Hiroshima University Doctoral Thesis

# Design and Synthesis of Photolabile Protecting Group with Two Photon Absorption and Reactivity: Application to Caged Compounds

# ２光子吸収と反応性に優れた光解離性保護基の設計と合成：ケージド化合物への応用

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## 1. Main Thesis

Design and Synthesis of Photolabile Protecting Group with Two Photon Absorption and Reactivity: Application to Caged Compounds
(２光子吸収と反応性に優れた光解離性保護基の設計と合成：
ケージド化合物への応用)

## 2. Articles

(1) "*p*-Nitroterphenyl Units for Near-Infrared Two-Photon Uncaging of Calcium Ions"
Thuy Thi Thu Pham, Satish Jakkampudi, Ko Furukawa, Fung-Yu Cheng, Tzu-Chau Lin, Yoki Nakamura, Norimitsu Morioka, Manabu Abe
*Journal of Photochemistry & Photobiology, A: Chemistry* 2021, 409, 113154-113167.

(2) "Impact of five-membered heterocyclic ring on photophysical property including two-photon absorption character"
Thuy Thi Thu Pham, Youhei Chitose, Tran Thi Thanh Tam, Wei-Lun Tseng, Tzu-Chau Lin, Manabu Abe
*Chem.Lett* 2021, CL-210420, *in press*.

## 3. Thesis Supplements

(1) "Design and Synthesis of Two-Photon Responsive Chromophores for Near-Infrared Light Induced Uncaging Reactions"
M. Abe, Y. Chitose, S. Jakkampudi, P. T. T. Thuy, Q. Lin, B. T. Van, A. Yamada, R. Oyama, M. Sasaki, C. Katan
*Synthesis* 2017, 49, 3337-3346.

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# Chapter 1

# General Introduction

## 1-1. Caged compound

Biologically active compounds play an extremely important role in our life. They are potential sources of new drugs development. To make use of these compounds, their roles and mechanisms in life phenomena must be elucidated. One of the research methods for elucidating mechanism of such physiologically active substances is using caged compounds. A caged compound in which a physiologically active substance is protected by a photolabile protecting groups (PPGs) and made inactive can regenerate the physiologically active substance by light irradiation[1–10] (Figure 1). Since the process needs only light irradiation, the release of physiologically active substances can be controlled temporally and spatially, which is very useful for elucidating biological phenomena.

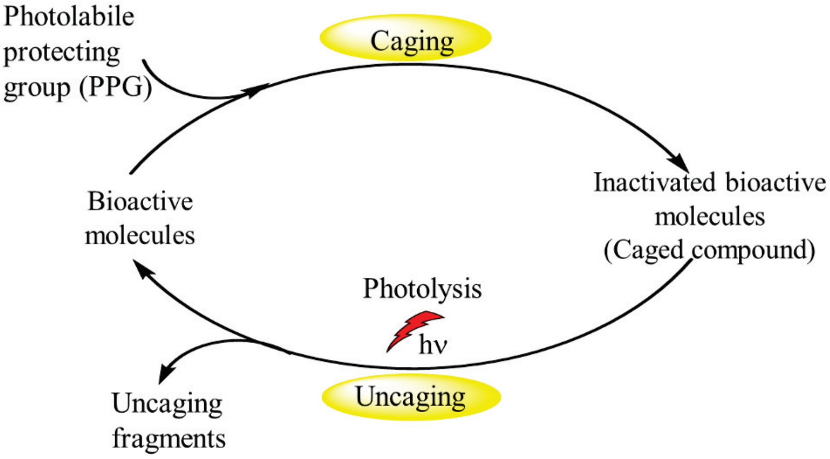


**Figure 1.** Caging and uncaging process of bioactive substances.

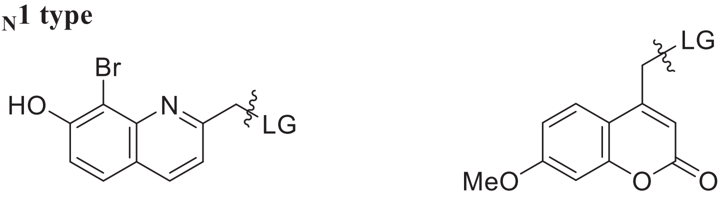
Until now, various types of PPGs have been developed and used to investigate the bioactivity of substances such as *ortho*-nitrobenzyl (*o*-NB) type[11,12] and photo $S_N1$ type[13,14] (Figure 2). Among them, the *o*-NB type photocleavable protecting group is most often used for caged compounds, and many reports have been made on its synthesis method and excellent photoreactivity. The *o*-nitrophenyl moiety has been widely used not only as a PPGs, but also as an electron-withdrawing group to induce nonlinear optical properties[15]. A donor–acceptor substitution pattern in π-conjugated systems endows molecules with good 2P absorption (2PA) properties.

***ortho*-nitrobenzyl type**

***ortho*-nitro benzyl**
*Chem. Commun.* **1966**, 22, 822-823

***ortho*-nitrophenyl ethyl**
*Tetrahedron Lett.* **1997**, 53, 4247

**Photo-$S_N1$ type**



**Quinoline**
*Org. Lett.* **2002**, 4, 3419

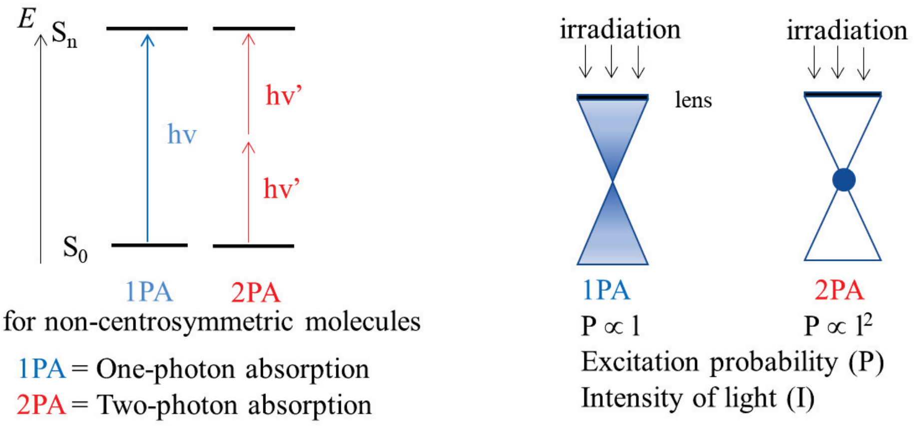
**Coumarin**
*J.Org. Chem.* **1995**, 60, 3953-3956

**Figure 2.** PPGs of uncaging reaction.

## 1-2. One-photon excitation (1PE) and two-photon excitation (2PE).

The bioactive molecules used to be uncaged by 1PE using ultraviolet and visible light. However, conventional 1PE does not allow the three-dimensional spatial localization of the released molecules deep within living tissues. Furthermore, high energy light can induce cell damage. Thus, 1PE processes, especially with an ultraviolet light source, are not suitable for physiological experiments. As a result, the 2PE was introduced to solve these problems.

In contrast, a two-photon excitation (2PE) process, in which molecules are excited by the simultaneous absorption of two lower energy photons[7–9,16–21], decreases the risk of cell damage. In contrast to 1PE, because 2PE is nonlinear process, the excitation probability is proportional to the square of light intensity, leading to molecules at the focal point of the laser will be electronically excited. Moreover, if wavelengths in the near-infrared (NIR) region (680–1050 nm) can be used for 2PE, molecules located deep within tissues can be activated with three-dimensional control because tissues are relatively transparent to NIR light[22–26] (Figure 3).



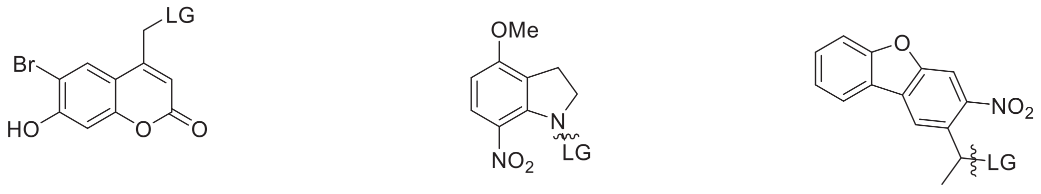
**$\delta_u = \sigma_2 \times \Phi$**
$\delta_u$: 2P uncaging efficiency
$\sigma_2$: 2P absorption cross-section
$\Phi$: uncaging quantum yield

**Figure 3.** One-photon excitation and two-photon excitation process.

The 2P uncaging efficiency ($\delta_u = \sigma_2 \times \Phi$) was calculated from 2P absorption cross-section ($\sigma_2$ in GM), (1 GM = $10^{-50}$ cm$^4$ s photon$^{-1}$), multiplied by the quantum yield ($\Phi$) of the corresponding uncaging reaction. The unit of GM was named in honor of Göppert-Mayer, who introduced the theory of two-photon absorption (2PA) in 1931[27].

### 1-3. Example for two-photon uncaging reaction

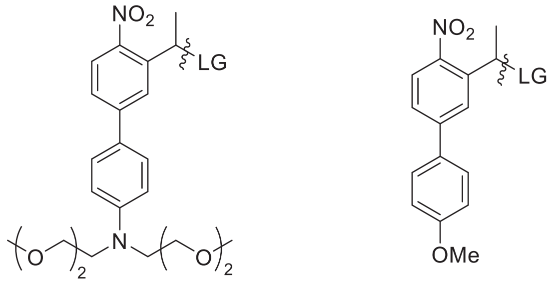
Since the last few decades, several caged compounds have been developed for 2PA application but not many of them show high two-photon efficiency. For example, in 2006, Ellis-Davies and co-workers successfully developed a nitrodibenzofuran (NDBF) skeleton substituted with ethylene glycol tetraacetic acid (EGTA), which is known to be a selective $Ca^{2+}$ chelator[28,29], as a 2P-responsive caged calcium species (Figure 1). The $Ca^{2+}$ uncaging efficiency of NDBF-EGTA using 2PE at 720 nm was ~0.6 GM[30]. Since then, new caged calcium compounds with better 2PA characteristics have been designed and synthesized. In 2012, Goeldner and co-workers developed biphenyl derivatives as highly 2P-responsive chromophores for caged glutamates and caged γ-aminobutyric acids with 2P-uncaging efficiencies of up to 11 GM at 800 nm and 3.2 GM at 740 nm[31] (Figure 4). Some physiologists suggested that 2P uncaging efficiency should be more than 3 GM for application to physiological studies[32]. Therefore, the design of chromophores with a larger 2PA cross-section and uncaging quantum yield is promising.



**Bhc**
**Tsien, R.** ***et al*** **(1999)**
***PNAS***
**1 GM at 740 nm**

**Indoline**
**Ellis-Davies.** ***et al*****(2001)**
***Nat. Neurosci***
**0.06 GM at 730 nm**

**NDBF**
**Ellis-Davies.** ***et al*** **(2006)**
***Nat. Method***
**0.6 GM at 720 nm**



**EANBP**
**Goeldner, M.** ***et al*** **(2012)**
***Photochem. Photobiol. Sci***
**11 GM at 800 nm**

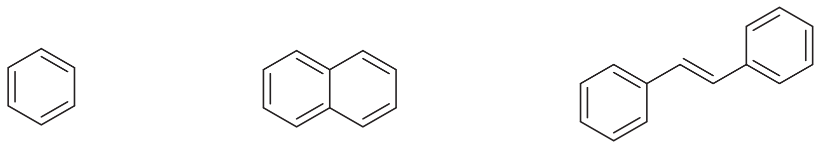
**PMNB**
**Goeldner, M.** ***et al*** **(2012)**
***Photochem. Photobiol. Sci***
**3.2 GM at 740 nm**

**Figure 4.** Example for two-photon uncaging reaction

## 1-4. Molecular design for two-photon chromophores

To design the chromophores with a larger 2PA cross-section, several factors that affect about 2PA cross-section should be considered. The parameter to increase 2PA cross-section are extension of π-conjugation and donor/acceptor group that increase the transition dipole moment.

Extension of π-conjugation: Benzene has no 2PA cross-section, naphthalene has 2PA cross-section with a value of 0.9 GM at 530 nm[33]. Moreover, stilbene, which has a double bond between two benzene rings, shows an improvement of 2PA cross-section with a value of 12 GM at 514 nm[34]. These values clearly demonstrated that the extension of π-conjugation can enhance the 2PA cross-section.



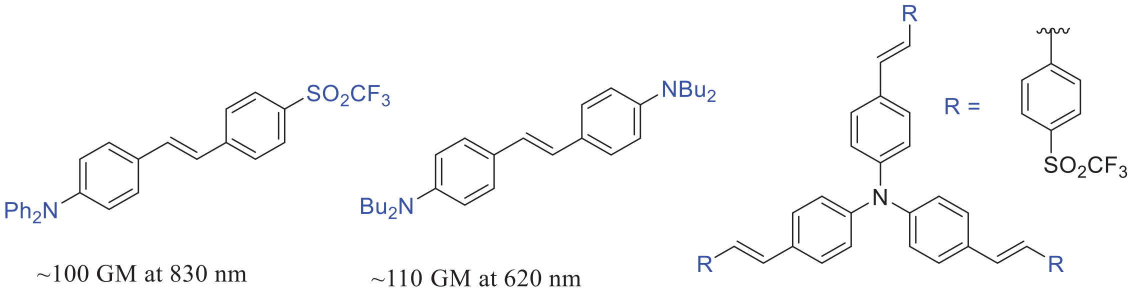
$\sigma_2$ = 0 GM

$\sigma_2$= 0.9 GM at 530 nm

$\sigma_2$ = 12 GM at 514 nm

**Figure 5.** Influence of π-extension on 2PA cross-section.

Donor/Acceptor group: Donor and acceptor groups are a key strategy to enhance 2PA cross-section value[35–37]. When the strong donor and acceptor groups was introduced to the π-conjugation system, the chromophores have higher transition dipole moments. For example, the simple systems such as a dipolar system (D-π-A) and a quadrupolar system (D-π-D, A-π-A, D-π-A-π-D or A-π-D-π-A) show a significantly larger 2PA cross-section than that of the stilbene. The triangular or star-shaped structures which were called octupolar chromophores $D(-\pi-A)_3$ or $A(-\pi-D)_3$, exhibit the same principle and show even more considerable TPA cross-section values than simple systems[37] (Figure 6).



~100 GM at 830 nm
D-π-A
(dipolar)

~110 GM at 620 nm
D-π-D
(quardrupolar)

~450 GM at 740 nm
$D\text{-}(\pi\text{-}A)_3$
(octupolar)

**Figure 6.** Influence of donor-acceptor groups on 2PA cross-section.

## 1-5. Caged calcium

The importance of $Ca^{2+}$ in physiological and cells was investigated over 100 years ago. $Ca^{2+}$ contributes significantly to numerous biological processes such as second messengers in cells, secretion of neurotransmitters, muscle contraction, nerve impulses and non-muscle motility[38]. Based on these reasons, an explanation about the mechanism of calcium ion in cells is needed for physiologists to elucidate the mechanism related to memory and learning.

In 1980's, the structures of ethylene glycol tetraacetic acid (EGTA)[39] have been known as $Ca^{2+}$ selective chelators (Figure 7). Since 1990's, Ellis-Davies and co-workers used an EGTA chelator[30] for the photo triggering of biologically active $Ca^{2+}$.

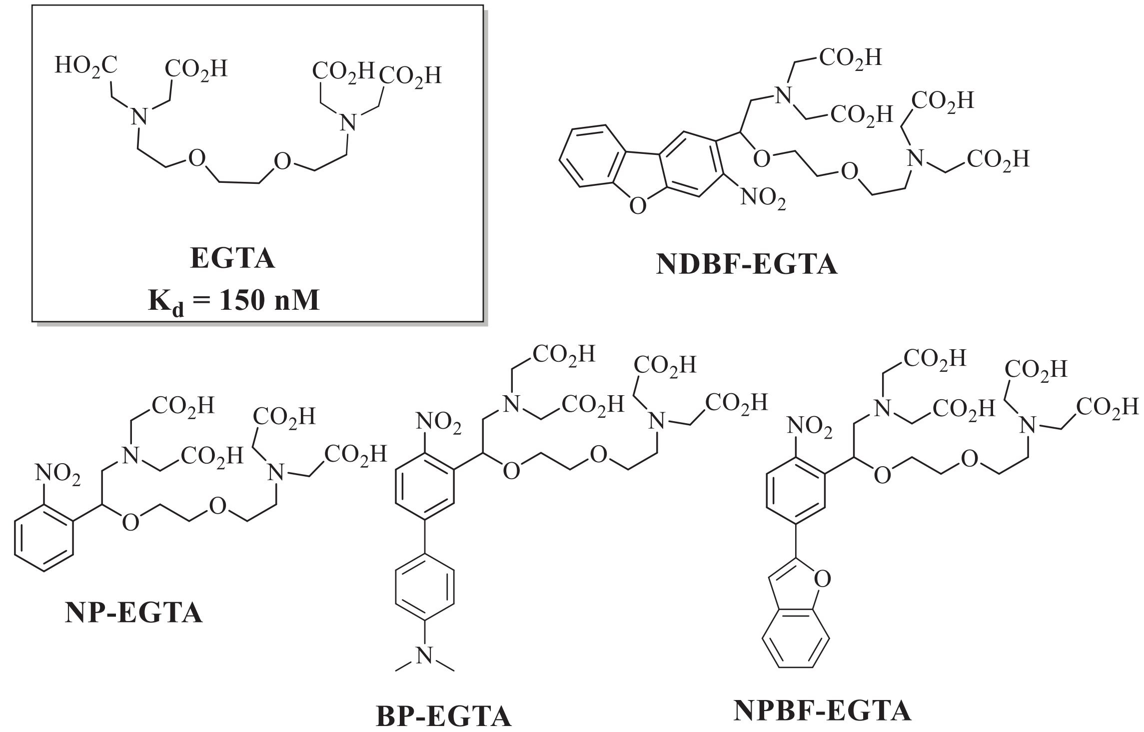


**Figure 7.** EGTA based calcium chelators.

## 1-6. Purpose of this research study

As mentioned above, in 2006, nitrodibenzofuran (NDBF) skeleton substituted with ethylene glycol tetraacetic acid (EGTA), which is known to be a selective Ca$^{2+}$ chelator[28,29], was reported to have the 2P uncaging efficiency value of about 0.6 GM at 720 nm. Nonetheless, to be applied to physiological studies, a high cross-section value in the TP uncaging reaction, at least 3 GM, is required. Therefore, in this research, new chromophores have been designed based on *ortho*-nitro (NB) PPG with dipolar character (D-π-A) to increase the 2P-uncaging efficiencies of caged calcium compounds.

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# Chapter 2

# Design and synthesis of two-photon responsive photolabile protecting group with a terphenyl unit for near IR calcium ion uncaging reaction

## 1-1. Introduction

In this study, new NIR-2P-responsive chromophores with *para*-terphenyl backbones featuring an ethylene glycol tetraacetic acid (EGTA) unit as a $Ca^{2+}$ selective chelator. One- and two-photon photochemical excitations of the synthesized *para*-terphenyl derivatives featuring two different electron-donating groups (dimethylamino ($NMe_2$) and methoxyl (OMe)) was investigated.

## 1-2. Design and synthesis of *p*-nitroterphenyl-EGTA derivatives

In 2012, Goeldner and co-workers developed biphenyl derivatives as highly 2P-responsive chromophores for caged glutamates and caged γ-aminobutyric acids with 2P-uncaging efficiencies of up to 11 GM at 800 nm and 3.2 GM at 740 nm[15]. In 2016, this laboratory reported EGTA-substituted nitrophenylbenzofuran and biphenyl derivatives (NPBF-EGTA and BP-EGTA) as caged calcium compounds with 2P uncaging efficiencies of 7.4 GM at 800 nm and 20.7 GM at 740 nm[40], respectively (Figure 8a). In comparison with these compounds, the addition of another benzene ring has been shown to give higher 2PA cross-section values (Figure 8b), as reported by Turro and co-workers in 2004[41] and Kamath and co-workers in 2014[42].

Computationally, the hyperpolarizability (β) of paraphenylenes has been predicted to be maximized in terphenylenes[43]. Indeed, a donor–acceptor-substituted terphenyl derivative was reported to possess a large dipole moment of 6.75 D[44]. Under such a background, in this study, EGTA-substituted p-nitroterphenyl (PNTP) derivatives with two different electron-donating groups (dimethylamino ($NMe_2$) and methoxy (OMe)) were synthesized and their photoreactions were investigated (Figure 8c).

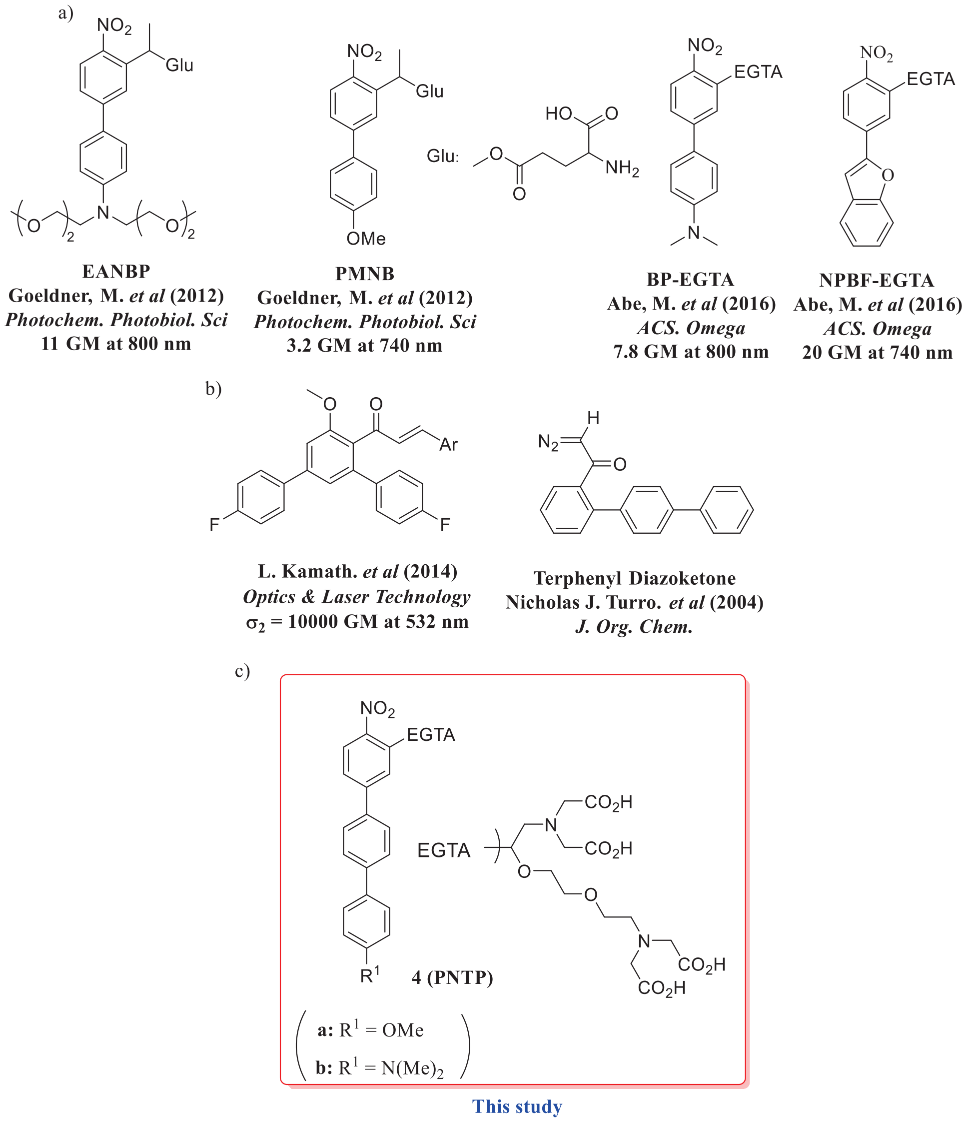
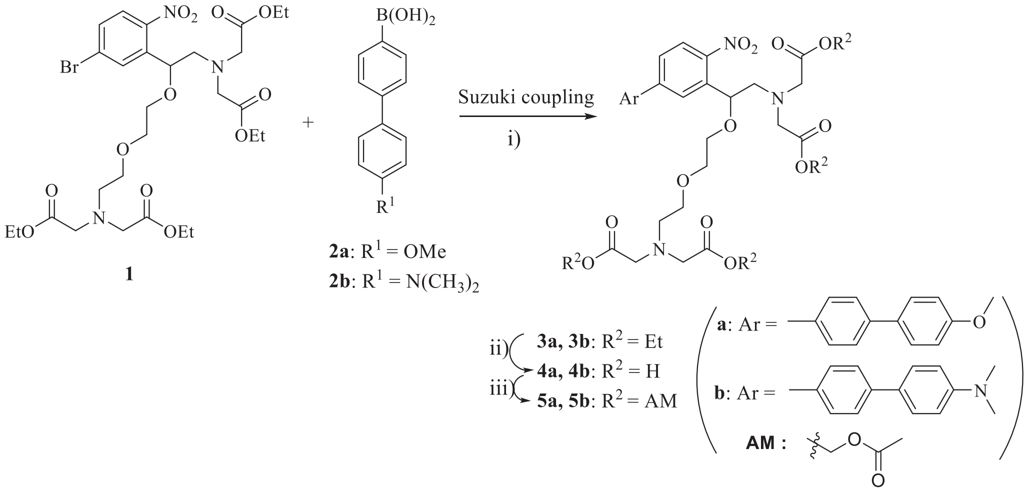


**Figure 8.** a) Structures and two-photon (2P) uncaging efficiencies of selected chromophores. b) example of 2P chromophores having terphenyl unit. c) this study.

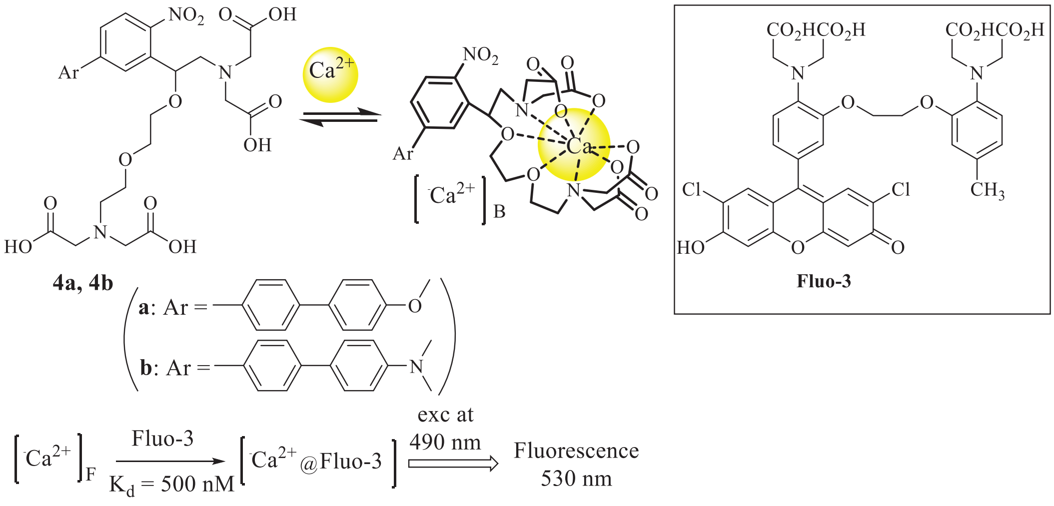
First, *p*-nitroterphenyl-EGTA derivatives with OMe and $NMe_2$ substituents is shown in Scheme 1. The Suzuki–Miyaura coupling reactions of key compound **1**[40] with biphenyl-substituted boronic acids **2a,b**[45,46] were conducted in the presence of $Pd(PPh_3)_4$ and $K_2CO_3$ to give target terphenyl derivatives **3a** (R = Et) and **3b** (R = Et) in 92% and 51% yield, respectively. Ethyl esters **3a,b** were hydrolyzed with KOH to afford tetraacids **4a** (R = H) and **4b** (R = H) in 90% and 89% yield, respectively. Corresponding acetoxy methyl (AM) esters **5a,b** (R = AM), which can be directly used for physiological studies[47], were synthesized in 30% and 17% yield, respectively. Because compounds **4a,b** are intended for use in physiological experiments, their thermal stability was investigated at room temperature and 37 °C in HEPES buffer (pH 7.4) under air. HPLC analyses demonstrated that compounds **4a,b** were stable for 36 h at 37 °C (Table S1).



**Scheme 1.** (i) **2a** or **2b**, $Pd(PPh_3)_4$, $K_2CO_3$, THF, $H_2O$, RT to 60 °C, 3 h, 92% for **3a** and 51% for **3b**; (ii) KOH, MeOH, 0 °C to RT, 16 h, 90% for **4a** and 89% for **4b**. ; (iii) bromomethyl acetate, DIPEA, DMF, 0 °C to RT, 16 h, 30% for **5a** and 17% for **5b**. DIPEA = *N,N*-diisopropylethylamine.

### 1-3. Measurement of calcium ion binding affinity

The dissociation constants ($K_d$) of **4a**,**b** for $Ca^{2+}$ were determined by titration using fluo-3 as a fluorescent dye[39,48,49] (Figure 9), which has a dissociation constant for $Ca^{2+}$ of 500 nM. For these experiments, the concentrations of free $Ca^{2+}$ ions ($[Ca^{2+}]_F$) in 1.0 mM solutions of **4a** and **4b** were obtained from the fluorescence intensity of fluo-3 at 530 nm (Figure 9a,c). Using Scatchard analyses (Figure 9b,d), the dissociation constants were determined to be $K_d$ = 202 nM for compound **4a** and $K_d$ = 213 nM for compound **4b**, which were similar values reported for the NPBF derivative[28].



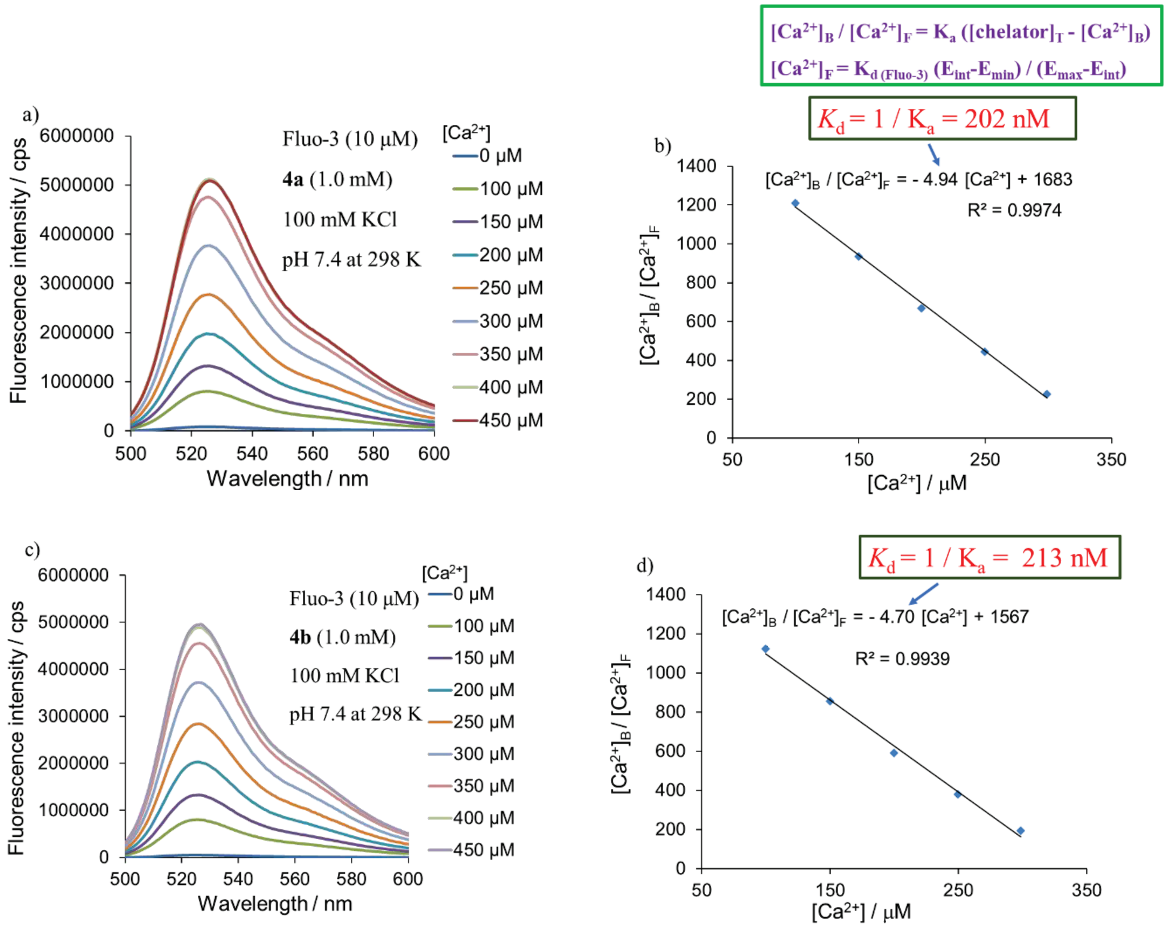


**Figure 9.** Emission spectra of fluo-3 (10 µM, excitation at 490 nm) obtained by titrating compound (a) **4a** and (c) **4b** (1.0 mM in HEPES/100 mM KCl, pH 7.4 at 298 K) with $Ca^{2+}$. (b) Scatchard analyses for (b) **4a** and (d) **4b** using a $K_d$ value of 500 nM for fluo-3 ($[Ca^{2+}]_B$ = bound calcium and $[Ca2^{+}]_F$ = free calcium).

## 1-4. Photophysical property

The photophysical properties including the 2P absorption values of **3a**,**b** and **4a**,**b** in DMSO and in HEPES buffer (pH 7.4) are summarized in Table 1. The electronic absorption spectra of **3a**,**b** and **4a**,**b** were obtained in DMSO and HEPES buffer (pH 7.4), respectively (Figure S25). The absorption maxima of **3a**,**b** were observed at 350 and 392 nm, respectively, in DMSO (entries 1 and 2), whereas those of **4a**,**b** were found at 344 and 363 nm, respectively, in HEPES buffer at pH 7.4 (entries 3 and 4). Thus, the 2PA maxima in the NIR region are expected to be ~700 nm for **3a**, ~780 nm for **3b**, ~690 nm for **4a**, and ~720 nm for **4b**.

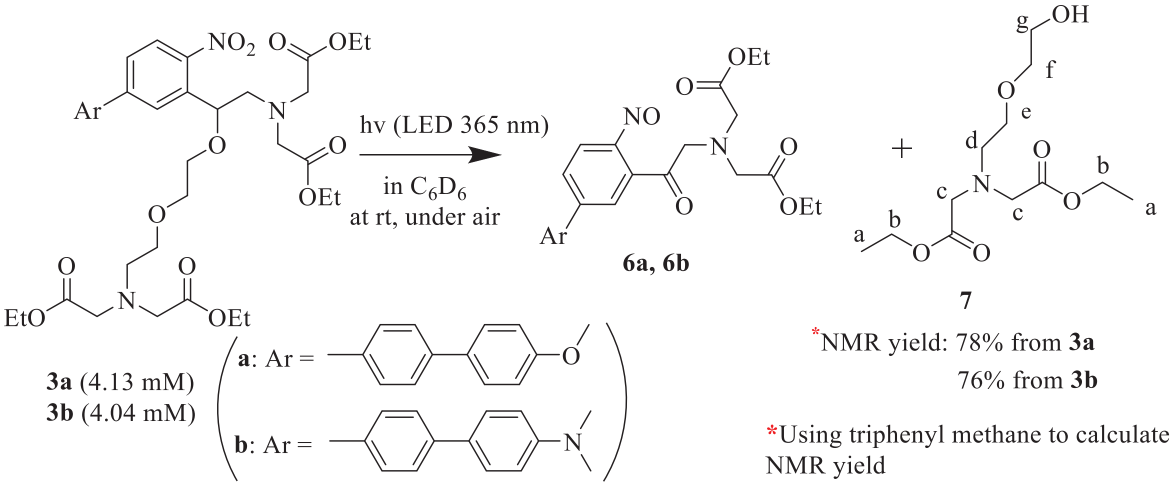
**Table 1.** Photophysical properties, and binding constants of compounds **3a,b** and **4a,b**

| entry | | Solv. | $K_d$ / nM[a] | $\lambda_{abs}$ / nm[b] | $\varepsilon$ / $M^{-1}$ $cm^{-1}$[c] |
|---|---|---|---|---|---|
| 1 | **3a**<br>($R^1$ = OMe) | DMSO | - | 350 | 16030 |
| 2 | **3b**<br>($R^1$ = $NMe_2$) | DMSO | - | 392 | 17102 |
| 3 | **4a**<br>($R^1$ = OMe) | HEPES buffer pH 7.4 | 202 | 344 | 14351 |
| 4 | **4b**<br>($R^1$ = $NMe_2$) | HEPES buffer pH 7.4 | 213 | 363 | 10371 |

[a]Dissociation constant determined by Scatchard analysis (Figure 9). [b]Absorption maximum. [c]Molar extinction coefficient.

### 1-5. One-photon (1P) photolysis

First, the 1P photochemical reactions of compounds **3a,b** in $C_6D_6$ were investigated using a 365 nm LED lamp. The photochemical reaction was directly monitored by $^1$H NMR (400 MHz) spectroscopy (Figure 10). The photolysis of **3a,b** results in the clean formation of bond-breaking product **7**. After 100% consumption of **3a,b**, triphenylmethane was added to the photolysate as an NMR standard to determine the NMR yields of compound **7** (78% from **3a** and 76% from **3b**; Figure 10). Compounds **6a,b**, which are thermally and photolabile, were not clearly identified in the photolysate. However, following quick column chromatography, the formation of compound **6b** was confirmed based on $^1$H-NMR and MS spectra (Figure S23 and S24). The quantum yield for the decomposition of **3a** ($R_1$ = OMe) was much higher than that of **3b** ($R_1$ = $NMe_2$) ($\Phi$ = 0.27 and 0.02, respectively). Ferric oxalate was used as a chemical actinometer to determine the quantum yield of the bond-breaking process (see experimental section)[50].



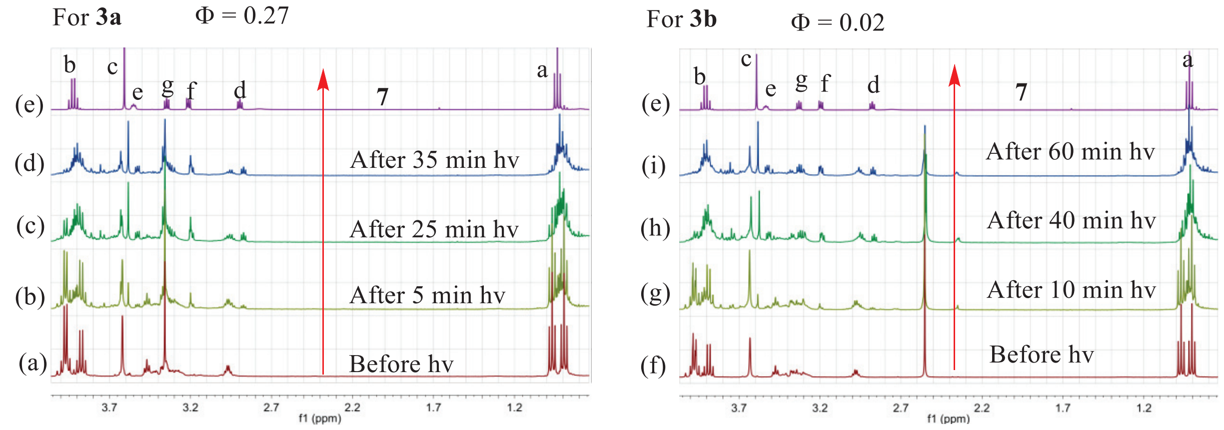
**3a** (4.13 mM)
**3b** (4.04 mM)

**6a, 6b**

**7**

*NMR yield: 78% from **3a**
76% from **3b**

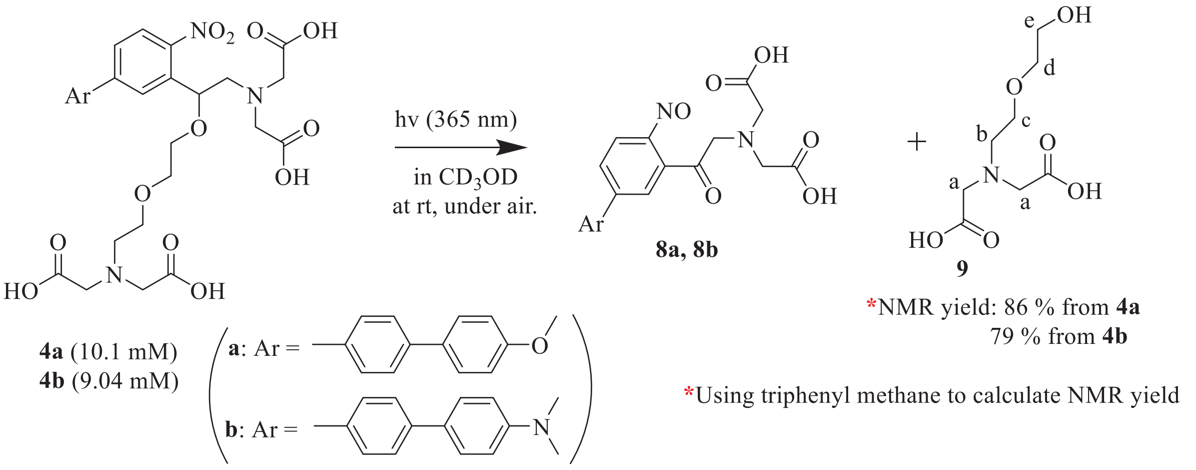
*Using triphenyl methane to calculate NMR yield


For **3a** Φ = 0.27

For **3b** Φ = 0.02

**Figure 10**. $^1$H NMR (400 MHz, δ 1-4 ppm) spectra during the photolysis of compounds **3a,b** in $C_6D_6$ using a 365 nm LED: (a) before irradiation of **3a**, (b) after 5 min irradiation of **3a**, (c) after 25 min irradiation of **3a**, (d) after 35 min irradiation of **3a**, (e) compound **7**, (f) before irradiation of **3b**, (g) after 10 min irradiation of **3b**, (h) after 40 min irradiation of **3b**, and (i) after 60 min irradiation of **3b**.

The 1P photochemical reactivities of compounds **4a,b** in $CD_3OD$ were also investigated using a 365 nm LED. The clean formation of compound **9** was observed during photolysis (Figure 11), indicating that EGTA derivatives **4a,b** can be used as caged $Ca^{2+}$ compounds. After photoirradiation, triphenylmethane was added to the photolysate as an NMR standard to determine the NMR yields of compound **9** (86% from **4a** and 79% from **4b**; Figure 11). The quantum yield for the decomposition of **4a** was also much higher than that of **4b** (Φ = 0.40 and 0.04, respectively). Thus, the quantum yields of *p*-nitroterphenyl compounds **3a** and **4a** with OMe substituents were much higher than those for *p*-nitrobiphenyl and *p*-nitroterphenyl compounds **3b** and **3b** with $NMe_2$ substituents. As $NMe_2$ is a better electron-donating group than OMe, the zwitterionic character of the $NMe_2$-substituted chromophore tends to slow down hydrogen abstraction from the benzylic position[51]. Similarly, low quantum yields have also been observed for amino-substituted caged compounds[52].



*NMR yield: 86 % from **4a**
79 % from **4b**

*Using triphenyl methane to calculate NMR yield

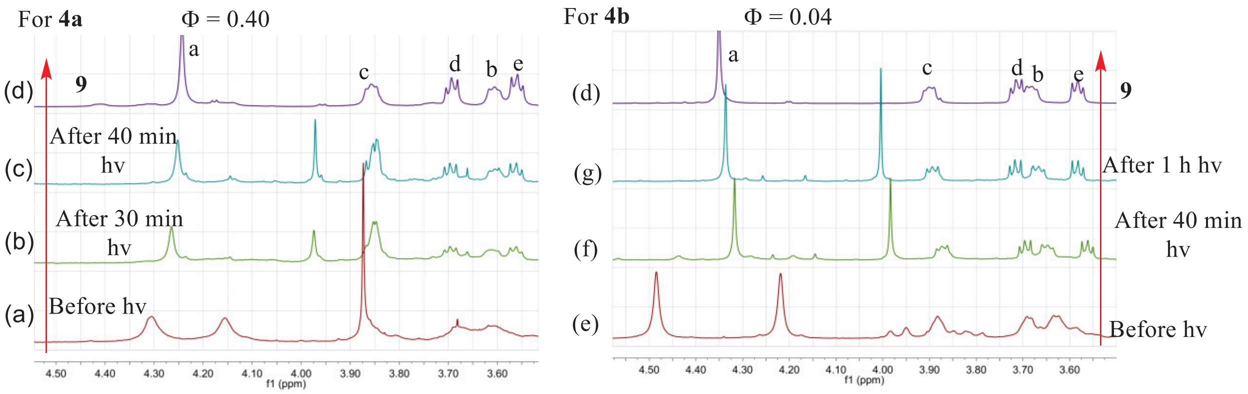
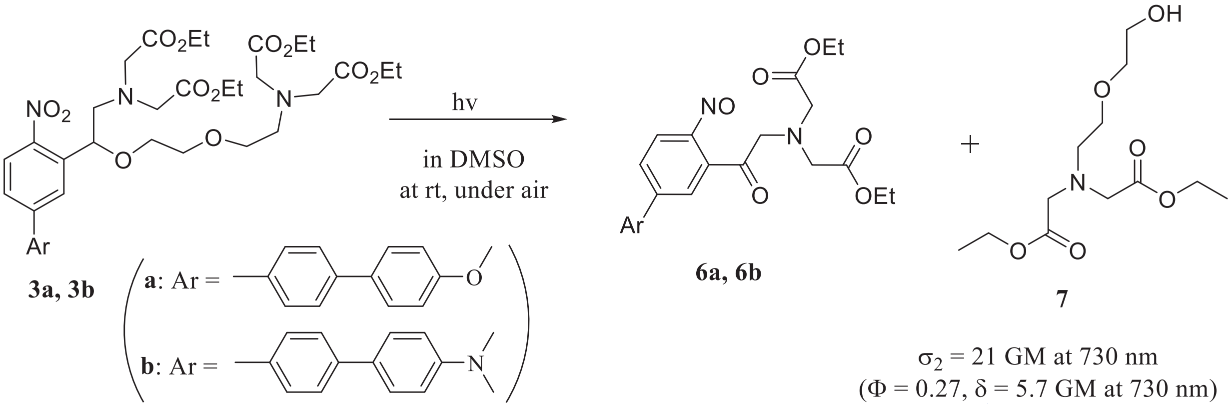


**Figure 11.** $^1$H NMR (400 MHz, δ 3.5–4.6 ppm) spectra during the photolysis of compounds **4a,b** in CD$_3$OD using a 365 nm LED: (a) before irradiation of **4a**, (b) after 30 min irradiation of **4a**, (c) after 40 min irradiation of **4a**, (d) compound **9**, (e) before irradiation of **4b**, (f) after 40 min irradiation of **4b**, and (g) after 1 h irradiation of **4b**.

## 1-6. Two-photon (2P) photolysis

2P excitation using NIR light was performed for **3a,b** in DMSO and **4a,b** in HEPES buffer pH 7.4[47]. The 2PE reactions were conducted at different wavelengths using a femtosecond Ti:sapphire laser (~700 mW) at ~25 °C (Figure 12,13). The 2P-induced decomposition of the compounds was monitored by HPLC. As shown by the time profiles in Figure 12a,c, and 13a,c, the photochemical decomposition of **3a,b**, and **4a,b** mainly depended on the photolysis wavelength. The action 2PA cross-sections at each wavelength were determined by comparing the rate constants with that of 2-(4-nitrophenyl)benzofuran, which has a cross-section of 18 GM at 720 nm[53]. The action 2PA spectra were extrapolated as shown in Figure 12b,d and 13b,d. The 2PA cross-sections and 2PA uncaging efficiencies are summarized in Table 2. NMe$_2$-substituted derivatives **4b** and **3b** had higher 2PA cross-section values (75 and 220 GM, respectively) than OMe-substituted derivatives **4a** and **3a** because the stronger electron-donating ability of $NMe_2$, which increased the 2P responsiveness of the chromophores. However, the 2P-uncaging efficiencies ($\delta_u = \sigma_2 \times \Phi_u$) of **4b** and **3b** (3.0 and 4.4 GM, respectively) were lower than those of **4a** and **3a** (3.3 and 5.7 GM, respectively) due to the lower quantum yields for the decomposition of **4b** and **3b**.



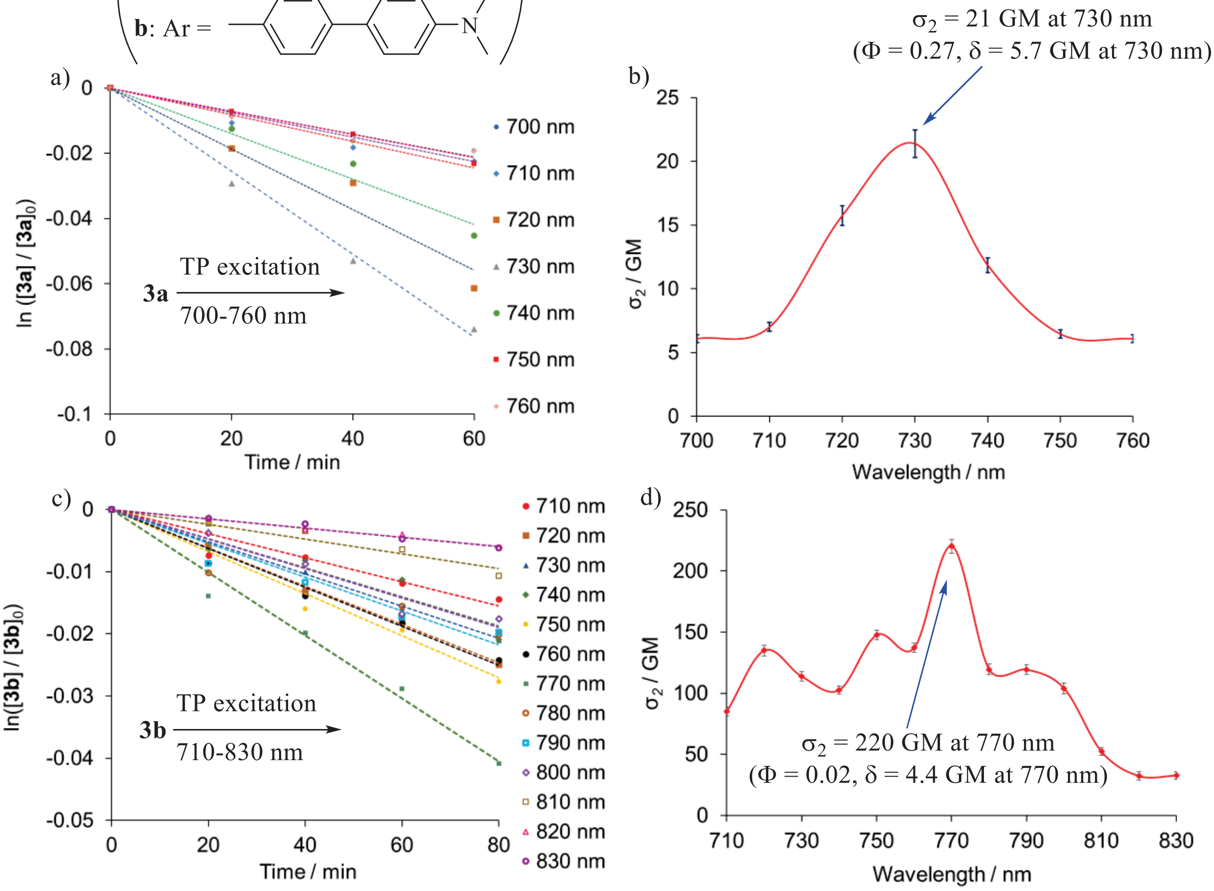


**Figure 12.** Time profiles for the 2P uncaging of (a) **3a**, ln([**3a**]/[**3a**]$_0$) vs. irradiation time at 700–760 nm, and (c) **3b**, ln([**3b**]/[**3b**]$_0$) vs. irradiation time at 710–830 nm. 2PA spectra (b) **3a** and (d) **3b**.

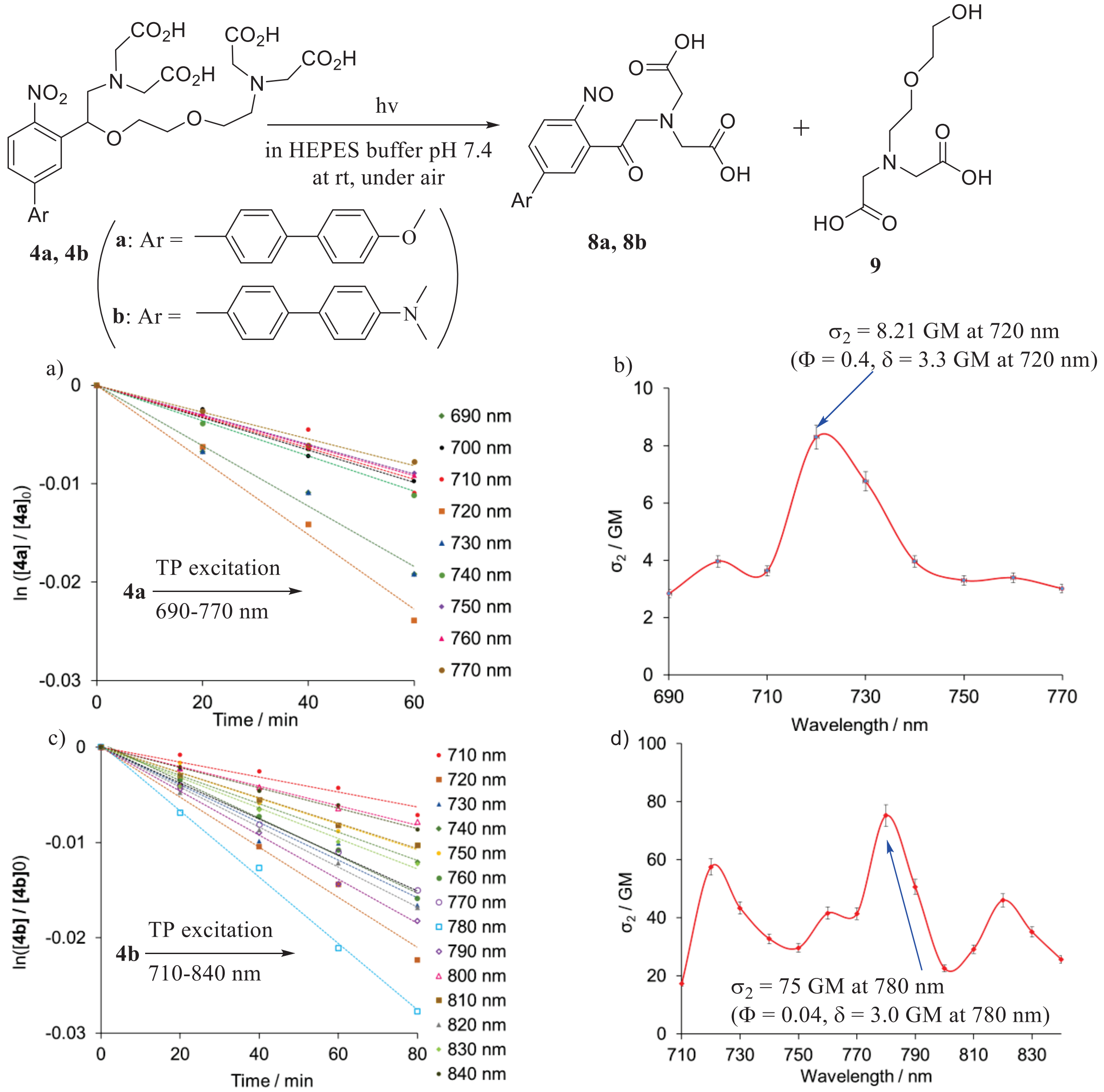


**Figure 13.** Time profiles for the 2P uncaging of (a) **4a**, ln([**4a**]/[**4a**]$_0$) vs. irradiation time at 690–770 nm, and (c) **4b**, ln([**4b**]/[**4b**]$_0$) vs. irradiation time at 710–840 nm. 2PA spectra of (b) **4a** and (d) **4b**.

## 1-7. Photochemical release of calcium ion

The release of $Ca^{2+}$ from $Ca^{2+}$@**4a**,**b** upon photolysis was confirmed by the 360 nm irradiation of a solution of **4a** or **4b** (1.00 mM), fluo-3 (0.01 mM), KCl (100 mM), and $CaCl_2$ (1.08 mM) in HEPES buffer at pH 7.4 (Figure 14). The fluorescence emission from $Ca^{2+}$@fluo-3 was used to confirm the release of $Ca^{2+}$. As shown in Figure 14, the emission intensity of $Ca^{2+}$@fluo-3 clearly increased during irradiation, indicating that photolysis results in the release of $Ca^{2+}$ from $Ca^{2+}$@**4a** or **4b**.

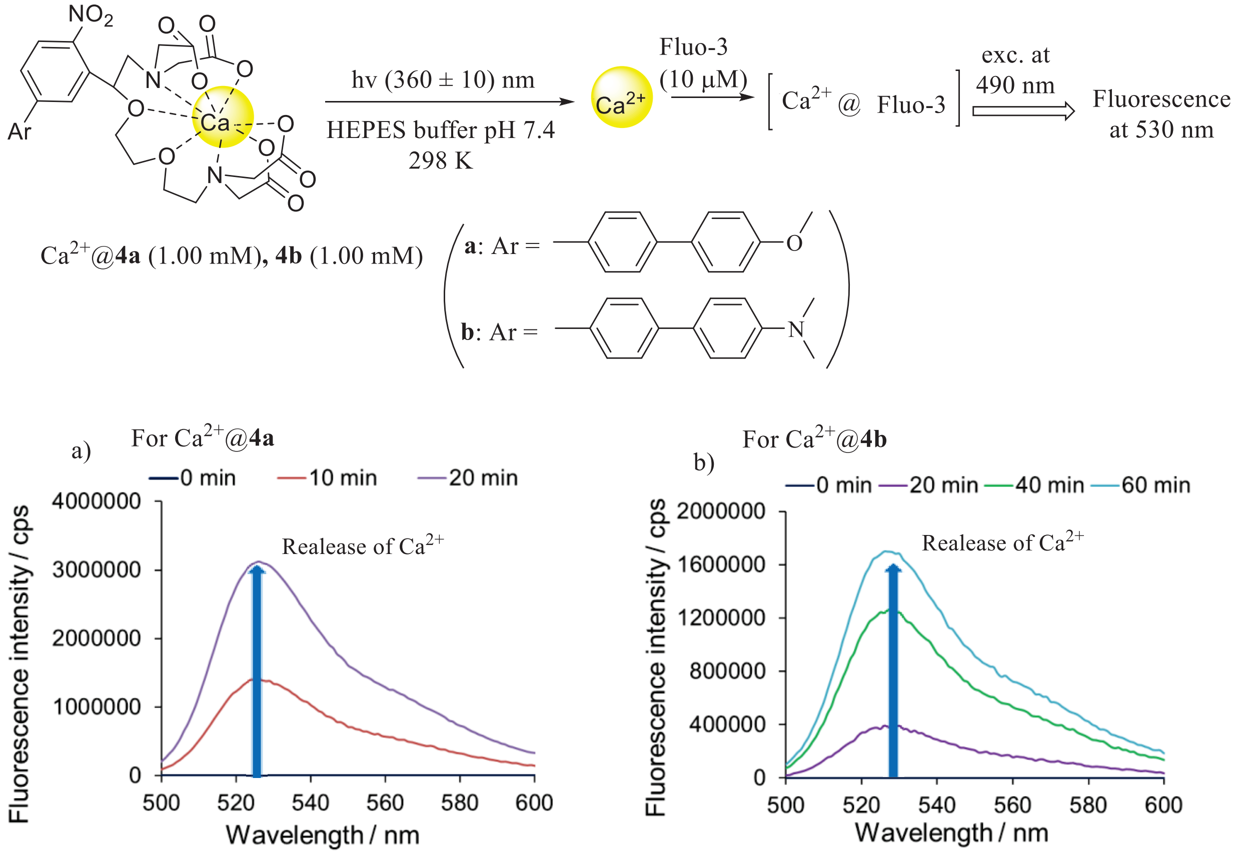
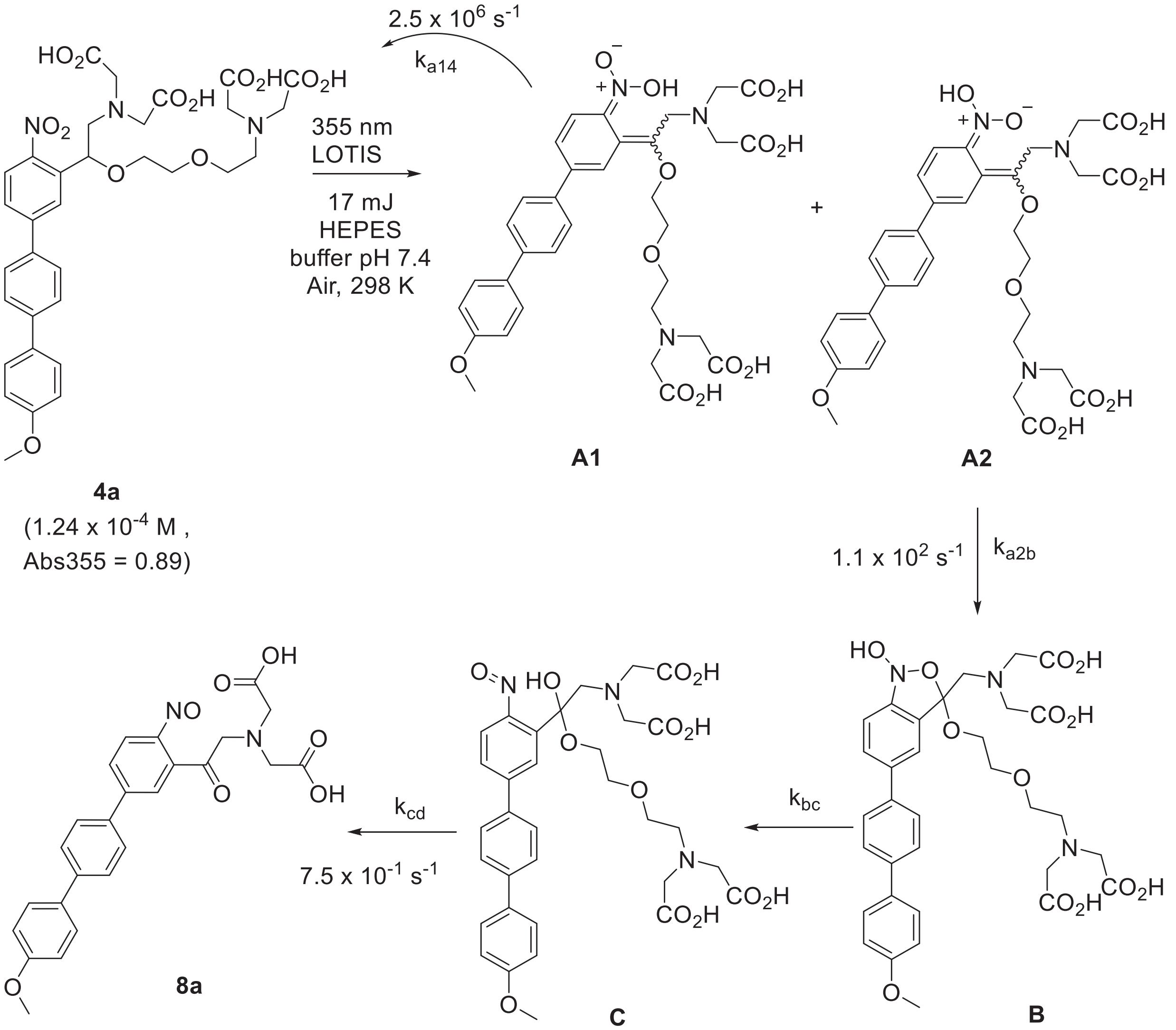


**Figure 14.** Emission spectra of $Ca^{2+}$@fluo-3 (0.01 mM, excitation at 490 nm) (a) after 20 min irradiation at 360 nm of **4a** (1.00 mM) and $Ca^{2+}$ (1.08 mM) in HEPES/100 mM KCl at pH 7.4, 298 K, and (b) after 60 min irradiation at 360 nm of **4b** (1.00 mM) and $Ca^{2+}$ (1.08 mM) in HEPES/100 mM KCl at pH 7.4, 298 K.

## 1-8. Laser flash photolysis

Based on the well-studied mechanism for the uncaging of *o*-nitrophenyl PPGs, the reaction pathway for the uncaging process of **4a** is shown in Scheme 2[54–57]. To obtain information on the rate constants of each process, transient absorption (TA) spectroscopy of **4a** was conducted using laser flash photolysis (LFP) at 355 nm (Nd-YAG, 10 ns pulse width, 17 mJ/pulse) on sub-nanosecond and sub-microsecond time scales (Figure 15a,b). Compound **4a** was selected for the LFP experiments because its quantum yield for photochemical decomposition was much higher than that of **4b**. First, the TA spectroscopy on the sub-microsecond time scale was used to investigate the photolysis of **4a** ($1.24 \times 10^{-4}$ M, Abs at 355 nm = 0.89) in HEPES buffer (pH 7.4) under air at ~298 K (Figure 8). LFP of **4a** resulted in bleaching at ~340 nm, the generation of an *aci*-nitro intermediate at ~420–440 nm, and a broad signal above 500 nm (Figure 15b).



**Scheme 2.** Reaction pathway for the uncaging of **4a**.

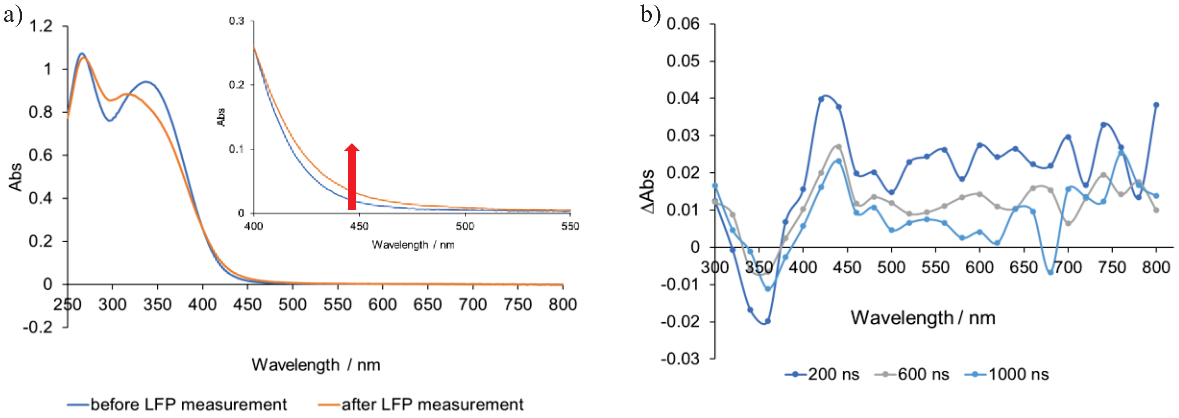
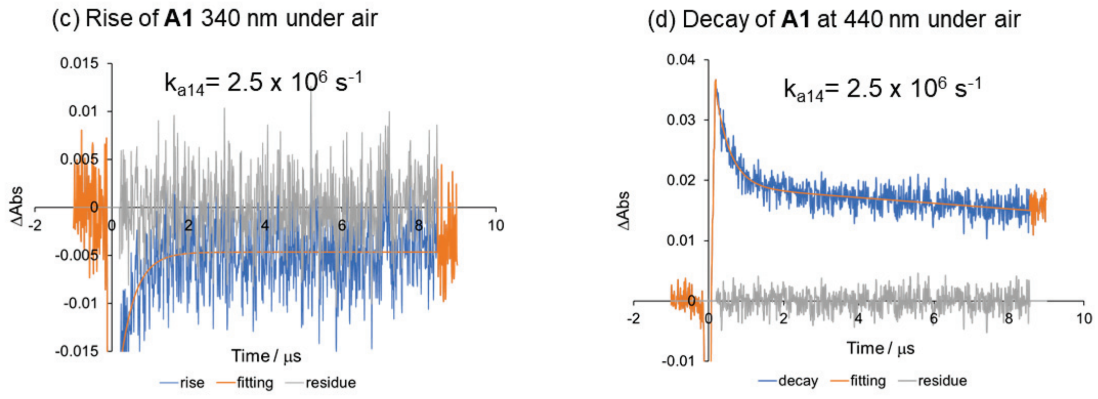


**Figure 15.** (a) UV-vis spectra of **4a** (0.124 mM, HEPES buffer (pH 7.4), Abs$_{355}$ = 0.89) under air before and after LFP measurements. (b) Sub-microsecond transient absorption of **4a** (0.124 mM, HEPES buffer (pH 7.4), Abs$_{355}$ = 0.89) under air.



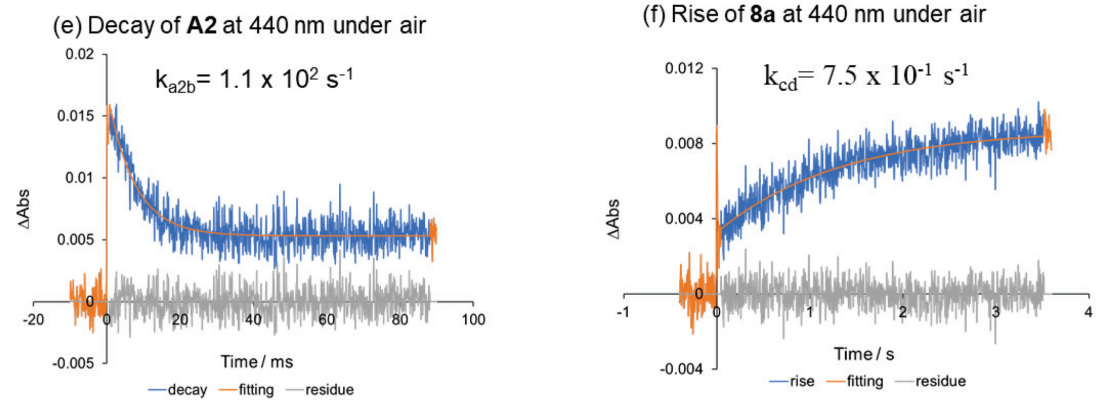


**Figure 16.** LFP time profiles (355 nm, Nd-YAG, 10 ns pulse width, 17 mJ/pulse) of **4a** (0.124 mM, HEPES buffer (pH 7.4), $Abs_{355} = 0.89$) at ~298 K: (c) rise of **4a** at 340 nm under air, (d) decay of **A1** at 420 nm under air, (e) decay of **A2** at 420 nm under air, (f) rise of **8a** at 420 nm under air.

The rate constant of the signal growth at 340 nm was determined to be $2.5 \times 10^6$ s$^{-1}$ (Figure 16c), and this process was assigned to the recovery of **4a** from *aci*-nitro intermediate **A1** via a [1,5] sigmatropic rearrangement[56]. This rate constant was consistent with one of the dual decay rate constants at 440 nm (those are $2.5 \times 10^6$ s$^{-1}$ and $1.1 \times 10^2$ s$^{-1}$; Figure 16d,e). The slow decay process was assigned to the formation of cyclic compound **B** from another isomer of *aci*-nitro intermediate **A2**[56] (Scheme 2). In addition to this relatively fast process, very slow signal growth was observed at 440 nm with $k = 7.5 \times 10^{-1}$ s$^{-1}$ (Figure 16f). This process was assigned to the formation of nitroso ketone compound **8a**[56], which is a product of the uncaging reaction. Indeed, an increase in the absorbance at ~420–450 nm was observed after the LFP experiments (Figure 15a).

## 1-9. Experiment section

**Diethyl 3,12-bis(2-ethoxy-2-oxoethyl)-5-(4''-methoxy-4-nitro-[1,1':4',1''-terphenyl]-3-yl)-6,9-dioxa-3,12-diazatetradecanedioate (3a):** Compound **1**[40] (300 mg, 0.43 mmol), (4'-methoxy-[1,1'-biphenyl]-4-yl)boronic acid **2a** (118 mg, 0.52 mmol), $Pd(PPh_3)_4$ (25 mg, 0.02 mmol), potassium carbonate (138 mg, 0.65 mmol) were mixed in 10 mL of $THF:H_2O$ (9:1) in a round-bottom flask. The resulting mixture was stirred for 3h at 60 °C. Then, the reaction mixture was filtered. The filtrate was washed with water and extracted with EtOAc. The organic layer was dried over $Na_2SO_4$. The solvent was removed under reduced pressure. The products were purified through silica gel column chromatography to give the desired coupling product **3a** (92%) as yellow oil. $^1$H-NMR of compound **3a** (400 MHz, $CDCl_3$): δ 8.11-8.04 (m, 2 H), 7.75-7.56 (m, 7 H), 7.03-6.97 (m, 2 H), 5.31 (dd, $J$ = 7.6 and 2.6 Hz, 1 H), 4.21-4.02 (m, 8 H), 3.87 (s, 3 H), 3.83-3.71 (m, 4 H), 3.63-3.43 (m, 10 H), 3.21-3.04 (m, 2 H), 2.96-2.81 (m, 2 H), 1.26 (t, $J$ = 7.21 Hz, 6 H), 1.19 (t, $J$ = 7.21 Hz, 6 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 171.67, 171.29, 159.46, 146.88, 145.97, 141.24, 137.51, 136.75, 132.57, 128.04, 127.68, 127.18, 126.13, 125.38, 114.26, 78.09, 70.23, 70.19, 68.90, 61.29, 60.30, 55.75, 55.65, 55.27, 53.61, 14.16, 14.09. IR: ν 2980, 2910, 2870, 1740, 1605, 1580, 1520, 1510, 1470, 1350, 1255, 1180, 1090, 1015 cm$^{-1}$. HRMS-ESI calcd for $C_{41}H_{53}N_3O_{13}Na$ $[M + Na]^+$ 818.34706, found 818.34625.

**3,12-Bis(carboxymethyl)-5-(4''-methoxy-4-nitro-[1,1':4',1''-terphenyl]-3-yl)-6,9-dioxa-3,12-diazatetradecanedioic acid (4a):** Compound **3a** (50 mg, 0.06 mmol) was dissolved in methanol (2 ml), and then hydrolyzed by the addition of KOH (17 mg, 0.31 mmol). The reaction mixture was stirred for 2 h at 60 °C. After evaporation of the solvent, the reaction mixture was acidified with 2N aqueous HCl to pH 2. The resulted yellow solid was taken and dried to afford **4a** (90%). $^1$H-NMR (400 MHz, $CD_3OD$) of compound **4a**: δ 8.26 (d, $J$ = 8.56 Hz, 1 H), 8.16-8.13 (m, 1 H), 7.96 (dd, $J$ = 8.62 and 2.02 Hz, 1 H), 7.86-7.76 (m, 4 H), 7.67-7.62 (m, 2H), 7.05-6.99 (m, 2H), 5.70-5.64 (m, 1 H), 4.60-4.43 (m, 3 H), 4.24-3.95 (m, 4 H), 3.92-3.44 (m, 14 H). $^{13}$C-NMR (100 MHz, $CD_3OD$): 169.75, 168.59, 161.31, 148.44, 148.14, 143.02, 135.11, 133.56, 129.14, 129.07, 128.39, 127.80, 127.43, 115.58, 75.20, 71.40, 69.60, 66.83, 61.18, 57.24, 56.88, 56.07, 55.94. IR: ν 3000, 2900, 2850, 1740, 1600, 1580, 1520, 1510, 1410, 1350, 1250, 1210, 1180, 1110, 1020 cm$^{-1}$. HRMS-ESI calcd for $C_{28}H_{36}N_4O_{12}$ $[M - H]^-$ 682.22536, found 682.22534, mp 170-172 °C.

**Bis(acetoxymethyl) 3,12-bis(2-(acetoxymethoxy)-2-oxoethyl)-5-(4''-methoxy-4-nitro-[1,1':4',1''-terphenyl]-3-yl)-6,9-dioxa-3,12-diazatetradecanedioate (5a):** To a solution of compound **4a** (80 mg, 0.1 mmol) in 3 mL of EtOH : THF : $H_2O$ (1: 1 : 1) was added LiOH (42 mg, 1.0 mmol) at 0 °C. and then, the reaction mixture was stirred for 16 h at room temperature. The reaction mixture was evaporated and dried under reduced pressure. The yellow color solid was dissolved in freshly distilled dry DMF (3 mL). *N,N*-Diisopropylethylamine (113 mg, 0.88 mmol) and bromomethyl acetate (449 mg, 2.94

mmol) were added at 0 °C, after 16 h stirring at room temperature the reaction mixture was diluted with water and extracted with ethyl acetate. The organic layer was washed with water, brine, dried over $Na_2SO_4$, and evaporated under reduced pressure. The reaction products were purified by silica gel column chromatography and recycling HPLC with GPC column to give the pure AM ester as a yellow color oil **5a** (30%). $^1$H-NMR (400 MHz, $CDCl_3$) of compound **5a**: δ 8.10 (d, $J$ = 8.5 Hz, 1 H), 8.05 (d, $J$ = 2.02 Hz, 1 H), 7.74-7.57 (m, 7 H), 7.04-6.98 (m, 2 H), 5.76 (s, 4 H), 5.67 (s, 4 H), 5.31-5.26 (m, 1 H), 3.91-3.80 (m, 7 H), 3.64-3.40 (m, 10 H), 3.21-3.05 (m, 2 H), 2.94-2.80 (m, 2 H), 2.11 (s, 6 H), 2.06 (s, 6 H). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ 170.71, 170.21, 169.77, 169.65, 159.78, 147.08, 146.40, 141.63, 137.53, 136.96, 132.78, 128.32, 127.96, 127.50, 126.88, 126.56, 125.78, 114.58, 79.38, 79.37, 78.42, 77.40, 70.52, 69.13, 61.40, 55.61, 55.56, 55.52, 53.83, 20.87, 20.81. IR: $v$ 3000, 2950, 2870, 1765, 1605, 1580, 1520, 1510, 1470, 1410, 1370, 1340, 1290, 1250, 1230, 1140, 1040 cm$^{-1}$. HRMS-ESI calcd for $C_{45}H_{53}N_3O_{21}Na$ $[M + Na]^+$ 994.30638, found 994.30621.

**Diethyl-5-(4’’-(dimethylamino)-4-nitro-[1,1’:4’,1”-tephenyl]-3-yl)-3.12-bis(2-ethoxyl-2-oxoethyl)-6,9-dioxa-3,12-diazatetradecanedioate (3b):** In a round-bottom flask, compound **1** (114 mg, 0.20 mmol), (4'-methoxy-[1,1'-biphenyl]-4-yl)boronic acid **2b** (231 mg, 1.00 mmol), $Pd(PPh_3)_4$ (10.1 mg, 0.24% mmol) was degassed with $N_2$ for 30 min. potassium carbonate (41 mg, 0.22 mmol) dissolved in $H_2O$ (2 mL) and THF (18 mL) was added in the mixture. The solution heated to 60 °C for 3 h. The reaction was cooled to room temperature and the reaction mixture was filtered. The filtrate was washed with water and extracted with EtOAc. The organic layer was dried over $Na_2SO_4$. The solvent was removed under reduced pressure. The products were purified through silica gel column chromatography and further purified by recycling HPLC with gel permeation chromatography (GPC) column to give the desired coupling product **3b** (82 mg, 51%) as an orange color oil. $^1$H-NMR (400 MHz, $CDCl_3$) of compound **3b**: δ 8.09 ppm (m, 2H), 6.82 ppm (d, $J$ = 8.6 Hz, 2H), 7.57 ppm (d, $J$ = 8.6 Hz, 2H), 7.64 ppm (s, 4H), 7.64 ppm (dd, $J$ = 8.6 Hz & $J$ = 1.9 Hz, 1H), 5.31 ppm (m, 1H), 4.13 (q, 4H), 4.06 (q, 4H), 3.74 ppm – 3.83 ppm (m, 4H), 3.60 ppm – 3.47 ppm (m, 10H), 3.07 ppm – 3.19 ppm (m, 2H), 2.85 ppm - 2.91 ppm (m, 2H), 1.24 (t, $J$ = 7.3 Hz, 6H), 1.17 (t, $J$ = 7.3 Hz, 6H), 3.02 ppm (s, 6H). $^{13}$C-NMR (100 Hz, $CDCl_3$): δ 171.8, 171.3, 150.3, 146.9, 146.3, 141.8, 137.6, 136.0, 127.9, 127.7, 126.7, 126.1, 125.5, 112.8, 78.3, 70.3, 69.0, 61.4, 60.3, 55.9, 55.7, 53.9, 40.5, 14.3, 14.2. IR: $v$ 2917, 2849, 1766, 1600, 1512, 1369, 1347, 1225, 1139, 1048, 1007, 985, 815. HRMS-ESI: calcd for $C_{42}H_{56}N_4O_{12}Na$ $[M + Na]^+$ 831.37869, found 831.37860.

**3,12-Bis(carboxymethyl)-5-(4-(dimethylamino)-4-nitro-[1,1-terphenyl]-3-yl)-6,9-dioxa-3,12-diazatetradecanedioic acid (4b):** In a round-bottom flask, compound **3b** (26 mg, 0.03 mmol) was dissolved in methanol (1 mL) and then hydrolyzed by the addition of KOH (10 mg, 0.19 mmol). The reaction mixture was stirred for 2 h at 60 °C. After evaporation of the solvent, the reaction mixture was acidified with 1N aqueous HCl to pH

1. The resulted yellow solid was taken and dried to afford **4b** (19 mg, 89%). $^1$H-NMR (400 MHz, $CD_3OD$) of compound **4b**: δ 8.28 ppm (d, *J* = 9.10 Hz, 1H), 8.17 ppm (s, 1H), 8.00 – 7.93 ppm (m, 7H), 7.80 ppm (d, *J* = 8.3 Hz, 2H), 5.69 ppm (d, *J* = 7.9 Hz, 1H), 4.50 ppm (s, 4H), 4.21 ppm (s, 4H), 4.00-3.57 (m, 10H), 4.06 (q, *J* = 7.1 Hz, 4H), 3.74 ppm – 3.83 ppm (m, 4H), 3.60 ppm – 3.47 ppm (m, 10H), 3.35 ppm (s, 3H) , 3.35 ppm (s, 3H). $^{13}$C-NMR (100 Hz, $CD_3OD$): δ 167.5, 166.9, 147.3, 146.3, 142.3, 141.7, 139.7, 137.9, 133.3, 128.7, 128.1, 127.9, 127.7, 126.7, 126.0, 120.9, 73.2, 69.9, 68.1, 65.3, 59.4, 55.8, 55.1, 45.7. IR: *v* 2928, 2581, 1735, 1604, 1517, 1341, 1253, 1133, 1107, 899, 822. HRMS-ESI: calcd for $C_{34}H_{39}N_4O_{12}$ $[M - H]^-$ 695.25590, found 695.25873, mp 148-150 °C.

**3,12-Bis(carboxymethyl)-5-(4-(dimethylamino)-4-nitro-[1,1-terphenyl]-3-yl)-6,9-dioxa-3,12-diazatetradecanedioate (5b):** In a round-bottom flask, compound **4b** (26 mg, 0.04 mmol) was dissolved in freshly distilled dry DMF (0.56 mL). *N,N*-Diisopropylethylamine (0.13 mL, 0.76 mmol) and bromomethyl acetate (0.07 mL, 0.76 mmol) were added at 60 °C. After 24 h of stirring at room temperature, the reaction mixture was diluted with water and extracted with dichloromethane. The organic layer was washed with water and brine solution, dried over $Na_2SO_4$, and evaporated under reduced pressure. The reaction products were purified using silica gel column chromatography and further purified by recycling HPLC with gel permeation chromatography column (GPC) to give compound **5b** (6.50 mg, 17%) as a yellow color oil. $^1$H-NMR (400 MHz, $CDCl_3$) of compound **5b**: δ 8.08 ppm (d, *J* = 8.64 Hz, 1H), 8.06 ppm (m, 1H), 7.64 ppm (s, 4H), 7.64 ppm (m, 1H), 7.57 ppm (d, *J* = 8.6 Hz, 2H), 6.82 ppm (d, *J* = 8.6 Hz, 2H), 5.77 (s, 4H), 5.68 (s, 4H), 5.29 ppm (m, 1H), 3.87 ppm (m, 4H), 3.70 ppm – 3.47 ppm (m, 12H), 3.08 ppm – 3.17 ppm (m, 2H), 3.08 ppm – 3.17 ppm (m, 2H), 2.87 ppm - 2.90 ppm (m, 2H), 2.07 (s, 6H), 2.12 (s, 6H), 3.02 ppm (s, 6H). $^{13}$C-NMR (100 Hz, $CDCl_3$): δ 170.5, 170.0, 169.6, 169.4, 150.3, 146.7, 146.4, 141.9, 137.3, 135.9, 127.8, 127.7, 127.6, 126.7, 126.5, 126.2, 125.5, 112.7, 79.2, 77.2, 70.5, 70.3, 68.9, 61.2, 56.4, 56.3, 53.6, 40.4 ($CH_3$), 20.7, 20.6. HRMS-ESI: calcd for $C_{46}H_{56}O_{20}N_4Na$ $[M + Na]^+$ 1007.33765, found 1007.33801.

**$Ca^{2+}$ binding affinities:** The association constant ($K_a$) of newly synthesized chelator **1a** and **1b** was determined using the reported method[39,48,49] by Ellis-Davies *et al.* by the equation:

$[Ca^{2+}]_B / [Ca^{2+}]_F = K_a ([\text{chelator}]_T - [Ca^{2+}]_B)$

Here $[Ca^{2+}]_B$ is the concentration of $Ca^{2+}$ bound to the chelator, $[Ca^{2+}]_F$ is the concentration of the free $Ca^{2+}$ and $[\text{chelator}]_T$ is the total concentration of chelator **4a** (TP-EGTA acid with methoxyl-substituted) or **4b** (TP-EGTA acid with dimethylamino-substituted) in the solution. The free calcium concentration and bound calcium concentration were measured from emission spectra of calcium sensitive dye (fluo-3, $K_d$ = 500 nM) through the titration with aqueous calcium chloride solution.

In this procedure, chelator (1.0 mM), fluo-3 (0.01 mM), HEPES (10 mM), and 100 mM KCl solutions were used. A 3.0 mL solution of 1.0 mM of chelator was used. The solution was buffered to pH 7.4 with HEPES and the ionic strength was set with 100 mM KCl. Titration with incremental addition of $Ca^{2+}$ gave the plot shown in Figure 9. $[Ca^{2+}]_B/[Ca^{2+}]_F$ were obtained from the emission spectra in Figure 9. The concentration of chelator was adjusted to be 1.0 mM and the $CaCl_2$ concentrations were 0.1, 0.15, 0.2, 0.25, 0.3, 0.35, 0.4 and 0.45 mM for the compound **4a** and **4b**, respectively. The intensity of the emission at 530 nm did not change over 0.45 mM of $CaCl_2$ for these two compounds.

The free calcium concentrations were calculated from the following equation.

$$[Ca^{2+}]_F = K_d\ (E_{int}-E_{min})\ /\ (E_{max}-E_{int})$$

Where $K_d$ = 500 nM (fluo-3), $E_{int}$ = emission intensity of chelator at setted $Ca^{2+}$ concentration, $E_{min}$ = emission intensity of chelator without $Ca^{2+}$, $E_{max}$ = emission intensity of chelator with excess $Ca^{2+}$.

**Chemical actinometer for quantum yield measurement[50]:** The rate of photo uncaging reaction can be quantified by quantum yield (Φ).

$$\Phi = \frac{\text{number of reacted molecules per time unit}}{\text{number of photons absorbed per time unit}}$$

Chemical actinometers are widely used to measure photon fluxes, one of the most popular and reliable one i.e., ferrioxalate, during the photo irradiation the potassium ferrioxalate decomposes according to the following equations.

$$Fe(C_2O_4)_3^{3+} \xrightarrow{hv} Fe^{2+} + C_2O_4^{-} + 2C_2O_4^{2-}$$

$$Fe^{2+} + 3phen \longrightarrow Fe(phen)_3^{2+}$$

The number of ferrous ions formed during a photoirradiation is measured by conversion to the colored tris-phenanthroline compound at 510 nm (ε = 11100 $M^{-1}$ $cm^{-1}$). The original ferric ions are not substantially complexed by 1,10-phenanthroline and the complex does not absorb at 510 nm.

TP-EGTA has absorption maximum around 360 nm, in this study measured the light quantities at 360 nm using a xenon lamp with a monochromator as a light source. The equation as below

$$I\ (\text{mol/s}) = \frac{\text{moles of } Fe^{2+}}{\Phi_\lambda \times t \times F} = \frac{V_1 \times V_3 \times \Delta A(510\ \text{nm})}{10^3 \times V_2 \times l \times \varepsilon\ (510\ \text{nm}) \times \Phi_\lambda \times t}$$

$V_1$: the irradiated volume (mL)

$V_2$: the aliquot of the irradiated solution taken for the determination of the ferrous ions (mL)

$V_3$: the final volume (mL)

ΔA: the optical difference in absorbance between the irradiated solution and that taken in the dark l: optical pathlength of the irradiation cell

ε (510 nm): ε of the complex $Fe(phen)_3^{2+}$

$\Phi_\lambda$: the quantum yield of ferrous ion production at the irradiation wavelength

t: the irradiation time

F: mean function of light absorbed by the ferrioxalate solution

Procedure for measurement:

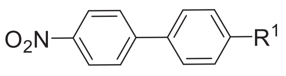
1. 117.7 mg of $K_3[Fe(C_2O_4)_3] \cdot 3H_2O$ was dissolved in 20 mL of 0.05 M $H_2SO_4$. (0.012 M Ferrioxalate was prepared)-solution-1
2. 10.2 mg of 1,10-phenanthroline monohydrate and 2.25 gram of $CH_3COONa \cdot 3H_2O$ were dissolved in 10 mL of 0.5 M $H_2SO_4$- solution-2
3. Both solutions were degassed with nitrogen for 20 minutes.
4. 3 mL solution of solution-1 irradiated at 360 nm for 0, 10, 20 and 30 seconds, 0.5 mL of solution solution-2 was added each time then measured the absorption spectra at 510 nm to measure the change in absorbance with respect to an irradiation time was used to calculate the light amount.

Calculated number of photons from Xe-lamp at 360 nm= $3.94 \times 10^{-7}$ mol/min.

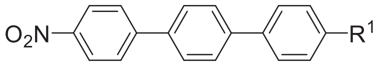
## 1-10. Supplementary material

### 1PA and 2PA of compounds 1'a,b and 2'a,b.

First, *p*-nitrobiphenyl **1'a**,**b** and *p*-nitroterphenyl **2'a**,**b** without EGTA groups were synthesized and their photophysical properties were investigated to understand the effects of extending $\pi$-conjugation and the OMe and NMe$_2$ substituents on the 1P and 2P responses. These four compounds were synthesized via Suzuki–Miyaura coupling reactions[44,45,58,59] (Scheme S1 and Figure S6–S10)



**1'a-b**



**2'a-b**

**a**: $R^1$ = OMe
**b**: $R^1$ = NMe$_2$

As shown in Table 1 (Figure S1), the absorption maxima of **1'a** and **2'a** ($R^1$ = OMe) shifted bathochromically with increases in the number of phenyl rings and the solvent polarity (335 nm for **1'a** in toluene (Tol) (entry 1), 338 nm for **1'a** in CHCl$_3$ (entry 2), 348 nm for **1'a** in dimethyl sulfoxide (DMSO) (entry 3), 339 nm for **2'a** in Tol (entry 4), 344 nm for **2'a** in CHCl$_3$ (entry 5), and 352 nm for **2'a** in DMSO (entry 6)). The observation is rationalized by the extension of the $\pi$-system and the stabilization of the intramolecular charge transfer (ICT) state in polar solvents. In contrast, in the case of NMe$_2$, which is a stronger electron-donor compared to OMe, the absorption maximum of terphenyl derivative **2'b** was hypsochromically shifted relative to that of biphenyl derivative **1'b**, despite the increase in the number of phenyl rings (398 nm for **1'b** in Tol (entry 7), 407 nm for **1'b** in CHCl$_3$ (entry 8), 423 nm for **1'b** in DMSO (entry 9), 361 nm for **2'b** in Tol (entry 10), 362 nm for **2'b** in CHCl$_3$ (entry 11), and 372 nm for **2'b** in DMSO (entry 12)). Compound **2'b** showed a much smaller bathochromic shift in polar solvents than **1'b**, indicating that the excited state of **2'b** has less ICT character of than that of **1'b**. In other words, the strong ICT character in the excited state of **1'b** is predominant in determining the absorption maximum of **1'b**, whereas the conjugation effect dominates the absorption maximum of **2'b**[60].

Interestingly, compounds **1'b** and **2'b** exhibited strong emission in nonpolar Tol (Figure S2c,e) but manifested nil or very weak emission in polar solvent (entries 7–12, Figure S2d). The fluorescence quantum yields of **1'b** and **2'b** were 0.66 and 0.20 in Tol, respectively (entries 7 and 10). In contrast, compound **1'a** showed weak emission in DMSO (entry 3, Figure S2a) but no emission in nonpolar solvents (entry 1). Similarly, **2'a** only exhibited weak emission in chloroform (entry 5, Figure S2b). This behavior can be explained using the lowest-energy excited state, at least for the behavior in Tol. In the case of chromophores with strong donor–acceptor groups, the ICT of the $\pi$–$\pi^*$ transition shifts to a lower energy, resulting in the corresponding excited state lying below that of the n–$\pi^*$ transition. For the weaker electron-donating group (–OMe), because the n–$\pi^*$ transition is at a lower energy, no emission or weak emission occurs[51] (Table S1). The fluorescence lifetimes of **1'b** and **2'b** were determined to be <1 ns by time-correlated single-photon counting technique (entries 7 and 10). The 2PA cross-sections ($\sigma_2$) of **1'b** and **2'b**, as determined by 2P-excited florescence measurements, were 44 and 13.9 at 830 nm and 810 nm, respectively (entries 7 and 10, Figure S4).

To gain further insight into the electronic excitation process, the absorption spectra of compounds **1'a,b** and **2'a,b** were computed at the TD-B3LYP/6-31G(d) level of theory in the gas phase. In the computed geometries, all the chromophores possessed significant twist angles between the phenyl groups (~35°). In all cases, the $NO_2$ moiety was coplanar with the adjacent ring. The $NMe_2$ group was also nearly coplanar with the adjacent benzene ring (Figure S26). A bathochromic shift of **2'b** (477 nm) relative to **1'b** (423 nm) was found in the TD-DFT calculation, which was not consistent with the experimental observation (entries 7 and 10, Table S1). However, it has been reported that the charge transfer transition from the highest-occupied-molecular-orbital (HOMO) to the lowest-unoccupied-molecular-orbital (LUMO) is overestimated by the TD-B3LYP/6-31G(d) level of theory[61–63]. When the four compounds were calculated at the TD-M06-2X and TD-CAM-B3LYP level of theory with the SMD solvent model[64], the trend experimentally observed in the absorption spectra was well reproduced, although the absolute values were all blue-shifted (~30 nm for **1'a** and **2'a** and ~60–70 nm for **1'b** and **2'b**; Table S1). For example, the computed absorption maxima in Tol, $CHCl_3$, and DMSO were 338, 346, and 349 nm, respectively, for compound **1'b** (entries 7–9), whereas the experimentally observed absorption maxima were 398, 407, and 423 nm, respectively.

**Table S1.** Experimental and theoretical photophysical data for 1PA and 2PA of **1’a,b** and **2’a,b**.

| Entry | | Solv. | $\lambda_{abs}$ / nm[a] | $\varepsilon$ / $M^{-1}$ $cm^{-1}$[b] | $\lambda_{abs}$ / nm[c] ($f$)[k] | $\lambda_{abs}$/ nm[d] ($f$)[k] | $\lambda_{abs}$ / nm[e] ($f$)[l] | $\lambda_{em}$ / nm[f] | $\Phi_{flu}$[g] | $\tau$ / ns[i] | $\sigma_2$ / GM[j] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Bi-OMe **1’a** | Tol | 335 | 15756 ± 97 | 360 (0.38) | 296 (0.78) | 300 (0.59) | nd | nd | nd | nd |
| 2 | | $CHCl_3$ | 340 | 14512± 100 | | 301 (0.76) | 305 (0.74) | nd | nd | nd | nd |
| 3 | | DMSO | 349 | 13481 ± 6 | | 302 (0.75) | 307 (0.74) | 554 | 0.032 ± 0.005 | nd | nd |
| 4 | Ter-OMe **2’a** | Tol | 341 | 33089 ± 87 | 400 (0.37) | 302 (1.15) | 304 (0.59) | nd | nd | nd | nd |
| 5 | | $CHCl_3$ | 343 | 27710 ± 135 | | 306 (1.04) | 311 (1.06) | 589 | 0.053 ± 0.0006 | nd | nd |
| 6 | | DMSO | 352 | 23827 ± 112 | | 308 (1.09) | 312 (1.08) | 680 | nd | nd | nd |
| 7 | Bi-$NMe_2$ **1’b** | Tol | 398 | 17219 ± 167 | 423 (0.39) | 338 (0.84) | 339 (0.83) | 536 | 0.66 ± 0.01 | (<1 ns, 2.61) | 44 (830 nm) |
| 8 | | $CHCl_3$ | 407 | 17613 ± 146 | | 346 (0.83) | 347 (0.81) | 668 | 0.012± 0.00036[h] | nd | nd |
| 9 | | DMSO | 423 | 17718 ± 3 | | 349 (0.81) | 350 (0.80) | nd | nd | nd | nd |
| 10 | Ter-$NMe_2$ **2’b** | Tol | 361 | 8860 ± 32 | 477 (0.28) | 331 (1.02) | 328 (1.02) | 565 | 0.20 ± 0.005 | (<1 ns, 2.09) | 13.9 (810 nm) |
| 11 | | $CHCl_3$ | 362 | 15243 ± 5 | | 335 (1.01) | 331 (1.00) | nd | nd | nd | nd |
| 12 | | DMSO | 372 | 9099 ± 5 | | 339 (1.03) | 336 (1.01) | nd | nd | nd | nd |

[a] Absorption maximum measured in Tol, $CHCl_3$, or DMSO. [b] Molar extinction coefficient. [c] Absorption maximum in the gas phase calculated at the TD-DFT/B3LYP/6-31G(d) level of theory in Gaussian 09. [d] Absorption maximum calculated at the TD-M06-2X/6-31G(d) level in Gaussian 09 using the SMD solvent model. [e] Absorption maximum calculated at the TD-DFT/CAM-B3LYP/6-31G(d) level in Gaussian 09 using the SMD solvent model. [f] Emission maximum measured in Tol, $CHCl_3$, or DMSO. [g] Fluorescence quantum yield measured in Tol, $CHCl_3$ or DMSO using 9,10-diphenylanthracene ($\Phi_f = 0.84$) as a standard. [h] Rhodamine B ($\Phi_f = 0.5$) was used as the fluorescence quantum yield standard. [i] Fluorescence lifetimes observed at 536 and 565 nm for **1’b** and **2’b**, respectively. [j] 2P cross-section measured using the 2PE fluorescence method in Tol with a chromophore concentration $1 \times 10^{-3}$ M. [k] Oscillator strength.

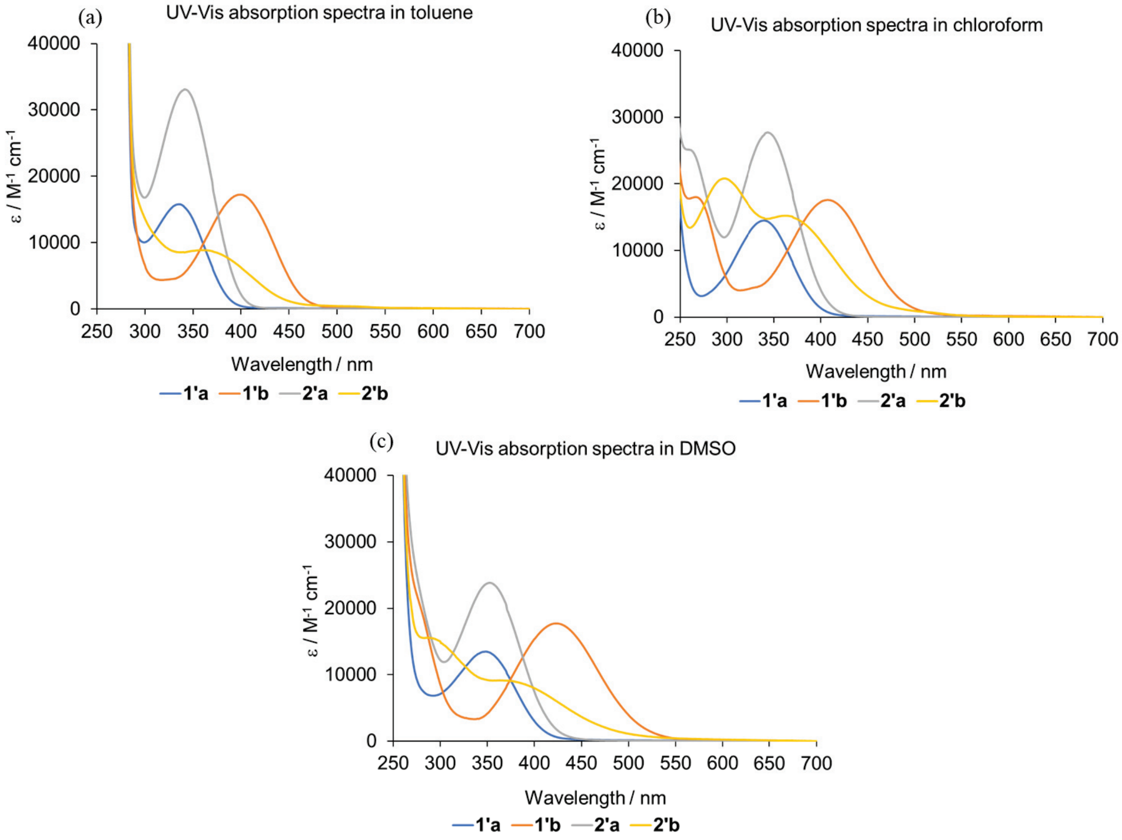


**Figure S1.** UV-Vis absorption spectra of **1'a,b** and **2'a,b**. (a) In toluene, (b) In chloroform, (c) In DMSO.

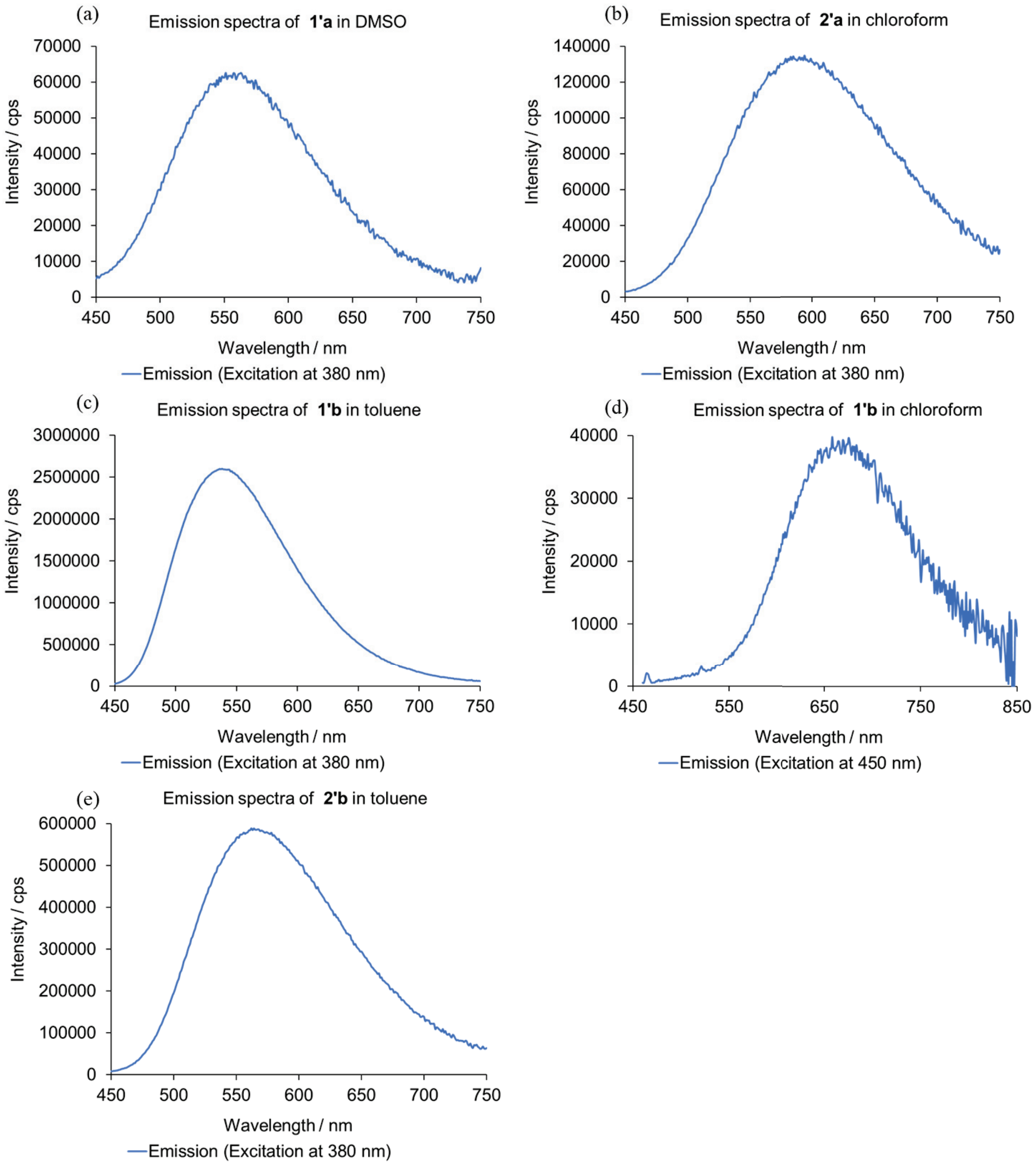


**Figure S2.** (a) Emission spectra of compound **1’a** in DMSO, (b) Emission spectra of compound **2’a** in chloroform, (c) Emission spectra of compound **1’b** in toluene, (d) Emission spectra of compound **1’b** in chloroform, (e) Emission spectra of compound **2’b** in toluene.

## 2PA spectroscopic measurement of 1’b and 2’b

Two-photon-excited fluorescence spectra of the studied model fluorophores **1’b** and **2’b** in solution phase (concentration: 1 x $10^{-3}$ M) were measured according to the reported protocols using Rhodamine 610 (in MeOH) as the standard[65,66]. The excitation light source was a mode-locked Ti:Sapphire laser (Chameleon Ultra II, Coherent Inc.) which delivers ~140 fs pulses with the repetition rate of 80 MHz and the beam diameter of 2 mm. The intensity level of the excitation beam was carefully controlled by the combination of a λ/2 wave plate and a polarizer in order to avoid the saturation of absorption and photodegradation. To minimize the effects of re-absorption, the excitation beam was focused as close as possible to the front-wall of the quartz cell (10 mm x 10 mm cuvette) and the up-converted emissions were collected at a right angle to the incident excitation beam and was induced by a fiber bundle into a CCD imaging spectrometer (USB-4000, Ocean Optics) for the spectra recording. This optical system was also utilized for the characterization of the quadratic dependence of the 2PA-induced up-conversion emission intensity on the pumping intensity for every data point. The measured 2PA spectra of the studied compounds are shown in Figure S4.

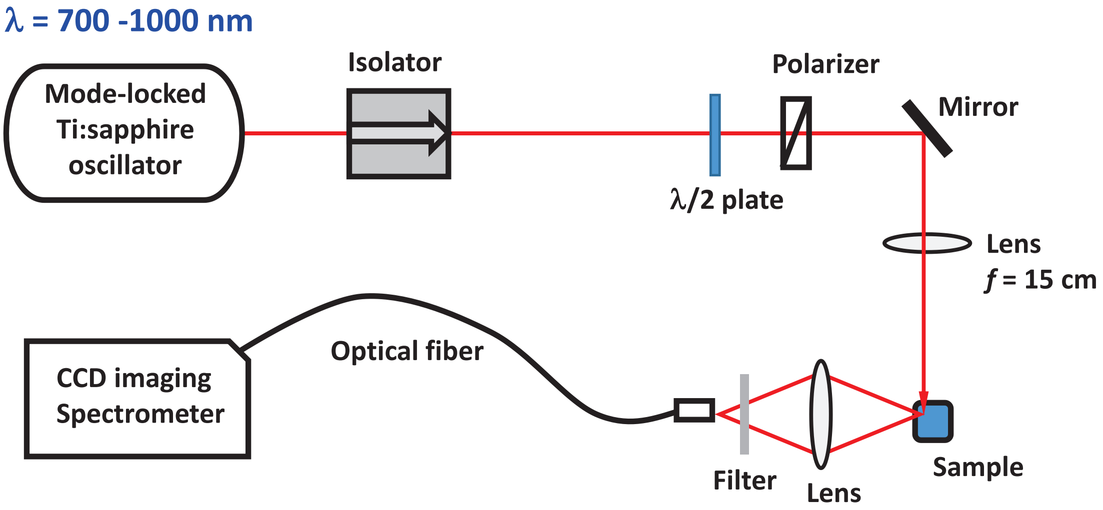


**Figure S3.** Optical setup for two-photon-excited-fluorescence-related experiments.

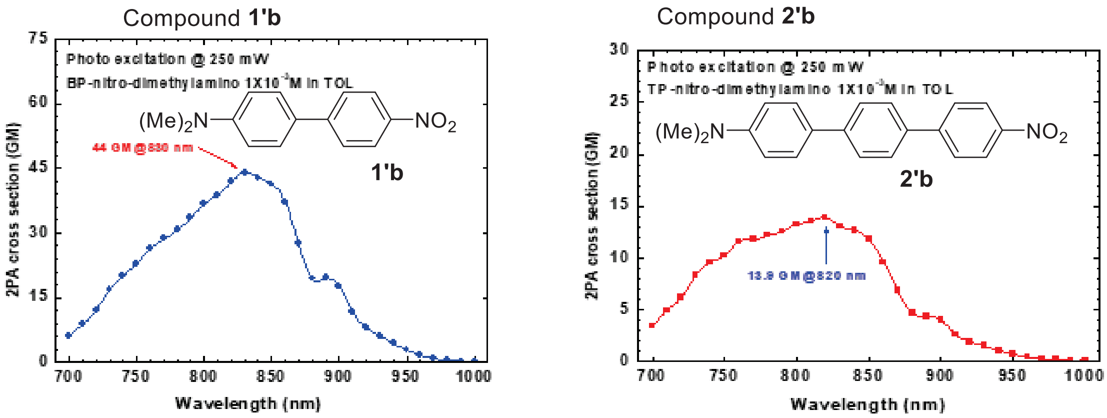


**Figure S4.** TPA spectra of **1’b** and **2’b** was determined by the 2P-induced fluorescence measurement in Toluene.

In this experiment, the mode-locked Ti: Sapphire laser (Mai Tai, Spectra Physic Inc.) was used as the light excitation source which delivers ~80 fs pulses with the repetition rate of 80 MHz. The excitation wavelength range was used in these experiments at 690 – 840 nm. Three mirrors were used to deliver the laser beam and a lens on top of the sample to focus a light (Figure S5).

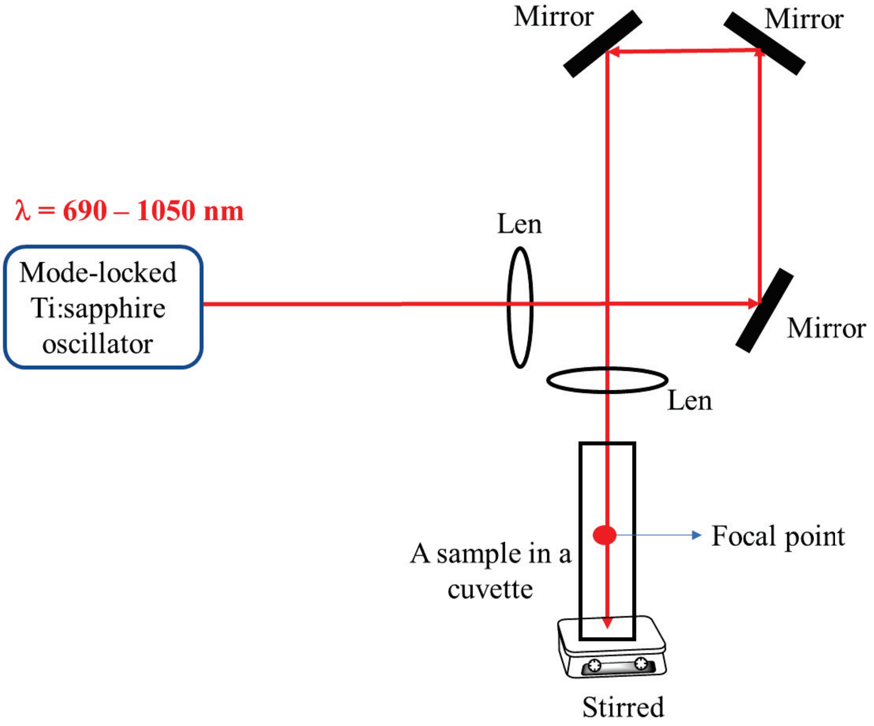


**Figure S5.** Optical setup for two-photon-excited-related experiments.

## $^1$H-NMR and $^{13}$C-NMR spectrum

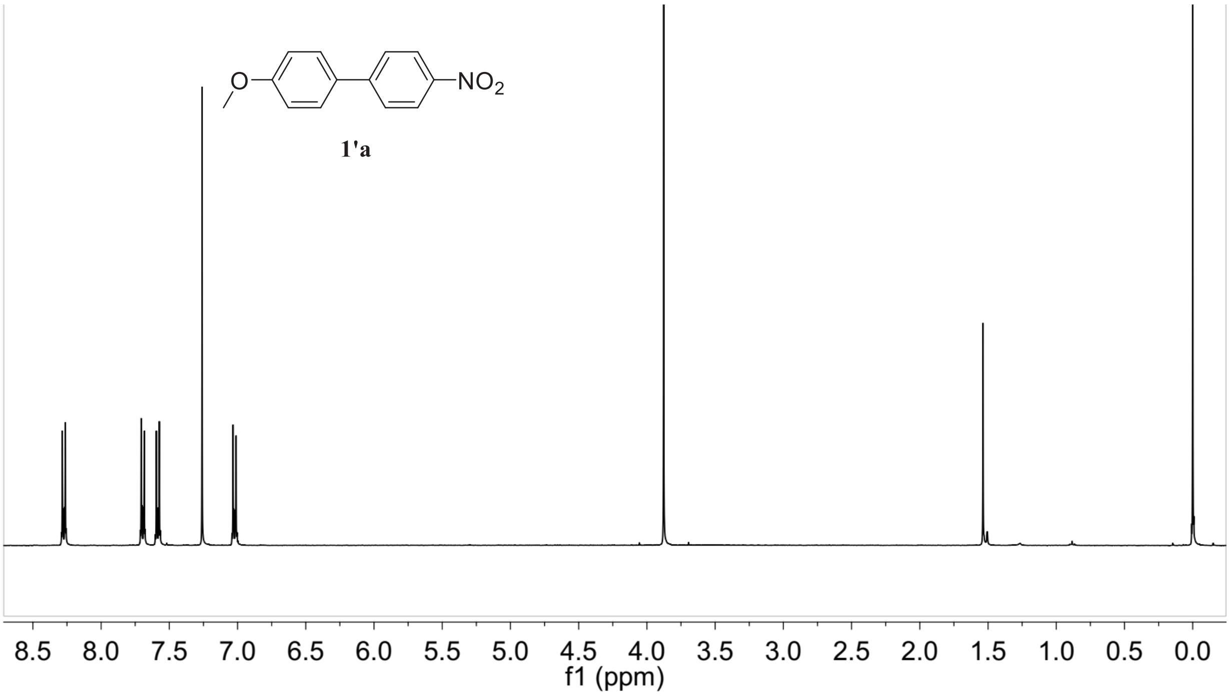


**Figure S6.** **$^1$H-NMR** spectrum of compound **1’a**[58] in $CDCl_3$.

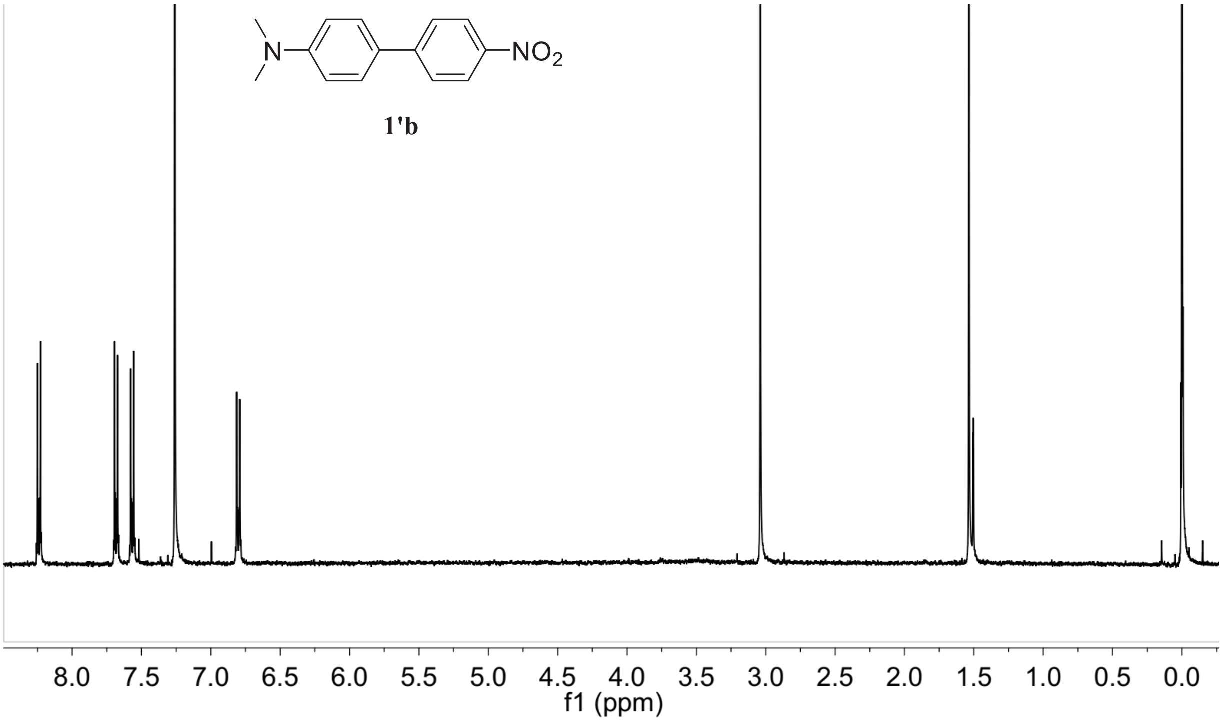
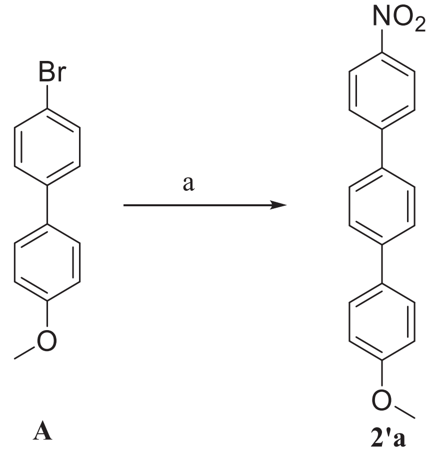


**Figure S7.** **$^1$H-NMR** spectrum of compound **1’b**[59] in $CDCl_3$.



**A**

**2'a**

**Scheme S1.** Synthesis of compound **2’a**. Reagents and conditions: (a) **2’a**, $Pd(PPh_3)_4$, $K_2CO_3$, THF, $H_2O$, rt to 80 °C, overnight, 50% for **2’a**.

**4-(Dimethylamino)-4’’-nitro-*p*-terphenyl (2’a):** In a round-bottom flask, the compound **A**[46] (426 mg, 1.62 mmol), 4-nitrophenylboronic acid (272 mg, 1.63 mmol), $Pd(PPh_3)_4$ (94.1 mg, 0.08 mmol) was degassed with $N_2$ for 30 min. Potassium carbonate (315 mg, 2.28 mmol) dissolved in $H_2O$ (10 mL) and THF (10 mL) was added in the mixture. The solution heated to 80 °C for overnight. The reaction was cooled to room temperature and the reaction mixture was filtered. The filtrate was washed with water and extracted with EtOAc. The organic layer was dried over $Na_2SO_4$. The solvent was removed under reduced pressure. The products were purified through silica gel column chromatography to give the desired coupling product **2’a** (245 mg, 50%) as a yellow color solid. $^1$H-NMR (400 MHz, $CDCl_3$): δ 8.33 ppm (d, $J = 9.2$ Hz, 2H), 7.80 ppm (d, $J = 9.0$ Hz, 2H), 7.69 ppm (s, 4H), 7.60 ppm (d, $J = 9.0$ Hz, 2H), 7.03 ppm (d, $J = 9.2$ Hz, 2H), 3.87 ppm (s, 3H). $^{13}$C-NMR (400 Hz, $CDCl_3$): δ 171.8, 171.3, 150.3, 146.9, 146.3, 141.8, 137.6, 136.0, 127.9, 127.7, 126.7, 126.1, 125.5, 112.8, 78.3, 70.3, 69.0, 61.4, 60.3, 55.9, 55.7, 53.9, 40.5, 14.3, 14.2. IR: $\nu$ 2917, 2849, 1766, 1600, 1512, 1369, 1347, 1225, 1139, 1048, 1007, 985, 815. HRMS-ESI: calcd for $C_{42}H_{56}N_4O_{12}Na$ $[M + Na]^+$ 831.37869, found 831.37860.

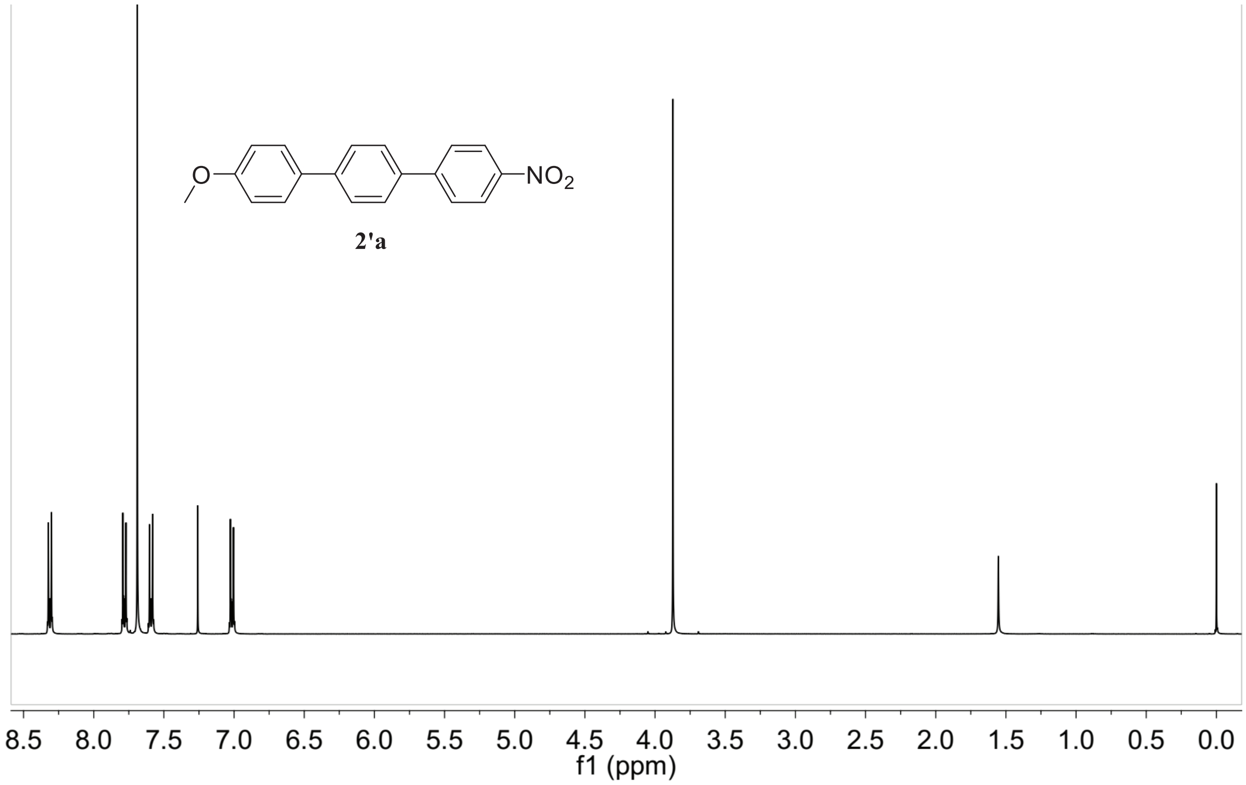


**Figure S8.** $^1$H-NMR spectrum of compound **2’a** in $CDCl_3$.

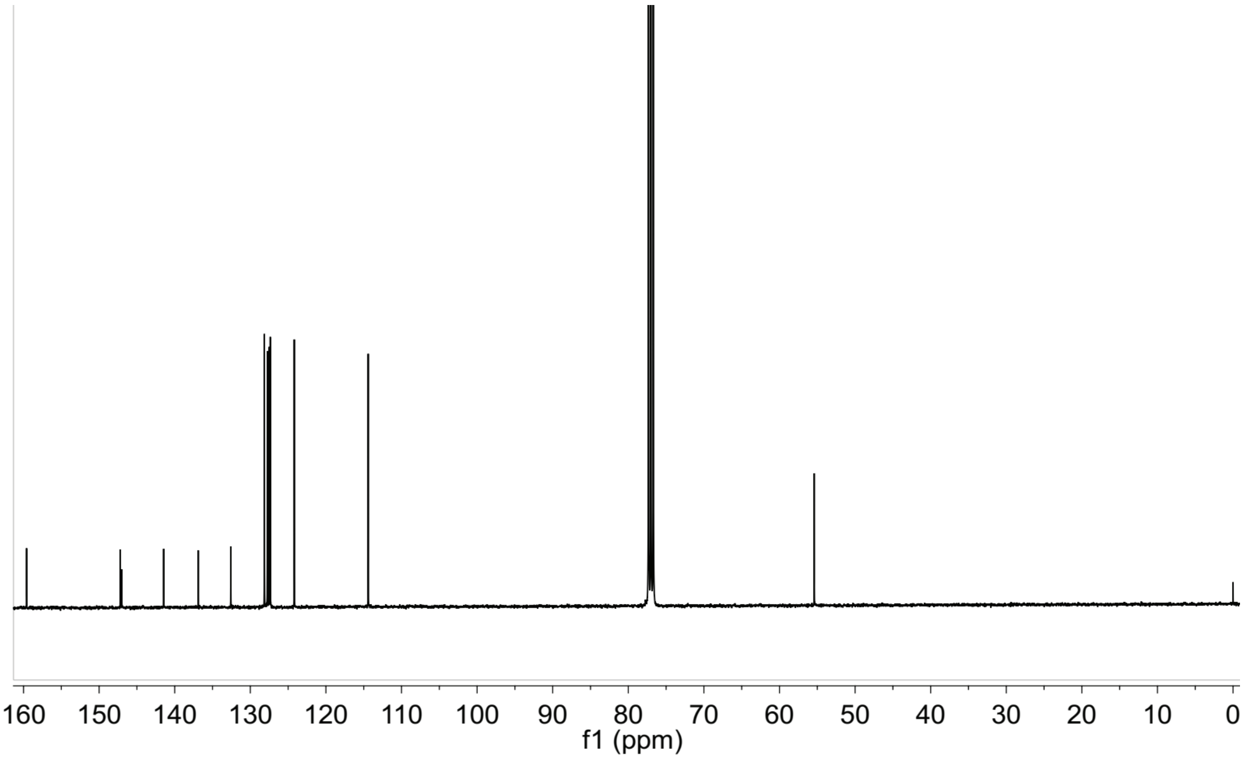


**Figure S9.** $^{13}$C-NMR spectrum of compound **2’a** in $CDCl_3$.

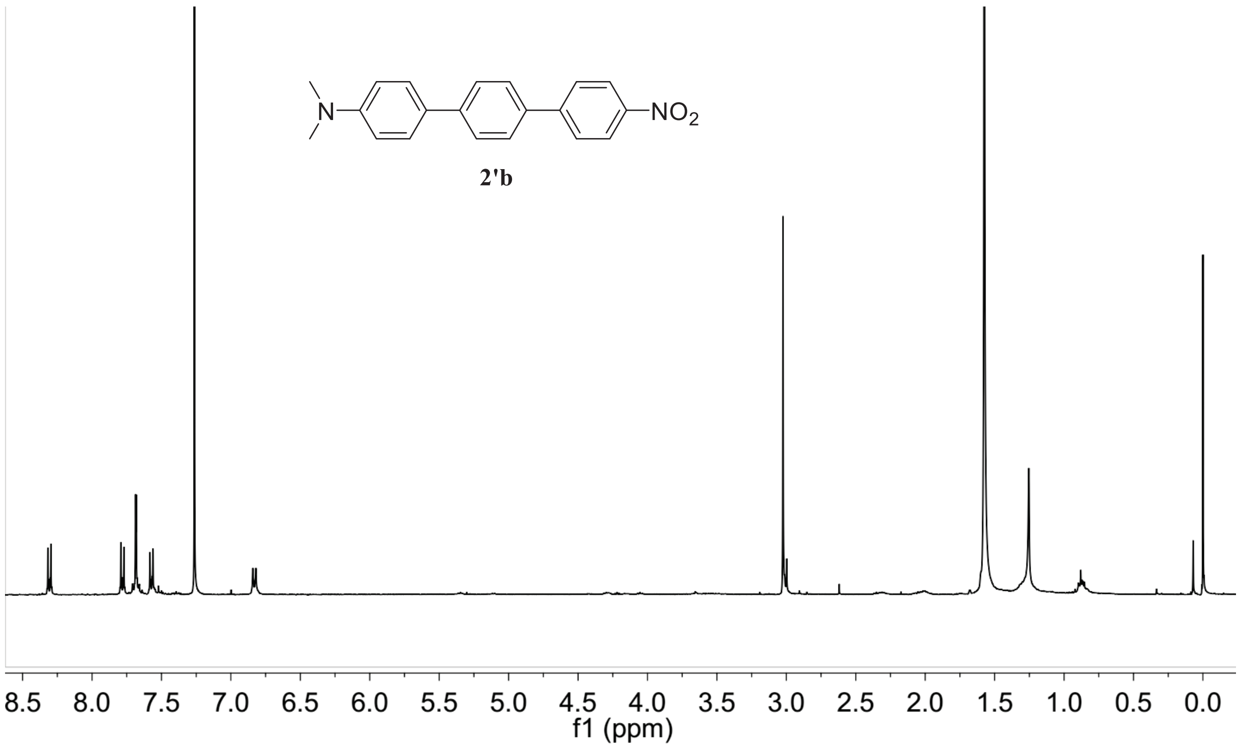


**Figure S10.** $^1$H-NMR spectrum of compound **2’b**[44,45] in $CDCl_3$.

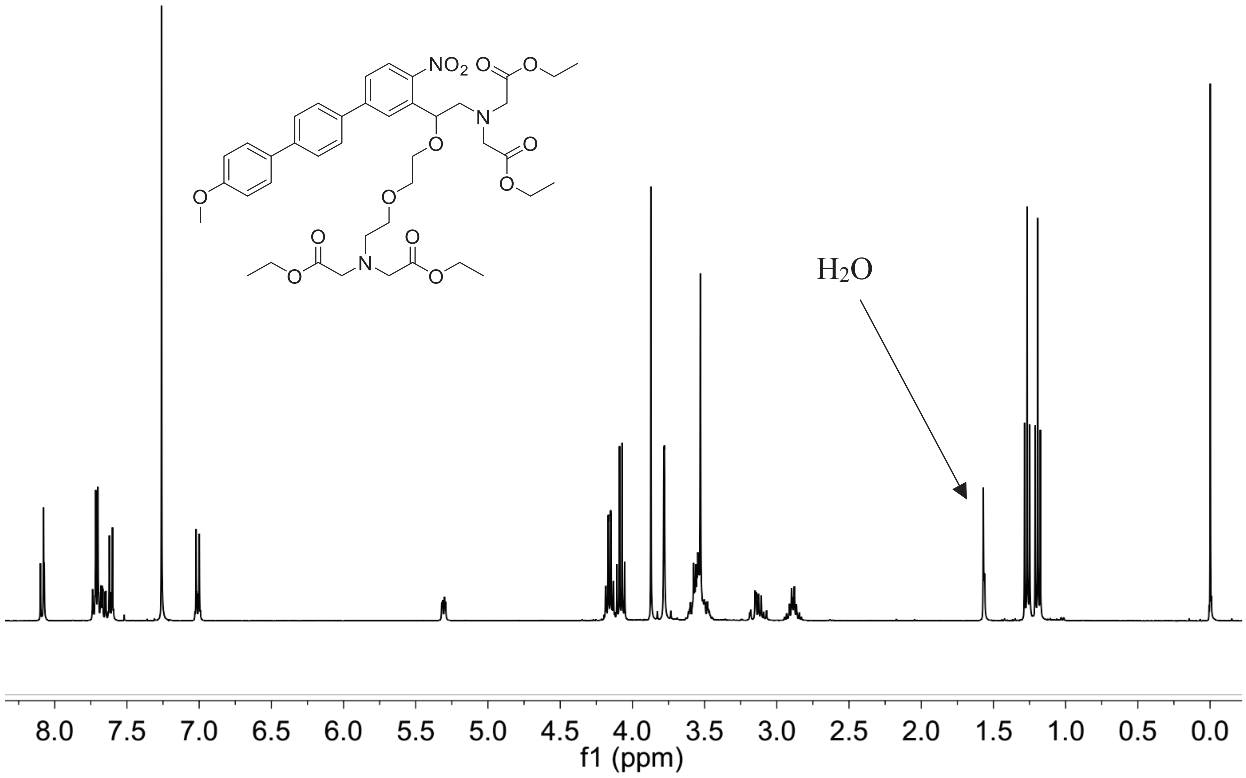


**Figure S11.** $^1$H-NMR spectrum of compound **3a** in CDCl3.

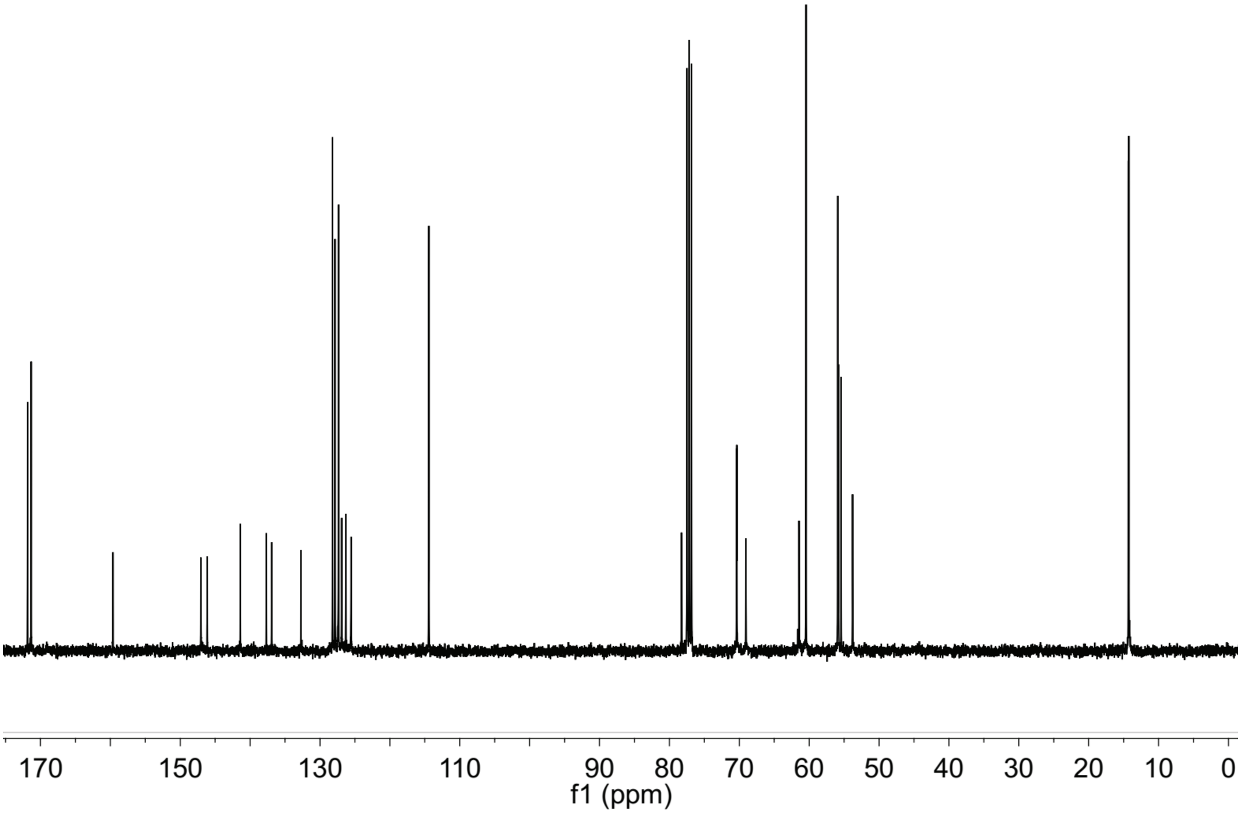


**Figure S12.** $^{13}$**C-NMR** spectrum of compound **3a** in $CDCl_3$.

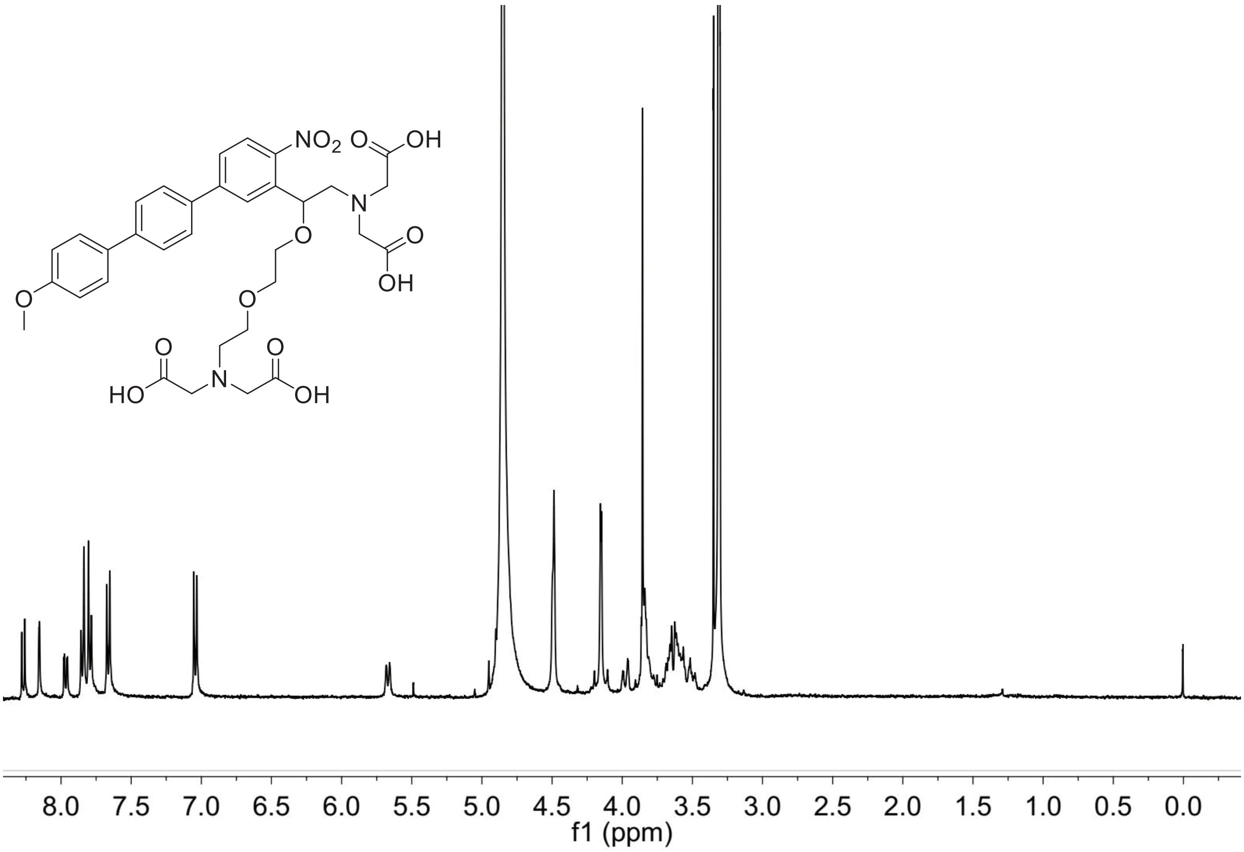


**Figure S13.** $^{1}$**H-NMR** spectrum of compound **4a** in $CD_3OD$.

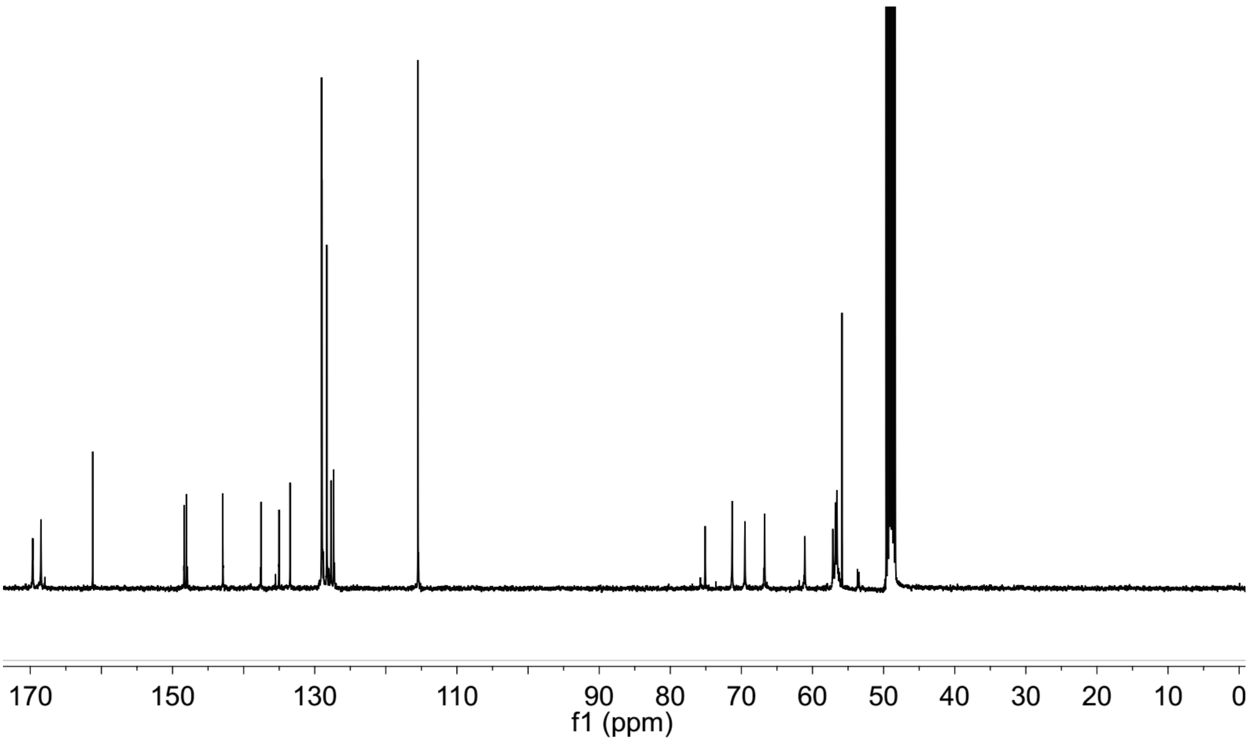


**Figure S14.** $^{13}$**C-NMR** spectrum of compound **4a** in $CD_3OD$.

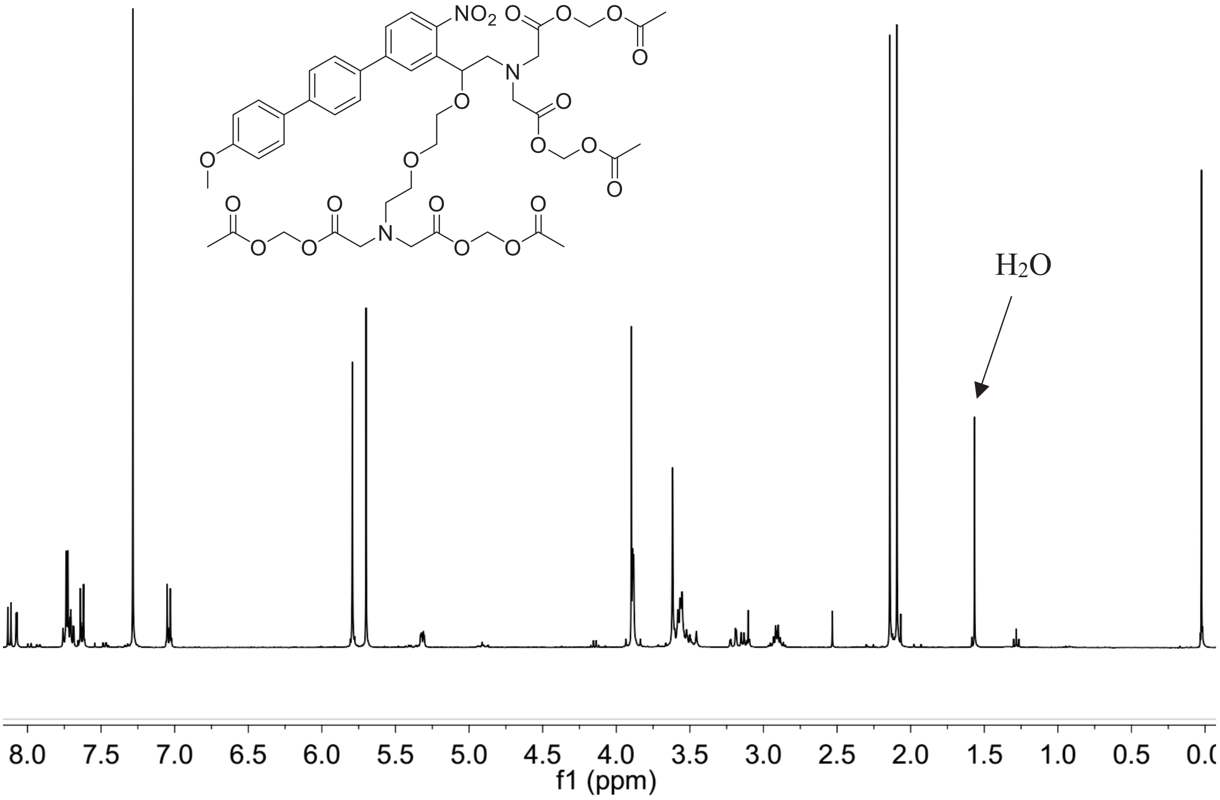


**Figure S15.**$^{1}$**H-NMR** spectrum of compound **5a** in $CDCl_3$.

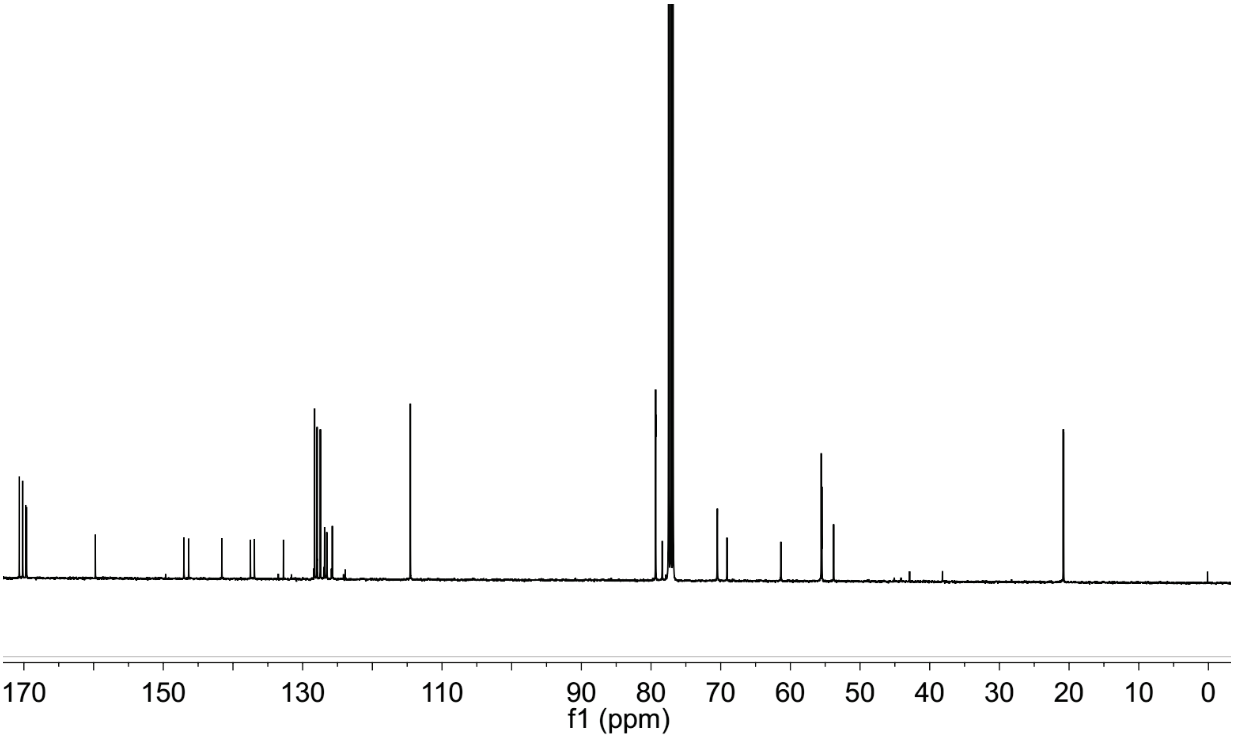


**Figure S16.** $^{13}$**C-NMR** spectrum of compound **5a** in $CDCl_3$.

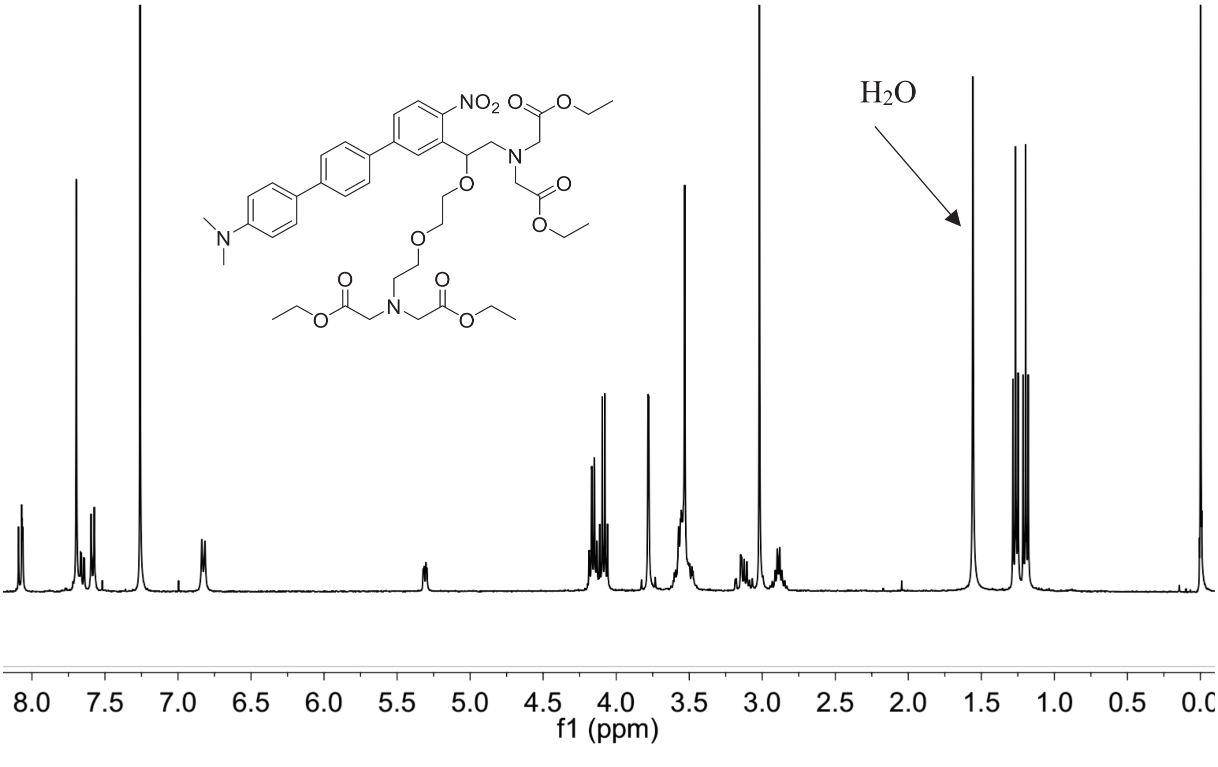


**Figure S17.** $^{1}$**H-NMR** spectrum of compound **3b** in $CDCl_3$.

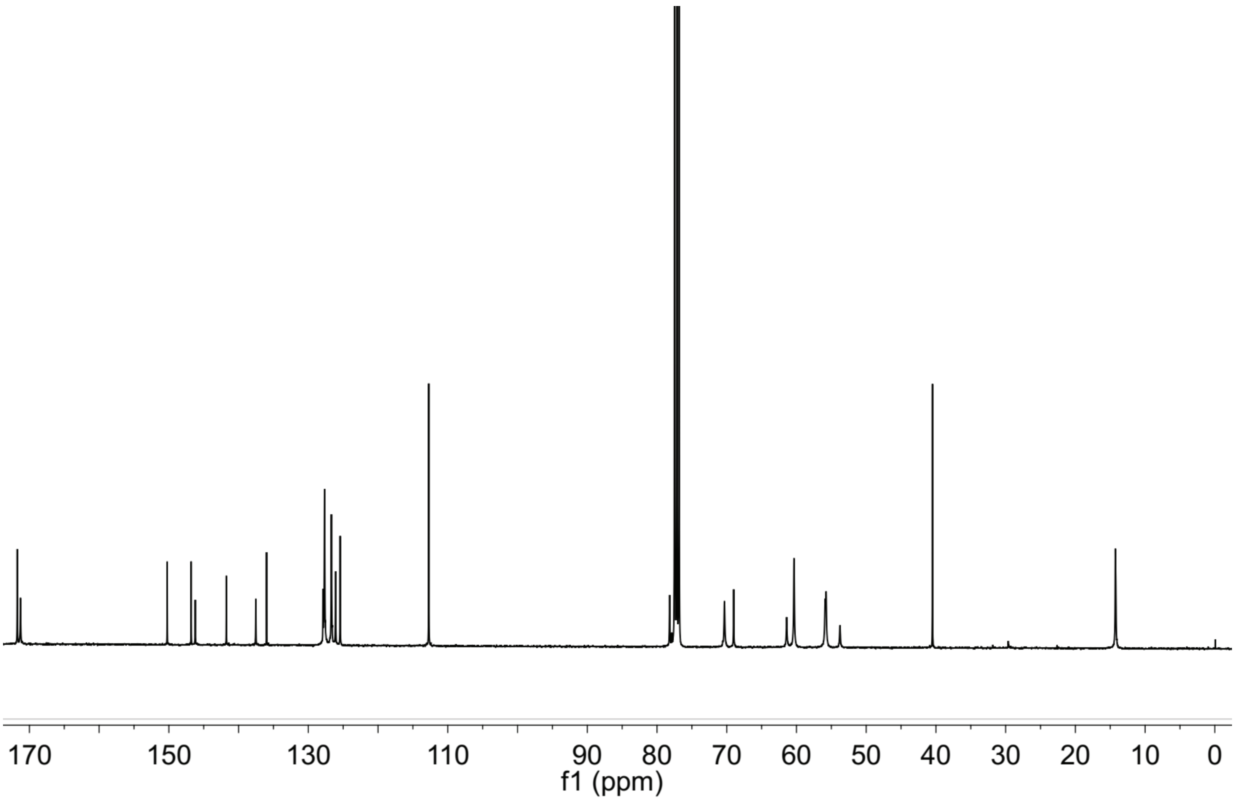


**Figure S18.** $^{13}$**C-NMR** spectrum of compound **3b** in $CDCl_3$.

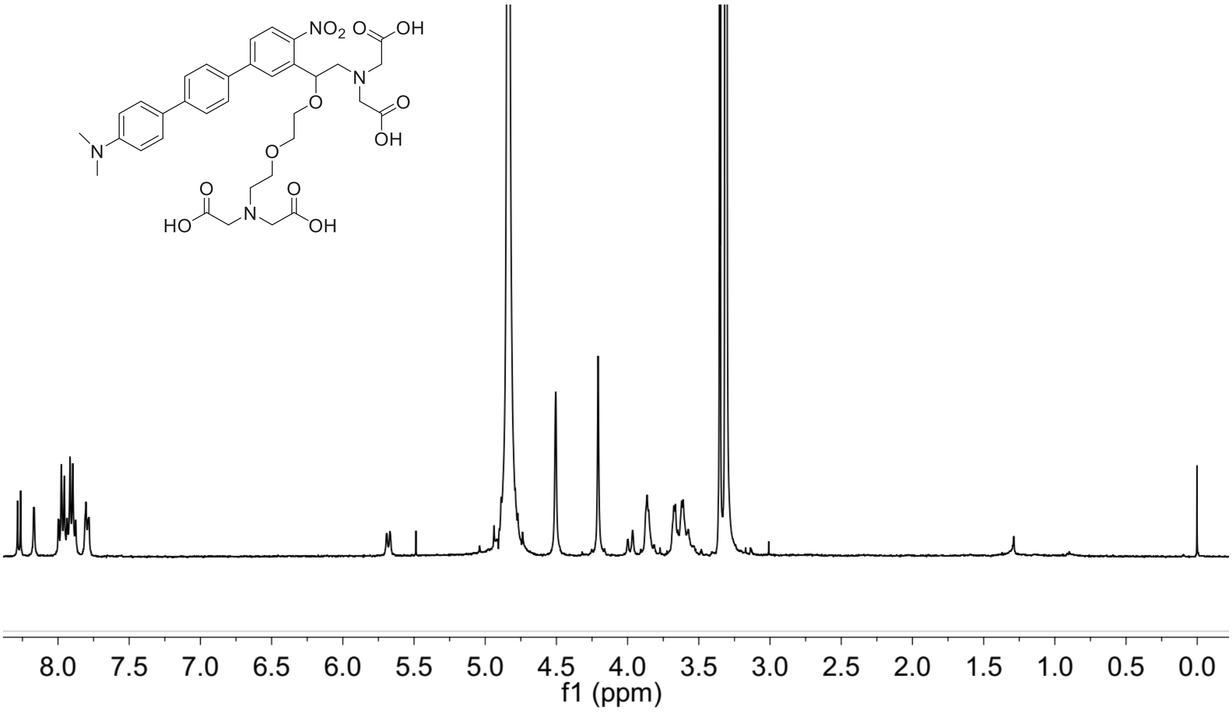


**Figure S19.** $^{1}$**H-NMR** spectrum of compound **4b** in $CD_3OD$.

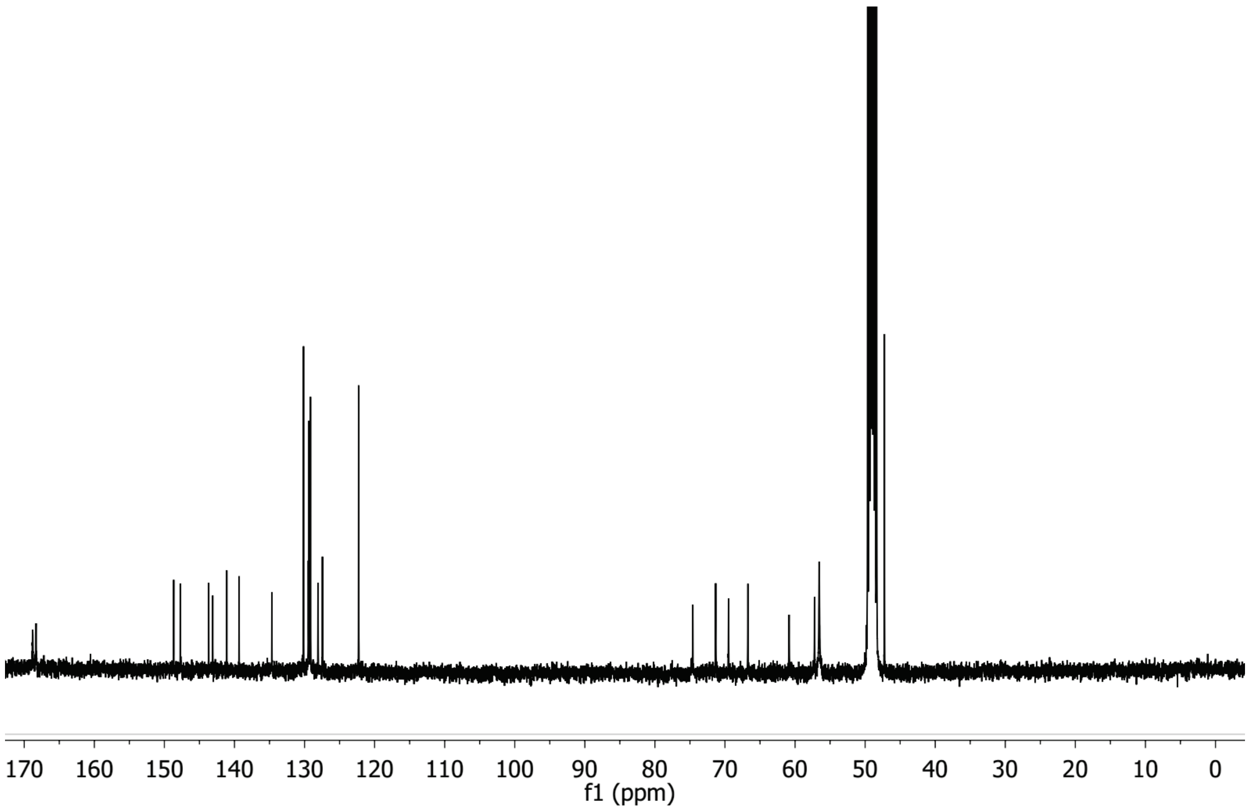


**Figure S20.** $^{13}$**C-NMR** spectrum of compound **4b** in $CD_3OD$.

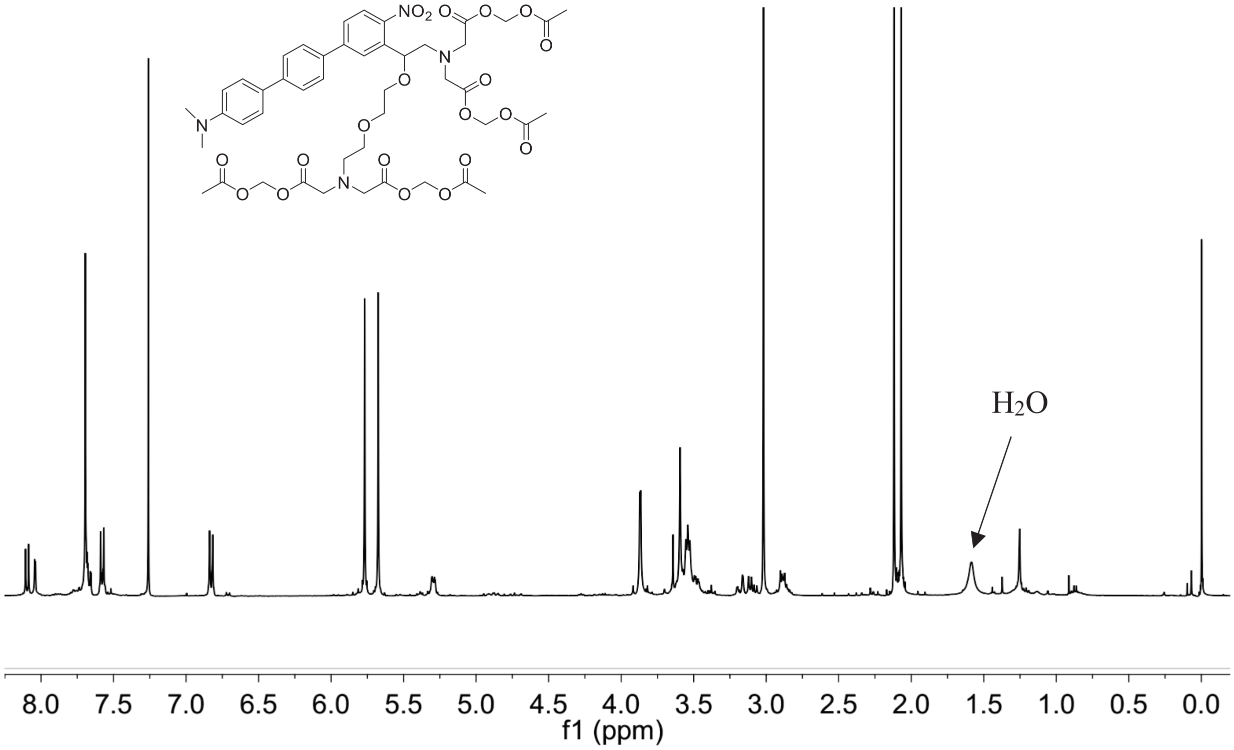


**Figure S21.** $^{1}$**H-NMR** spectrum of compound **5b** in $CDCl_3$.

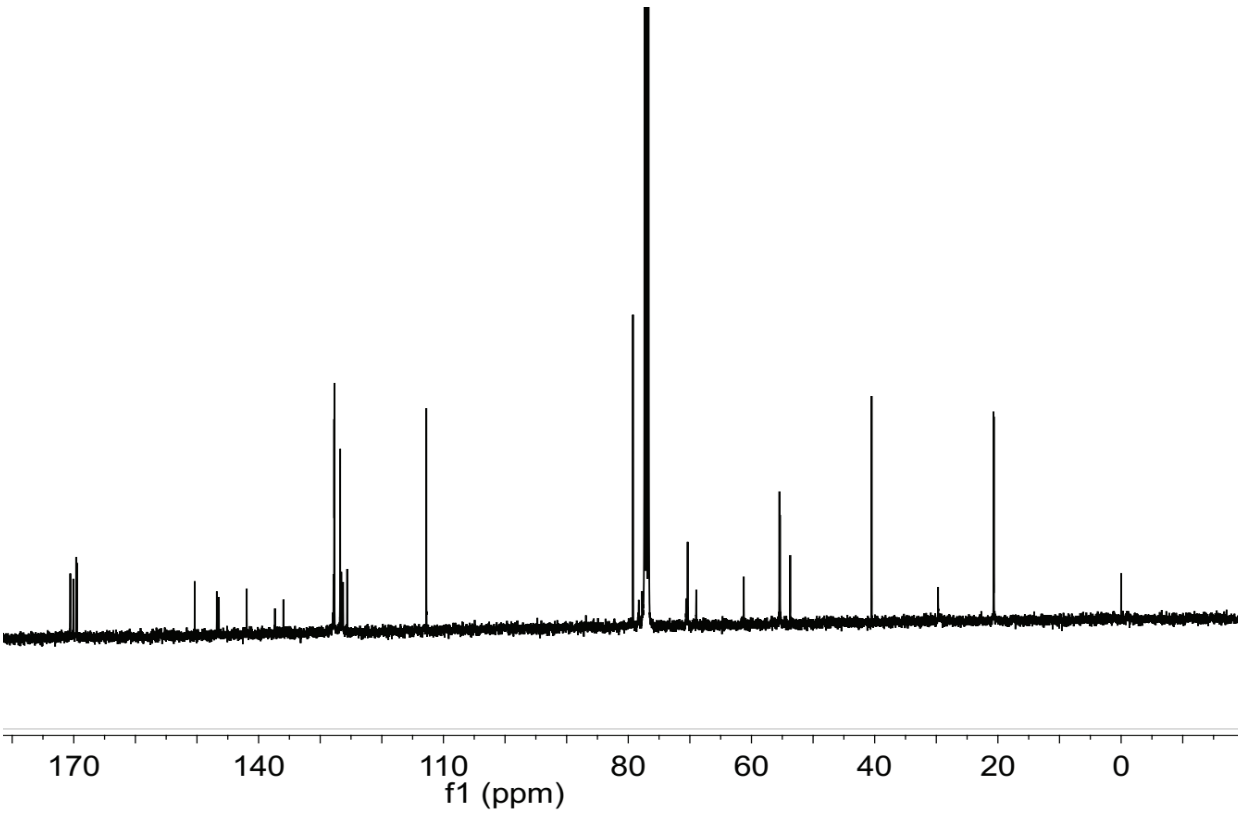


**Figure S22.** $^{13}$C-NMR spectrum of compound **5b** in $CDCl_3$.

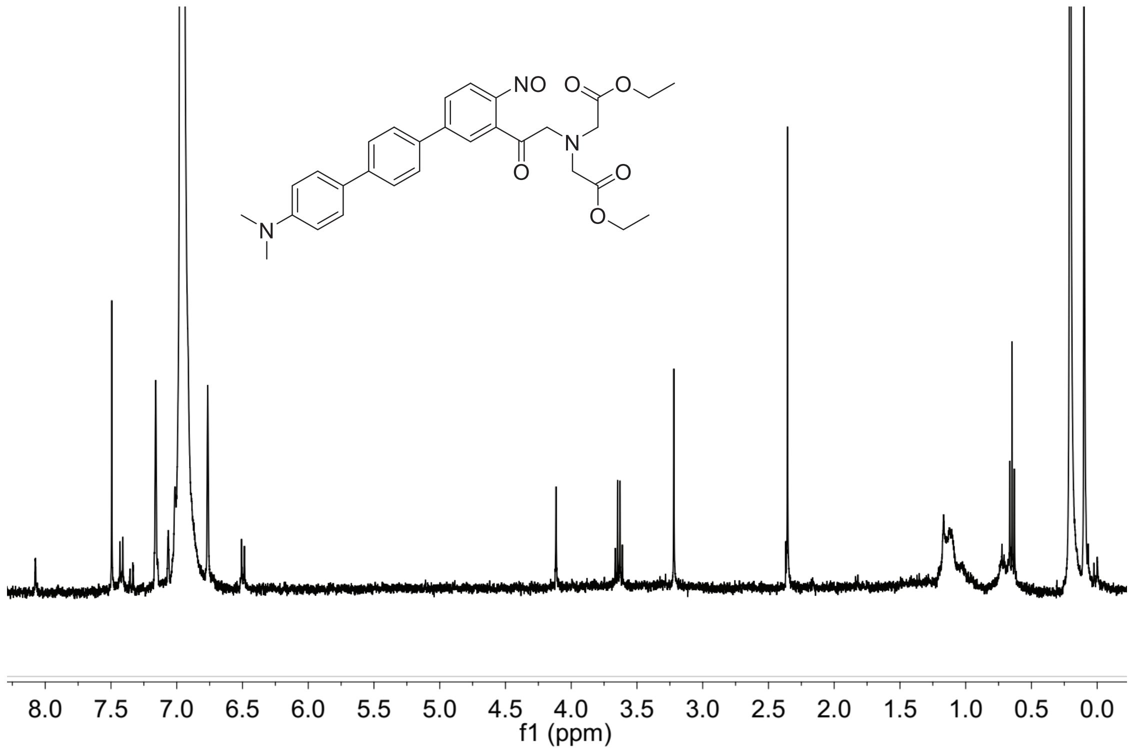


**Figure S23. $^{1}$H-NMR** spectrum of compound **6b** in $C_6D_6$.

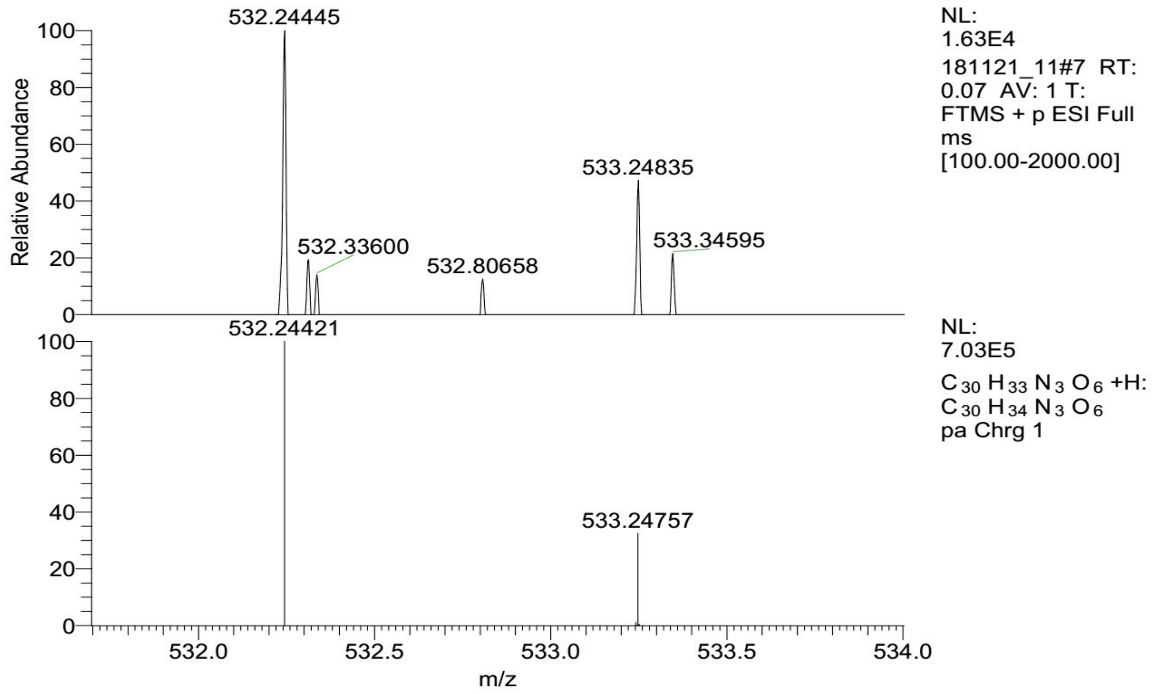


**Figure S24. MS** spectrum of compound **6b**

## UV-vis absorption spectra of 3a,b and 4a,b

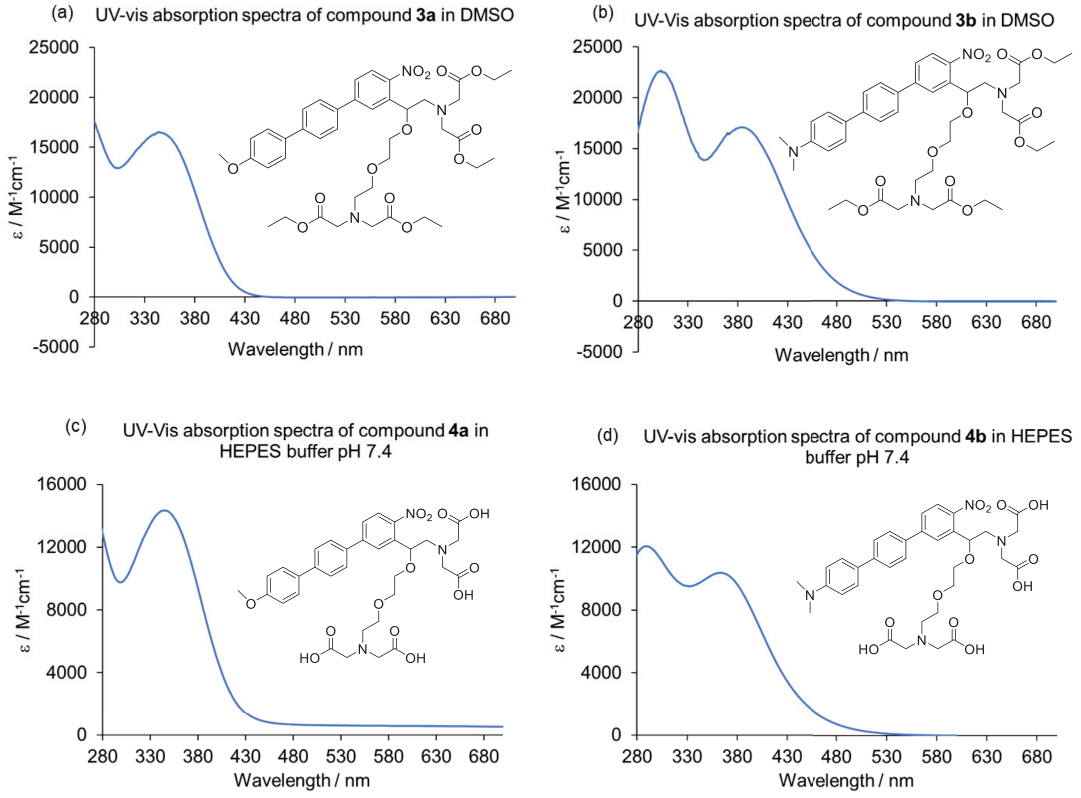


**Figure S25.** UV-vis absorption spectra. (a) Compound **3a** in DMSO, (b) Compound **3b** in DMSO, (c) Compound **4a** in HEPES buffer pH 7.4, (d) Compound **4b** in HEPES buffer pH 7.4.

### Computational details

We used density functional theory (DFT) and time-dependent (TD) DFT approaches, as implemented in the Gaussian 09 packages[67], to model the four chromophores of interest. Calculations have been performed in vacuum, in SMD solvent model[64] and were limited to properties related to the ground state geometry: geometry optimization, one photon absorption related to the electronically excited states (ES). One-photon absorption (1PA) were obtained at the TD-B3LYP/6-31G(d), TD-M062X/6-31G(d) and TD-CAM-B3LYP/6-31G(d) level of theory, including up to 20 singlet ES.

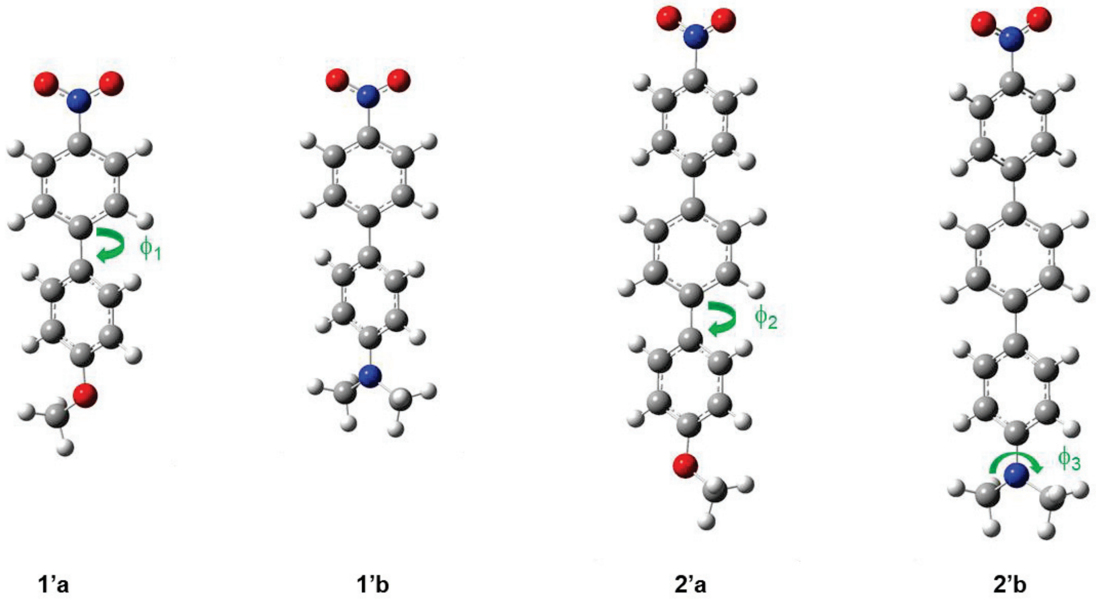


**Figure S26.** Molecular scheme of the chromophores of interest and selected dihedral angles.

**B3LYP/6-31G(d) in gaussian 09 packages in gas phase**

Compound **1'a**

Number of Imaginary Frequencies = 0

Zero-point correction = 0.217420 (Hartree/Particle)

Thermal correction to Energy = 0.231446

Thermal correction to Enthalpy = 0.232390

Thermal correction to Gibbs Free Energy = 0.175262

Sum of electronic and zero-point Energies = -782.114608

Sum of electronic and thermal Energies = -782.100582

Sum of electronic and thermal Enthalpies = -782.099638

Sum of electronic and thermal Free Energies = -782.156765

```
-------------------------------------------------------------------
 Center     Atomic                   Forces (Hartrees/Bohr)
 Number      Number          X                  Y                  Z
-------------------------------------------------------------------
      1          6      -0.000028886    -0.000002341    -0.000000725
      2          6       0.000046497    -0.000008619     0.000002340
      3          6       0.000009091    -0.000000295    -0.000000781
      4          6       0.000010530    -0.000001224     0.000001587
      5          6      -0.000002710    -0.000010829    -0.000005612
      6          6      -0.000002518     0.000009979    -0.000002557
      7          1       0.000003300    -0.000004798     0.000001446
      8          1       0.000002613     0.000002155    -0.000002953
      9          1      -0.000009032     0.000005536     0.000002906
     10          1      -0.000008405    -0.000005542    -0.000001999
     11          6      -0.000048652     0.000013625     0.000022010
     12          6       0.000026038    -0.000004717    -0.000007153
     13          6       0.000003454     0.000010976    -0.000003739
     14          6       0.000006108    -0.000011801    -0.000005940
     15          6      -0.000007949     0.000003888    -0.000001655
     16          6      -0.000008778    -0.000001593     0.000004578
     17          1       0.000008085    -0.000005398     0.000004437
     18          1       0.000007936     0.000003254    -0.000006477
     19          1      -0.000003097     0.000003208     0.000000663
     20          1      -0.000002715    -0.000001000    -0.000000610
     21          7       0.000016796    -0.000000087    -0.000009098
     22          8      -0.000000828    -0.000010775     0.000000892
     23          8      -0.000002104     0.000005849     0.000004560
     24          8      -0.000014209     0.000002259     0.000004568
     25          6       0.000001146     0.000004741    -0.000001669
     26          1      -0.000000694     0.000000788    -0.000000016
     27          1      -0.000000565     0.000001834     0.000000709
     28          1      -0.000000453     0.000000925     0.000000286
-------------------------------------------------------------------
```

Compound **1’b**

Number of Imaginary Frequencies = 0

Zero-point correction = 0.258055 (Hartree/Particle)

Thermal correction to Energy = 0.273988

```
Thermal correction to Enthalpy = 0.274932
Thermal correction to Gibbs Free Energy = 0.213121
Sum of electronic and zero-point Energies = -801.519761
Sum of electronic and thermal Energies = -801.503828
Sum of electronic and thermal Enthalpies = -801.502884
Sum of electronic and thermal Free Energies = -801.564695

-------------------------------------------------------------------
 Center     Atomic                   Forces (Hartrees/Bohr)
 Number      Number             X                 Y                 Z
 -------------------------------------------------------------------
      1          6         0.000015176   -0.000000025   -0.000000773
      2          6        -0.000000624   -0.000002445    0.000008044
      3          6        -0.000001288    0.000000389   -0.000000556
      4          6        -0.000000979   -0.000002849    0.000000229
      5          6         0.000000796    0.000001195    0.000001594
      6          6         0.000004503   -0.000001659   -0.000006594
      7          1        -0.000001086    0.000000518   -0.000004866
      8          1        -0.000000844   -0.000000796    0.000003738
      9          1        -0.000003245   -0.000000279    0.000000778
     10          1        -0.000001194    0.000002296   -0.000004248
     11          6        -0.000000010    0.000004788   -0.000003763
     12          6        -0.000009644   -0.000002822   -0.000000218
     13          6        -0.000002397   -0.000003630    0.000001507
     14          6        -0.000002516    0.000000813    0.000001420
     15          6         0.000003146    0.000001389    0.000000356
     16          6        -0.000001397    0.000001350   -0.000003090
     17          1         0.000000787    0.000000050   -0.000004177
     18          1         0.000004439    0.000001724    0.000004338
     19          1         0.000001377    0.000000654    0.000002789
     20          1        -0.000001616   -0.000001737   -0.000001973
     21          7        -0.000015745   -0.000000589   -0.000000753
     22          8         0.000001785   -0.000003529   -0.000003569
     23          8         0.000002298    0.000003249    0.000002189
     24          7         0.000009311    0.000002418    0.000012161
     25          6        -0.000002726    0.000002373   -0.000000712
     26          1         0.000001640   -0.000001792    0.000002417
     27          1         0.000000420    0.000000980    0.000004569
     28          1        -0.000001586    0.000002497    0.000002278
```

```
      29          6            -0.000000456    -0.000004107    -0.000007333
      30          1            -0.000000154    -0.000001240    -0.000001933
      31          1             0.000001516     0.000000894    -0.000002322
      32          1             0.000000314    -0.000000075    -0.000001527
 -------------------------------------------------------------------------------------------
```

Compound **2’a**
Number of Imaginary Frequencies = 0
Zero-point correction = 0.298398 (Hartree/Particle)
Thermal correction to Energy = 0.317134
Thermal correction to Enthalpy = 0.318078
Thermal correction to Gibbs Free Energy = 0.249288
Sum of electronic and zero-point Energies = -1013.090849
Sum of electronic and thermal Energies = -1013.072113
Sum of electronic and thermal Enthalpies = -1013.071169
Sum of electronic and thermal Free Energies = -1013.139959

```
 -------------------------------------------------------------------------------------------
 Center      Atomic                         Forces (Hartrees/Bohr)
 Number       Number               X                     Y                     Z
 -------------------------------------------------------------------------------------------
       1          6            -0.000010157    -0.000000868     0.000004948
       2          6             0.000006811     0.000001074     0.000001920
       3          6             0.000000351     0.000002543    -0.000002355
       4          6             0.000000751    -0.000002273    -0.000001574
       5          6             0.000000198     0.000000514    -0.000000747
       6          6            -0.000000912     0.000000367    -0.000000004
       7          1             0.000000086    -0.000001618    -0.000000342
       8          1             0.000000775     0.000001285    -0.000000061
       9          1             0.000000147     0.000000871    -0.000000049
      10          1            -0.000000693    -0.000000448    -0.000001216
      11          6             0.000009795    -0.000000075    -0.000005852
      12          6            -0.000004963     0.000000984    -0.000000325
      13          6            -0.000000132    -0.000002956     0.000001510
      14          6             0.000000033     0.000002131     0.000002257
      15          6             0.000001556     0.000000794    -0.000000519
      16          6            -0.000000139    -0.000000135     0.000000629
      17          1            -0.000000920     0.000000832     0.000000831
      18          1            -0.000000090    -0.000001150    -0.000001160
```

```
     19          1            0.000000683    -0.000000657      0.000000047
     20          1            0.000000614     0.000000224      0.000000480
     21          6            0.000001259    -0.000000562     -0.000000208
     22          6           -0.000000350    -0.000000314      0.000000305
     23          6           -0.000000145     0.000000323      0.000000716
     24          6            0.000000355    -0.000000218      0.000000353
     25          6            0.000000488    -0.000000428     -0.000000049
     26          6            0.000000527     0.000000026      0.000000437
     27          1           -0.000000086    -0.000000301      0.000000593
     28          1            0.000000275    -0.000000126     -0.000000338
     29          1            0.000000129    -0.000000127     -0.000000127
     30          1           -0.000000096    -0.000000314      0.000000653
     31          7            0.000001730    -0.000000831      0.000000657
     32          8           -0.000001330     0.000000772      0.000000057
     33          8           -0.000001400    -0.000001021      0.000000665
     34          8           -0.000004113    -0.000000984     -0.000000893
     35          6           -0.000000070     0.000002519     -0.000000798
     36          1           -0.000000243    -0.000000225     -0.000000129
     37          1           -0.000000268     0.000000065     -0.000000225
     38          1           -0.000000454     0.000000308     -0.000000087
 -------------------------------------------------------------------------------------------
```

Compound **2’b**

Number of Imaginary Frequencies = 0

Zero-point correction = 0.339035 (Hartree/Particle)

Thermal correction to Energy = 0.359632

Thermal correction to Enthalpy = 0.360576

Thermal correction to Gibbs Free Energy = 0.287391

Sum of electronic and zero-point Energies = -1032.495338

Sum of electronic and thermal Energies = -1032.474741

Sum of electronic and thermal Enthalpies = -1032.473797

Sum of electronic and thermal Free Energies = -1032.546983

```
-------------------------------------------------------------------------------------------
 Center        Atomic                           Forces (Hartrees/Bohr)
 Number         Number                X                        Y                         Z
 -------------------------------------------------------------------------------------------
      1          6           -0.000006076    -0.000000039      0.000000269
      2          6            0.000010997    -0.000003288      0.000005584
```

| | | | | |
|---|---|---|---|---|
| 3 | 6 | 0.000003038 | 0.000000315 | -0.000001296 |
| 4 | 6 | 0.000002517 | -0.000001629 | 0.000001862 |
| 5 | 6 | -0.000002368 | 0.000001077 | -0.000002147 |
| 6 | 6 | -0.000004846 | -0.000000549 | -0.000001242 |
| 7 | 1 | -0.000000082 | 0.000000818 | -0.00000127 |
| 8 | 1 | 0.000000105 | -0.000001077 | 0.000001653 |
| 9 | 1 | -0.000000238 | -0.000000846 | 0.000001899 |
| 10 | 1 | -0.000002464 | 0.000002786 | -0.000002596 |
| 11 | 6 | -0.000000267 | -0.000004766 | 0.000004063 |
| 12 | 6 | 0.000012440 | 0.000000658 | -0.000000331 |
| 13 | 6 | 0.000002456 | -0.000000614 | 0.000000121 |
| 14 | 6 | 0.000002260 | 0.000003244 | -0.000004168 |
| 15 | 6 | 0.000000704 | 0.000000922 | 0.000002944 |
| 16 | 6 | -0.000000383 | 0.000000070 | -0.000000068 |
| 17 | 1 | -0.000004069 | -0.000001433 | -0.000002782 |
| 18 | 1 | -0.000002071 | 0.000000676 | 0.000003415 |
| 19 | 1 | 0.000000703 | 0.000001847 | 0.000000929 |
| 20 | 1 | -0.000000315 | -0.000000894 | -0.000001080 |
| 21 | 7 | 0.000004600 | 0.000000149 | 0.000000366 |
| 22 | 8 | -0.000000522 | -0.000001394 | -0.000001458 |
| 23 | 8 | -0.000000383 | 0.000000767 | 0.000001791 |
| 24 | 7 | -0.000011269 | -0.000006626 | -0.000013254 |
| 25 | 6 | 0.000000715 | 0.000004862 | 0.000004427 |
| 26 | 1 | -0.000000380 | 0.000000032 | -0.000000198 |
| 27 | 1 | -0.000001154 | 0.000001730 | 0.000002017 |
| 28 | 1 | -0.000000212 | 0.000001421 | 0.000001953 |
| 29 | 6 | 0.000001977 | 0.000000937 | 0.00000585 |
| 30 | 1 | -0.000000049 | -0.000001708 | -0.000001336 |
| 31 | 1 | -0.000000527 | 0.000001183 | -0.000002151 |
| 32 | 1 | -0.000000438 | -0.000000829 | -0.000002395 |
| 33 | 6 | -0.000009713 | 0.000002105 | -0.000005140 |
| 34 | 6 | 0.000002457 | 0.000001207 | -0.000006693 |
| 35 | 6 | 0.000001374 | 0.000002621 | -0.000000759 |
| 36 | 6 | -0.000001202 | -0.000003022 | 0.000003636 |
| 37 | 6 | -0.000004753 | 0.000002607 | 0.000004024 |
| 38 | 6 | -0.000001796 | -0.000002718 | -0.000001949 |
| 39 | 1 | 0.000003283 | -0.000000805 | -0.000001030 |
| 40 | 1 | 0.000000967 | 0.000001142 | 0.000003632 |
| 41 | 1 | 0.000001672 | -0.000000958 | 0.000002781 |

```
       42           1                0.000003312      0.000000019      0.000000136
 -------------------------------------------------------------------------------------------------
```

**M062X/6-31G (D) in gaussian 09 packages using SMD solvent model**

Compound **1'a**

In toluene

Number of Imaginary Frequencies = 0

Zero-point correction = 0.220491 (Hartree/Particle)

Thermal correction to Energy = 0.234341

Thermal correction to Enthalpy = 0.235286

Thermal correction to Gibbs Free Energy = 0.178352

Sum of electronic and zero-point Energies = -781.801458

Sum of electronic and thermal Energies = -781.787608

Sum of electronic and thermal Enthalpies = -781.786664

Sum of electronic and thermal Free Energies = -781.843598

```
-------------------------------------------------------------------------------------------------
 Center       Atomic                          Forces (Hartrees/Bohr)
 Number        Number                   X                      Y                      Z
 -------------------------------------------------------------------------------------------------
        1           6                0.000060496     -0.000006423      0.000002436
        2           6                0.000003461     -0.000004507     -0.000002142
        3           6               -0.000017069     -0.000005767     -0.000001511
        4           6               -0.000020516     -0.000000351      0.000002838
        5           6               -0.000000123     -0.000004729      0.000000709
        6           6                0.000004051      0.000001875      0.000002806
        7           1                0.000002385     -0.000003788      0.000000671
        8           1               -0.000002135     -0.000005962      0.000001466
        9           1               -0.000003814     -0.000003272      0.000002480
       10           1                0.000003229     -0.000001362     -0.000000700
       11           6               -0.000005955      0.000006288      0.000001730
       12           6               -0.000011662      0.000015273      0.000003049
       13           6                0.000007917     -0.000001641     -0.000002384
       14           6                0.000002234     -0.000000127     -0.000000377
       15           6                0.000004397     -0.000003835      0.000000479
       16           6               -0.000000088      0.000001628     -0.000000443
       17           1                0.000002056      0.000000597     -0.000001244
       18           1               -0.000000050     -0.000000228     -0.000000996
       19           1                0.000001200      0.000004320     -0.000001172
```

```
     20          1            0.000003627      0.000003687     -0.000001319
     21          7           -0.000023250     -0.000006747      0.000000172
     22          8            0.000000343     -0.000005752      0.000003119
     23          8           -0.000005142     -0.000007013      0.000001215
     24          8            0.000011008      0.000003115     -0.000011534
     25          6           -0.000009071     -0.000000475      0.000006930
     26          1           -0.000003680      0.000009005     -0.000002865
     27          1           -0.000001579      0.000007004     -0.000000738
     28          1           -0.000002270      0.000009188     -0.000002678
 -------------------------------------------------------------------------------------------------
```

In chloroform
Number of Imaginary Frequencies = 0
Zero-point correction = 0.220421 (Hartree/Particle)
Thermal correction to Energy = 0.234296
Thermal correction to Enthalpy = 0.235240
Thermal correction to Gibbs Free Energy = 0.178184
Sum of electronic and zero-point Energies = -781.803028
Sum of electronic and thermal Energies = -781.789153
Sum of electronic and thermal Enthalpies = -781.788209
Sum of electronic and thermal Free Energies = -781.845264

```
-------------------------------------------------------------------------------------------------
 Center      Atomic                      Forces (Hartrees/Bohr)
 Number        Number              X                       Y                       Z
 -------------------------------------------------------------------------------------------------
      1          6           -0.000040429     -0.000006863      0.000006343
      2          6           -0.000010637      0.000000613      0.000000240
      3          6            0.000023290      0.000002294      0.000010885
      4          6            0.000022276     -0.000009567     -0.000005150
      5          6           -0.000003843      0.000005909     -0.000001820
      6          6            0.000002172     -0.000008455      0.000002316
      7          1            0.000003195     -0.000009405      0.000007705
      8          1           -0.000001066     -0.000000682     -0.000002618
      9          1           -0.000005351      0.000001653     -0.000004551
     10          1            0.000001534     -0.000004963      0.000009003
     11          6            0.000012092     -0.000007910      0.000005799
     12          6            0.000020349     -0.000006597      0.000008600
     13          6           -0.000006727      0.000004976     -0.000000623
```

```
      14          6           -0.000006069      0.000005181     -0.000006255
      15          6           -0.000005646      0.000009192     -0.000008543
      16          6            0.000003201      0.000005602      0.000003963
      17          1            0.000003501      0.000001531      0.000006310
      18          1           -0.000001931     -0.000000989     -0.000005801
      19          1           -0.000001288      0.000002994     -0.000007682
      20          1            0.000002535      0.000005141      0.000006077
      21          7            0.000019348     -0.000000741     -0.000019284
      22          8           -0.000004791     -0.000013158      0.000007601
      23          8           -0.000006611     -0.000006352      0.000012542
      24          8           -0.000011110      0.000008150     -0.000008968
      25          6           -0.000006120      0.000003905     -0.000002333
      26          1           -0.000002085      0.000008136     -0.000005261
      27          1            0.000002327      0.000008704     -0.000001989
      28          1           -0.000002118      0.000001702     -0.000006508
 -------------------------------------------------------------------------------------------
```

In DMSO

Number of Imaginary Frequencies = 0

Zero-point correction = 0.220420 (Hartree/Particle)

Thermal correction to Energy = 0.234313

Thermal correction to Enthalpy = 0.235257

Thermal correction to Gibbs Free Energy = 0.177862

Sum of electronic and zero-point Energies = -781.800101

Sum of electronic and thermal Energies = -781.786208

Sum of electronic and thermal Enthalpies = -781.785264

Sum of electronic and thermal Free Energies = -781.842659

```
-------------------------------------------------------------------------------------------
 Center      Atomic                        Forces (Hartrees/Bohr)
 Number       Number              X                    Y                    Z
 -------------------------------------------------------------------------------------------
       1          6            0.000041651     -0.000001943      0.000000977
       2          6            0.000006069     -0.000002879      0.000000437
       3          6           -0.000009505     -0.000004949      0.000000382
       4          6           -0.000013294      0.000000220      0.000000593
       5          6           -0.000003830     -0.000003212     -0.000001207
       6          6           -0.000003253      0.000001455      0.000002977
       7          1            0.000000262     -0.000002712      0.000002525
```

| | | | | |
|---|---|---|---|---|
| 8 | 1 | -0.000002163 | -0.000001802 | -0.000000719 |
| 9 | 1 | -0.000001449 | -0.000000789 | -0.000000424 |
| 10 | 1 | 0.000001290 | -0.000001368 | 0.000001282 |
| 11 | 6 | -0.000008659 | 0.000002774 | 0.000000266 |
| 12 | 6 | -0.000001064 | 0.000004082 | 0.000000171 |
| 13 | 6 | 0.000005791 | 0.000001421 | 0.000000019 |
| 14 | 6 | 0.000007006 | 0.000000741 | -0.000000307 |
| 15 | 6 | -0.000006662 | 0.000000713 | -0.000001540 |
| 16 | 6 | 0.000000313 | 0.000001755 | 0.000000503 |
| 17 | 1 | 0.000001707 | 0.000000885 | 0.000001672 |
| 18 | 1 | -0.000000862 | -0.000000460 | -0.000002561 |
| 19 | 1 | -0.000000202 | 0.000000956 | -0.000002476 |
| 20 | 1 | 0.000001488 | 0.000002227 | 0.000000927 |
| 21 | 7 | -0.000029842 | -0.000004892 | 0.000005998 |
| 22 | 8 | 0.000009267 | -0.000002530 | 0.000001717 |
| 23 | 8 | 0.000008393 | -0.000004124 | -0.000001410 |
| 24 | 8 | -0.000002764 | -0.000005130 | -0.000000193 |
| 25 | 6 | 0.000005281 | 0.000012720 | -0.000003707 |
| 26 | 1 | -0.000001509 | 0.000002448 | -0.000003189 |
| 27 | 1 | -0.000001347 | 0.000003172 | -0.000001114 |
| 28 | 1 | -0.000002113 | 0.000001219 | -0.000001601 |

---

Compound **1’b**

In toluene

Number of Imaginary Frequencies = 0

Zero-point correction = 0.261588 (Hartree/Particle)

Thermal correction to Energy = 0.277189

Thermal correction to Enthalpy = 0.278133

Thermal correction to Gibbs Free Energy = 0.217441

Sum of electronic and zero-point Energies = -801.191098

Sum of electronic and thermal Energies = -801.175497

Sum of electronic and thermal Enthalpies = -801.174553

Sum of electronic and thermal Free Energies = -801.235245

```
 -------------------------------------------------------------------
 Center     Atomic                   Forces (Hartrees/Bohr)
 Number     Number              X              Y              Z
 -------------------------------------------------------------------
      1          6       -0.000008446    0.000000135   -0.000002192
      2          6       -0.000002809    0.000000010    0.000000280
      3          6        0.000001445    0.000000702    0.000004409
      4          6        0.000003990    0.000001622   -0.000002175
      5          6        0.000001555   -0.000001212   -0.000003833
      6          6       -0.000000894    0.000000422    0.000003051
      7          1       -0.000002220    0.000001650    0.000006168
      8          1        0.000000997   -0.000000903   -0.000003012
      9          1        0.000001739   -0.000000874   -0.000003856
     10          1       -0.000000052    0.000001206    0.000005055
     11          6        0.000001912   -0.000000599   -0.000000654
     12          6        0.000020938   -0.000001395   -0.000001525
     13          6       -0.000000779   -0.000002870    0.000000606
     14          6       -0.000000210    0.000000406   -0.000003295
     15          6       -0.000006010   -0.000002223   -0.000005413
     16          6       -0.000008005   -0.000000974    0.000000385
     17          1       -0.000001247   -0.000002804    0.000003929
     18          1        0.000000228    0.000001320   -0.000005870
     19          1        0.000000065    0.000000053   -0.000006730
     20          1       -0.000001945   -0.000003608    0.000002904
     21          7        0.000008769    0.000000833    0.000002744
     22          7       -0.000006804   -0.000002695   -0.000002487
     23          8        0.000000560    0.000001132    0.000000902
     24          8        0.000001634   -0.000005966   -0.000007214
     25          6       -0.000001154    0.000000706    0.000006651
     26          1       -0.000000017    0.000001634    0.000005095
     27          1       -0.000000249    0.000004700    0.000004948
     28          1       -0.000000563    0.000000807    0.000006890
     29          6       -0.000002649    0.000004252   -0.000001941
     30          1       -0.000001531   -0.000001247   -0.000001250
     31          1        0.000001196    0.000002952   -0.000003215
     32          1        0.000000556    0.000002827    0.000000644
 -------------------------------------------------------------------
```

In choloform
Number of Imaginary Frequencies = 0
Zero-point correction = 0.261583 (Hartree/Particle)
Thermal correction to Energy = 0.277131
Thermal correction to Enthalpy = 0.278075
Thermal correction to Gibbs Free Energy = 0.217529
Sum of electronic and zero-point Energies = -801.193282
Sum of electronic and thermal Energies = -801.177735
Sum of electronic and thermal Enthalpies = -801.176790
Sum of electronic and thermal Free Energies = -801.237336

```
-------------------------------------------------------------------------------------------
 Center      Atomic                      Forces (Hartrees/Bohr)
 Number       Number              X                      Y                      Z
 -------------------------------------------------------------------------------------------
      1           6           0.000011602       0.000000030      -0.000000501
      2           6           0.000000594      -0.000001284       0.000002825
      3           6          -0.000004772      -0.000001830       0.000005797
      4           6          -0.000004465       0.000002850      -0.000005065
      5           6           0.000001776      -0.000004146      -0.000004582
      6           6           0.000002352       0.000004004       0.000004688
      7           1           0.000002671       0.000004214       0.000008074
      8           1           0.000002188      -0.000003735      -0.000005720
      9           1           0.000001581      -0.000002247      -0.000006629
     10           1           0.000001192       0.000001672       0.000006518
     11           6          -0.000008006       0.000000677      -0.000003755
     12           6           0.000077689       0.000000013       0.000000845
     13           6           0.000007979      -0.000001943       0.000003669
     14           6           0.000007766      -0.000000483      -0.000003056
     15           6          -0.000014034       0.000001637      -0.000003198
     16           6          -0.000016176      -0.000004528      -0.000000281
     17           1          -0.000001571      -0.000003074       0.000006848
     18           1          -0.000000182       0.000001776      -0.000007568
     19           1           0.000001920       0.000001169      -0.000008739
     20           1           0.000000784      -0.000003226       0.000006514
     21           7          -0.000012048      -0.000000520       0.000001143
     22           7          -0.000038105      -0.000000339      -0.000003296
     23           8          -0.000010995      -0.000006421       0.000004566
     24           8          -0.000010236       0.000002787      -0.000007052
```

```
      25          6           0.000002582      0.000004986      0.000006083
      26          1          -0.000000134      0.000000698      0.000004116
      27          1          -0.000000211      0.000006290      0.000004360
      28          1          -0.000003288      0.000001639      0.000009204
      29          6           0.000002515     -0.000001097     -0.000006090
      30          1          -0.000000327     -0.000004080     -0.000003253
      31          1          -0.000000923      0.000002648     -0.000006046
      32          1           0.000000282      0.000001867     -0.000000419
 -------------------------------------------------------------------------------------------------
```

In DMSO

Number of Imaginary Frequencies = 0

Zero-point correction = 0.261602 (Hartree/Particle)

Thermal correction to Energy = 0.277096

Thermal correction to Enthalpy = 0.278040

Thermal correction to Gibbs Free Energy = 0.217789

Sum of electronic and zero-point Energies = -801.189072

Sum of electronic and thermal Energies = -801.173578

Sum of electronic and thermal Enthalpies = -801.172634

Sum of electronic and thermal Free Energies = -801.232885

```
-------------------------------------------------------------------------------------------------
 Center       Atomic                       Forces (Hartrees/Bohr)
 Number        Number                X                      Y                        Z
 -------------------------------------------------------------------------------------------------
       1          6           0.000025204      0.000000562      0.000010422
       2          6          -0.000009507     -0.000001207      0.000000987
       3          6          -0.000010685     -0.000000304      0.000000623
       4          6          -0.000005828      0.000003795      0.000000548
       5          6           0.000006108     -0.000001017     -0.000001039
       6          6           0.000005682      0.000001772      0.000000023
       7          1           0.000001239      0.000000848      0.000000537
       8          1           0.000003035     -0.000002576      0.000003786
       9          1           0.000001984     -0.000000023      0.000002537
      10          1           0.000000366      0.000000740     -0.000000809
      11          6           0.000004385      0.000001352     -0.000000654
      12          6           0.000045143     -0.000000241     -0.000001117
      13          6           0.000002183     -0.000001308     -0.000005041
      14          6           0.000001802     -0.000000680     -0.000000790
```

| | | | | |
|---|---|---|---|---|
| 15 | 6 | -0.000009900 | 0.000001805 | -0.000002583 |
| 16 | 6 | -0.000011595 | -0.000003339 | -0.000005183 |
| 17 | 1 | -0.000001167 | 0.000001257 | -0.000002270 |
| 18 | 1 | -0.000001878 | -0.000000648 | -0.000002410 |
| 19 | 1 | 0.000000977 | -0.000002280 | -0.000003217 |
| 20 | 1 | -0.000000390 | 0.000001352 | -0.000004145 |
| 21 | 7 | -0.000025058 | -0.000002673 | -0.000004335 |
| 22 | 7 | -0.000027741 | 0.000002133 | -0.000013088 |
| 23 | 8 | 0.000000841 | 0.000008055 | -0.000000656 |
| 24 | 8 | 0.000001632 | -0.000011134 | -0.000006295 |
| 25 | 6 | 0.000005668 | 0.000005704 | 0.000003650 |
| 26 | 1 | -0.000000767 | -0.000000410 | 0.000006287 |
| 27 | 1 | 0.000001187 | -0.000001129 | 0.000001872 |
| 28 | 1 | -0.000000988 | 0.000000543 | 0.000002736 |
| 29 | 6 | 0.000002680 | -0.000003552 | 0.000003130 |
| 30 | 1 | -0.000003257 | 0.000000043 | 0.000005080 |
| 31 | 1 | -0.000000265 | 0.000000728 | 0.000003972 |
| 32 | 1 | -0.000001087 | 0.000001832 | 0.000007444 |

Compound **2’a**
In toluene
Number of Imaginary Frequencies = 0
Zero-point correction = 0.302607 (Hartree/Particle)
Thermal correction to Energy = 0.320895
Thermal correction to Enthalpy = 0.321839
Thermal correction to Gibbs Free Energy = 0.254757
Sum of electronic and zero-point Energies = -1012.687089
Sum of electronic and thermal Energies = -1012.668802
Sum of electronic and thermal Enthalpies = -1012.667857
Sum of electronic and thermal Free Energies = -1012.734940

| Center | Atomic | Forces (Hartrees/Bohr) | | |
|---|---|---|---|---|
| Number | Number | X | Y | Z |
| 1 | 6 | 0.000019255 | 0.000003036 | 0.000001388 |
| 2 | 6 | 0.000031060 | -0.000015400 | 0.000008309 |
| 3 | 6 | -0.000007123 | 0.000001202 | 0.000015337 |

```
    4          6          -0.000010842     0.000004097    -0.000012543
    5          6          -0.000011360     0.000006338    -0.000005748
    6          6          -0.000004250     0.000003371     0.000000417
    7          1          -0.000000395     0.000012811     0.000012899
    8          1          -0.000002509    -0.000012365    -0.000013101
    9          1          -0.000003052    -0.000012636    -0.000017811
   10          1           0.000000937     0.000011762     0.000018157
   11          6          -0.000025772    -0.000001923     0.000001286
   12          6           0.000026670    -0.000002121     0.000004071
   13          6           0.000018866     0.000009636    -0.000012443
   14          6           0.000015261    -0.000005439     0.000014396
   15          6          -0.000015657    -0.000004482     0.000004892
   16          6          -0.000014838     0.000009164    -0.000005547
   17          1           0.000002612    -0.000000531    -0.000020389
   18          1           0.000002978     0.000002793     0.000022604
   19          1           0.000003714     0.000003280     0.000020813
   20          1           0.000005031    -0.000002981    -0.000019690
   21          6          -0.000015560    -0.000001303    -0.000004031
   22          6           0.000027736     0.000001028    -0.000000276
   23          6          -0.000000911     0.000024386    -0.000004504
   24          6          -0.000002691    -0.000022025     0.000007125
   25          6           0.000006988     0.000003991     0.000019320
   26          6           0.000006248    -0.000003666    -0.000018420
   27          1          -0.000007441     0.000010382    -0.000013008
   28          1          -0.000006075    -0.000009541     0.000014555
   29          1           0.000001725    -0.000014475     0.000010146
   30          1           0.000001995     0.000014105    -0.000011207
   31          7          -0.000033749    -0.000002931     0.000004399
   32          8           0.000001767    -0.000009783     0.000000526
   33          8          -0.000002941     0.000013119    -0.000005778
   34          8          -0.000008480     0.000023879     0.000019936
   35          6          -0.000004407    -0.000018997    -0.000010478
   36          1           0.000002653     0.000002274    -0.000011856
   37          1           0.000005341    -0.000007754    -0.000004956
   38          1          -0.000002784    -0.000012299    -0.000008791
-------------------------------------------------------------------------------------------
```

In cholorform

Number of Imaginary Frequencies = 0

Zero-point correction = 0.302509 (Hartree/Particle)

Thermal correction to Energy = 0.320837

Thermal correction to Enthalpy = 0.321781

Thermal correction to Gibbs Free Energy = 0.254495

Sum of electronic and zero-point Energies = -1012.689455

Sum of electronic and thermal Energies = -1012.671127

Sum of electronic and thermal Enthalpies = -1012.670183

Sum of electronic and thermal Free Energies = -1012.737469

```
-------------------------------------------------------------------------------------------
 Center     Atomic                    Forces (Hartrees/Bohr)
 Number      Number          X                   Y                   Z
-------------------------------------------------------------------------------------------
      1          6        0.000015931        0.000004021       -0.000001655
      2          6        0.000034948       -0.000021410        0.000002372
      3          6       -0.000015762        0.000005432        0.000011348
      4          6       -0.000017044       -0.000002765       -0.000007640
      5          6       -0.000010435        0.000011973       -0.000004422
      6          6       -0.000000925        0.000001083        0.000000578
      7          1        0.000000529        0.000005222        0.000008645
      8          1       -0.000002681       -0.000005582       -0.000010011
      9          1       -0.000005870       -0.000007750       -0.000011291
     10          1       -0.000001297        0.000006534        0.000011392
     11          6       -0.000018261       -0.000002006        0.000003196
     12          6        0.000023857       -0.000002517        0.000005119
     13          6        0.000027199        0.000000870       -0.000003847
     14          6        0.000022438        0.000001030        0.000005835
     15          6       -0.000021250        0.000000582        0.000005167
     16          6       -0.000021633        0.000003939       -0.000006342
     17          1        0.000000833        0.000003114       -0.000015493
     18          1        0.000000483       -0.000000662        0.000015555
     19          1        0.000003304       -0.000000667        0.000012562
     20          1        0.000005235        0.000000271       -0.000013917
     21          6       -0.000020864        0.000000173       -0.000005692
     22          6        0.000012091        0.000001651        0.000000002
     23          6        0.000010332        0.000011953       -0.000000683
     24          6        0.000007123       -0.000011734        0.000003600
     25          6        0.000004569        0.000007818        0.000015196
```

```
   26          6            0.000001984    -0.000007221    -0.000015700
   27          1           -0.000006899     0.000008713    -0.000007769
   28          1           -0.000003802    -0.000009112     0.000010361
   29          1            0.000003895    -0.000011382     0.000006817
   30          1            0.000003994     0.000010368    -0.000007587
   31          7           -0.000040731     0.000000511     0.000002934
   32          8            0.000008120    -0.000005609     0.000000153
   33          8            0.000005042     0.000005084    -0.000003548
   34          8           -0.000012799     0.000025924     0.000021664
   35          6            0.000002220    -0.000019620    -0.000014126
   36          1            0.000003531     0.000003021    -0.000005898
   37          1            0.000005161    -0.000003339    -0.000002449
   38          1           -0.000002565    -0.000007912    -0.000004425
 -------------------------------------------------------------------------------------------
```

In DMSO

```
Number of Imaginary Frequencies = 0
Zero-point correction = 0.302432 (Hartree/Particle)
Thermal correction to Energy = 0.320792
Thermal correction to Enthalpy = 0.321736
Thermal correction to Gibbs Free Energy = 0.254328
Sum of electronic and zero-point Energies = -1012.684587
Sum of electronic and thermal Energies = -1012.666226
Sum of electronic and thermal Enthalpies = -1012.665282
Sum of electronic and thermal Free Energies = -1012.732690
```

```
-------------------------------------------------------------------------------------------
 Center      Atomic                      Forces (Hartrees/Bohr)
 Number       Number              X                   Y                   Z
 -------------------------------------------------------------------------------------------
    1          6            0.000003631     0.000009040    -0.000004801
    2          6            0.000007345    -0.000000299     0.000006926
    3          6           -0.000009527     0.000000177     0.000004566
    4          6           -0.000014763    -0.000012736    -0.000002429
    5          6            0.000002569     0.000003654    -0.000005425
    6          6           -0.000003682    -0.000002789     0.000003735
    7          1            0.000000988     0.000004662     0.000009553
    8          1           -0.000001693    -0.000003687    -0.000011060
    9          1            0.000000120    -0.000007533    -0.000009889
```

| | | | | |
|---|---|---|---|---|
| 10 | 1 | -0.000000073 | 0.000005643 | 0.000008073 |
| 11 | 6 | 0.000000706 | 0.000001602 | 0.000002812 |
| 12 | 6 | 0.000002290 | 0.000002429 | 0.000003690 |
| 13 | 6 | 0.000017696 | -0.000005601 | -0.000003321 |
| 14 | 6 | 0.000015223 | 0.000004570 | 0.000005821 |
| 15 | 6 | -0.000012568 | 0.000002403 | 0.000008418 |
| 16 | 6 | -0.000012230 | -0.000001216 | -0.000005789 |
| 17 | 1 | -0.000002001 | 0.000004200 | -0.000013290 |
| 18 | 1 | -0.000003011 | -0.000003152 | 0.000011979 |
| 19 | 1 | -0.000000233 | -0.000002455 | 0.000009727 |
| 20 | 1 | 0.000001709 | 0.000003345 | -0.000011455 |
| 21 | 6 | -0.000005567 | -0.000000478 | -0.000004043 |
| 22 | 6 | -0.000047823 | -0.000001727 | 0.000004270 |
| 23 | 6 | 0.000004639 | 0.000007773 | 0.000000635 |
| 24 | 6 | 0.000003971 | -0.000005256 | 0.000004143 |
| 25 | 6 | 0.000020881 | 0.000004441 | 0.000010140 |
| 26 | 6 | 0.000021455 | -0.000002677 | -0.000003476 |
| 27 | 1 | 0.000000260 | 0.000009405 | -0.000008269 |
| 28 | 1 | 0.000000575 | -0.000007994 | 0.000011192 |
| 29 | 1 | 0.000001297 | -0.000007277 | 0.000010034 |
| 30 | 1 | 0.000003219 | 0.000008675 | -0.000008166 |
| 31 | 7 | 0.000032332 | 0.000017413 | -0.000015398 |
| 32 | 8 | -0.000011854 | -0.000024256 | 0.000002676 |
| 33 | 8 | -0.000015060 | 0.000015651 | 0.000012826 |
| 34 | 8 | 0.000009729 | 0.000022538 | 0.000003243 |
| 35 | 6 | -0.000017954 | -0.000033209 | -0.000007757 |
| 36 | 1 | 0.000000894 | 0.000003151 | -0.000005805 |
| 37 | 1 | 0.000006211 | -0.000002628 | -0.000005898 |
| 38 | 1 | 0.000000297 | -0.000005805 | -0.000008189 |

-------------------------------------------------------------------------------------------------

Compound **2’b**

In toluene

Number of Imaginary Frequencies = 0

Zero-point correction = 0.343190 (Hartree/Particle)

Thermal correction to Energy = 0.363452

Thermal correction to Enthalpy = 0.364396

Thermal correction to Gibbs Free Energy = 0.292355

Sum of electronic and zero-point Energies = -1032.076402

```
Sum of electronic and thermal Energies = -1032.056140
Sum of electronic and thermal Enthalpies = -1032.055196
Sum of electronic and thermal Free Energies = -1032.127237

-------------------------------------------------------------------
 Center     Atomic                   Forces (Hartrees/Bohr)
 Number     Number              X              Y              Z
 -------------------------------------------------------------------
      1          1          0.000000428   -0.000002389    0.000002751
      2          6          0.000001921    0.000001865    0.000002664
      3          6          0.000001221   -0.000001386   -0.000002584
      4          6         -0.000000790    0.000001041   -0.000000695
      5          6          0.000001139    0.000001094    0.000003781
      6          6         -0.000000396   -0.000000042    0.000000589
      7          6          0.000000856   -0.000002294   -0.000002144
      8          1          0.000000955   -0.000001965    0.000002780
      9          1          0.000000313    0.000002345   -0.000002698
     10          1          0.000001035    0.000001816   -0.000001921
     11          6          0.000001328   -0.000001982    0.000000606
     12          6          0.000012675   -0.000000499    0.000007838
     13          6         -0.000001915    0.000005238    0.000001569
     14          6         -0.000000853   -0.000003602   -0.000003998
     15          6         -0.000003569    0.000003760   -0.000004165
     16          6         -0.000001677   -0.000001547    0.000000459
     17          1         -0.000000941   -0.000000438    0.000001885
     18          1         -0.000000851    0.000000555   -0.000002577
     19          1         -0.000001501   -0.000001061   -0.000003727
     20          1         -0.000001292    0.000001342    0.000000533
     21          6         -0.000002347    0.000000661    0.000001717
     22          6         -0.000015513    0.000000121    0.000001245
     23          6         -0.000000952   -0.000001447    0.000000352
     24          6         -0.000001588    0.000000222    0.000001128
     25          6          0.000004972    0.000000165    0.000006475
     26          6          0.000004057   -0.000001012   -0.000001765
     27          1         -0.000000154   -0.000001574   -0.000003020
     28          1          0.000000451    0.000001017    0.000003908
     29          1         -0.000000776    0.000000736    0.000003149
     30          1         -0.000001260   -0.000001317   -0.000000628
     31          7         -0.000005845   -0.000001280   -0.000013697
```

```
    32          7            -0.000005519    -0.000000955      0.000000616
    33          8             0.000007510    -0.000012049      0.000004047
    34          8             0.000007366     0.000011394      0.000000444
    35          6            -0.000000673    -0.000002063     -0.000000084
    36          1            -0.000000295     0.000002133     -0.000002975
    37          1            -0.000000490    -0.000001222     -0.000002632
    38          1             0.000002437     0.000000586     -0.000004868
    39          6            -0.000001583     0.000003401      0.000005692
    40          1             0.000001843     0.000001329     -0.000000645
    41          1             0.000000252     0.000000299      0.000000991
    42          1             0.000000024    -0.000000996     -0.000000398
 -------------------------------------------------------------------------------------------
```

In cholofrom
Number of Imaginary Frequencies = 0
Zero-point correction = 0.342911 (Hartree/Particle)
Thermal correction to Energy = 0.363209
Thermal correction to Enthalpy = 0.364153
Thermal correction to Gibbs Free Energy = 0.291919
Sum of electronic and zero-point Energies = -1032.079594
Sum of electronic and thermal Energies = -1032.059296
Sum of electronic and thermal Enthalpies = -1032.058352
Sum of electronic and thermal Free Energies = -1032.130586

```
 -------------------------------------------------------------------------------------------
 Center      Atomic                          Forces (Hartrees/Bohr)
 Number       Number                X                      Y                        Z
 -------------------------------------------------------------------------------------------
     1          1            -0.000003609     0.000000492     -0.000002225
     2          6             0.000004120     0.000001165      0.000000445
     3          6            -0.000002891     0.000001788      0.000002553
     4          6            -0.000000744    -0.000003692      0.000001991
     5          6            -0.000005123     0.000000120     -0.000001207
     6          6             0.000003228    -0.000002260      0.000001098
     7          6             0.000004560     0.000002276     -0.000001194
     8          1            -0.000001061     0.000000400      0.000000581
     9          1            -0.000001251    -0.000000562      0.000001079
    10          1            -0.000000313    -0.000000554      0.000000960
    11          6            -0.000004116    -0.000001836     -0.000002726
```

| | | | | |
|---|---|---|---|---|
| 12 | 6 | 0.000011141 | -0.000002693 | 0.000004384 |
| 13 | 6 | -0.000000873 | 0.000000981 | -0.000002323 |
| 14 | 6 | 0.000001658 | 0.000002430 | 0.000002519 |
| 15 | 6 | -0.000005655 | 0.000001813 | 0.000000695 |
| 16 | 6 | -0.000000305 | 0.000000758 | -0.000003818 |
| 17 | 1 | 0.000004114 | -0.000000791 | -0.000000895 |
| 18 | 1 | 0.000001437 | 0.000000793 | 0.000000090 |
| 19 | 1 | -0.000001351 | 0.000000434 | -0.000002184 |
| 20 | 1 | 0.000001879 | -0.000001696 | -0.000002616 |
| 21 | 6 | -0.000002907 | -0.000000604 | 0.000001099 |
| 22 | 6 | 0.000036930 | -0.000000582 | 0.000002168 |
| 23 | 6 | 0.000008161 | -0.000000446 | 0.000001340 |
| 24 | 6 | 0.000007929 | 0.000001418 | 0.000001418 |
| 25 | 6 | -0.000014935 | 0.000002805 | -0.000002989 |
| 26 | 6 | -0.000014176 | -0.000001803 | 0.000007285 |
| 27 | 1 | -0.000000070 | 0.000001208 | 0.000003605 |
| 28 | 1 | -0.000000008 | -0.000001124 | -0.000001284 |
| 29 | 1 | 0.000002759 | -0.000001242 | 0.000002247 |
| 30 | 1 | 0.000002800 | 0.000001442 | 0.000001911 |
| 31 | 7 | -0.000011036 | -0.000000164 | -0.000003061 |
| 32 | 7 | -0.000029019 | -0.000001086 | 0.000004185 |
| 33 | 8 | 0.000000807 | 0.000001968 | -0.000000884 |
| 34 | 8 | 0.000002149 | -0.000000657 | 0.000004561 |
| 35 | 6 | 0.000004035 | 0.000004513 | -0.000003046 |
| 36 | 1 | -0.000000244 | -0.000000221 | -0.000001987 |
| 37 | 1 | 0.000000134 | 0.000001024 | -0.000001878 |
| 38 | 1 | 0.000000752 | -0.000000858 | -0.000001226 |
| 39 | 6 | 0.000001897 | -0.000004299 | -0.000001489 |
| 40 | 1 | -0.000001854 | -0.000000810 | -0.000002661 |
| 41 | 1 | 0.000000868 | 0.000000420 | -0.000003819 |
| 42 | 1 | 0.000000184 | -0.000000266 | -0.000002702 |

---

In DMSO

Number of Imaginary Frequencies = 0

Zero-point correction = 0.342819 (Hartree/Particle)

Thermal correction to Energy = 0.363062

Thermal correction to Enthalpy = 0.364006

Thermal correction to Gibbs Free Energy = 0.292108

```
Sum of electronic and zero-point Energies = -1032.073641
Sum of electronic and thermal Energies = -1032.053398
Sum of electronic and thermal Enthalpies = -1032.052454
Sum of electronic and thermal Free Energies = -1032.124351

-------------------------------------------------------------------
 Center     Atomic                   Forces (Hartrees/Bohr)
 Number     Number              X              Y              Z
 -------------------------------------------------------------------
      1        1          -0.000002613    0.000000890   -0.000005981
      2        6           0.000005775    0.000003244   -0.000000674
      3        6          -0.000004209   -0.000004200    0.000000990
      4        6          -0.000005292    0.000001566   -0.000001303
      5        6          -0.000004630    0.000003835   -0.000000926
      6        6           0.000003415    0.000000969    0.000001185
      7        6           0.000004321   -0.000003690    0.000001737
      8        1           0.000003522    0.000000971   -0.000005978
      9        1          -0.000002871   -0.000001728    0.000006925
     10        1           0.000003384   -0.000001713    0.000007443
     11        6           0.000005949   -0.000004542    0.000001126
     12        6           0.000019738   -0.000003673    0.000003439
     13        6          -0.000003431    0.000003615   -0.000005915
     14        6          -0.000000463   -0.000000420    0.000003518
     15        6          -0.000003993    0.000004839    0.000004587
     16        6          -0.000001514   -0.000002060   -0.000005326
     17        1           0.000001763   -0.000001894   -0.000006425
     18        1           0.000002163    0.000001552    0.000005513
     19        1           0.000000229    0.000001056    0.000005209
     20        1           0.000000165   -0.000000854   -0.000008630
     21        6          -0.000005215   -0.000001196    0.000000413
     22        6          -0.000041487    0.000000119    0.000003384
     23        6           0.000005622   -0.000000305    0.000005835
     24        6           0.000005040   -0.000000328   -0.000003921
     25        6           0.000009116    0.000000182   -0.000003130
     26        6           0.000008313   -0.000001190    0.000006416
     27        1          -0.000003533    0.000001763    0.000006909
     28        1          -0.000002762   -0.000002280   -0.000005202
     29        1           0.000003538   -0.000001588   -0.000004949
     30        1           0.000003324    0.000000786    0.000008086
```

```
      31          7          -0.000014048     -0.000001627     -0.000007961
      32          7           0.000022027     -0.000003014     -0.000007457
      33          8          -0.000005144     -0.000005982      0.000007619
      34          8          -0.000004844      0.000006565      0.000002656
      35          6          -0.000001547     -0.000001402      0.000001229
      36          1          -0.000000532      0.000003333      0.000000439
      37          1          -0.000000732      0.000004789      0.000003560
      38          1           0.000001665      0.000000320      0.000004406
      39          6          -0.000003349      0.000006255      0.000002000
      40          1          -0.000000643     -0.000002737     -0.000009045
      41          1           0.000003202      0.000002467     -0.000009135
      42          1           0.000000583     -0.000002692     -0.000002666
 -------------------------------------------------------------------------------------------------
```

**CAM-B3LYP/6-31G (d) in Gaussian 09 packages using SMD solvent model.**

Compound **1’a**

In toluene

Number of Imaginary Frequencies = 0

Zero-point correction = 0.220523 (Hartree/Particle)

Thermal correction to Energy = 0.234356

Thermal correction to Enthalpy= 0.235300

Thermal correction to Gibbs Free Energy = 0.178479

Sum of electronic and zero-point Energies = -781.739468

Sum of electronic and thermal Energies = -781.725636

Sum of electronic and thermal Enthalpies = - -781.724692

Sum of electronic and thermal Free Energies = -781.781512

```
 -------------------------------------------------------------------------------------------------
 Center      Atomic                        Forces (Hartrees/Bohr)
 Number        Number              X                          Y                         Z
 -------------------------------------------------------------------------------------------------
       1          6          -0.000060414      0.000004730     -0.000002646
       2          6          -0.000023301      0.000006891     -0.000010930
       3          6           0.000033147      0.000001631     -0.000002921
       4          6           0.000032338      0.000001047     -0.000001138
       5          6           0.000000090     -0.000002962      0.000004415
       6          6           0.000001710      0.000004081      0.000001970
       7          1           0.000000788      0.000000086      0.000001529
       8          1           0.000003062      0.000002805     -0.000003827
```

| | | | | |
|---|---|---|---|---|
| 9 | 1 | 0.000005535 | 0.000003127 | -0.000001523 |
| 10 | 1 | 0.000007544 | -0.000005148 | 0.000004268 |
| 11 | 6 | 0.000021130 | 0.000001816 | 0.000006825 |
| 12 | 6 | 0.000011408 | 0.000004777 | 0.000010828 |
| 13 | 6 | -0.000005208 | 0.000004388 | 0.000000190 |
| 14 | 6 | -0.000011974 | -0.000008537 | -0.000004020 |
| 15 | 6 | -0.000000949 | -0.000000525 | -0.000002240 |
| 16 | 6 | -0.000009535 | 0.000000311 | 0.000001126 |
| 17 | 1 | -0.000008394 | -0.000004851 | -0.000001912 |
| 18 | 1 | -0.000004112 | 0.000003598 | -0.000000729 |
| 19 | 1 | -0.000005855 | -0.000001071 | -0.000000873 |
| 20 | 1 | -0.000001397 | -0.000002242 | 0.000002625 |
| 21 | 7 | 0.000017533 | 0.000000436 | 0.000004390 |
| 22 | 8 | 0.000003626 | 0.000029678 | 0.000007336 |
| 23 | 8 | -0.000000119 | -0.000022851 | -0.000013694 |
| 24 | 8 | -0.000024549 | -0.000035396 | 0.000002397 |
| 25 | 6 | 0.000016129 | 0.000046633 | -0.000011771 |
| 26 | 1 | 0.000001249 | -0.000011748 | 0.000001886 |
| 27 | 1 | -0.000001629 | -0.000006761 | 0.000004410 |
| 28 | 1 | 0.000002148 | -0.000013944 | 0.000004031 |

In chloroform

Number of Imaginary Frequencies = 0

Zero-point correction = 0.220483 (Hartree/Particle)

Thermal correction to Energy = 0.234320

Thermal correction to Enthalpy= 0.235264

Thermal correction to Gibbs Free Energy = 0.178458

Sum of electronic and zero-point Energies = -781.740817

Sum of electronic and thermal Energies = -781.726980

Sum of electronic and thermal Enthalpies = -781.726036

Sum of electronic and thermal Free Energies = -781.782842

| Center Number | Atomic Number | Forces (Hartrees/Bohr) X | Y | Z |
|---|---|---|---|---|
| 1 | 6 | -0.000024487 | 0.000003800 | -0.000000459 |
| 2 | 6 | -0.000011393 | 0.000003849 | -0.000013330 |

```
      3          6           0.000014884    -0.000012285    -0.000002976
      4          6           0.000013808     0.000015282     0.000000717
      5          6           0.000003451     0.000005552     0.000009165
      6          6           0.000005862    -0.000003532     0.000000947
      7          1          -0.000003927     0.000002786     0.000005279
      8          1          -0.000001758     0.000001263    -0.000006633
      9          1           0.000013815     0.000001922    -0.000005601
     10          1           0.000017155    -0.000005622     0.000010501
     11          6           0.000010916     0.000001996     0.000008106
     12          6          -0.000034255     0.000003305    -0.000000995
     13          6          -0.000010092    -0.000001094     0.000009866
     14          6          -0.000015147     0.000000321    -0.000012441
     15          6           0.000006880     0.000010783    -0.000002672
     16          6           0.000002857    -0.000008711     0.000002016
     17          1          -0.000017002    -0.000002670    -0.000002332
     18          1          -0.000011320     0.000002134    -0.000002045
     19          1          -0.000008183    -0.000004881    -0.000004636
     20          1           0.000000153     0.000000170     0.000004992
     21          7           0.000004891     0.000001998     0.000001130
     22          8          -0.000004096    -0.000009158     0.000001546
     23          8          -0.000003118     0.000014395    -0.000003106
     24          8           0.000025552    -0.000019512     0.000014487
     25          6           0.000017577     0.000015555    -0.000009188
     26          1           0.000004602    -0.000004453    -0.000002141
     27          1           0.000002488    -0.000001603     0.000001696
     28          1          -0.000000114    -0.000011592    -0.000001895
 -------------------------------------------------------------------
```

In DMSO
Number of Imaginary Frequencies = 0
Zero-point correction = 0.220443 (Hartree/Particle)
Thermal correction to Energy = 0.234315
Thermal correction to Enthalpy= 0.235259
Thermal correction to Gibbs Free Energy = 0.178093
Sum of electronic and zero-point Energies = -781.737661
Sum of electronic and thermal Energies = -781.723788
Sum of electronic and thermal Enthalpies = -781.722844
Sum of electronic and thermal Free Energies = -781.780011

```
-------------------------------------------------------------------
 Center     Atomic                   Forces (Hartrees/Bohr)
 Number     Number              X              Y              Z
 -------------------------------------------------------------------
      1        6          -0.000005099    0.000003739   -0.000000845
      2        6           0.000017115   -0.000000270    0.000003226
      3        6          -0.000000306    0.000003819    0.000000355
      4        6           0.000001177    0.000002939   -0.000002848
      5        6           0.000000492    0.000000519   -0.000005922
      6        6          -0.000002778    0.000003295    0.000002988
      7        1          -0.000000577    0.000001302    0.000001907
      8        1           0.000003824    0.000006062   -0.000004011
      9        1          -0.000000079    0.000004600   -0.000002976
     10        1          -0.000005384   -0.000000953    0.000001385
     11        6          -0.000018097   -0.000003048   -0.000000238
     12        6           0.000024560   -0.000012187    0.000008716
     13        6          -0.000003687    0.000002903   -0.000002174
     14        6           0.000009684    0.000001268    0.000001396
     15        6          -0.000013019    0.000000091   -0.000004230
     16        6          -0.000001225    0.000000872    0.000004198
     17        1           0.000001187   -0.000000709    0.000005628
     18        1           0.000002794   -0.000000157   -0.000003297
     19        1           0.000002258   -0.000002656   -0.000001556
     20        1          -0.000004239   -0.000003143    0.000004910
     21        7           0.000008973    0.000005185   -0.000001995
     22        8          -0.000004252    0.000000654   -0.000002197
     23        8          -0.000002558    0.000011065   -0.000001615
     24        8          -0.000017756   -0.000006506   -0.000006305
     25        6           0.000007895   -0.000001454    0.000005594
     26        1          -0.000000923   -0.000003650   -0.000001964
     27        1          -0.000000784   -0.000006958    0.000001610
     28        1           0.000000804   -0.000006623    0.000000259
 -------------------------------------------------------------------
```

Compound **1'b**

In toluene

Number of Imaginary Frequencies = 0

Zero-point correction = 0.261691 (Hartree/Particle)

Thermal correction to Energy = 0.277371

```
Thermal correction to Enthalpy= 0.278315
Thermal correction to Gibbs Free Energy = 0.217142
Sum of electronic and zero-point Energies = -801.118321
Sum of electronic and thermal Energies = -801.102641
Sum of electronic and thermal Enthalpies = -801.101697
Sum of electronic and thermal Free Energies = -801.162870

-------------------------------------------------------------------
 Center     Atomic                   Forces (Hartrees/Bohr)
 Number     Number              X              Y              Z
 ------------------------------------------------------------------
      1          6        0.000005742    0.000001668   -0.000000362
      2          6       -0.000009145    0.000000186    0.000001481
      3          6       -0.000002103    0.000002147   -0.000001470
      4          6        0.000000576    0.000001130    0.000000919
      5          6        0.000002545    0.000002351   -0.000001455
      6          6        0.000001518   -0.000002191   -0.000001793
      7          1       -0.000001738    0.000001191    0.000001029
      8          1        0.000002524    0.000000818    0.000003125
      9          1       -0.000000117   -0.000001138    0.000000539
     10          1       -0.000000824    0.000000537   -0.000001481
     11          6        0.000008168   -0.000001947   -0.000000887
     12          6       -0.000014838   -0.000003159   -0.000002398
     13          6       -0.000004415   -0.000002452   -0.000001115
     14          6       -0.000000634    0.000000884   -0.000000256
     15          6        0.000003942   -0.000004991    0.000000289
     16          6        0.000003463    0.000001096   -0.000000960
     17          1       -0.000000767   -0.000000375   -0.000002186
     18          1        0.000003175   -0.000002294    0.000001055
     19          1        0.000000074   -0.000001963   -0.000000470
     20          1       -0.000002684   -0.000003126   -0.000002847
     21          7       -0.000011739   -0.000001014   -0.000006012
     22          7        0.000007670   -0.000003361   -0.000002414
     23          8        0.000000865    0.000000474   -0.000000242
     24          8        0.000002630   -0.000007860   -0.000003968
     25          6        0.000003981    0.000009271    0.000003242
     26          1       -0.000001226    0.000003535   -0.000001987
     27          1       -0.000001576    0.000001908    0.000003200
     28          1        0.000000710    0.000003554    0.000000903
```

```
        29          6           0.000002379   -0.000001145    0.000008323
        30          1           0.000001675    0.000002798    0.000003905
        31          1           0.000000389    0.000002747    0.000005404
        32          1          -0.000000222    0.000000720   -0.000001109
 -------------------------------------------------------------------
```

In chloroform

Number of Imaginary Frequencies = 0

Zero-point correction = 0.261742 (Hartree/Particle)

Thermal correction to Energy = 0.277351

Thermal correction to Enthalpy= 0.278295

Thermal correction to Gibbs Free Energy = 0.217477

Sum of electronic and zero-point Energies = -801.120180

Sum of electronic and thermal Energies = -801.104571

Sum of electronic and thermal Enthalpies = -801.103627

Sum of electronic and thermal Free Energies = -801.164444

```
 -------------------------------------------------------------------
 Center     Atomic                   Forces (Hartrees/Bohr)
 Number     Number              X              Y              Z
 -------------------------------------------------------------------
         1          6           0.000012993    0.000002382    0.000004900
         2          6           0.000010838   -0.000000131    0.000002158
         3          6          -0.000001201    0.000000798   -0.000000072
         4          6          -0.000003077    0.000000813    0.000000576
         5          6          -0.000003506   -0.000003921   -0.000000194
         6          6          -0.000004614    0.000003054   -0.000000254
         7          1           0.000001840    0.000001868   -0.000001751
         8          1           0.000002003    0.000000535    0.000001755
         9          1           0.000002866    0.000001158    0.000002447
        10          1           0.000001291   -0.000001094   -0.000002109
        11          6          -0.000011957    0.000001427   -0.000002107
        12          6           0.000038323    0.000000292   -0.000000177
        13          6           0.000010758    0.000000515   -0.000001567
        14          6           0.000008788   -0.000005228    0.000001372
        15          6          -0.000009092    0.000002929    0.000001146
        16          6          -0.000013908   -0.000008225   -0.000004732
        17          1          -0.000004677   -0.000000052   -0.000001019
        18          1          -0.000002366   -0.000001523   -0.000000018
```

```
      19          1               0.000003684     -0.000004714     -0.000000769
      20          1               0.000001687      0.000000948     -0.000001013
      21          7              -0.000004242     -0.000000600     -0.000005519
      22          7              -0.000023692     -0.000002942      0.000000693
      23          8              -0.000003619     -0.000005830     -0.000004262
      24          8              -0.000002796     -0.000000026     -0.000000534
      25          6              -0.000003402     -0.000002902      0.000005112
      26          1               0.000000522      0.000002411      0.000000363
      27          1               0.000000092      0.000002006     -0.000003339
      28          1              -0.000003572      0.000003923     -0.000000243
      29          6              -0.000000725      0.000009172     -0.000000375
      30          1              -0.000000140      0.000000397      0.000003713
      31          1              -0.000000482     -0.000000454      0.000001175
      32          1               0.000001379      0.000003016      0.000004645
-------------------------------------------------------------------------------
```

In DMSO
Number of Imaginary Frequencies = 0
Zero-point correction = 0.261758 (Hartree/Particle)
Thermal correction to Energy = 0.277339
Thermal correction to Enthalpy= 0.278283
Thermal correction to Gibbs Free Energy = 0.217596
Sum of electronic and zero-point Energies = -801.115610
Sum of electronic and thermal Energies = -801.100029
Sum of electronic and thermal Enthalpies = -801.099085
Sum of electronic and thermal Free Energies = -801.159772

```
-------------------------------------------------------------------------------
 Center      Atomic                      Forces (Hartrees/Bohr)
 Number       Number             X                  Y                  Z
 ------------------------------------------------------------------------------
       1          6               0.000027838      0.000002244      0.000006480
       2          6               0.000013189     -0.000000135      0.000002537
       3          6              -0.000007179      0.000001725     -0.000002824
       4          6              -0.000008769     -0.000000175      0.000004512
       5          6              -0.000003215     -0.000001530      0.000006878
       6          6              -0.000002531      0.000002579     -0.000005792
       7          1               0.000002431     -0.000000653     -0.000008548
       8          1               0.000002652      0.000003219      0.000011376
```

```
    9        1          -0.000000865     0.000002779     0.000008200
   10        1          -0.000000106    -0.000003080    -0.000010169
   11        6          -0.000013064     0.000000795    -0.000004981
   12        6           0.000022910     0.000000061    -0.000003408
   13        6           0.000009571     0.000002274    -0.000006676
   14        6           0.000008779    -0.000005670     0.000003506
   15        6          -0.000006769     0.000004756     0.000002888
   16        6          -0.000011938    -0.000009270    -0.000012336
   17        1          -0.000004710     0.000003377    -0.000010571
   18        1          -0.000000273    -0.000004849     0.000006901
   19        1           0.000005301    -0.000008423     0.000002977
   20        1           0.000002497     0.000005302    -0.000011857
   21        7          -0.000018445     0.000003593     0.000003425
   22        7          -0.000014447    -0.000001609    -0.000005841
   23        8          -0.000001290    -0.000000056    -0.000013389
   24        8           0.000000010    -0.000006223    -0.000000173
   25        6           0.000002794     0.000001555    -0.000004388
   26        1          -0.000000513    -0.000002665     0.000001148
   27        1          -0.000001011    -0.000005531    -0.000003217
   28        1          -0.000003111     0.000003526    -0.000002869
   29        6           0.000002864    -0.000001045     0.000009424
   30        1          -0.000003033     0.000007057     0.000013384
   31        1           0.000000341    -0.000000876     0.000010996
   32        1           0.000000093     0.000006947     0.000012409
-------------------------------------------------------------------------------------------------
```

Compound **2’a**

In toluene

Number of Imaginary Frequencies = 0

Zero-point correction = 0.303026 (Hartree/Particle)

Thermal correction to Energy = 0.321329

Thermal correction to Enthalpy= 0.322273

Thermal correction to Gibbs Free Energy = 0.254859

Sum of electronic and zero-point Energies = -1012.584708

Sum of electronic and thermal Energies = -1012.566405

Sum of electronic and thermal Enthalpies = -1012.565461

Sum of electronic and thermal Free Energies = -1012.632875

```
 -------------------------------------------------------------------
 Center     Atomic                   Forces (Hartrees/Bohr)
 Number     Number              X              Y              Z
 -------------------------------------------------------------------
      1          6        -0.000001506    0.000002362   -0.000001776
      2          6         0.000020068   -0.000006438   -0.000008415
      3          6         0.000000867    0.000006602    0.000008723
      4          6        -0.000002984   -0.000007845   -0.000004254
      5          6         0.000002001   -0.000008162   -0.000003064
      6          6        -0.000004948    0.000007704    0.000007583
      7          1         0.000003165    0.000015336    0.000017878
      8          1         0.000002434   -0.000012146   -0.000014341
      9          1         0.000000899   -0.000010476   -0.000014637
     10          1        -0.000000799    0.000013488    0.000017119
     11          6         0.000002068    0.000000756    0.000003241
     12          6         0.000001477   -0.000000650    0.000001284
     13          6         0.000002838   -0.000002731   -0.000013020
     14          6         0.000004170    0.000004701    0.000013811
     15          6        -0.000003599    0.000004321    0.000008993
     16          6        -0.000001867   -0.000001547   -0.000008745
     17          1        -0.000002735    0.000001172   -0.000019540
     18          1        -0.000004004    0.000000739    0.000021338
     19          1         0.000004378    0.000001427    0.000022947
     20          1         0.000004908   -0.000000377   -0.000020408
     21          6        -0.000002217    0.000001063    0.000001201
     22          6        -0.000018791    0.000001023    0.000000155
     23          6        -0.000003946    0.000011796   -0.000009197
     24          6        -0.000004977   -0.000010346    0.000010580
     25          6         0.000006758   -0.000000282    0.000014138
     26          6         0.000007634    0.000001148   -0.000012567
     27          1        -0.000004128    0.000011750   -0.000014706
     28          1        -0.000004400   -0.000009165    0.000016329
     29          1        -0.000000255   -0.000013040    0.000015558
     30          1         0.000000298    0.000013872   -0.000014608
     31          7         0.000005132    0.000000549    0.000001101
     32          8         0.000005944   -0.000010481    0.000005318
     33          8         0.000005588    0.000011499   -0.000004726
     34          8        -0.000020931    0.000010096    0.000021281
     35          6         0.000003131   -0.000004407   -0.000025250
```

```
    36        1           0.000000636    -0.000004321    -0.000012013
    37        1           0.000000400    -0.000002975    -0.000004204
    38        1          -0.000002705    -0.000016018    -0.000003108
 -------------------------------------------------------------------------------------------
```

In chloroform
Number of Imaginary Frequencies = 0
Zero-point correction = 0.302941 (Hartree/Particle)
Thermal correction to Energy = 0.321284
Thermal correction to Enthalpy= 0.322228
Thermal correction to Gibbs Free Energy = 0.254587
Sum of electronic and zero-point Energies = -1012.586757
Sum of electronic and thermal Energies = -1012.568415
Sum of electronic and thermal Enthalpies = -1012.567471
Sum of electronic and thermal Free Energies = -1012.635112

```
-------------------------------------------------------------------------------------------
 Center     Atomic                   Forces (Hartrees/Bohr)
 Number     Number              X                  Y                  Z
 -------------------------------------------------------------------------------------------
     1        6           0.000004966     0.000003811    -0.000003319
     2        6           0.000012632    -0.000003914    -0.000002416
     3        6          -0.000001791     0.000002965     0.000007964
     4        6          -0.000009275    -0.000004259    -0.000003931
     5        6          -0.000001083    -0.000002017    -0.000002678
     6        6          -0.000003756     0.000001466     0.000003885
     7        1           0.000001145     0.000009335     0.000011068
     8        1           0.000000615    -0.000007599    -0.000009132
     9        1          -0.000001466    -0.000008133    -0.000010139
    10        1          -0.000001050     0.000008469     0.000011554
    11        6          -0.000003852     0.000000636     0.000002402
    12        6           0.000006515    -0.000000505     0.000000247
    13        6           0.000009274    -0.000000955    -0.000006771
    14        6           0.000008509     0.000001778     0.000008468
    15        6          -0.000009938     0.000003079     0.000006610
    16        6          -0.000009129    -0.000001313    -0.000005293
    17        1          -0.000000938     0.000001006    -0.000013707
    18        1          -0.000002130     0.000000412     0.000013964
    19        1           0.000002219     0.000000167     0.000013756
```

```
    20          1              0.000002764      0.000000912     -0.000012888
    21          6             -0.000005597      0.000000304      0.000000821
    22          6              0.000000538     -0.000000277      0.000002342
    23          6             -0.000001664      0.000009043     -0.000004914
    24          6             -0.000002549     -0.000007395      0.000005139
    25          6              0.000009102      0.000000960      0.000014703
    26          6              0.000010078     -0.000001407     -0.000012359
    27          1             -0.000003406      0.000009543     -0.000010206
    28          1             -0.000003859     -0.000007230      0.000010281
    29          1              0.000000799     -0.000009961      0.000007544
    30          1              0.000000672      0.000011215     -0.000007600
    31          7              0.000002821      0.000006701     -0.000010090
    32          8             -0.000001491     -0.000009426      0.000002633
    33          8             -0.000000872      0.000007003      0.000004440
    34          8             -0.000009697      0.000008097      0.000012681
    35          6             -0.000000739     -0.000008914     -0.000008966
    36          1              0.000002057      0.000000028     -0.000008394
    37          1              0.000001587     -0.000003193     -0.000002864
    38          1             -0.000002011     -0.000010432     -0.000004835
 -------------------------------------------------------------------------------------------
```

In DMSO
Number of Imaginary Frequencies = 0
Zero-point correction = 0.302848 (Hartree/Particle)
Thermal correction to Energy = 0.321213
Thermal correction to Enthalpy= 0.322158
Thermal correction to Gibbs Free Energy = 0.254436
Sum of electronic and zero-point Energies = -1012.581474
Sum of electronic and thermal Energies = -1012.56310
Sum of electronic and thermal Enthalpies = -1012.562165
Sum of electronic and thermal Free Energies = -1012.629887

```
-------------------------------------------------------------------------------------------
 Center       Atomic                        Forces (Hartrees/Bohr)
 Number        Number              X                    Y                    Z
 -------------------------------------------------------------------------------------------
     1          6             -0.000002918     -0.000004517      0.000001793
     2          6              0.000026992     -0.000015198     -0.000005101
     3          6             -0.000006255      0.000007503      0.000004523
```

```
      4          6          -0.000001000    -0.000001771    -0.000005716
      5          6          -0.000009478    -0.000004344    -0.000002939
      6          6          -0.000000018     0.000004793     0.000002201
      7          1           0.000001576     0.000005194     0.000009051
      8          1           0.000002745    -0.000006795    -0.000007937
      9          1           0.000000556    -0.000007006    -0.000008634
     10          1          -0.000002584     0.000003251     0.000008912
     11          6          -0.000003093    -0.000001194     0.000000082
     12          6           0.000008770    -0.000001280     0.000000460
     13          6           0.000009822    -0.000000239    -0.000004456
     14          6           0.000009977     0.000001341     0.000005891
     15          6          -0.000011705     0.000000080     0.000007116
     16          6          -0.000009252     0.000003709    -0.000006215
     17          1           0.000000647    -0.000000819    -0.000009985
     18          1          -0.000001757     0.000001198     0.000010986
     19          1          -0.000001245     0.000002703     0.000011332
     20          1           0.000000624    -0.000000246    -0.000009498
     21          6          -0.000002262     0.000002881     0.000001403
     22          6           0.000012321     0.000002637     0.000001462
     23          6           0.000005112     0.000006537    -0.000002149
     24          6           0.000004620    -0.000002205     0.000004372
     25          6          -0.000005221     0.000006299     0.000010389
     26          6          -0.000003618    -0.000000606    -0.000008782
     27          1          -0.000001280     0.000007884    -0.000007542
     28          1          -0.000003790    -0.000004381     0.000009800
     29          1           0.000000350    -0.000005507     0.000008265
     30          1           0.000002871     0.000011164    -0.000005580
     31          7          -0.000000137     0.000003555     0.000003472
     32          8          -0.000004603    -0.000003266     0.000001992
     33          8          -0.000003702     0.000011110    -0.000000637
     34          8          -0.000018885     0.000002221     0.000006329
     35          6           0.000007758    -0.000004454    -0.000006435
     36          1           0.000001364    -0.000002768    -0.000009499
     37          1          -0.000000560    -0.000006185    -0.000003698
     38          1          -0.000002737    -0.000011280    -0.000005027
-------------------------------------------------------------------------------------
```

Compound **2’b**

In toluene

Number of Imaginary Frequencies = 0

Zero-point correction = 0.343859 (Hartree/Particle)

Thermal correction to Energy = 0.364103

Thermal correction to Enthalpy= 0.365047

Thermal correction to Gibbs Free Energy = 0.292811

Sum of electronic and zero-point Energies = -1031.963106

Sum of electronic and thermal Energies = -1031.942862

Sum of electronic and thermal Enthalpies = -1031.941917

Sum of electronic and thermal Free Energies = -1032.014154

```
-------------------------------------------------------------------
 Center     Atomic                   Forces (Hartrees/Bohr)
 Number     Number              X              Y              Z
-------------------------------------------------------------------
      1          1        -0.000000590   -0.000003175    0.000004942
      2          6        -0.000007494   -0.000002090    0.000004883
      3          6         0.000008921    0.000001570   -0.000002684
      4          6         0.000009709   -0.000000162   -0.000000603
      5          6         0.000009740   -0.000002660    0.000002818
      6          6        -0.000007314    0.000001045    0.000001669
      7          6        -0.000007158    0.000002561   -0.000004596
      8          1         0.000000304   -0.000003045    0.000006791
      9          1        -0.000000182    0.000003242   -0.000005063
     10          1         0.000000331    0.000002906   -0.000005664
     11          6        -0.000009887   -0.000003824    0.000000481
     12          6         0.000008967   -0.000003357    0.000009058
     13          6         0.000001714    0.000005007    0.000001727
     14          6         0.000008215   -0.000000044   -0.000002734
     15          6        -0.000005424    0.000001572   -0.000003379
     16          6        -0.000003257   -0.000001656    0.000001399
     17          1         0.000001523    0.000000061    0.000006577
     18          1         0.000000816   -0.000000159   -0.000007238
     19          1         0.000000707    0.000000287   -0.000007932
     20          1        -0.000004575    0.000002106    0.000002330
     21          6         0.000003370    0.000000231   -0.000000227
     22          6        -0.000010289    0.000000297    0.000000556
     23          6        -0.000006224   -0.000000221   -0.000001933
```

```
    24          6          -0.000007767    -0.000001155     0.000004188
    25          6           0.000007007    -0.000004963     0.000006174
    26          6           0.000005861     0.000003668    -0.000003884
    27          1           0.000001006    -0.000002814    -0.000005186
    28          1           0.000001613     0.000002785     0.000006753
    29          1          -0.000002217     0.000003361     0.000006631
    30          1          -0.000002799    -0.000003960    -0.000004150
    31          7          -0.000009169     0.000004603     0.000006473
    32          7           0.000005060    -0.000000368     0.000003120
    33          8          -0.000000106    -0.000002651    -0.000001351
    34          8          -0.000000354     0.000001668     0.000003863
    35          6           0.000000660     0.000000439    -0.000016602
    36          1          -0.000000424     0.000002013    -0.000001445
    37          1           0.000001033    -0.000004514    -0.000005440
    38          1           0.000000193     0.000000211    -0.000008565
    39          6           0.000003966    -0.000002217     0.000002080
    40          1           0.000000295     0.000005477    -0.000000771
    41          1           0.000003910    -0.000001758     0.000001570
    42          1           0.000000311    -0.000000322     0.000005363
 -------------------------------------------------------------------------------------------------
```

In chloroform
Number of Imaginary Frequencies = 0
Zero-point correction = 0.343676 (Hartree/Particle)
Thermal correction to Energy = 0.363964
Thermal correction to Enthalpy= 0.364908
Thermal correction to Gibbs Free Energy = 0.292432
Sum of electronic and zero-point Energies = -1031.965811
Sum of electronic and thermal Energies = -1031.945524
Sum of electronic and thermal Enthalpies = -1031.944579
Sum of electronic and thermal Free Energies = -1032.017055

```
 -------------------------------------------------------------------------------------------------
 Center      Atomic                      Forces (Hartrees/Bohr)
 Number      Number                 X                 Y                  Z
 -------------------------------------------------------------------------------------------------
     1          1          -0.000001667    -0.000000706     0.000000154
     2          6           0.000006931     0.000000384     0.000002059
     3          6          -0.000006337     0.000000918     0.000000708
```

|  |  |  |  |  |
|---|---|---|---|---|
| 4 | 6 | -0.000007474 | -0.000000172 | -0.000001729 |
| 5 | 6 | -0.000006955 | 0.000000017 | 0.000001173 |
| 6 | 6 | 0.000008235 | -0.000000708 | -0.000000840 |
| 7 | 6 | 0.000006240 | 0.000000003 | -0.000000623 |
| 8 | 1 | -0.000001541 | -0.000000953 | 0.000002134 |
| 9 | 1 | -0.000001860 | 0.000000365 | 0.000000195 |
| 10 | 1 | -0.000000778 | 0.000000499 | -0.000000605 |
| 11 | 6 | 0.000005446 | 0.000001263 | 0.000000104 |
| 12 | 6 | -0.000002496 | 0.000002348 | -0.000005547 |
| 13 | 6 | -0.000002830 | -0.000000389 | -0.000001232 |
| 14 | 6 | -0.000004780 | -0.000000830 | 0.000000280 |
| 15 | 6 | 0.000002904 | -0.000001379 | -0.000000820 |
| 16 | 6 | -0.000000847 | -0.000000777 | -0.000001001 |
| 17 | 1 | 0.000001401 | -0.000000154 | 0.000000231 |
| 18 | 1 | 0.000001991 | 0.000000112 | -0.000001953 |
| 19 | 1 | 0.000000231 | 0.000000638 | -0.000001762 |
| 20 | 1 | 0.000000240 | 0.000000250 | 0.000000576 |
| 21 | 6 | -0.000006916 | -0.000000562 | 0.000002150 |
| 22 | 6 | 0.000004478 | -0.000000424 | 0.000002133 |
| 23 | 6 | 0.000004967 | 0.000000841 | 0.000000058 |
| 24 | 6 | 0.000005830 | -0.000000022 | 0.000001706 |
| 25 | 6 | -0.000003629 | 0.000002799 | 0.000000571 |
| 26 | 6 | -0.000003249 | -0.000002612 | 0.000002397 |
| 27 | 1 | 0.000000417 | 0.000000075 | 0.000000778 |
| 28 | 1 | 0.000000979 | -0.000000453 | 0.000000439 |
| 29 | 1 | 0.000001878 | -0.000001108 | 0.000003091 |
| 30 | 1 | 0.000001681 | 0.000000834 | 0.000000091 |
| 31 | 7 | 0.000004386 | 0.000000677 | 0.000004518 |
| 32 | 7 | -0.000004530 | -0.000000464 | 0.000001419 |
| 33 | 8 | -0.000000922 | -0.000002384 | 0.000001541 |
| 34 | 8 | -0.000000260 | 0.000002274 | 0.000002767 |
| 35 | 6 | -0.000000180 | 0.000000093 | -0.000001030 |
| 36 | 1 | 0.000000263 | -0.000000813 | -0.000003171 |
| 37 | 1 | -0.000000582 | 0.000000332 | -0.000003036 |
| 38 | 1 | -0.000000997 | 0.000000289 | -0.000001959 |
| 39 | 6 | 0.000000792 | -0.000000368 | -0.000004208 |
| 40 | 1 | 0.000000658 | 0.000000057 | 0.000000696 |
| 41 | 1 | -0.000001336 | -0.000000735 | -0.000000257 |
| 42 | 1 | 0.000000220 | 0.000000944 | -0.000002197 |

In DMSO
Number of Imaginary Frequencies = 0
Zero-point correction = 0.343857 (Hartree/Particle)
Thermal correction to Energy = 0.364029
Thermal correction to Enthalpy= 0.364973
Thermal correction to Gibbs Free Energy = 0.293199
Sum of electronic and zero-point Energies = -1031.959080
Sum of electronic and thermal Energies = -1031.938908
Sum of electronic and thermal Enthalpies = -1031.937964
Sum of electronic and thermal Free Energies = -1032.009738

```
-------------------------------------------------------------------
 Center     Atomic                   Forces (Hartrees/Bohr)
 Number     Number              X              Y              Z
 -------------------------------------------------------------------
      1          1        -0.000003793    0.000008598   -0.000006431
      2          6         0.000014065    0.000001784    0.000002046
      3          6        -0.000017338    0.000003655    0.000007657
      4          6        -0.000014740   -0.000001230   -0.000001095
      5          6        -0.000015592   -0.000003700   -0.000005726
      6          6         0.000031666   -0.000002119   -0.000001763
      7          6         0.000016153   -0.000002194   -0.000001048
      8          1        -0.000001511    0.000008513   -0.000002860
      9          1        -0.000004270   -0.000008530    0.000006191
     10          1        -0.000000657   -0.000009003    0.000002775
     11          6        -0.000002643    0.000004288   -0.000000060
     12          6         0.000015077   -0.000000304    0.000006908
     13          6        -0.000001574    0.000001330   -0.000008680
     14          6        -0.000003676   -0.000001965    0.000008370
     15          6        -0.000008514   -0.000002353    0.000005142
     16          6        -0.000000660    0.000005505   -0.000006968
     17          1         0.000007823    0.000002829   -0.000004624
     18          1         0.000006828   -0.000002102    0.000004797
     19          1        -0.000002939   -0.000000944    0.000005565
     20          1         0.000006314   -0.000001034   -0.000004402
     21          6        -0.000014460    0.000000857    0.000000807
     22          6         0.000064863   -0.000000917    0.000000134
     23          6        -0.000001756    0.000003949    0.000003332
     24          6         0.000000037   -0.000005058   -0.000002559
```

```
   25          6          -0.000011916     0.000022727    -0.000006384
   26          6          -0.000011772    -0.000023609     0.000006330
   27          1          -0.000006914    -0.000001499     0.000005767
   28          1          -0.000006136     0.000000582    -0.000005251
   29          1           0.000000899    -0.000008985    -0.000003986
   30          1           0.000000604     0.000007767     0.000004950
   31          7          -0.000015782    -0.000002166    -0.000031331
   32          7          -0.000008218     0.000000011     0.000005562
   33          8          -0.000005209     0.000000413     0.000005183
   34          8          -0.000005161    -0.000002580    -0.000007652
   35          6           0.000009869     0.000014020     0.000008917
   36          1           0.000000833    -0.000004292     0.000006054
   37          1          -0.000004479     0.000000071     0.000005969
   38          1          -0.000000275    -0.000002872     0.000008094
   39          6           0.000007911    -0.000009765     0.000005683
   40          1          -0.000006864    -0.000001651    -0.000003216
   41          1          -0.000005674     0.000005955    -0.000005090
   42          1          -0.000000423     0.000006018    -0.000007105
-------------------------------------------------------------------
```

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# Chapter 3

# Impact of five-membered heterocyclic ring on photophysical property including two-photon absorption character

## 3-1. Introduction

Dipolar, quadrupolar, and octopolar systems[35–37] have been developed to design chromophores with larger 2PA cross-section ($\sigma_2$ in GM = $10^{-50}$ cm$^4$ s photon$^{-1}$). In addition to the polarity effect, π-conjugation and planarity[33,34,68,69] effects are also known to be crucial to increase the 2P character of molecules. In the previous study, *p*-nitroterphenyl (**TP**) and *p*-nitrobiphenyl (**BP**) backbone application for the 2P-responsive caged compounds was investigated (Figure 17a). However, because the dihedral angel of **BP** was smaller than that of **TP**, leading to the 2PA cross-section ($\sigma_2$) of **TP**, $\sigma_2$ = 13.9 GM at 820 nm, was relatively lower than that of the biphenyl skeleton (**BP**: $\sigma_2$ = 44 GM at 830 nm), although the number of π electron increases. The planarity would increase the transition dipole moment between the acceptor and donor moieties, and π-conjugation. Therefore, a new chromophore having more planar structure would increase the 2P response in NIR region, reducing the damage of cells in physiological experiments. It has been reported that thiophene derivatives featuring the electron donor (D) and acceptor (A) possess the relatively high 2PA cross section[51] (Figure 17c). The advantage of heteroaromatic rings to benzene rings has been reported by Bhanuparakash[70] in 2006, Achelle in 2017[71] and Maeda in 2020[72] (Figure 17b). Several heteroaromatic molecules with large 2PA cross-section were reported in the literature[48,51,73,74] (Figure 17c). In this study, we designed the teraryl derivatives 10-12, in which the central aromatic ring is replaced by heteroaromatic rings such as thiophene, furan, and pyrrole. The donor (*p*-$NMe_2C_6H_4$ group) and acceptor (-$NO_2C_6H_4$ group) substituents are connected with the π-linker (Figure 17a). The effect of the central heterocyclic rings system would play a vital role in the photophysical properties and two-photon absorption character.

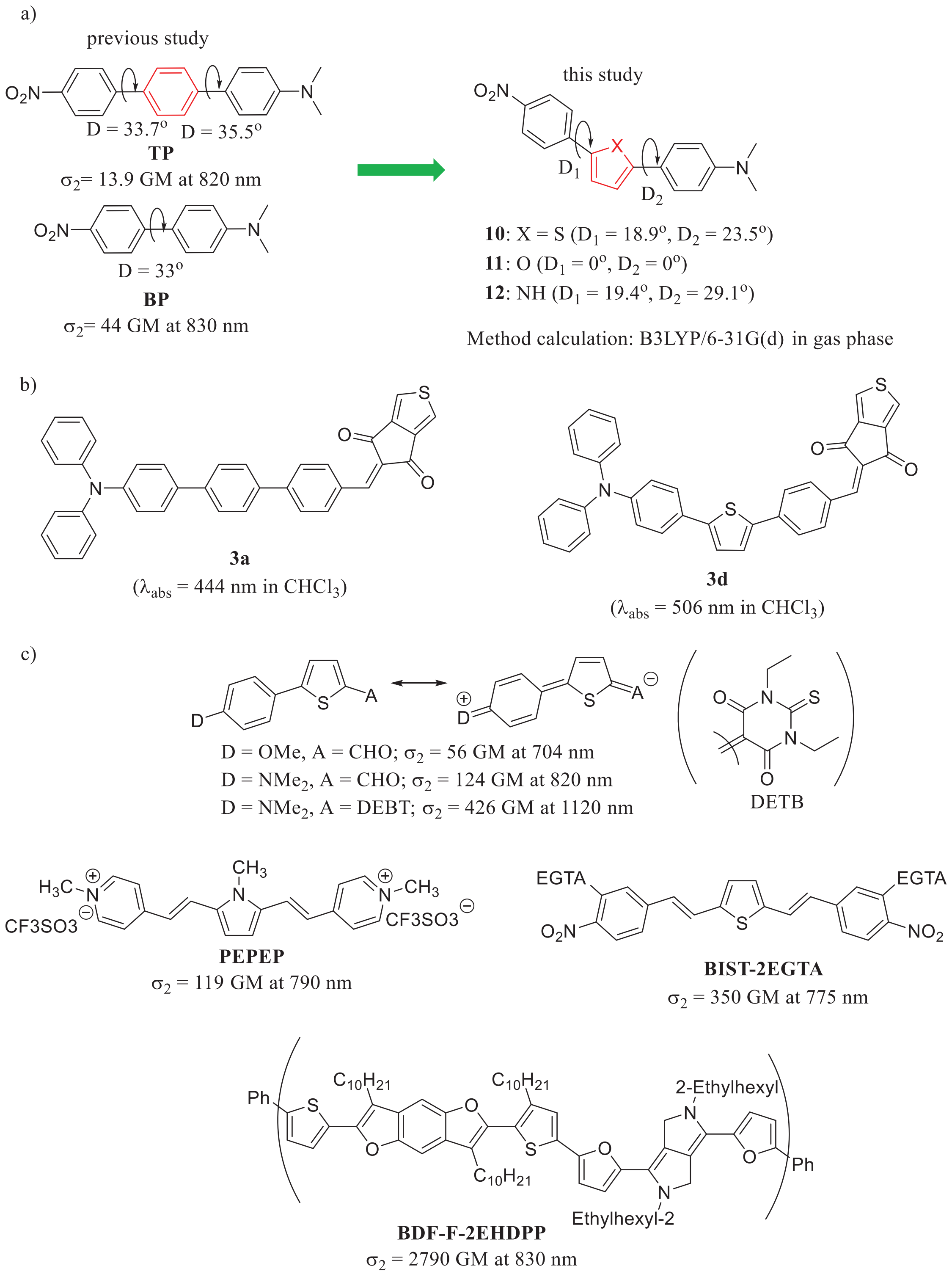
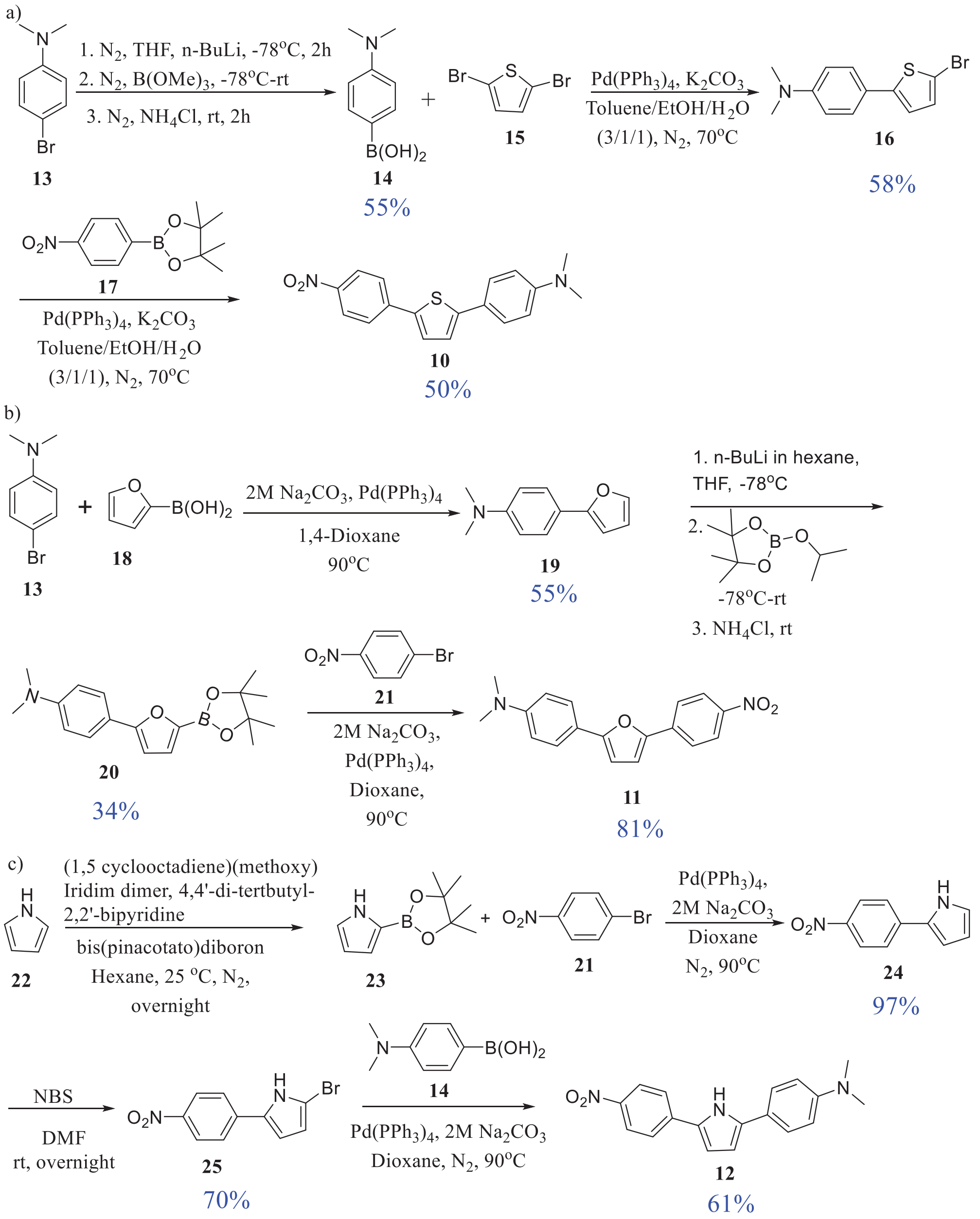


**Figure 17.** a) previous study and this study. b) example of one photon absorption of hetero terphenyl derivatives. c) example of two-photon absorption

## 3-2. Synthesis of hetero terphenyl derivatives.

First, compound **10** was synthesized in three steps from the commercially available compound **13**. Borylation of compound **13** using trimethoxylborane gave compound **14**[45] in 55% yield, followed by the Suzuki-Miyaura coupling reaction with 2,5-dibromothiophene **15** to afford compound **16**[75] in 58%. The coupling reaction of compound **17**[76] produced the desired compound **10** in 50%. Similarly, compounds **11** and **12** were synthesized as shown in Scheme 3 in 81% and 61%, respectively.



**Scheme 3.** Synthesis routine of a) Compound **10.** b) Compound **11**. c) Compound **12**.

## 3-3. Photophysical properties

### UV-vis absorption and fluorescence emission measurement

To understand the effects of the central heterocyclic rings system on 1P and 2P responses, the photophysical properties of three compounds **10-12** were investigated and compared with those of TP (Table 3). The absorption and emission of **12** were measured also in 2-propanol because compound **12** was soluble in 2-propanol (entry 18).

As shown in Table 1, the absorption maxima of compounds **10-12**, ~430-450 nm for **10**, ~440-460 nm for **11**, ~460-490 nm for **12**, did not change significantly when the solvent polarity increased. In contrast, the strong bathochromic-shift of the fluorescence spectra was observed, for example 598 nm in toluene (Tol) (entry 1), 701 nm in ethyl acetate (AcOEt) (entry 3), 706 nm in tetrahydrofuran (THF) (entry 4) for compound **10** (Figures 18a), demonstrating the charge transfer character in their excited states due to the donor-acceptor combination in the chromophores[52,77]. The absorption and fluorescence maxima of the parent terphenyl **TP** were found to be 361 and 565 nm in Tol (entry 20). Thus, as expected, the absorption and emission spectra of compounds **10-12** featuring the heterocyclic ring system were bathochromically shifted than those of **TP**. It should be noted that the molar absorption coefficients ($\varepsilon$ in $M^{-1}$ $cm^{-1}$) of compounds **10-12** were 2-3 times higher than that of **TP**, demonstrating that the π-conjugation of **10-12** is significantly higher than **TP**.

The blue shift of the emission wavelength of compound **12** was observed in the protic solvent, 2-propanol, in comparison with those in the aprotic solvent (AcOEt and THF) (Figures 18c). This can be accounted for because the dipole moment of AcOEt and THF solvent is larger than that of 2-propanol solvent which leads to the stabilization of the excited state. When comparing the absorption maxima of compounds **10-12**, the absorption maximum of **12** is the most red-shifted in all solvents used in this study. For example, compound **12** showed the absorption maximum at 491 nm in DMSO (entry 19), which is the longest wavelength. The fluorescence quantum yield ($\Phi$) was found to decrease with increasing solvent polarity. For example, $\Phi$ values of compound **10** were 0.6 and 0.015 in Tol and AcOEt, respectively (entries 1, 3). The fluorescence lifetimes of compounds in toluene, AcOEt, THF, and 2-propanol were determined by time-correlated single-photon counting (TCSPC) technique.

**Table 3.** Photophysical properties of compounds **10-12**, and **TP** in different organic solvent.

| Entry | Comp. | Sol. | μ[a] | $\lambda_{abs}$ / nm[b] | ε / $M^{-1}cm^{-1}$[c] | $\lambda_{emi}$ / nm[d] | Φ[e] | τ[g]/ ns | $\sigma_2$[j] / GM (nm) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | **10** X = S | Tol | 1.0 | 436 | 24932 ± 48 | 598 | 0.60 ± 0.002 | 2.83 ± 0.02[h] | 143 GM (900 nm) |
| 2 | | $CHCl_3$ | 3.8 | 442 | 18109 ± 40 | –[k] | –[k] | –[k] | nd[l] |
| 3 | | AcOEt | 5.9 | 432 | 21660 ± 11 | 701 | 0.015 ± 0.0001 | 1.49 ± 0.02[i] | nd[l] |
| 4 | | THF | 5.8 | 438 | 26478 ± 4 | 706 | 0.032 ± 0.0003 | 1.64 ± 0.04[i] | nd[l] |
| 5 | | ACN | 13 | 434 | 19183 ± 546 | –[k] | –[k] | –[k] | nd[l] |
| 6 | | DMSO | 13.5 | 453 | 23995 ± 193 | –[k] | –[k] | –[k] | nd[l] |
| 7 | **11** X = O | Tol | 1.0 | 444 | 20722 ± 293 | 608 | 0.52 ± 0.002 | 2.85 ± 0.03[h] | 93 GM (910 nm) |
| 8 | | $CHCl_3$ | 3.8 | 451 | 17618 ± 12 | –[k] | –[k] | –[k] | nd[l] |
| 9 | | AcOEt | 5.9 | 440 | 15245 ± 21 | 714 | 0.018 ± 0.001 | 1.79 ± 0.01[i] | nd[l] |
| 10 | | THF | 5.8 | 446 | 19885 ± 42 | 717 | 0.039 ± 0.001 | 1.70 ± 0.01[i] | nd[l] |
| 11 | | ACN | 13 | 442 | 16782 ± 32 | –[k] | –[k] | –[k] | nd[l] |
| 12 | | DMSO | 13.5 | 462 | 18234 ± 7 | –[k] | –[k] | –[k] | nd[l] |
| 13 | **12** X = NH | Tol | 1.0 | 456 | 27359 ± 369 | 625 | 0.11 ± 0.01 | 1.13 ± 0.04[h] | 150 GM (960 nm) |
| 14 | | $CHCl_3$ | 3.8 | 461 | 16598 ± 153 | –[k] | –[k] | –[k] | nd[l] |
| 15 | | AcOEt | 5.9 | 459 | 11453 ± 20 | 698 | 0.0038 ± 0.0006 | 1.66 ± 0.02[i] | nd[l] |
| 16 | | THF | 5.8 | 467 | 21931 ± 120 | 705 | 0.0027 ± 0.0068 | 1.82 ± 0.02[i] | nd[l] |
| 17 | | ACN | 13 | 460 | 19188 ± 95 | –[k] | –[k] | –[k] | nd[l] |
| 18 | | 2-propanol | 5.5 | 465 | 17772 ± 177 | 644 | 0.0029 ± 0.0003 | 1.69 ± 0.007[i] | nd[n] |
| 19 | | DMSO | 13.5 | 491 | 18805 ± 99 | –[k] | –[k] | –[k] | nd[n] |
| 20 | **TP** | Tol | 1.0 | 361 | 8860 ± 32 | 565 | 0.20 ± 0.005[f] | 2.09 | 13.9 (810 nm) |
| 21 | | $CHCl_3$ | 3.8 | 362 | 15243 ± 5 | –[k] | –[k] | –[k] | nd[l] |
| 22 | | DMSO | 13.5 | 372 | 9099 ± 5 | –[k] | –[k] | –[k] | nd[l] |

[a]Dipole moment (μ x $10^{30}$ / Cm)[78]. [b]Absorption maximum measured in Tol, $CHCl_3$, AcOEt, ACN, THF, 2-propanol or DMSO. [c]Molar extinction coefficient. [d]Fluorescence maximum measured in Tol, $CHCl_3$, AcOEt, ACN, THF, 2-propanol or DMSO. [e]Fluorescence quantum yield measured in Tol, $CHCl_3$, AcOEt, ACN, THF, 2-propanol or DMSO using absolute PL quantum yield spectrometer. [f]Fluorescence quantum yield measured in Tol using Rhodamine B ($\Phi_f = 0.5$) as a standard. [g]Fluorescence lifetime. [h]Fluorescence lifetime monitored at 600 nm. [i]Fluorescence lifetime monitored at 700 nm. [j]TP cross-section measured using the two-photon excited (2PE) fluorescence method in toluene-$d_8$ with a chromophore concentration $1 \times 10^{-4}$ M. [k]not detected or very weak. [l]not determined.

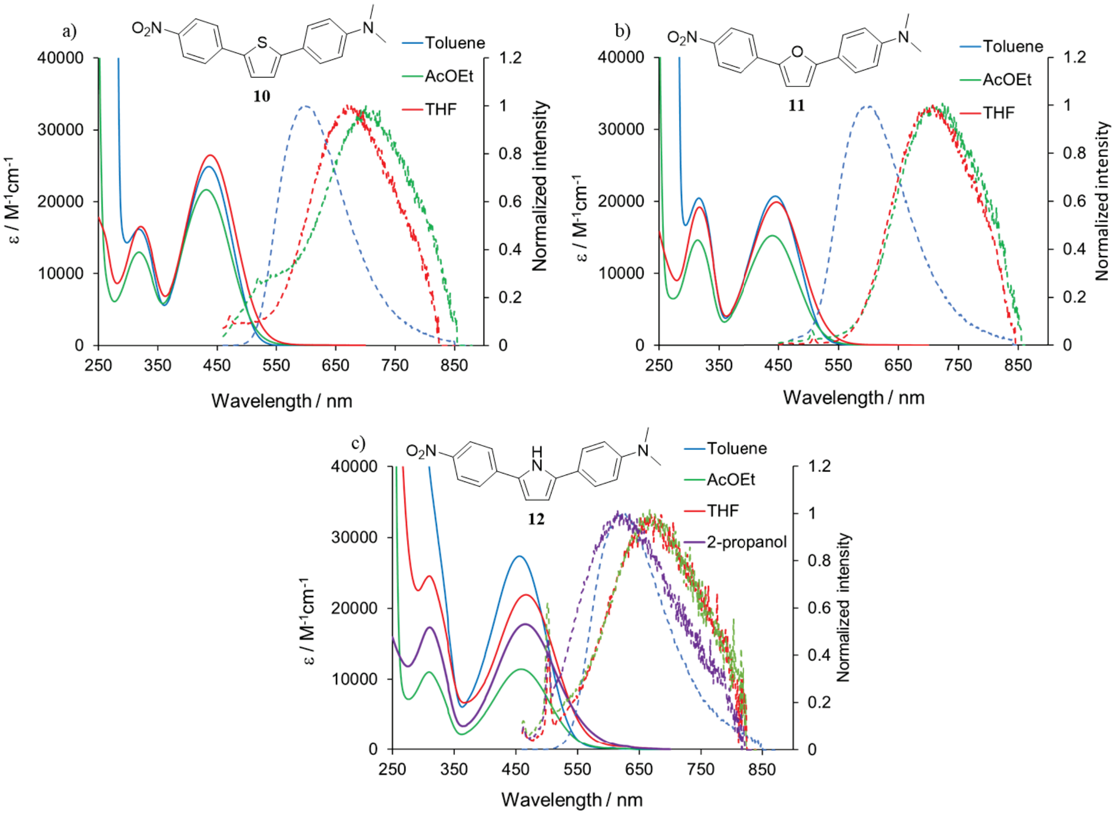


**Figure 18.** Absorption spectra (full line) and emission spectra (dashed line) of a) compound **10**; b) compound **11**; c) compound **12**.

### Cyclic voltammetry measurement

The HOMO and LUMO levels of compounds **10-12** were estimated by cyclic voltammetry (CV) data (Figure 19 and Table 4). Thus, the HOMO and LUMO level were calculated from the value of oxidation and reduction potentials, by considering the redox potentials relative to ferrocene/ferrocenium (Fc/Fc$^+$) (SI, Figure S45) using the equation (1) and (2)[79]:

$$E_{\mathrm{HOMO}}\ (\mathrm{eV}) = -4.8 + E_{\mathrm{Ferrocene}} - E_{\mathrm{ox}} \quad (1)$$

$$E_{\mathrm{LUMO}}\ (\mathrm{eV}) = -4.8 + E_{\mathrm{Ferrocene}} - E_{\mathrm{red}} \quad (2)$$

Compounds **10** and **11** showed HOMO levels at –5.12 eV and –5.11 eV, while compound **12** had the highest HOMO value of –4.82 eV. For the LUMO level, compound **10,11** were ~ 0.1 eV lower than compound **12**. The smallest HOMO-LUMO gap (1.47 eV) was found for compound **12** (Table 4).

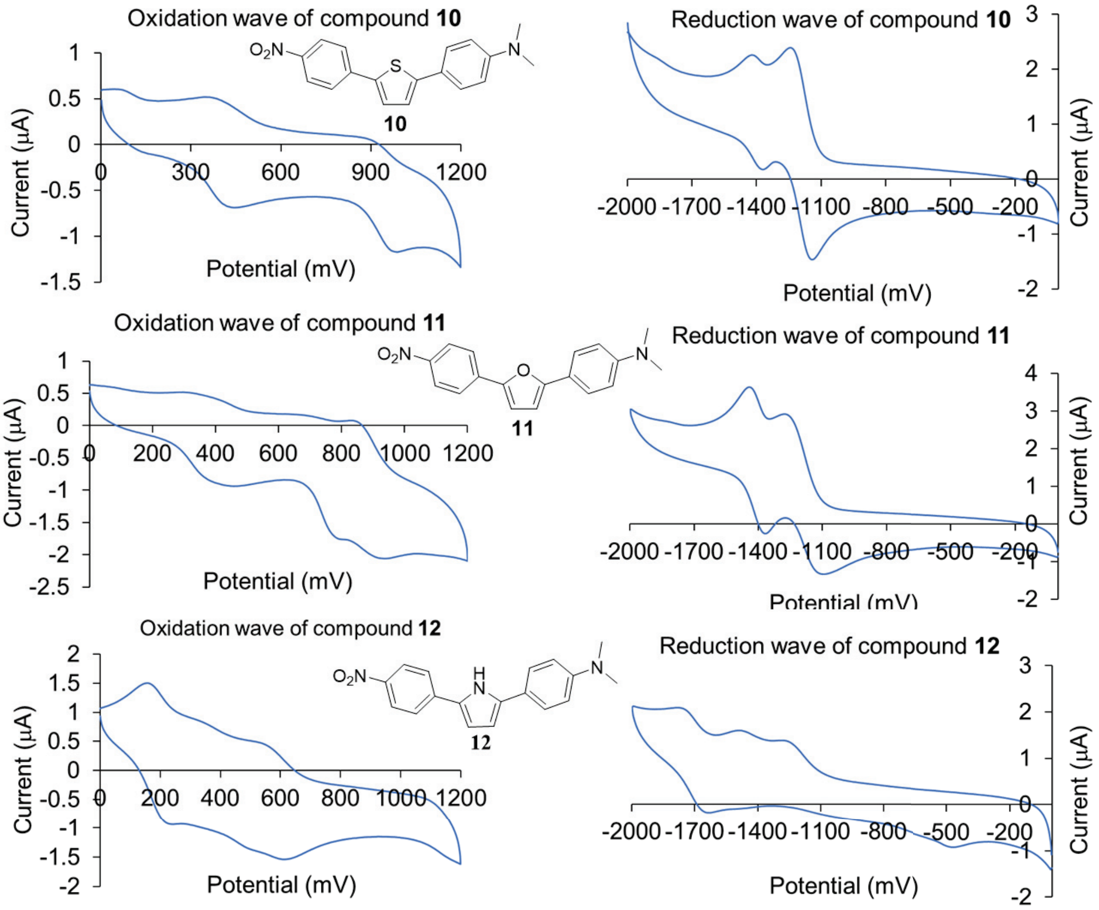


**Figure 19.** Cyclic voltammetry of compounds **10-12** (0.23 M) recorded in acetonitrile (ACN)/0.1 M tetrabutylammonium hexafluorophosphate (TBAHFP) electrolyte with 0.01 M Ag/AgNO3 reference electrode *vs.* 0.1 M Fc/Fc$^+$. a) oxidation wave of compound **10**; b) reduction wave of compound **10**; c) oxidation wave of compound **11**; b) reduction wave of compound **11**; e) oxidation wave of compound **12**; f) reduction wave of compound **12**.

**Table 4.** Optical and electrochemical studies of compounds **10-12**.

| Comp. | $E^1_{\mathrm{red}}{}^a$ / V | $E^1_{\mathrm{ox}}{}^a$ / V | HOMO$^b$ / eV | LUMO$^c$ / eV | $E_{\mathrm{gap(elec)}}{}^d$ / eV |
|---|---|---|---|---|---|
| **10** (X=S) | -1.23 | 0.43 | -5.12 | -3.46 | 1.66 |
| **11** (X=O) | -1.26 | 0.42 | -5.11 | -3.43 | 1.68 |
| **12** (X=NH) | -1.24 | 0.23 | -4.82 | -3.35 | 1.47 |

[a]Electrochemical potentials *vs.* Fc/Fc$^+$ of the indicated compounds **10-12** in ACN. [b]Measured from onset value of oxidation half cycle of CV. [c]Measured from onset value of reduction half cycle of CV. [d]Electrochemical HOMO-LUMO gap.

### 3-4. Two-photon absorption

The 2P response of compounds **10-12** were determined by two-photon excited (2PE) fluorescence measurements in Tol (entries 1,7,13). The 2PA spectra are shown in Figure 20 in 680-1000 nm. Compound **12** (X = NH) had the largest 2PA cross-section of 150 GM at 960 nm (entry 13), whereas compound **10** (X = S) showed a slightly smaller 2PA maximum cross-section of 143 GM at 900 nm (entry 1). Compound **11** (X = O) showed the smallest response of 93 GM at 910 nm (entry 7). Thus, the heterocyclic linkers that connect donor-acceptor units significantly enhance the 2P response of the terphenyl derivatives as compared to **TP** ($\sigma_2$ = 13.9 GM at 820 nm). The smaller dihedral angles of **10-12** enhance the molecular planarity to increase the transition dipole moment of **10-12**. The higher 2PA cross-section of these more-planar (compounds **10-12**) could be observed.

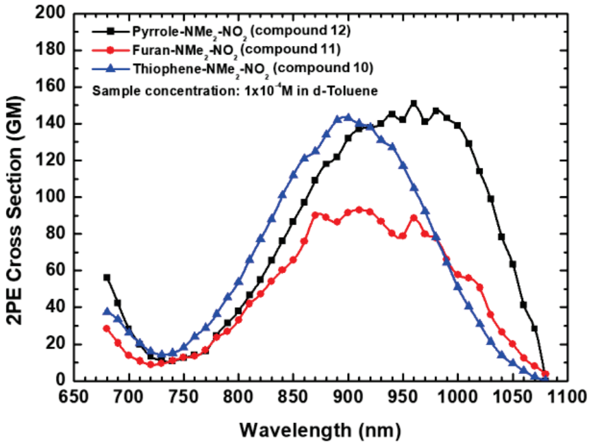


**Figure 20.** Two-photon absorption spectra of compounds **10-12** in $d_8$-toluene.

## 3-5. Experiment section

**4-(*N,N*-Dimethylamino)phenylboronic acid (14):** Compound **13** (4.00 g, 0.02 mol) was dissolved in dry 80 mL THF and cooled down to -78 °C. 2.3 M *n*-BuLi (12.6 mL, 0.03 mol) was slowly added over 10 minutes and stirred for 2 h at -78°C. $B(OMe)_3$ (8.50 mL, 0.07 mol) was slowly added to the mixture. The reaction was stirred for another 2 h at -78 °C, and for overnight at room temperature (rt). After quenching with saturated aq. $NH_4Cl$, the reaction was stirred for another 2 h at rt. The organic phase was collected and the water phase was extracted with DCM. The combined organic phases were dried over MgSO4 and solvents removed under reduced pressure. The crude was washed with a mixture of Hexane:EtOAc (1:1) to deliver **14** (1.81 g, 55%) as a colorless solid. $^1$H-NMR of compound **14** (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.82 Hz, 2 H), 6.79 (d, *J* = 8.82 Hz, 2 H), 3.06 (s, 6 H).

**4-(5-Bromothiophen-2-yl)-*N,N*-dimethylaniline** (**16**): Compound **14** (260 mg, 1.57 mmol) and **15** (381 mg, 1.57 mmol) were dissolved in mixture toluene and EtOH (3:1) and degassed under $N_2$ for 30 minutes. Then, $Pd(PPh_3)_4$ (37.0 mg, 0.03 mmol) and a solution of $K_2CO_3$ (435 mg, 3.15 mmol) in $H_2O$ (5.00 mL) were added. The reaction mixture was degassed with $N_2$ again and stirred for 70 °C for overnight. After evaporation of the organic solvent, the residue was extracted with DCM, washed with $H_2O$ and brine, dried over $Na_2SO_4$ and the solvent was removed under reduced pressure. The crude compound was purified by Flash column chromatography (Hexane:AcOEt = 2:1,…) to give desired product **16** (258 mg, 58%) as a yellow solid. $^1$H-NMR of compound **16** (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.58 Hz, 2 H), 6.96 (d, *J* = 3.74 Hz, 2 H), 6.88 (d, *J* = 3.74 Hz, 2 H), 6.71 (d, *J* = 8.58 Hz, 2 H), 2.98 (s, 6 H).

**4,4,5,5-tetramethyl-2-(4-nitrophenyl)-1,3,2-dioxaborolane** (**17**): Compound **19** (50.0 mg, 0.25 mmol), bis(pinacolato)diboron (64.1 mg, 0.25 mmol), AcOK (77.3 mg, 0.79 mmol) and $PdCl_2(dppf)$ (22.1 mg, 0.03 mmol) were degassed under $N_2$ for 30 minutes. Then, dioxane (3.30 mL) was added, the reaction mixture was degassed with $N_2$ again and stirred for 80 °C for overnight. After evaporation of the organic solvent, the residue was extracted with DCM, washed with $H_2O$ and brine, dried over $Na_2SO_4$ and the solvent was removed under reduced pressure. The crude was purified through silica gel column chromatography using 100%AcOEt to give the desired coupling product **17** (50.4 mg, 81%) as grey solid. $^1$H-NMR of compound **17** (400 MHz, $CDCl_3$): δ 8.19 (d, *J* = 8.56 Hz, 2 H), 7.96 (d, *J* = 8.56 Hz, 2 H), 2.98 (s, 6 H), 1.36 (s, 12 H).

***N,N*-dimethyl-4-(5-(4-nitrophenyl)thiophen-2-yl)aniline** (**10**)**:** Compound **17** (200 mg, 0.71 mmol) and **16** (160 mg, 0.64 mmol) were dissolved into a mixture of toluene (3.90 mL) and ethanol (1.30 mL) and degassed under $N_2$ for 30 minutes. Then, $Pd(PPh_3)_4$ (72.8 mg, 0.06 mmol) and an aqueous solution of $Na_2CO_3$ (134 mg, 1.26 mmol) (1.3 mL) were added. The reaction mixture was degassed with $N_2$ again and stirred at 70 °C overnight.

After evaporation of the organic solvent, the residue was extracted with DCM, washed with $H_2O$ and brine, dried over $Na_2SO_4$. The solvent was removed under reduced pressure. The crude was purified through silica gel column chromatography and recycling HPLC with GPC to give the desired coupling product **10** (98 mg, 48%) as red solid. $^1$H-NMR (400 MHz, $CDCl_3$): δ 8.24 (d, $J$ = 9.02 Hz, 2H), 7.72 (d, $J$ = 9.02 Hz, 2H), 7.53 (d, $J$ = 8.86 Hz, 2H), 7.43 (d, $J$ = 3.81 Hz, 2H), 7.19 (d, $J$ = 3.81 Hz, 2H), 6.74 (d, $J$ = 8.86 Hz, 2H), 3.02 (s, 6H). $^{13}$C NMR (100 MHz, pyridine-d6): δ 150.65, 148.68, 146.06, 140.83, 137.92, 127.78, 126.96, 125.31, 124.55, 122.68, 121.74, 112.65, 39.73. HRMS-ESI calcd for $C_{18}H_{17}N_2O_2S$ $[M + H]^+$ 325.10354, found 325.10095. Mp: 265°C, IR [KBr, $cm^{-1}$]: 2911, 1608, 1589, 1541, 1503, 1500, 1440, 1367, 1328, 1226, 1196, 1186, 1109,1064, 947, 849, 815, 796, 751, 742, 690.

**4-(furan-2-yl)-*N,N*-dimethylaniline** (**19**): Compound **13** (50.1 mg, 0.25 mmol), **18** (56.6 mg, 0.51 mmol) and $Pd(PPh_3)_4$ (15.2 mg, 0.013 mmol) were degassed under $N_2$ for 30 minutes. Then, a solution of 2M $Na_2CO_3$ (0.3 mL) and 1,4-dioxane (5.00 mL) were added. The reaction mixture was degassed with $N_2$ again and stirred for 90 °C for overnight. After reaction, the reaction mixture was extracted with EtOAc, washed with $H_2O$ and brine, dried over $Na_2SO_4$ and the solvent was removed under reduced pressure. The crude was separated by column chromatography. The products were purified through silica gel column chromatography using Hex:AcOEt (98:2) to give the desired coupling product **19** (30.3 mg, 65%) as yellow solid. $^1$H-NMR of compound **19** (400 MHz, $CDCl_3$): δ 7.56 (d, $J$ = 9.02 Hz, 2 H), 7.39-7.40 (m, 1 H), 6.74 (d, $J$ = 9.02 Hz, 2 H), 6.42-6.42 (m, 2 H), 2.98 (s, 6 H).

***N,N*-dimethyl-4-(5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)furan-2-yl)aniline (20):** Compound **19** (563 mg, 3.01 mmol) was dissolved in dry THF (30.0 mL) and cooled down to -78 °C. *n*-BuLi (2.3 M in *n*-hexane, 4.60 mL, 10.6 mmol) was slowly added over 10 minutes and the mixture was stirred for 3 h at -78 °C. Then, 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (4.30 mL, 21.1 mmol) was slowly added to the mixture. The reaction was stirred for another 2 h at -78 °C, and overnight at rt. After quenching with saturated aqueous solution of $NH_4Cl$ (30 mL), the reaction was stirred for another 2 h at rt. After evaporation of the organic solvent, the residue was extracted with DCM, washed with $H_2O$ and brine, dried over $Na_2SO_4$ and the solvent was removed under reduced pressure. The crude was washed with *n*-hexane to give the desired product **20** (150 mg, 34%) as white solid. $^1$H-NMR (400 MHz, $CDCl_3$): δ 7.66 (d, $J$ = 8.55 Hz, 2H), 7.13 (d, $J$ = 3.51 Hz, 2H), 6.71 (d, $J$ = 8.55 Hz, 2H), 6.49 (d, $J$ = 3.51 Hz, 2H), 2.99 (s, 6H), 2.99 (s, 12H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 159.76, 150.21, 126.01, 125.91, 112.09, 103.17, 83.93, 83.20, 40.40, 24.76, 24.56. HRMS-ESI calcd for $C_{18}H_{25}BNO_3$ $[M + H]^+$ 314.19220, found 314.19211. Mp: 160°C, IR [KBr, $cm^{-1}$]: 2981, 1616, 1589, 1546, 1501, 1371, 1341, 1320, 1271, 1193, 1143, 1105, 1061, 1017, 966, 853, 823, 818, 782, 689, 672.

***N,N*-dimethyl-4-(5-(4-nitrophenyl)furan-2-yl)aniline (11):** Compound **20** (80 mg, 0.26 mmol) and **21** (29.0 mg, 0.14 mmol) were dissolved into 1,4-dioxane (2.90 mL) and degassed under $N_2$ for 30 minutes. Then, $Pd(PPh_3)_4$ (8.03 mg, 6.94 μmol) and an aqueous solution of 2M $Na_2CO_3$ (0.1 mL) were added. The reaction mixture was degassed with $N_2$ again and stirred for 90 °C for overnight. After evaporation of the organic solvent, the residue was extracted with DCM, washed with $H_2O$ and brine, dried over $Na_2SO_4$. The solvent was removed under reduced pressure. The products were purified through silica gel column chromatography and recycling HPLC with GPC to give the desired coupling product **11** (35 mg, 81%) as red solid. $^1$H-NMR (400 MHz, $CDCl_3$): δ 8.24 (d, *J* = 9.10 Hz, 2H), 7.80 (d, *J* = 9.10 Hz, 2H), 7.65 (d, *J* = 8.87 Hz, 2H), 6.95 (d, *J* = 3.52 Hz, 2H), 6.76 (d, *J* = 8.87 Hz, 2H), 6.60 (d, *J* = 3.52 Hz, 2H), 3.03 (s, 6H). $^{13}$C-NMR (100 MHz, $CDCl_3$): δ 157.06, 150.57, 149.79, 145.86, 136.85, 125.64, 124.58, 123.31, 118.54, 112.37, 111.94, 105.21, 40.19. HRMS-ESI calcd for $C_{18}H_{17}N_2O_2S$ $[M + Na]^+$ 331.10532, found 331.10535. Mp: 235°C, IR [KBr, $cm^{-1}$]: 2921, 1613, 1598, 1505, 1441, 1363, 1327, 1224, 1195, 1107, 1055, 1022, 925, 849, 820, 788, 753, 695.

**2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrrole** (**23**): First, Bis(pinacolato)diboron (381 mg, 1.5 mmol), (1,5-cyclooctadiene)(methoxy)iridium (I) Dimer (40.0 mg, 0.06 mmol) and 4,4'-di-tertbutyl-2,2'-bipyridine (32.2 mg, 0.12 mmol) was added into round bottom flask and degassed under $N_2$ for 30 minutes. Then, dry hexane (15.0 mL) and compound **22** (201 mg, 3.00 mmol) was added into and bubbling under $N_2$ for 30 minutes again. The reaction mixture was stirred at 25 °C for overnight. The reaction mixture was through silica, washed with DCM and the solvent was removed under reduced pressure. The products were purified through recycling HPLC with GPC to give the desired coupling product **23** (74.0 mg, 21%) as yellow oil. $^1$H-NMR of compound **23** (400 MHz, $CDCl_3$): δ 8.94 (br, 1H of NH), 7.00-7.01 (m, 1 H), 6.86-6.88 (m, 1 H), 6.30-6.32 (m, 1 H), 1.33 (s, 12H).

**2-(4-nitrophenyl)-1H-pyrrole** (**24**): Compound **21** (28.3 mg, 0.14 mmol), **23** (54.5 mg, 0.28 mmol) and $Pd(PPh_3)_4$ (8.1 mg, 0.007 mmol) were added into round bottom flask and degassed under $N_2$ for 30 minutes. Then, a solution of 2M $Na_2CO_3$ (0.15 mL) and 1,4-dioxane (1.4 mL) were added. The reaction mixture was degassed with $N_2$ again and stirred for 90 °C for overnight. After reaction, the reaction mixture was extracted with EtOAc, washed with $H_2O$ and brine, dried over $Na_2SO_4$ and the solvent was removed under reduced pressure. The products were purified through silica gel column chromatography using Hex:AcOEt (2:1) to give the desired coupling product **24** (23.7 mg, 97%) as orange solid. $^1$H-NMR of compound **24** (400 MHz, $CDCl_3$): δ 8.60 (br, 1H of NH), 8.23 (d, *J* = 8.85 Hz, 2 H), 7.57 (d, *J* = 8.85 Hz, 2 H), 6.99-7.00 (m, 1 H), 6.73-6.75 (m, 1 H), 6.38-6.36 (m, 1 H).

**2-bromo-5-(4-nitrophenyl)-1H-pyrrole (25):** Compound **24** (20.9 mg, 0.11 mmol) was dissolved into DMF (1.10 mL) and then, NBS (23.0 mg, 0.13) was slowly added into at 0 °C. The reaction mixture was cooled to room temperature and stirred for overnight. The rection mixture was extracted with EtOAc, washed with $H_2O$ and brine, dried over $Na_2SO_4$ and solvent was removed under reduced pressure. The crude was purified by Flash column chromatography to give compound **25** (20.7 mg, 70%). $^1$H-NMR of compound **25** (400 MHz, $CDCl_3$): δ 8.54 (br, 1H of NH), 8.24 (d, *J* = 8.87 Hz, 2 H), 7.53 (d, *J* = 8.87 Hz, 2 H), 6.65-6.63 (m, 1 H), 6.31-6.29 (m, 1 H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 145.46, 138.59, 129.84, 124.66, 123.39, 121.58, 111.35, 109.65. HRMS-ESI calcd for $C_{18}H_{18}N_3O_2$ $[M + H]^-$ 264.96198, found 264.96181. Mp: 65°C, IR [KBr, $cm^{-1}$]: 3311, 1598, 1500, 1440, 1416, 1332, 1197, 1112,1045, 915,852, 767, 752.

***N,N*-dimethyl-4-(5-(4-nitrophenyl)-1H-pyrrol-2-yl)aniline (12):** Compound **25** (20.7 mg, 0.08 mmol) and **14** (52.8 mg, 0.32 mmol) were dissolved into 1,4-dioxane (0.8 mL) and degassed under $N_2$ for 30 minutes. Then, $Pd(PPh_3)_4$ (4.6 mg, 4.0 μmol) and an aqueous solution of 2M $Na_2CO_3$ (0.07 mL) were added. The reaction mixture was degassed with $N_2$ again and stirred for 90 °C for overnight. After evaporation of the organic solvent, the residue was extracted with DCM, washed with $H_2O$ and brine, dried over $Na_2SO_4$. The solvent was removed under reduced pressure. The products were purified through silica gel column chromatography and recycling HPLC with GPC to give the desired coupling product **12** (14 mg, 61%) as dark red solid. $^1$H NMR (400 MHz, $CDCl_3$): δ 8.57 (br, 1H of NH), 8.22 (d, *J* = 9.02 Hz, 2H), 7.57 (d, *J* = 9.02 Hz, 2H), 7.45 (d, *J* = 7.78 Hz, 2H), 6.87 (m, 3H), 6.49 (m, 1H), 3.01 (s, 6H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ 149.91, 144.84, 138.47, 138.47, 137.10, 129.63, 125.42, 124.75, 122.66, 120.11, 112.68, 111.83, 107.27, 40.45. HRMS-ESI calcd for $C_{18}H_{18}N_3O_2$ $[M + H]^+$ 308.13935, found 308.13940. Mp: 275°C, IR [KBr, $cm^{-1}$]: 3452, 2920, 1613, 1594, 1503, 1441, 1366, 1328, 1281, 1227, 1189, 1110, 1085, 1048, 846, 820, 778, 753, 528.

## 3-6. Supplementary material

### $^1$H and $^{13}$C NMR spectra.

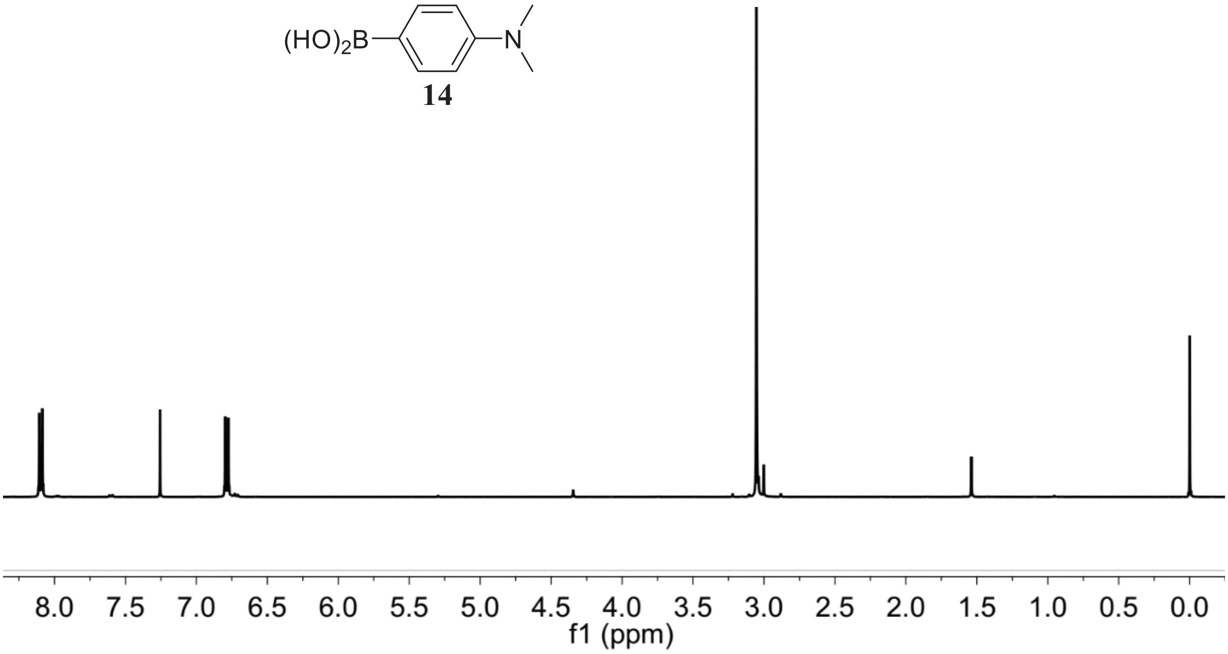


**Figure S27. $^1$H NMR** spectrum of compound **14** in $CDCl_3$.

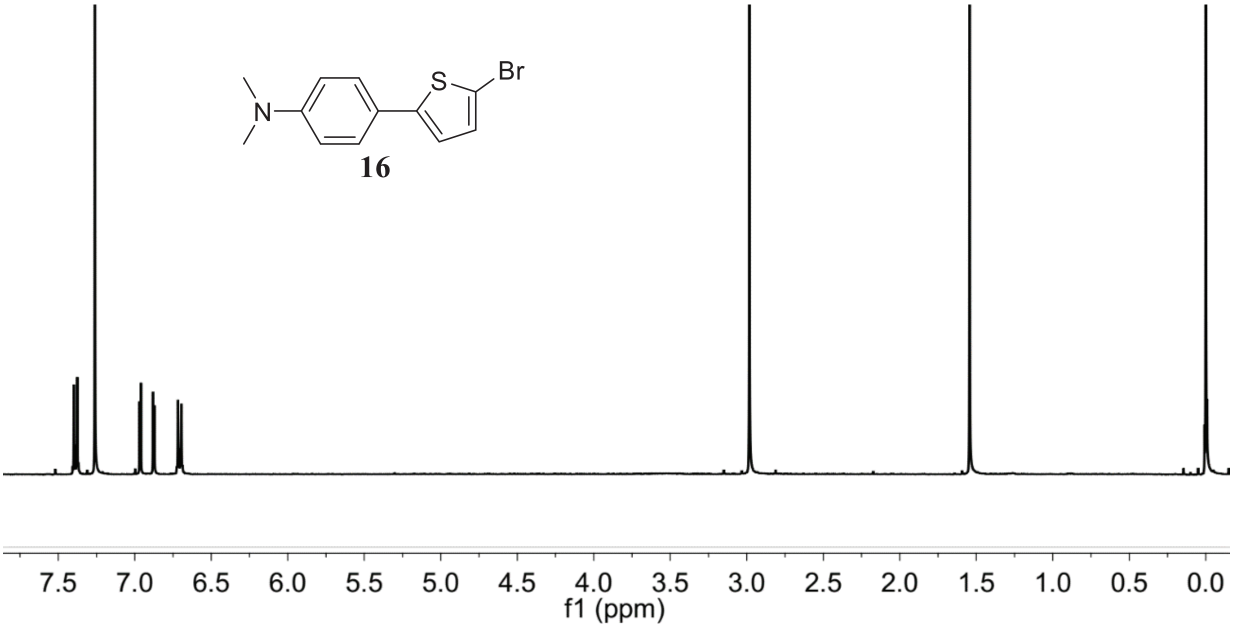


**Figure S28.** $^1$H NMR spectrum of compound **16** in $CDCl_3$.

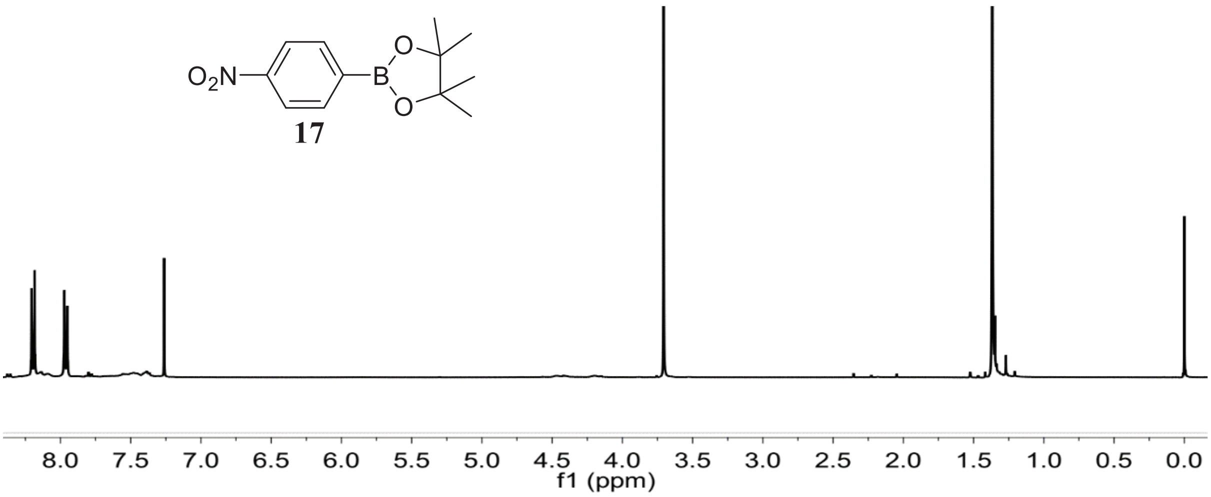


**Figure S29. $^1$H NMR** spectrum of compound **17** in $CDCl_3$.

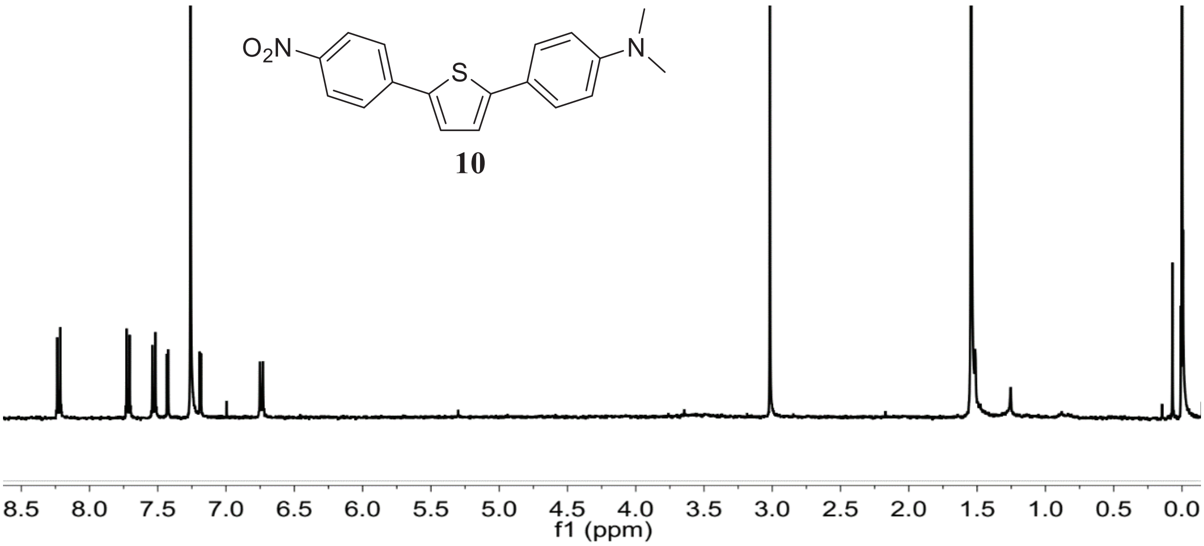


**Figure S30. $^1$H NMR** spectrum of compound **10** in $CDCl_3$.

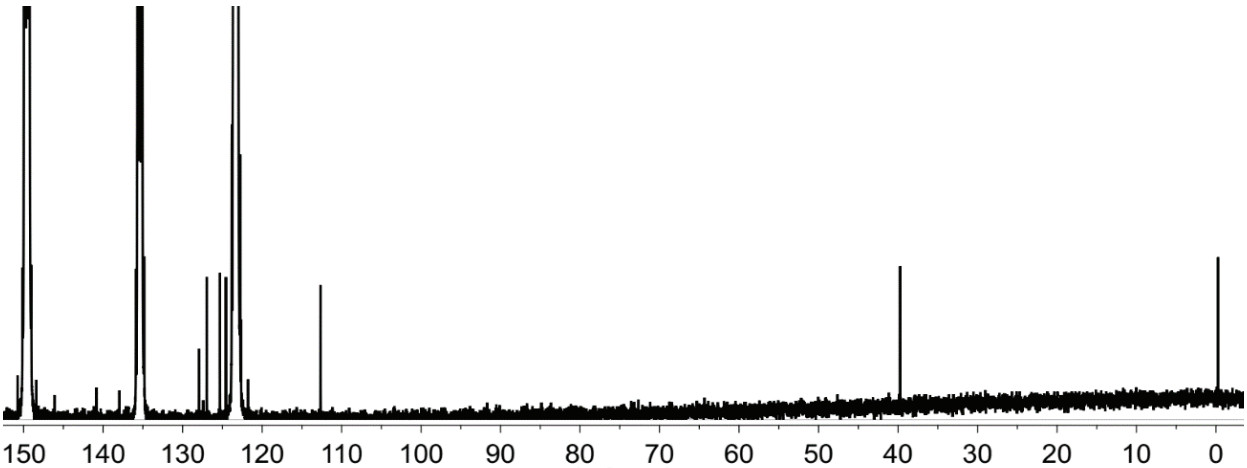


**Figure S31. $^{13}$C NMR** spectrum of compound **10** in pyridine-d6.

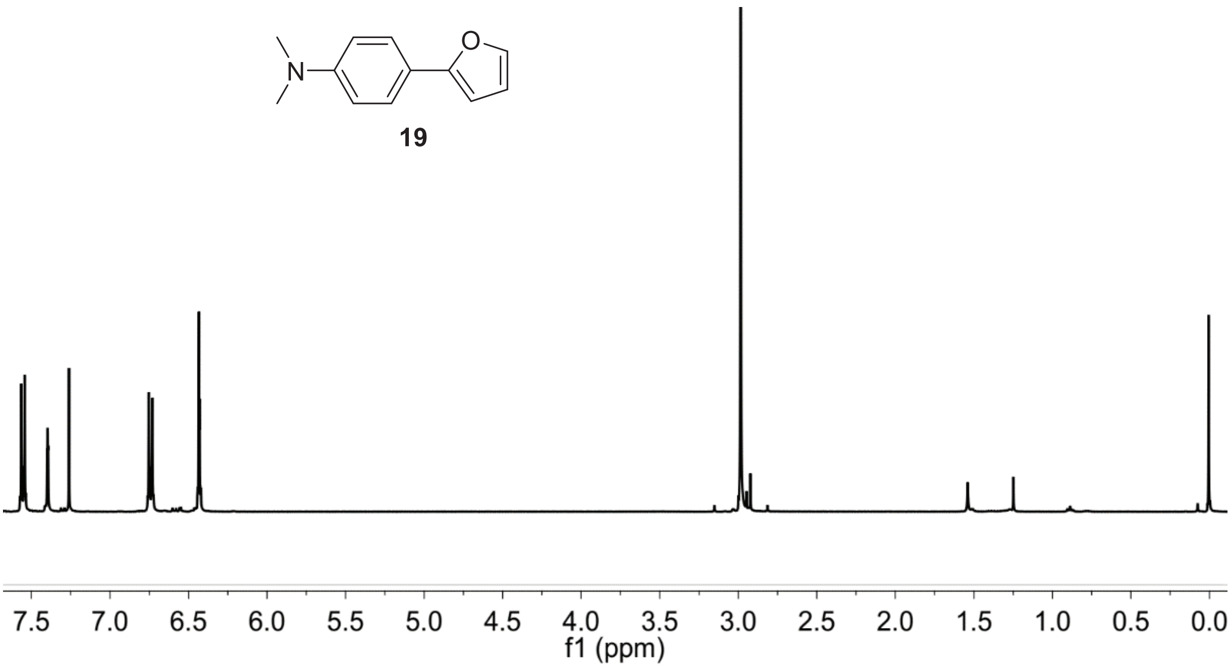


**Figure S32.** $^1$**H NMR** spectrum of compound **19** in $CDCl_3$.

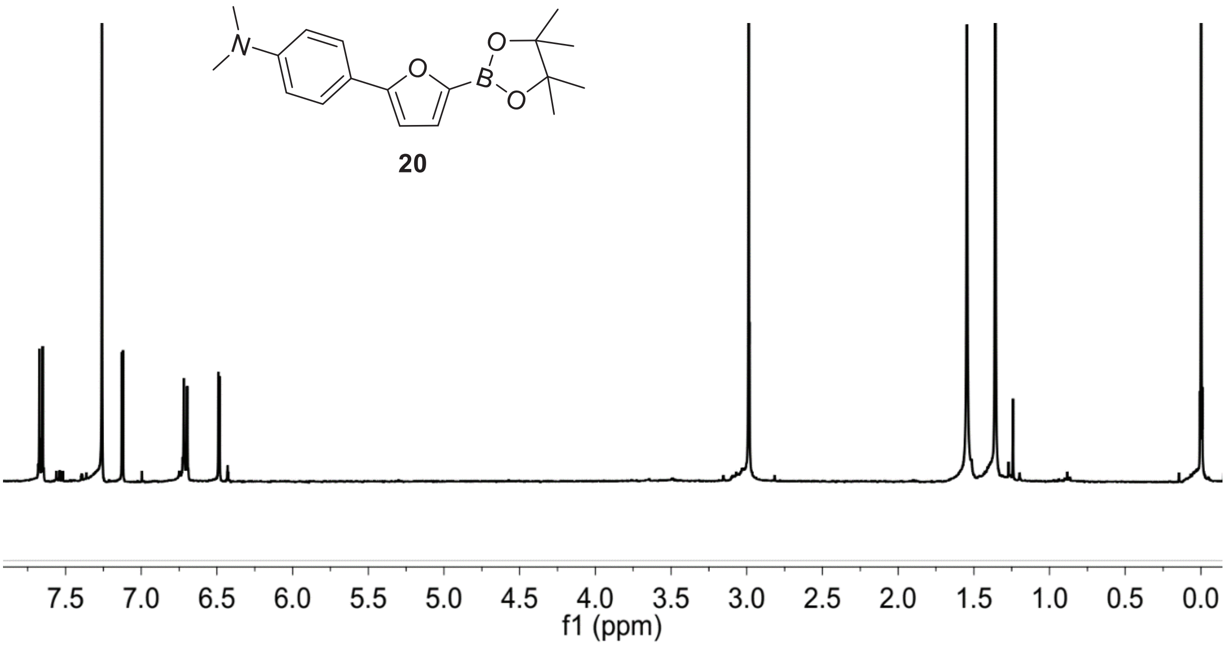


**Figure S33.** $^1$**H NMR** spectrum of compound **20** in $CDCl_3$.

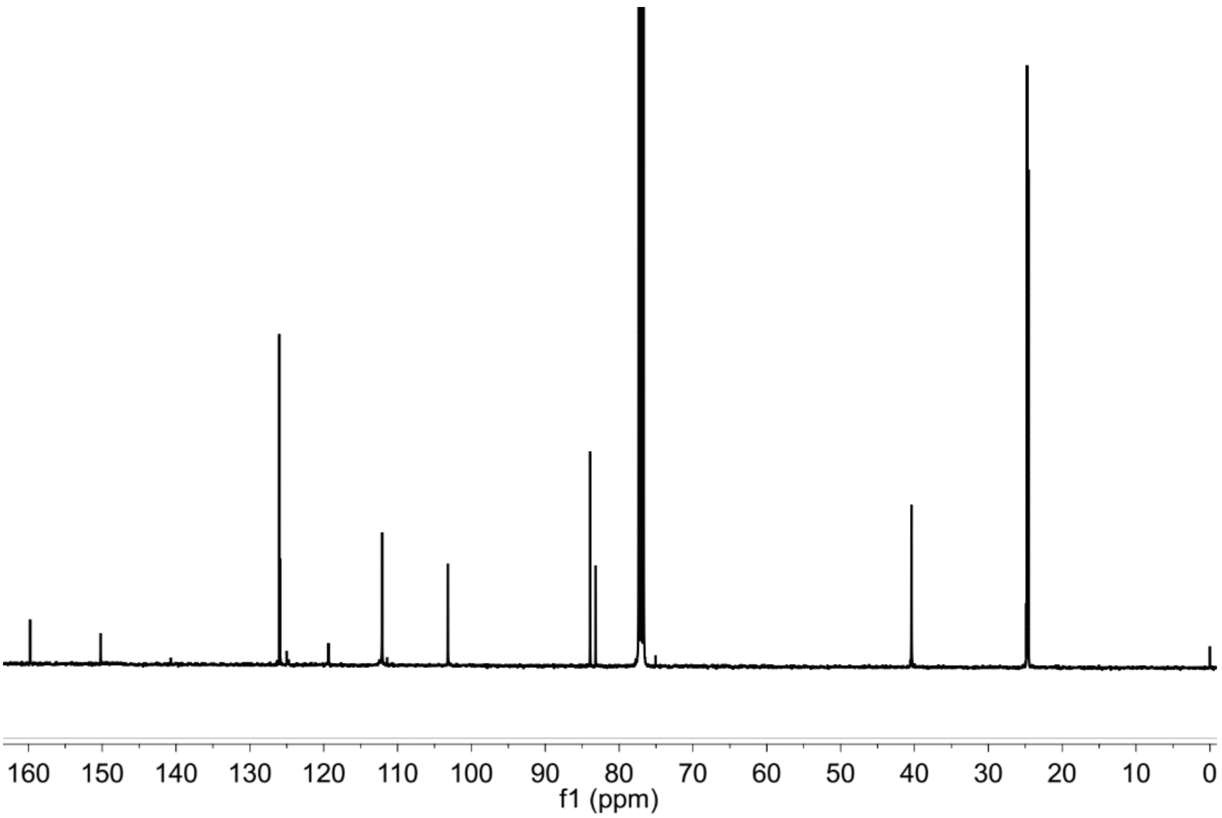


**Figure S34.** $^{13}$**C NMR** spectrum of compound **20** in $CDCl_3$.

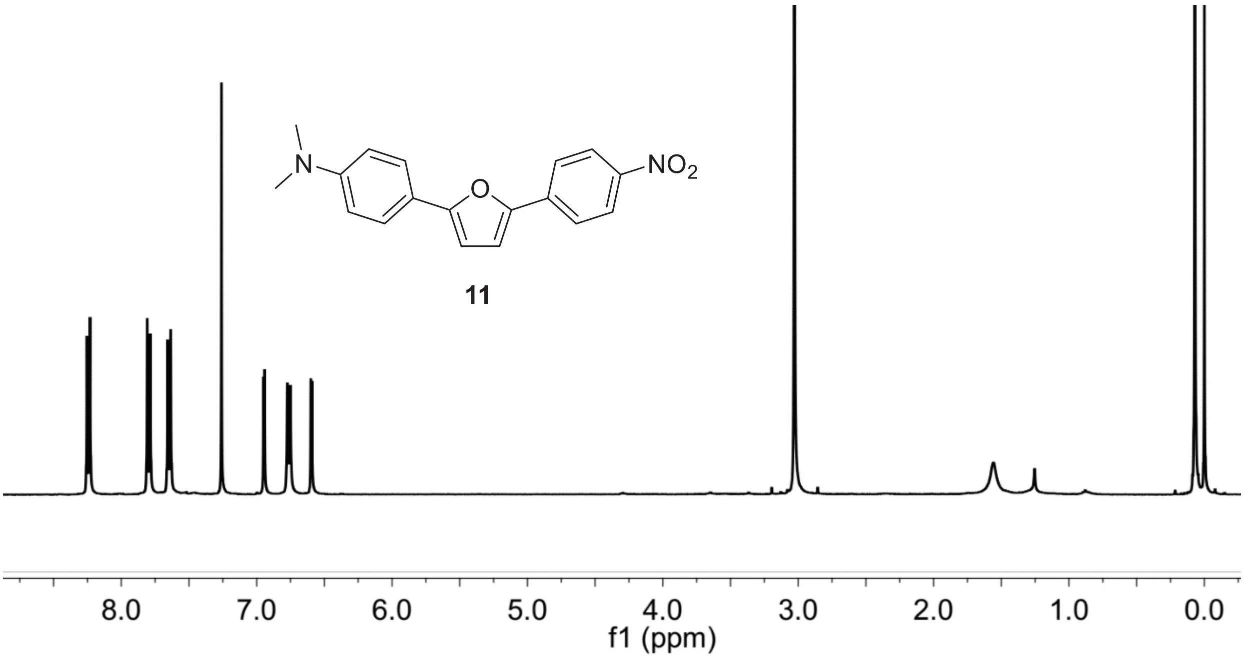


**Figure S35.** $^{1}$**H NMR** spectrum of compound **11** in $CDCl_3$.

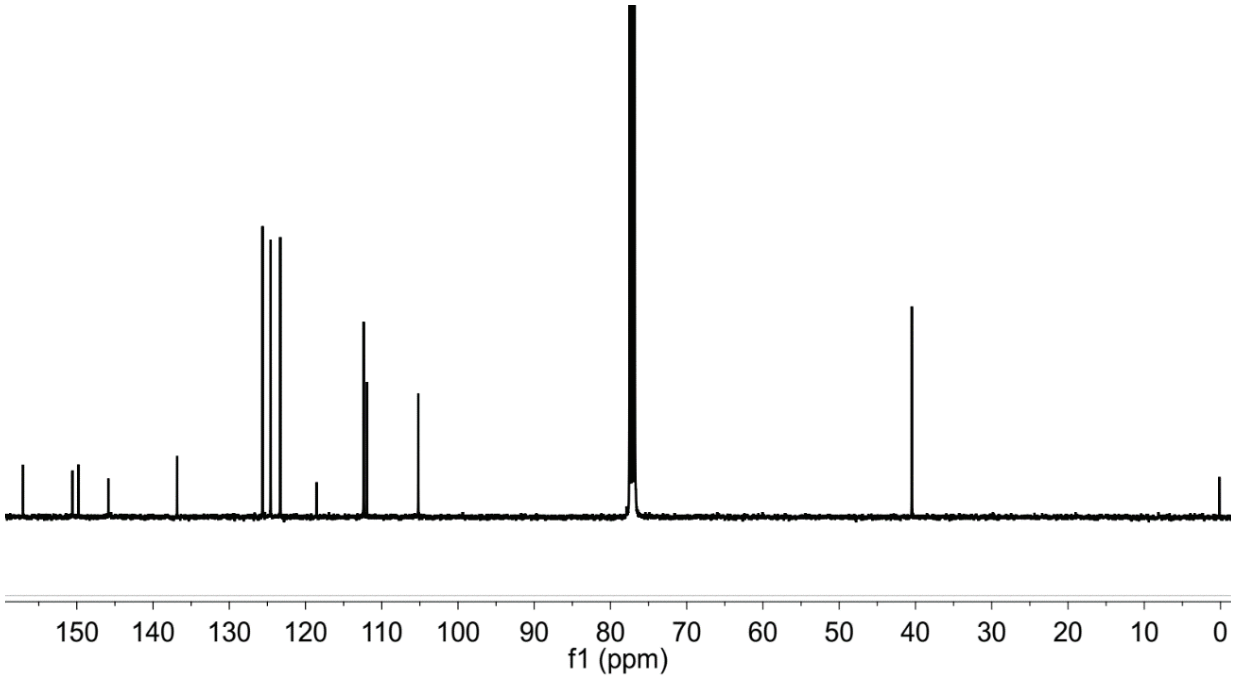


**Figure S36.** **$^{13}$C NMR** spectrum of compound **11** in $CDCl_3$.

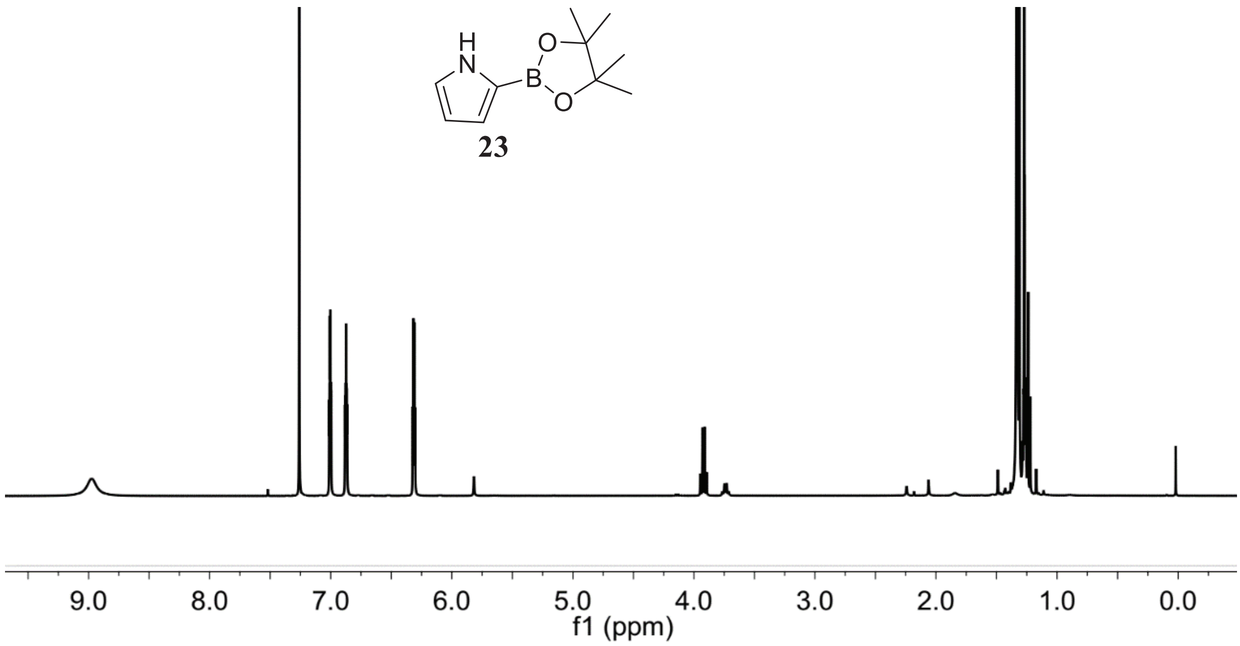


**Figure S37.** **$^{1}$H NMR** spectrum of compound **23** in $CDCl_3$.

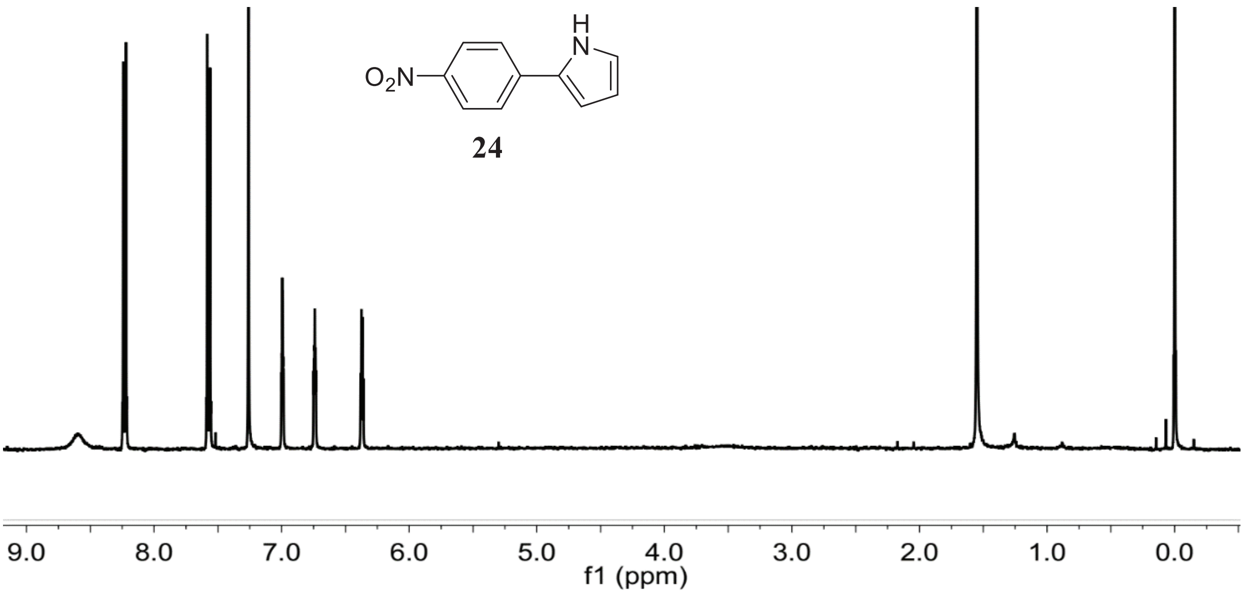


**Figure S38.** $^{1}$**H NMR** spectrum of compound **24** in $CDCl_3$.

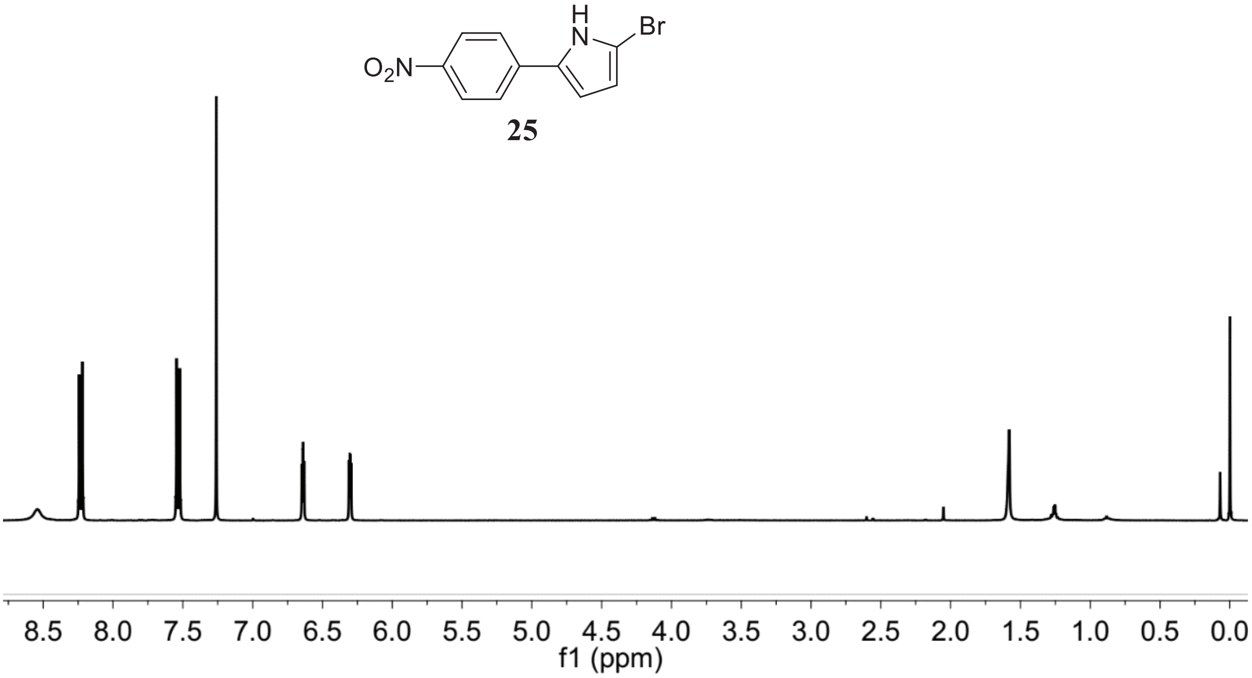


**Figure S39.** $^{1}$**H NMR** spectrum of compound **25** in $CDCl_3$.

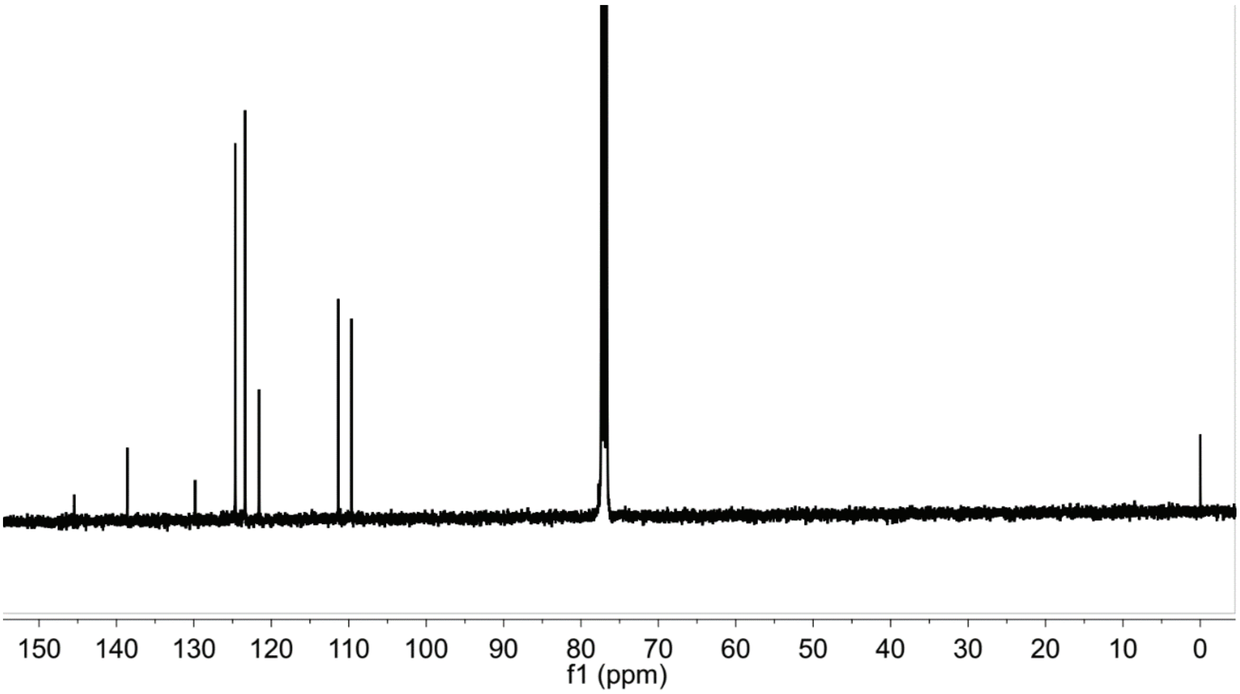


**Figure S40.** $^{13}$**C NMR** spectrum of compound **25** in CDCl$_3$.

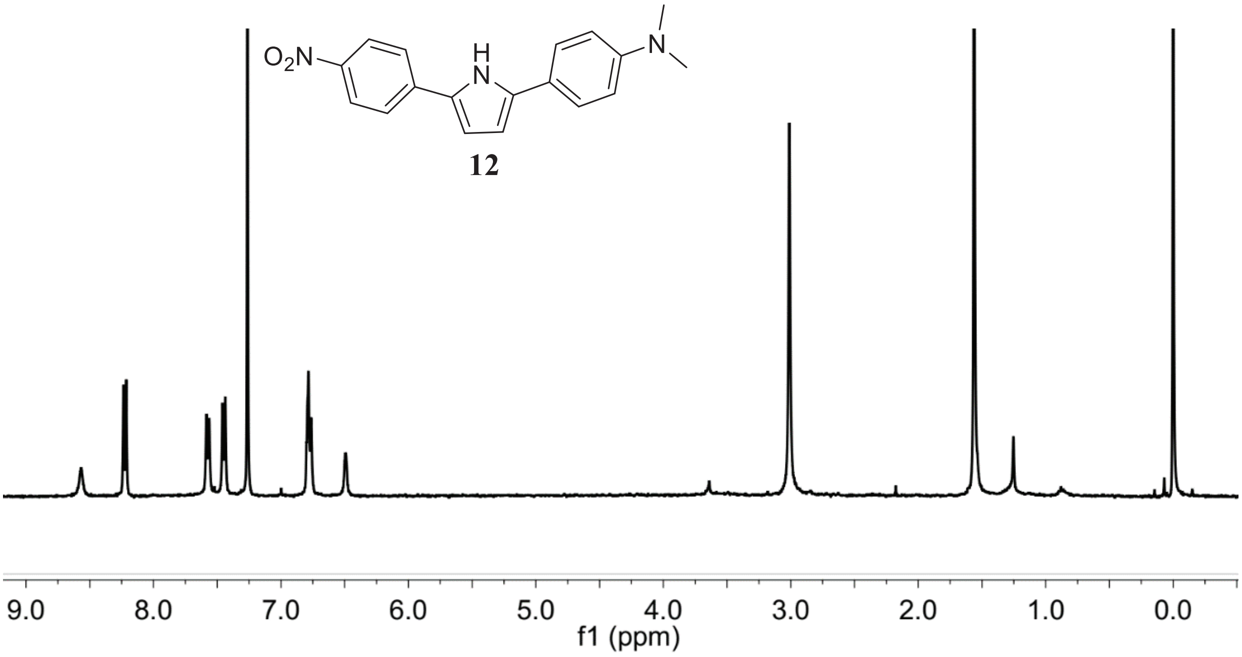


**Figure S41.** $^{1}$**H NMR** spectrum of compound **12** in CDCl$_3$.

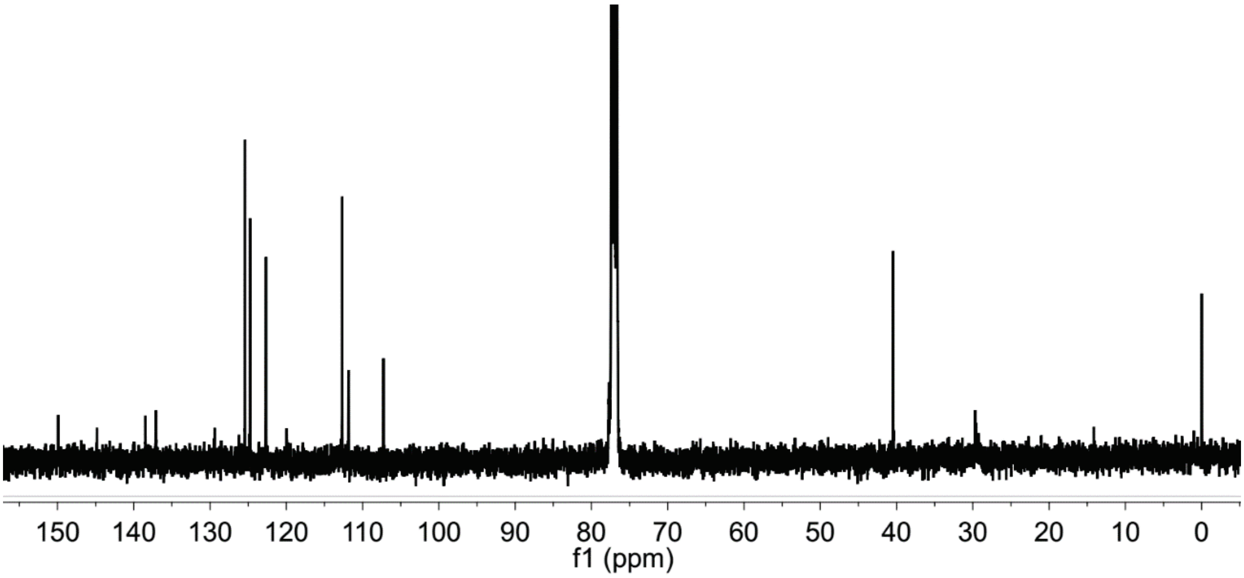


**Figure S42.** $^{13}$C NMR spectrum of compound **12** in CDCl$_3$.

## UV-vis absorption spectra of 10-12

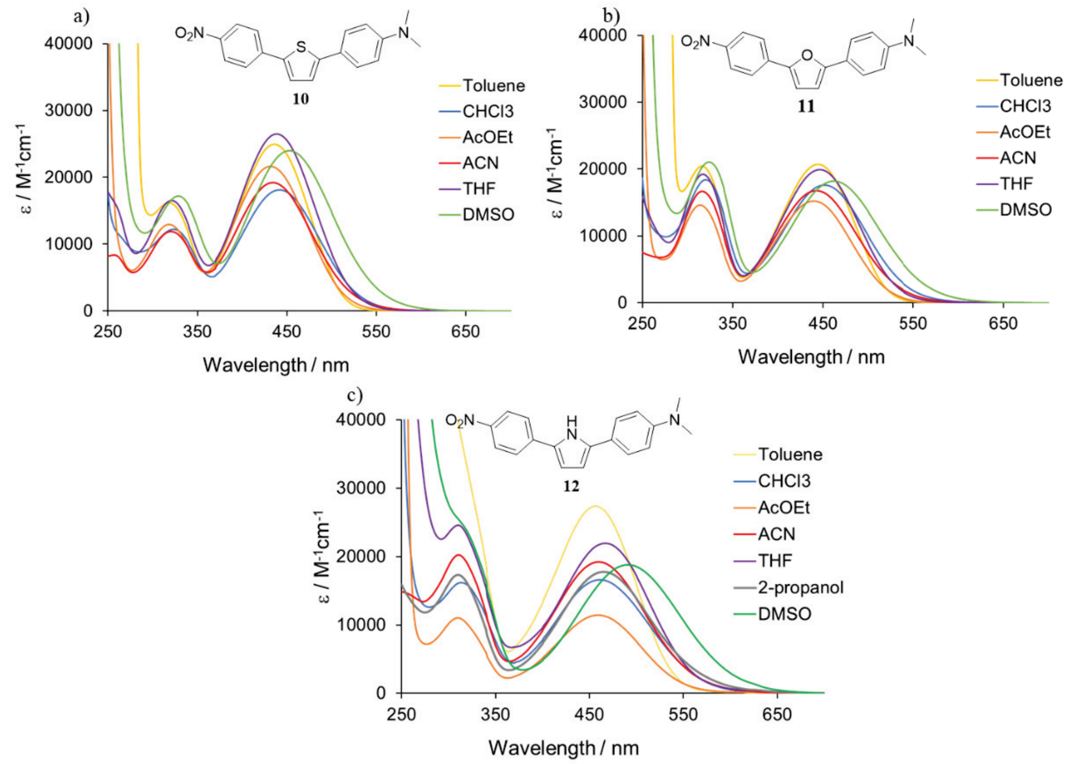


**Figure S43.** UV-vis absorption spectra of **10-12** in different solvents.

## Fluorescence decay of 10-12

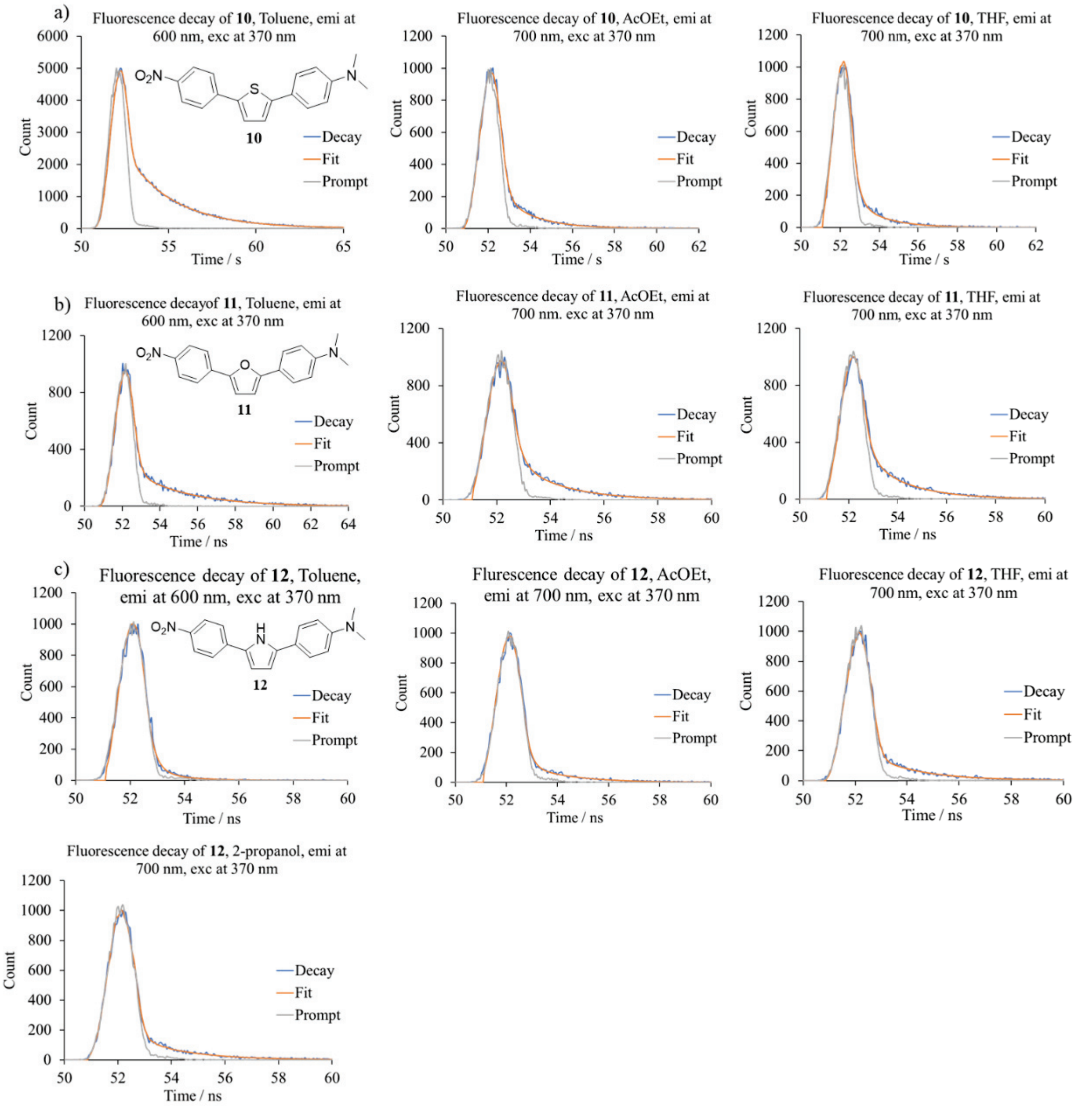


**Figure S44.** Fluorescence decay measured in Tol, AcOEt, THF and 2-propanol of (a) compound **10**, (b) compound **11**, (c) compound **12**.

## Cyclic voltammetry

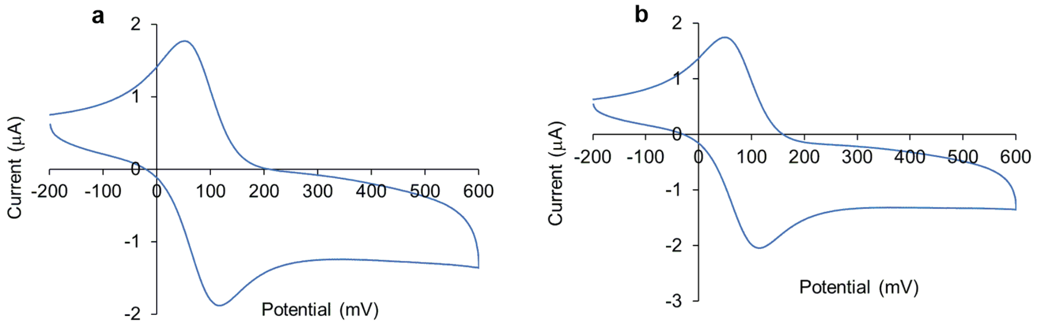


**Figure S45.** Cyclic voltammetry of ferrocene (0.1 M) recorded in acetonitrile (ACN)/0.1 M tetrabutylammonium hexafluorophosphate (TBAHFP) electrolyte with 0.01 M Ag/AgNO$_3$ reference electrode. (a) Redox potential of ferrocene was used to calculate the HOMO and LUMO level of **10,11. (**b) Redox potential of ferrocene was used to calculate the HOMO and LUMO level of **12.**

**Table S2.** Optical and electrochemical studies of compounds **10-12**.

| Comp. | $E^{1}_{\mathrm{red}}$[a] / V | $E^{2}_{\mathrm{red}}$[a] / V | $E^{3}_{\mathrm{red}}$[a] / V | $E^{1}_{\mathrm{ox}}$[a] / V | $E^{2}_{\mathrm{ox}}$[a] / V | $E^{3}_{\mathrm{ox}}$[a] / V | HOMO[b] / eV | LUMO[c] / eV | $E_{\mathrm{gap(elec)}}$[d] / eV |
|---|---|---|---|---|---|---|---|---|---|
| **10** | -1.23 | -1.41 | - | 0.43 | 0.98 | - | -5.12 | -3.46 | 1.66 |
| **11** | -1.26 | -1.43 | - | 0.42 | 0.78 | 0.92 | -5.11 | -3.43 | 1.68 |
| **12** | -1.24 | -1.47 | -1.75 | 0.23 | 0.51 | 0.62 | -4.82 | -3.35 | 1.47 |

[a] Electrochemical potentials *vs.* Fc/Fc$^{+}$ of the indicated compounds **10-12** in ACN. [b] Measured from onset value of oxidation half cycle of CV. [c] Measured from onset value of reduction half cycle of CV. [d] Electrochemical HOMO-LUMO gap.

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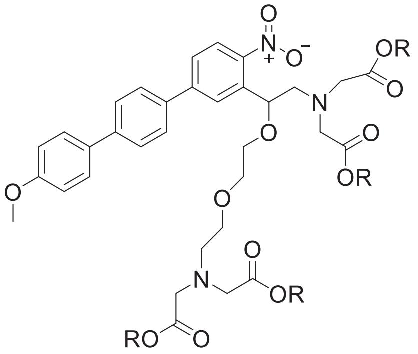
# Chapter 4

# Conclusion and Outlook

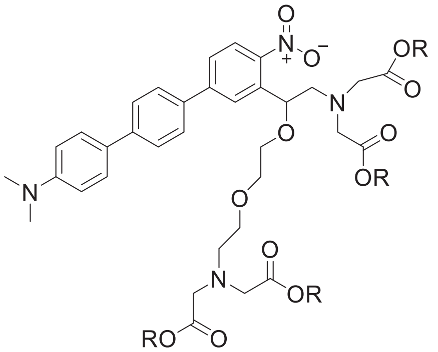
## Conclusion and Outlook

In this research, the investigation one-photon of EGTA substituted *p*-nitroterphenyl (PNTP) derivatives with two different electron-donating -NMe$_2$ and -OMe substituents showed that a high quantum yield of up to 0.40 was observed for the photolysis of the caged calcium species featuring -OMe substituent, whereas that with the more strongly electron-donating -NMe$_2$ group showed a sizeable 2PA cross-section.



**3a, 4a**

**3a:** R = Et
**4a:** R = H

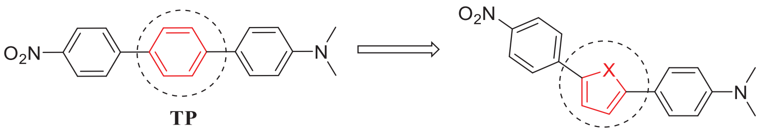


**3b, 4b**

**3b:** R = Et
**4b:** R = H

| Comp. | Solv. | $K_d$ / nM | $\lambda_{abs}$ / nm | $\Phi_{decomposition}$ | $\sigma_2$ / GM | $\delta_u$ / GM |
|---|---|---|---|---|---|---|
| **3a** | DMSO | - | 350 | 0.27 | 21<br>(730 nm) | 5.7<br>(730 nm) |
| **3b** | DMSO | - | 392 | 0.02 | 220<br>(770 nm) | 4.4<br>(770 nm) |
| **4a** | HEPES buffer pH 7.4 | 202 | 344 | 0.4 | 8.2<br>(720 nm) | 3.3<br>(720 nm) |
| **4b** | HEPES buffer pH 7.4 | 213 | 363 | 0.04 | 75<br>(780 nm) | 3.0<br>(780 nm) |

In addition, the synthesis and investigation of one- and two-photon of teraryl derivatives, in which the heterocycle linkers such as thiophene, furan, and pyrrole replaced the central aromatic ring showed much improved 2PA cross-section value. These compounds can be used for chromophores in investigating for 2P-responsive photolabile protecting groups for physiological processes.



**TP**
$\sigma_2$= 13.9 GM at 820 nm

**10**: X = S, $\sigma_2$= 143 GM at 900 nm
**11:** X = O, $\sigma_2$= 93 GM at 910 nm
**12:** X = NH, $\sigma_2$= 150 GM at 960 nm

# List of Publications

# Articles

(1) "*p*-Nitroterphenyl Units for Near-Infrared Two-Photon Uncaging of Calcium Ions"
Thuy Thi Thu Pham, Satish Jakkampudi, Ko Furukawa, Fung-Yu Cheng, Tzu-Chau Lin, Yoki Nakamura, Norimitsu Morioka, Manabu Abe
*Journal of Photochemistry & Photobiology, A: Chemistry* **2021**, 409, 113154-113167.

(2) "Impact of five-membered heterocyclic ring on photophysical property including two-photon absorption character"
Thuy Thi Thu Pham, Youhei Chitose, Tran Thi Thanh Tam, Wei-Lun Tseng, Tzu-Chau Lin, Manabu Abe
*Chem. Lett* **2021,** CL-210420, *in press*.

# Thesis Supplements

(1) “Design and Synthesis of Two-Photon Responsive Chromophores for Near-Infrared Light Induced Uncaging Reactions”
M. Abe, Y. Chitose, S. Jakkampudi, P. T. T. Thuy, Q. Lin, B. T. Van, A. Yamada, R. Oyama, M. Sasaki, C. Katan
*Synthesis* **2017**, 49, 3337-3346.

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July 2021
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Hiroshima University