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A new fluorescent chemosensor for F^- based on inhibition of excited-state intramolecular proton transfer

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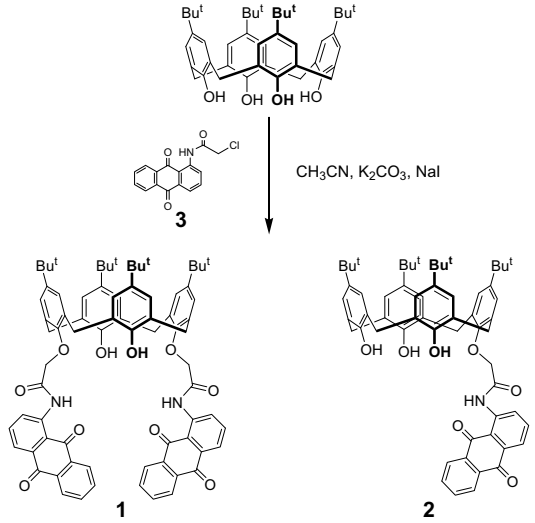
ABSTRACT

New fluorescent chemosensor **1** with two amidoanthraquinone groups (1-AAQs) at the lower rim of *p-tert*-butylcalix[4]arene has been synthesized. The significant changes of absorption and fluorescence bands show that chemosensor **1** is selective toward fluoride ion (F^-) over other anions such as Cl^-, Br^-, I^-, CH_3COO^-, $H_2PO_4^-$, HSO_4^-, and OH^-. The ESIPT process of **1** is inhibited by the fluoride-induced H-bonding followed by deprotonation of NH of the 1-AAQ.

The design and synthesis of systems able to sense analytes are of major interest for anions involved in chemical and biological processes.[1] Fluoride ion (F^-) is of particular interest because of its role in preventing from dental caries and in treatment of osteoporosis.[2] However, an excess of fluoride ion can lead to fluorosis, which corresponds to a fluoride 'disease'. The development of reliable sensing methods for F^- is, therefore, needed for environment and human health care. Calixarenes are useful macrocycles because they are ideal platforms for creating host molecules with ion-sensing properties.[3] Linkage of fluorogenic tags to *p-tert*-butylcalix[4]arenes with appropriate functions as to be anion receptors, such as amide,[4] urea,[5] thiourea[6], and pyrrole[7] has afforded a large variety of efficient chemosensors. Usually, fluorescent chemosensors based on calix[4]arenes utilize photophysical changes upon anion binding: photo-induced electron transfer (PET),[8] excimer/exciplex formation and extinction,[9] or energy transfer.[10] 1-Aminoanthraquinone (1-AAQ), a chromofluorophore exhibiting excited-state intramolecular proton transfer (ESIPT), has been reported to show intrinsic photophysical properties such as intense luminescence, large Stokes shifts, and significant photostability, and has been applied in various chemical fields.[11] Recently, a large number of excellent examples for the sensing of F^- have been reported.[12] This led us to prepare *p-tert*-butylcalix[4]arene functionalized by 1-AAQ residues.

Thus, in this Note, we report on the synthesis of chemosensor **1** with two 1-AAQs, 1,3-linked to the lower rim of a *p-tert*-butylcalix[4]arene, by amido groups exhibiting a selective fluorescence response to F^- ion. Analogue **2** was prepared as a reference. According to Scheme 1, the reaction of *p-tert*-butylcalix[4]arene with 2 equiv of the chloride derivative of 1-AAQ (**3**)[13] in the



Scheme 1. Synthesis of **1** and **2**.

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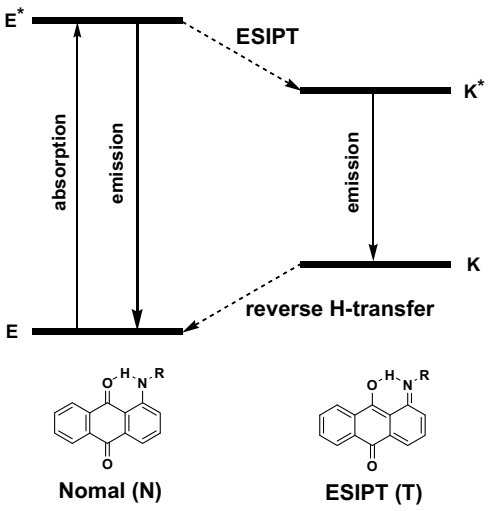
presence of K_2CO_3 as base and NaI as catalyst in refluxing CH_3CN afforded **1** and **2** in 52% and 23% yields, respectively.[14]

The photophysical properties of **1** and **2** were investigated by monitoring UV–vis and fluorescence changes in various solvents (toluene, acetonitrile, and DMSO). Absorption spectra of **1** were dependent on the solvent polarity (Fig. 1a). The absorption band maximum underwent blue shifts from non-polar (toluene) to polar solvent (DMSO). In toluene and acetonitrile, both normal and Stokes-shifted tautomer emissions appeared at 515 and 560 nm, respectively. In DMSO, the tautomer emission (ESIPT band) was not observed because this solvent is known to form H-bonds with H-donors (Fig. 1b).[15,16] This prevented **1** from forming the intramolecular H-bonding between NH group and the carbonyl group of 1-AAQ which is one of the driving forces that allow the ESIPT process to occur. This solvent dependency was the first evidence to show that ESIPT took place with the transfer of amido NH hydrogen to the neighboring oxygen atom in the excited state (Scheme 2). A useful method to differentiate a normal band (N) from an ESIPT band (T) is the excitation spectrum. Figure 1c indicates that the excitation spectra of **1** in toluene monitored at 560 nm corresponding to ESIPT band are red-shifted ($\Delta\lambda$ = 24 nm) in comparison to that recorded at 406 nm original UV band. This is explicit evidence for the formation



Scheme 2. Forms of 1-AAQ in **1** in the ground state (N) and the excited state (T).

of intermolecular ESIPT of **1** in non-polar solvent. Thus, it should be noteworthy that the chemical species corresponding to 406 and 430 nm in absorption spectra are different.

1 showed high sensitivity and selectivity toward F^- ion over competing anions. Variations of UV–vis and fluorescence spectra of **1** in the presence of various anions including F^-, Cl^-, Br^-, I^-, CH_3COO^-, HSO_4^-, $H_2PO_4^-$, and OH^- (30 equiv as their tetrabutylammonium (TBA) salts) in CH_3CN are given in Figure 2. All the anions neither lead to any significant absorption in the visible region nor lead to fluorescence changes, but F^- ion which gave an emission peak at 527 and 560 nm. Competing anions + F^- gave absorption and fluorescence changes similar to those of single F^- experiment. In addition, the color changes from pale-yellow to deep-yellow and fluorescence changes from colorless to green

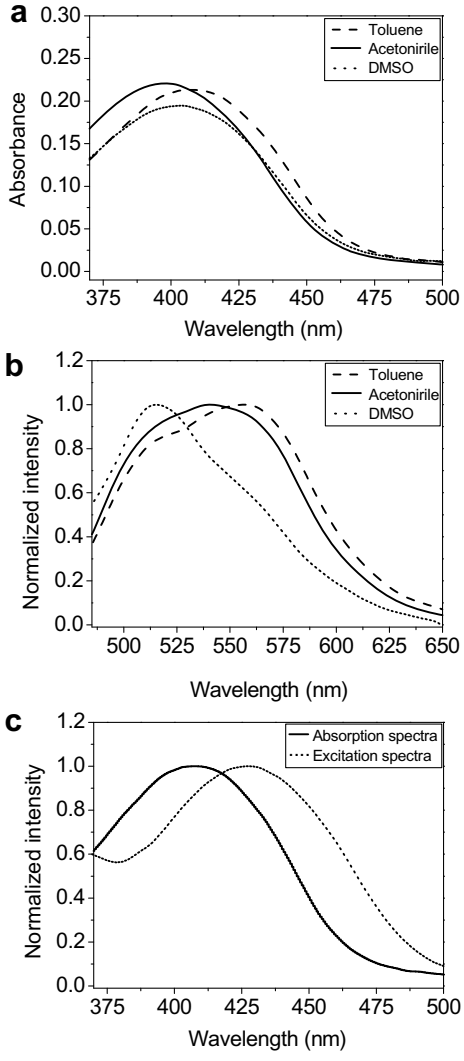


Figure 1. (a) UV–vis absorption and (b) normalized fluorescence emission spectra at 455 nm of **1** (20 μM) in various solvents. (c) Absorption and excitation spectra of **1** (20 μM) in toluene at 560 nm.

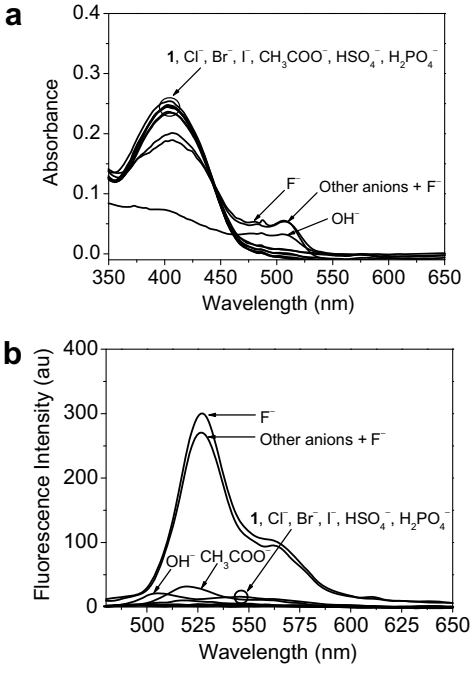


Figure 2. (a) UV–vis and (b) fluorescence spectra of **1** (20 μM) in CH_3CN solution in the presence of TBA salts of various anions (F^-, Cl^-, Br^-, I^-, CH_3COO^-, HSO_4^-, $H_2PO_4^-$, and OH^- (20 mM, respectively). Excitation at 455 nm.

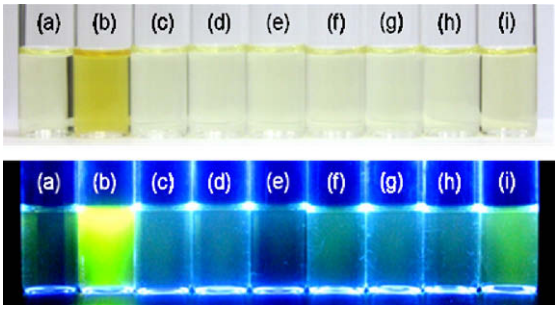


Figure 3. Color (top) and fluorescence (bottom) changes of **1** upon addition of 100 equiv of various anions in CH_3CN solution: (a) no anion, (b) F^-, (c) Cl^-, (d) Br^-, (e) I^-, (f) CH_3COO^-, (g) HSO_4^-, (h) $H_2PO_4^-$, and (i) OH^-.

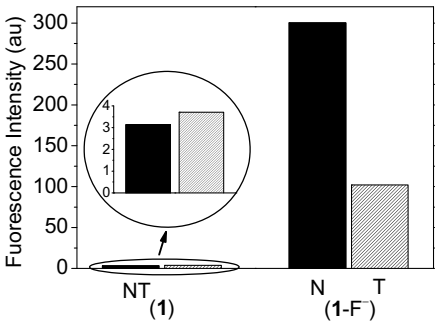


Figure 5. Relative responses at N (black bars) and T (dense bars) bands of **1** (20 μM) with addition of TBAF (30 equiv, respectively) in CH_3CN with an excitation at 455 nm. (N and T denote Normal and Tautomer bands, respectively).

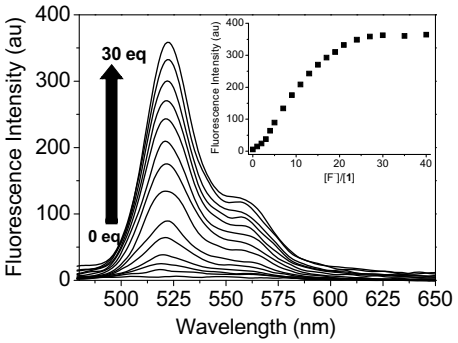


Figure 4. Fluorescence titration spectra of **1** (20 μM) upon gradual addition of TBAF in CH_3CN from 0 to 600 μM excited at 455 nm. The Inset shows the plot of fluorescence intensity versus the ratio of F^- to **1**. (λ_{em} = 527).

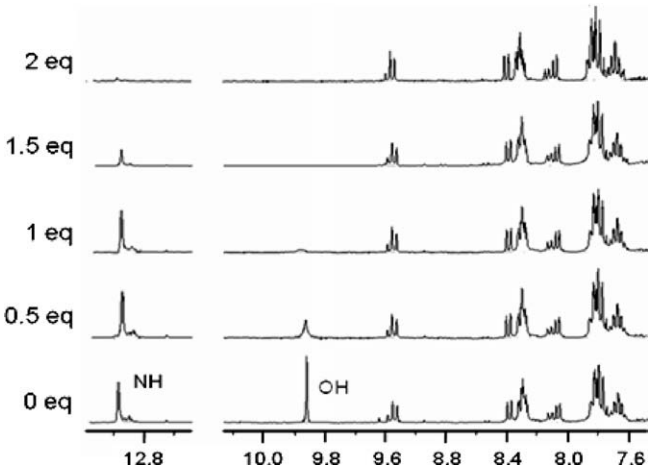


Figure 6. Partial ^1H NMR (300 MHz) spectra of **1** (1.0×10^{-2} M) in $CDCl_3$ upon gradual addition of TBAF.

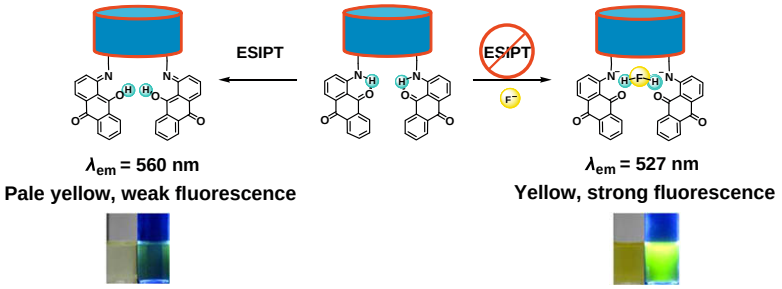
(OFF-ON) as shown in Figure 3. These facts were indicative of a high selectivity of **1** toward F^- ion over other competitive anions.

The absorption spectra of **1** show the spectral variation of the CH_3CN solution of **1** upon gradual addition of TBAF. As a function of F^-, a new red-shifted absorption band centered at 510 nm increased with a concomitant decrease of the band at 405 nm. The band at 510 nm is attributable to the Internal Charge Transfer (ICT) developed by deprotonation of NH in **1**.[17] Upon excitation at 455 nm, new bands at 527 and 560 nm appeared in the emission spectrum with the F^- ion (Fig. 4). The high selectivity of **1** for F^- ion is probably due to the formation of intramolecular H-bonds, NH···F^-, (or deprotonation) which promotes the delocalization of π-electrons through the 1-AAQ, causing changes in π–π transition with a fluorescence color change from colorless to green (Figs. 3 and 4).

A slight change of the tautomer emission band at 560 nm is accompanied by a strong increase of the normal emission band at 527 nm (Fig. 5) showing that ESIPT is inhibited by the presence of F^- anions, which interact with the NH groups of **1** (Scheme 3). Inhibition of ESIPT by F^- has already been observed in the case of some aromatic urea derivatives.[18]

We investigated **1**-F^- interactions in the ground state by running ^1H NMR titrations. It was found that the two OH and the two NH protons signals in the downfield part of the spectrum broadened and finally disappeared upon addition of F^- (Fig. 6). These observations clearly support that the proton-transfer interaction between **1** and F^- involved the amide NH groups. Aromatics protons were not shifted showing that no charge was delocalized in the anthraquinone moieties.

UV–vis and fluorescence changes of **2** were recorded under conditions similiar to those of **1** (Fig. 7). **2** showed less selectivity for F^-



Scheme 3. Proposed mechanism for the inhibition of ESIPT in **1** induced by F^- ion.

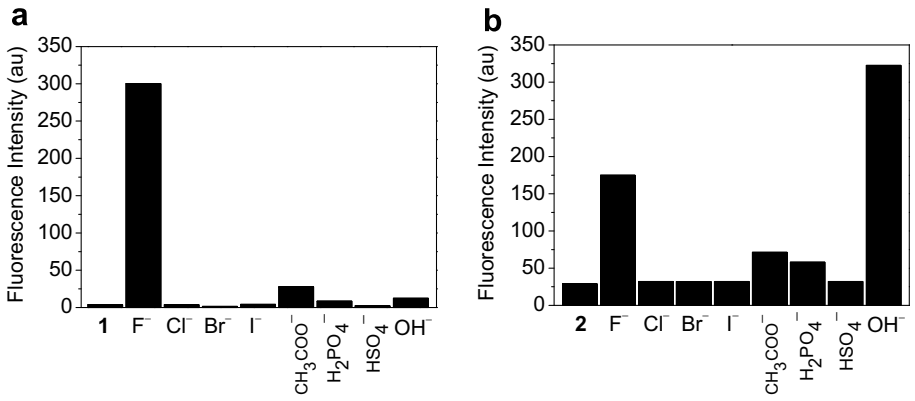


Figure 7. Relative responses at 527 nm of (a) **1** and (b) **2** (20 μM, respectively) with addition of various anions (30 equiv, respectively) (black bars) in CH_3CN with an excitation at 455 nm.

Table 1
ESIPT inhibition efficiency ($E_{inhibition}$) and association constants (K_a)[20] of **1** and **2** (20 μM) for F^- ion (20 mM)

Compound	$E_{inhibition}$[a] (I_N/I_T)	K_a (M^{-1})
1	0.84	—
1-F^-	2.94	279.0
2	0.63	—
2-F^-	1.49	29.2

[a] I_N: Fluorescence intensity of normal band. I_T: Fluorescence intensity of tautomer band (excitation at 455 nm).

than **1** leading to a conclusion that two amido NH functional linkers-1-AAQ are needed for selectivity. Similarly, the involvement of two –CH=N–N*H* has recently been reported for the binding of F^- by calix[4]arene derivatives with hydrazone functionalities in 1,3-positions at the lower rim.[19] Interestingly, it was observed that the emission intensity of **2** increased using NaOH, while it did not for **1**. This could be due to a deprotonation of NH, whereas that of **1** scarcely showed responses.

Table 1 summarizes the ESIPT-inhibition efficiencies and association constants of **1** and **2** calculated for 1:1 stoichiometry.

In conclusion, we have presented *p-tert*-butylcalix[4]arene (**1**) bearing two 1-amidoanthraquinone as both colorimetric and fluorescent-selective chemosensors for fluoride anion in CH_3CN which operates by inhibition of ESIPT signaling mechanism. The obvious absorption and fluorescence variations upon the addition of fluoride ion can be observed by naked-eyes and by optical responses. Other anions Cl^-, Br^-, I^-, CH_3COO^-, HSO_4^-, $H_2PO_4^-$, and OH^- were found to not induce any variation in either the absorption or fluorescence spectra. Importantly, such a possibility of preparing a sensor whose design could be correlated to the properties of an ion and its ability to inhibit the ESIPT will be a useful clue to design more delicate ESIPT-based chemosensors.

Acknowledgments

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14. *General*: Uncorrected melting points (Mps), Buchi 500. ^1H NMR and ^{13}C NMR, Varian 300 MHz (δ in ppm from TMS, *J* in Hertz). FAB MS mass spectra, JEOL-JMS-HX 110A/110A High Resolution Tendem Mass Spectrometry in Seoul National University (Korea). All the reactions were run under a nitrogen atmosphere. SiO_2 (Geduran 1.11567) was used for column chromatography. All reagents and solvents were commercial and used without further purification. Fluorescence spectra were recorded with a RF-5301PC spectrofluorophotometer. Stock solutions of **1** and **2** (20 μM) were prepared in CH_3CN. For all measurements, excitation was at 455 nm with excitation and emission slit widths at 1.5 nm. Fluorescence titration experiments were performed using 20 μM solutions of **1** and **2** in CH_3CN and various concentrations of metal perchlorate in CH_3CN.
Preparation of 1. *p-tert*-butylcalix[4]arene (0.51 g; 0.79 mmol), **3**[7] (0.44 g; 1.44 mmol), K_2CO_3 (0.11 g, 0.79 mmol), NaI (catalytic amount), and CH_3CN (100 mL) were refluxed for 24 h. After removal of the solvents in vacuo, the resulting solid was dissolved in CH_2Cl_2 (100 mL) and aqueous $NaHCO_3$ solutions (100 mL). The filtrate was washed with water (3 × 50 mL) and dried over anhydrous sodium sulfate, and the solvent was removed in vacuo. The crude product was further purified by column chromatography on silica gel (eluant: ethyl acetate/*n*-hexane, 1:5 v/v) to afford **1** (0.48 g; 52%) and **2** (0.17 g; 23%) as yellow solids, respectively). Mp: 235–237 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 12.94 (d, 2H, *NH*, *J* = 18.5 Hz), 9.69 (s, 2H, Ar_{calix}-O*H*), 9.20–9.12 (t, 2H, $Ar_{anthraquinone}$-H_m, *J* = 23.59 Hz), 8.39 (d, 1H, $Ar_{anthraquinone}$-H_m,

J = 8.52 Hz), 8.34–8.25 (m, 3H, $Ar_{anthraquinone}$-H_m), 8.14–8.04 (m, 1H, $Ar_{anthraquinone}$-H_m), 8.07 (d, 1H, $Ar_{anthraquinone}$-H_m, J = 14.53 Hz), 7.86–7.75 (m, 6H, $Ar_{anthraquinone}$-H_m) 7.20 (s, 8H, Ar_{calix}-H_m)), 4.91 (s, 4H, ArOCH_2CO), 4.55 (d, 4H, ArCH_2Ar, J = 12.8 Hz), 3.44 (d, 4H, ArCH_2Ar, J = 13.2 Hz), 1.04 (s, 18H, Ar-*t-bu*), 0.66 (s, 18H, Ar-*t-bu*); ^{13}C NMR (75 MHz, $CDCl_3$): 187.6, 185.9, 181.7, 168.2, 152.2, 151.2, 150.9, 150.6, 148.8, 148.4, 148.0, 147.2, 146.9, 144.6, 143.3, 143.0, 142.4, 142.1, 140.2, 136.2, 136.1, 135.6, 134.8, 134.7, 134.4, 134.3, 134.2, 134.1, 133.5, 1334.4, 133.0, 132.2, 131.3, 129.0, 128.6, 128.2, 128.1, 127.9, 127.6, 127.4, 126.8, 126.5, 126.3, 126.2, 126.1, 125.9, 125.8, 125.7, 34.3, 32.4, 31.5. HR-MS (ESI): Anal. Calcd for $C_{76}H_{74}N_2O_{10}$ $(M+1)^+$, 1175.5422; found, 1175.5431.

Preparation of 2. (0.17 g; 23%). Mp: 235–237 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.66 (s, 1H, *NH*), 10.34 (s, 1H, Ar_{calix}-O*H*), 10.11 (s, 1H, Ar_{calix}-O*H*), 9.17–9.15 (d, 1H, $Ar_{anthraquinone}$-H_m, J = 8.63 Hz), 9.11 (s, 1H, Ar_{calix}-O*H*), 8.47–8.44 (m, 1H, $Ar_{anthraquinone}$-H_m), 8.33–8.29 (m, 1H, $Ar_{anthraquinone}$-H_m), 8.19–8.15 (d, 1H, $Ar_{anthraquinone}$-H_m, J = 7.66 Hz), 7.87–7.79 (m, 3H, $Ar_{anthraquinone}$- H_m) 7.10–6.99 (m, 8H, Ar_{calix}-H_m), 5.01 (s, 2H, ArOCH_2CO), 4.55 (d, 4H, ArCH_2Ar, J = 12.8 Hz), 3.44 (d, 4H, ArCH_2Ar, J = 13.2 Hz), 1.04 (s, 18H, Ar-*t-bu*), 0.66 (s, 18H, Ar-*t-bu*); ^{13}C NMR (75 MHz, $CDCl_3$): 187.3, 182.8, 168.7, 150.7, 148.7, 148.6, 148.1, 146.9, 144.6, 143.7, 143.3, 140.9, 135.9, 134.7, 134.4, 134.3, 133.3, 133.1, 130.0, 128.3, 128.1, 127.9, 127.7, 127.3, 126.9, 126.2, 126.0, 125.9, 125.8, 123.7, 123.4, 119.2, 119.1, 75.2, 34.4, 34.2, 34.1, 33.1,32.9, 32.6, 31.7, 31.6, 31.4, 29.9. HR-MS (ESI): Anal. Calcd for $C_{60}H_{65}NO_7$ $(M+1)^+$, 912.4839; found, 912.4844.

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