analysis, and medical diagnosis.^{1,2} Fluorescence spectroscopy has several advantages over other methodologies due to its high sensitivity, easy visualization, and short response time for detection.^{3,4}

A fluorescent chemosensor is composed of an ion recognition unit (ionophore) and a fluorogenic unit (fluorophore).⁵ An effective fluorescent chemosensor must convert the cation recognition by an ionophore into an easily monitored and highly sensitive light signal from the fluorophore.⁶ The determination of Ca^{2+} in various biological systems has attracted much interest and many efficient systems are continually being developed.^{7,8} The sensitive and convenient determination of calcium ions, such as naked eye detection,^{9,10} is essential for the convenient monitoring of the ions in many chemical and biological systems.¹¹

Calixarenes with appropriate appended groups are good candidates for cation recognition because they have been shown to be highly specific ligands and their potential as sensing agents has received increasing interest.^{12,13}

Intramolecular cavities of calixarenes, formed by the phenolic rings, can host complementary cations,^{14–16} anions,^{17,18} and neutral molecules¹⁹ especially when several binding sites are preorganized at the wide or narrow rim of the macrocycle.²⁰

Calixarenes substituted on the upper or lower rim may show selective cation recognition dependent on the cation ligating group. This group, known as the ionophore, may be a crown ether, carboxylic acid, amide, or other functional group. Recently, the cation–ionophore interaction has been monitored by a signaling moiety

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attached to the calixarene framework. The signaling moiety may be a fluorogenic unit, such as a pyrene, anthracene, or naphthalene group.^{21,22}

Reported calixarene-based fluorescence sensors utilize photo-physical changes produced by cation binding: photo-induced electron transfer (PET),^{23–25} excimer/exciplex formation and extinction,²⁶ energy transfer,^{27,28} or fluorescence resonance energy transfer (FRET).²⁹

Recently, we have reported on the cation binding affinities of the calix[4]arene naphthylimide derivative, which was shown to be an efficient binder for Cu(II) cation in acetonitrile:dichloromethane.³⁰ In the present paper, we report on the synthesis and binding abilities of the novel fluorescent calix[4]arene derivative containing 2 anthracene units at the upper rim.

2. Results and discussion

2.1. Synthetic routes

In this paper, we describe the synthesis of a new anthracene based calix[4]arene fluorophore. *o*-Phenylenediamine (**1**) was reacted with 9-anthraldehyde (**2**) to give compound **3**. Compounds **4**, **5**, and **6** were prepared according to known previous procedures.^{31–34} Finally, sensor **7** was obtained by treatment of calix[4]arene **6** with amine **3** in chloroform/methanol (Scheme 1). The synthesized compounds were characterized by a combination of FTIR, ¹H NMR, and elemental analysis.

The ¹H NMR spectrum of **3** showed 3 multiplets at δ 6.83–6.89 ppm (2H), 7.12–7.19 ppm (1H), and 7.48–7.59 ppm (4H); 3 doublets at δ 7.28 ppm (1H), 8.04 ppm (2H), and 8.76 ppm (2H); and 1 singlet at δ 8.54 ppm (1H) for anthracene and phenyl protons and 1 singlet at δ 9.75 ppm (1H) for imine proton.

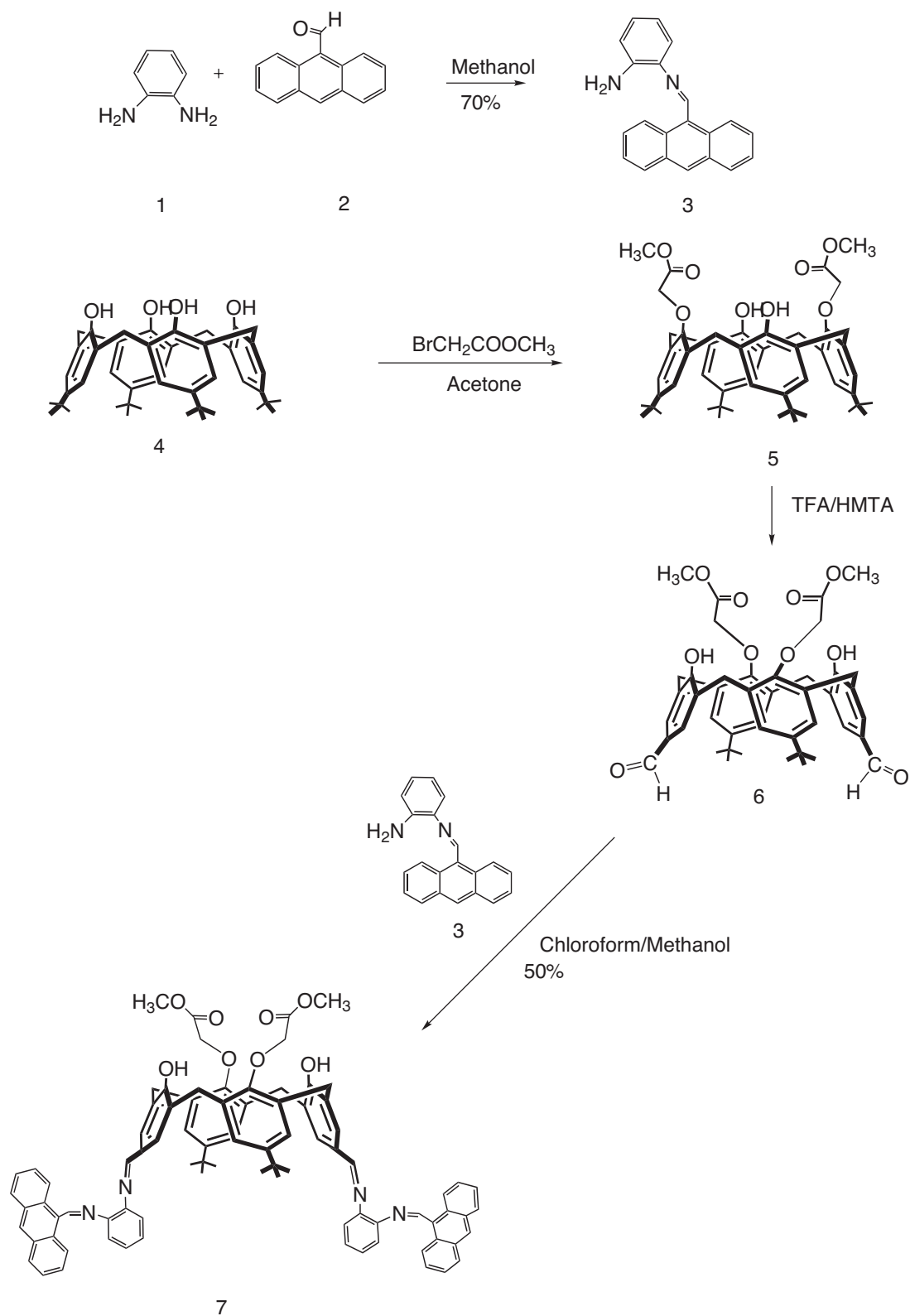
The ¹H NMR spectrum of **7** showed 1 singlet at δ 1.01 ppm (18H) for *tert-butyl* protons, one singlet at δ 3.79 ppm (6H) for OCH₃, 1 singlet at δ 4.83 ppm (4H) for OCH₂, 2 doublets at δ 3.52 and 4.37 ppm (8H) for ArCH₂Ar protons, 2 singlets (4H) at δ 8.83 ppm and 9.00 ppm for imino protons, and 2 doublets (8H) at δ 8.19 and 7.65 ppm, 1 singlet (2H) at δ 7.98 ppm, and 4 multiplets at δ 7.09–7.13, 7.27–7.31, 7.46–7.52, and 7.53–7.59 ppm for aromatic protons.

2.2. Absorption and fluorescence measurements

Absorption spectra of ligands (1×10^{-6} M for fluorescence measurements and 1×10^{-4} M for absorption measurements) in CH₃CN:CH₂Cl₂ solutions containing 10 mol equiv of the appropriate metal perchlorate salt were measured using a 1-cm absorption cell. Fluorescence spectra of the same solutions were measured with a 1-cm quartz cell. The excitation wavelength was 300 nm for **7**. The stoichiometries of the complexes and their stability constants were determined according to a literature procedure.

2.3. Fluorescence spectra and absorption spectra

Excess perchlorate salts (10 equiv) of Li⁺, Na⁺, Mg²⁺, Ca²⁺, Ba²⁺, Ni²⁺, Cu²⁺, Zn²⁺, and Pb²⁺ were tested to evaluate the metal ion binding properties of **7**. The results are shown in Figure 1. Ligand concentration was fixed at 1×10^{-6} M in CH₂Cl₂:CH₃CN (1:1, v/v). The fluorescence emission spectrum of the compound (**7**) was recorded by fixing the excitation wavelength at 300 nm, which exhibited a characteristic emission band at 348 nm.



Scheme 1. Synthesis of novel anthracene functionalized calix[4]arene.

Among the metal ions tested, Mg^{2+} , Ca^{2+} , Ba^{2+} , Ni^{2+} , Cu^{2+} , Zn^{2+} , and Pb^{2+} quenched the fluorescence of compound **7** (Figure 2). However, Ca^{2+} ion strongly quenched emission of compound **7** (98%). In this case, we reported of **7** + Ca^{2+} complex property (fluorescence titration, complex stability constant, and complex stoichiometry). The fluorescence intensity of **7** in the presence of increasing amounts of Ca^{2+} is shown in Figure 3. The fluorescence intensity of the emissions at 348 nm decreased with increasing Ca^{2+} concentrations (0–10 equiv). The quenching phenomenon can be clearly observable under UV light (Scheme 2).

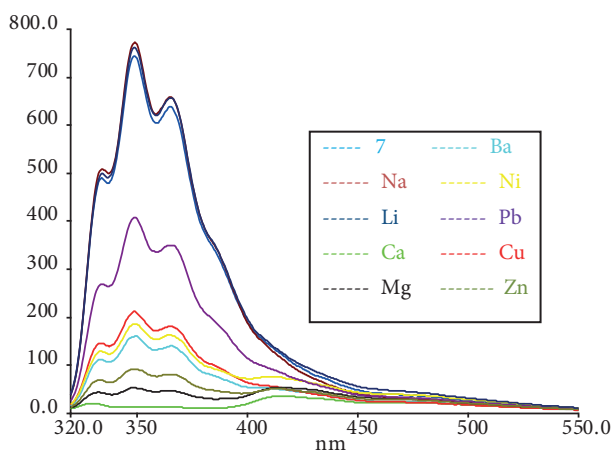


Figure 1. Fluorescence spectra of **7** upon addition of ClO_4^- salt of Ca^{2+} , Cu^{2+} , Li^+ , Mg^{2+} , Ba^{2+} , Na^+ , Ni^{2+} , Pb^{2+} , and Zn^{2+} (10 equiv) in $\text{CH}_2\text{Cl}_2:\text{CH}_3\text{CN}$ (1:1, v/v) (1×10^{-5} M).

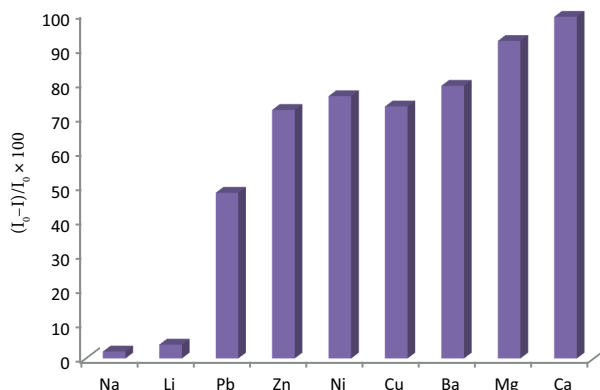
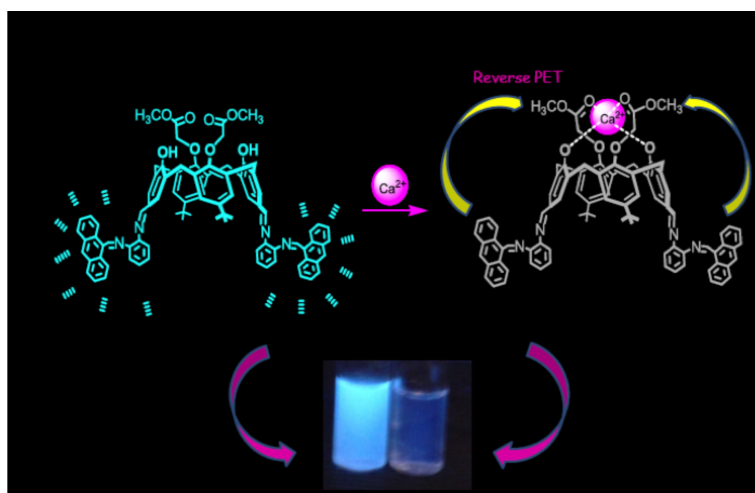


Figure 2. Fluorescence quenching ratio $[(I_o - I/I_o) \times 100]$ of **7** (1×10^{-6} M) at 348 nm upon addition of different metal ions (10.0 equiv) in $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{CN}$ (1:1, v/v).



Scheme 2. $\text{CH}_3\text{CN}/\text{CH}_2\text{Cl}_2$ solutions of **7** and **7** + Ca^{2+} under UV light.

The quenching phenomenon of **7** upon Ca^{2+} ion binding was attributed to the reverse- photo-induced electron transfer (PET) mechanism.^{35,36} As mentioned in the literature,³⁴ when the Ca^{2+} ion strongly interacts with the lone pair of electrons of the carbonyl oxygen atoms with the aid of 2 proximal OH,^{35–37} then electron transfer occurs from the anthracene unit behaving as a PET donor to the electron-lacking carbonyl group.²⁸

Metal ion binding properties of **7** were investigated by monitoring fluorescence and UV-vis changes upon the addition of Ca^{2+} ion. Compound **7** showed absorption bands at 431, 409, 390, 340, and 283 nm (Figure 4). On addition of Ca^{2+} ions (10 equiv) to a solution of **7**, the spectrum changed. The stoichiometry of the binding species was determined by Job's plot and was found to be 1:1.

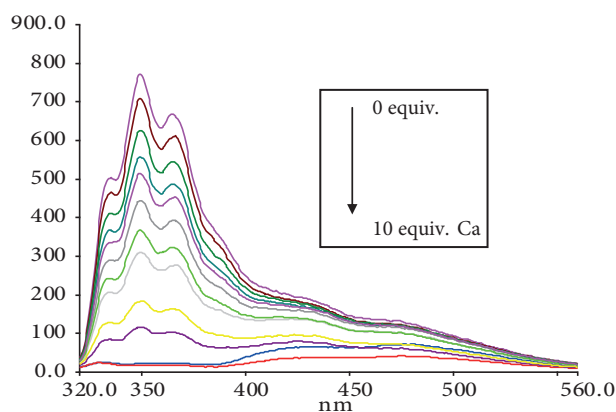


Figure 3. Fluorescence spectra of **7** (1×10^{-6}) in $\text{CH}_2\text{Cl}_2:\text{CH}_3\text{CN}$ (1:1, v/v) upon addition of increasing concentrations of $\text{Ca}(\text{ClO}_4)_2$ (0–10 equiv) with an excitation at 348 nm.

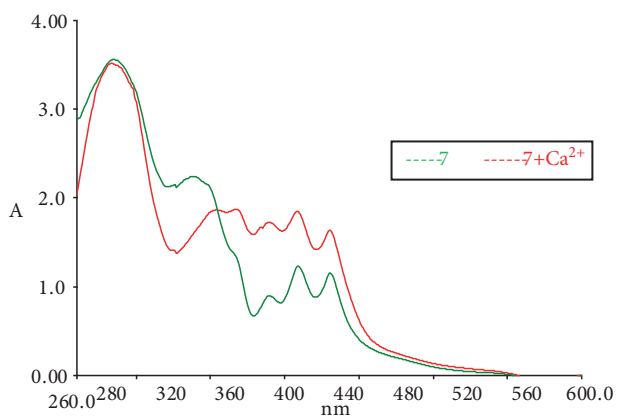


Figure 4. UV-vis spectra of **7** (1×10^{-4} M) upon addition of ClO_4^- salt of Ca^{2+} (10 equiv) in $\text{CH}_2\text{Cl}_2:\text{CH}_3\text{CN}$ (1:1, v/v).

UV-vis spectra of **3** and **6** were scanned in an attempt to make comments about the structure of the complex. There was no change in the absorption spectrum of compound **3** upon addition of Ca^{2+} ion to solution **3** (Figure 5). On addition of Ca^{2+} ions (10 equiv) to a solution of **6**, there was a new absorption band at 380 nm (Figure 6). It shows that calcium ion interacts with ester groups in **7** + Ca complex.

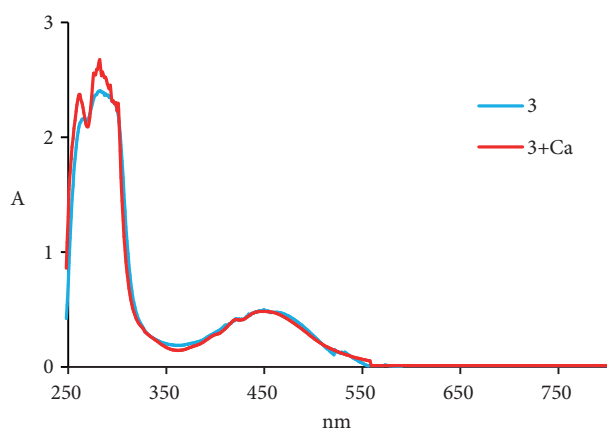


Figure 5. UV-vis spectra of **3** (1×10^{-4} M) upon addition of ClO_4^- salt of Ca^{2+} (10 equiv) in $\text{CH}_2\text{Cl}_2:\text{CH}_3\text{CN}$ (1:1, v/v).

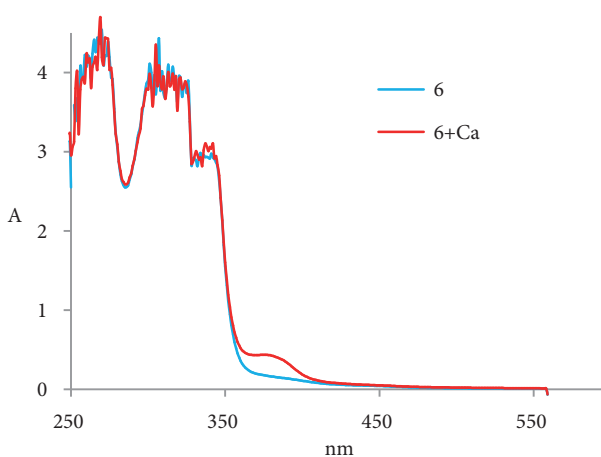


Figure 6. UV-vis spectra of **6** (1×10^{-4} M) upon addition of ClO_4^- salt of Ca^{2+} (10 equiv) in $\text{CH}_2\text{Cl}_2:\text{CH}_3\text{CN}$ (1:1, v/v).

2.4. Determination of stability constants

The complex stability constant (β) was calculated using Valeur's method.³⁸ Accordingly, the quantity $I_o/(I_o - I)$ was plotted versus $[\text{metal ion}]^{-1}$ with the stability constant given by the ratio of intercept/slope^{39,40} (Figure 7). The stability constants for complexation of Ca^{2+} with **7** were determined by fluorimetric titration. The titration experiments were performed by adding solutions with various concentrations of metal perchlorate in $\text{CH}_3\text{CN}/\text{CH}_2\text{Cl}_2$ to solutions of the ligand in the same solvent. From the fluorescent titrations, the stability constants ($(\log \beta) (\text{M})^{-1}$) of **7** with Ca^{2+} were calculated to be 5.12 ± 0.10 .

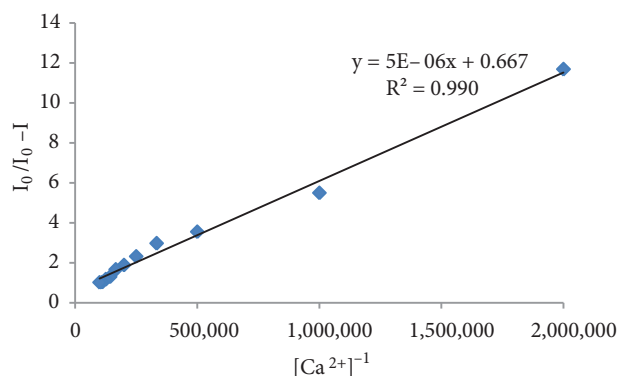


Figure 7. Plot of $I_o/(I_o - I)$ versus $[\text{Ca}^{2+}]^{-1}$ for the spectrofluorimetric titration of **7** with Ca^{2+} in $\text{CH}_3\text{CN}:\text{CH}_2\text{Cl}_2$ (1:1 v/v).

In conclusion, a new fluorogenic ionophore based on anthracene derivative of calix[4]arene was prepared. Upon the addition of Mg^{2+} , Ca^{2+} , Ba^{2+} , Ni^{2+} , Cu^{2+} , and Zn^{2+} ions to a solution of **7** in $\text{CH}_3\text{CN}:\text{CH}_2\text{Cl}_2$ (1:1 v/v), the fluorescence spectrum was quenched. Particularly, as the concentration of calcium ions increased the fluorescence intensity decreased; that is typical of a reverse-PET type mechanism from the anthracene unit to carbonyl group.²⁸ There was no change in the intensity of emission of compound **7** upon addition of Na^+ or Li^+ ions to solution **7**.

3. Experimental section

All starting materials and reagents used were of standard analytical grade from Fluka, Merck, and Aldrich and used without further purification. Other commercial grade solvents were distilled, and then stored over molecular sieves. The drying agent employed was anhydrous MgSO_4 . All aqueous solutions were prepared with deionized water that had been passed through a Millipore Milli-Q Plus water purification system. ^1H and ^{13}C NMR spectra were recorded with a Varian 400 MHz spectrometer in CDCl_3 . FT-IR spectra was recorded with a PerkinElmer spectrum 100. UV-visible spectra were obtained on a PerkinElmer UV-Visible recording spectrophotometer. Fluorescence spectra were recorded on a PerkinElmer spectrometer. Elemental analyses were performed using a Leco CHNS-932 analyzer. Thin layer chromatography (TLC) was performed using silica gel on glass TLC plates (silica gel H, type 60, Merck).

3.1. Synthesis

Compounds **4**, **5**, and **6** were prepared according to known previous procedures^{31–34} and the other compounds (**3** and **7**) employed in this work as illustrated in Scheme 1 were synthesized according to the methods given below.

3.1.1. Synthesis of compound 3

A stirred solution of **1** (1.0 g, 9.25 mmol) in methanol (25 mL) was cooled at $-5\text{ }^{\circ}\text{C}$. This solution was added a solution of **2** (1.9 g, 9.25 mmol) in methanol (25 mL) and stirred at $-5\text{ }^{\circ}\text{C}$ for 6 h to obtain a light orange precipitate. The precipitate was filtered and washed with methanol and ethanol. The residue obtained was further recrystallized from chloroform/n-hexane to furnish compound **3**. Yield (70%). Mp. 166–168 $^{\circ}\text{C}$. IR (cm^{-1}): 1610 (C=N). ^1H NMR (CDCl_3 , 400 MHz) δ (ppm): 4.30 (bs, 2H, NH_2), 6.83–6.89 (m, 2H, ArH), 7.12–7.19 (m, 1H, ArH), 7.28 (d, $J = 7.72$, 1H, ArH), 7.48–7.59 (m, 4H, ArH), 8.04 (d, $J = 8.60$, 2H, ArH), 8.54 (s, 1H, ArH), 8.76 (d, $J = 8.80$, 2H, ArH), 9.75 (s, 1H, CH=N). ^{13}C NMR (CDCl_3) δ : 115.53, 117.22, 118.52, 124.95, 125.39, 127.09, 127.85, 128.06, 129.01, 130.40, 130.63, 131.34, 138.21, 142.54, 156.90. Anal. Calcd for $\text{C}_{21}\text{H}_{16}\text{N}_2$: C 85.11; H 5.44; N 9.45. Found: C 85.25; H 5.62; N 9.54.

3.1.2. Synthesis of compound 7

To a stirred solution of **6** (0.3 g, 0.40 mmol) in chloroform (3 mL) was added a solution of **3** (0.24 g, 0.81 mmol) in methanol (10 mL), followed by refluxing for 6 h to obtain a light yellow precipitate. The precipitate was filtered and washed with methanol and diethyl ether. The residue obtained was further recrystallized from chloroform/n-hexane to furnish compound **9**. Yield (50%). Mp. 309–311 $^{\circ}\text{C}$. IR (cm^{-1}): 1742 (C=O), 1610, 1630 (C=N). ^1H NMR (DMSO, 400 MHz) δ (ppm): 1.01 (s, 18H, C (CH_3)₃), 3.79 (s, 6H, OCH_3), 3.52 (d, 4H, $J = 13.5$, ArCH_2Ar), 4.37 (d, 4H, $J = 13.5$, ArCH_2Ar), 4.83 (s, 4H, OCH_2), 7.05 (s, 4H, ArH), 7.09–7.13 (m, 6H, ArH), 7.27–7.31 (m, 2H, ArH), 7.46–7.52 (m, 4H, ArH), 7.53–7.59 (m, 6H, ArH, OH), 7.98 (s, 4H, ArH), 7.65 (d, 4H, $J = 9.4$, ArH), 7.96 (s, 2H, ArH), 8.19 (d, 4H, $J = 8.6$, ArH), 8.83 (s, 2H, CH = N), 9.00 (s, 2H, CH=N). Anal. Calcd for $\text{C}_{86}\text{H}_{76}\text{N}_4\text{O}_8$: C 79.85; H 5.92; N 4.33. Found: C 79.91; H 5.98; N 4.36.

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