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Aza-crown ether derivatives based on stilbene: Two-photon absorption and bioimaging

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ABSTRACT

Two novel aza-crown ether derivatives based on stilbene were synthesized and characterized. Their linear photophysical properties were systematically investigated in various solvents. The nonlinear photophysical properties were investigated by two-photon induced fluorescence method. The two-photon absorption cross sections values measured by two-photon excited fluorescence were determined to be 328.2 GM and 246.55 GM for the dyes derived from monoaza 15-crown-5 and 18-crown-6, respectively, which accorded with dipole moment changes under photoexcitation. In addition, a single-photon fluorescence cell imaging experiment proved that dye derived from monoaza 15-crown-5 was suitable for biomedical imaging.

1. Introduction

The development of materials displaying two-photon absorption (2PA) [1] has attracted great interest in past decades due to a variety of potential applications in photonics and optoelectronics, such as three-dimensional optical data storage, fluorescence imaging, optical limiting, up-converted lasing and microfabrication [2].

The applications of 2PA materials stimulated substantial research on structure-property relationship [3]. The significant issue is how to synthesize the materials with large 2PA cross sections. Some efficient molecular design strategies were put forward to provide guidelines for the development of materials with large two-photon absorption cross sections (σ), including donor–acceptor–donor (D–A–D)-type molecules, donor–π–acceptor (D–π–A)-type molecules, donor–π–donor (D–π–D)-type molecules, macrocycles, dendrimers, polymers, and multi-branched molecules. Reinhardt synthesized a variety of donor–π–acceptor (D–π–A) and donor–π–donor (D–π–D) derivatives, in which fluorene, biphenyl, or naphthyl groups are employed as the mobile π-electron bridge, and showed that the TPA cross sections become larger if a planar fluorene was used as the π-center [4]. The TPA properties of fluorene derivatives were subsequently optimized by Belfield by introducing a variety of donors and acceptors [5]. The important role of the π-center for the design of large TPA dyes was demonstrated by Prasad, who showed that the TPA cross sections of the D–π–D chromophores based on dithienothiophene as the π-center were larger by an order of magnitude than those of the fluorene derivatives [6]. By combining synthesis, characterization, and theory, Marder, Perry, and Webb found that bis(styryl)-benzene derivatives with donor–acceptor–donor (D–A–D) and acceptor–donor–acceptor (A–D–A) structural motifs, which were linear quadrupolar molecules, showed exceptionally large TPA cross sections [7].

Most organic dyes with large conjugated structures have a major defect that solubility is poor for bioimaging, as a result, it is necessary to enhance their biocompatibility by optimizing the

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structure [8]. In the design of the target molecules, the aza-crown ether often used as phase transfer catalyst was introduced. The aza-crown ether serves as the electron donor, meanwhile, it was also expected to endow the molecules hydrophilia. And that crown ether compounds having good solubility and environmental stability are also multidentate ligands that exhibit selectivity for specific metal ions in solutions containing other chemically similar ions, which can be applied to identify ions. In this paper, we designed and synthesized two novel aza-crown ether derivatives-based TPA dyes with dumbbell-shape (D–π–D), aza-crown ether as electron donor and stilbene as the conjugated chain. Compared with simple dimethyl amino substituents, the two dyes showed the similar two-photon absorption property and better solubility. Furthermore, a single-photon fluorescence cell imaging experiment proved the suitability of dye 1 for biomedical imaging.

2. Experimental section

2.1. Apparatus and materials

Chemicals were purchased and used as received. Every solvent was purified by conventional methods beforehand. IR spectra were recorded with a Nicolet FT-IR NEXUS 870 spectrometer (KBr discs) in the 4000–400 cm^{-1} region. ^1H NMR and ^{13}C NMR were recorded on 400 MHz and 100 MHz NMR instruments using $CDCl_3$ as solvent respectively. The mass spectra were obtained on a Bruker Autoflex III smartbeam mass spectrometer and a Finnigan LCQ Spectrometer. Elemental analyses data were measured by a Perkin Elmer 240B elemental analyzer. The one-photon absorption (OPA) spectra were recorded on a SPECORD S600 spectrophotometer. The one-photon excited fluorescence (OPEF) spectra measurements were performed using a Hitachi F-7000 fluorescence spectrophotometer. For time-resolved fluorescence measurements, the fluorescence signals were collimated and focused onto the entrance slit of a monochromator with the output plane equipped with a photomultiplier tube (HORIBA HuoroMax-4P). Two-photon absorption (TPA) cross sections (δ) of the samples were obtained by two-photon excited fluorescence (TPEF) method [9] at femtosecond laser pulse and Ti: sapphire system (680–1080 nm, 80 MHz, 140 fs) as the light source.

2.2. Synthesis

2.2.1. Synthesis of dye 1 (Scheme 1)

t-BuOK (1.2 g, 10 mmol) and 4-(1, 4, 7, 10-tetraoxa-13-aza cyclopentadecyl) benzaldehyde (1 g, 3 mmol) were placed into a dry mortar and milled vigorously for about 90 min under infrared ray lamp, in the process, 4, 4-Bis(diethylphosphonomethyl) biphenyl(1.36 g, 3.0 mmol) was added in batches. After completion of the reaction (monitored by Thin Layer chromatography (TLC)), the mixture was dissolved in Dichloromethane (150 mL). The residual solid was filtered and filtrate was concentrated. Yellow-green needle product (1.24 g, 1.565 mmol) was obtained by recrystallized from dichloromethane. Yield: 52.3%. mp 233 °C; ^1H NMR (400 MHz, $CDCl_3$, TMS) (Fig. S1): δ 7.59 ($J = 8$, *d*, 4H), 7.53($J = 8$, *d*, 4H), 7.40($J = 8$, *d*, 4H), 7.07($J = 16$, *d*, 2H), 6.92($J = 16$, *d*, 2H), 6.66($J = 8$, *d*, 4H), 3.78–3.76(*m*, 8H), 3.67–3.64(*m*, 32H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS) (Fig. S2): δ 146.25, 137.87, 136.16, 127.68, 126.80, 125.87, 125.37, 124.24, 122.60, 110.54, 70.32, 69.21, 69.15, 67.54, 51.55. IR (KBr): 3054 (m), 1610 (m), 1486 (s), 1208 (s), 1142 (s). MS (ESI): 397.22 $[(M+2)/2]^+$. Anal. Calcd for $C_{48}H_{60}N_2O_8$: C, 72.70; H, 7.63; N, 3.53%. Found: C, 72.35; H, 7.28; N, 3.26%.

Table 1
Photophysical properties of dye 1 and dye 2 in four different polar solvents.

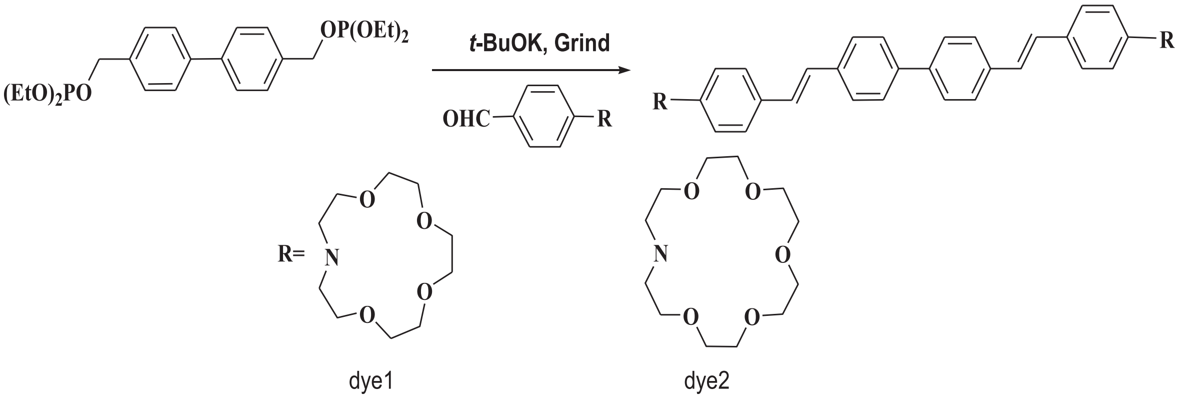
Ligand	Solvents	λ_{max}[a]	λ_{max}[b]	Φ[c]	$\Delta\nu$[d]
Dye 1	Benzene	395	455,482	0.373	3338.43
	DCM	395	494	0.361	5073.54
	THF	395	485	0.367	4697.90
	DMF	398	511	0.333	5306.15
Dye 2	Benzene	391	458, 479	0.372	3741.39
	DCM	392	489	0.368	5018.40
	THF	393	482	0.370	4698.40
	DMF	393	511	0.330	5875.82

[a] Peak position of the longest absorption band.
[b] Peak position of SPEF, excited at the absorption maximum.
[c] Quantum yields determined by using quinine sulfate as standard.
[d] Stokes' shift in cm^{-1}.

2.2.2. Synthesis of dye 2 (Scheme 1)

Dye 2 was obtained as orange powders in 40.6% yield by following a similar procedure of Dye 1. mp 207 °C;^1H NMR (400 MHz, $CDCl_3$, TMS) (Fig. S3): δ 7.59($J = 8$, *d*, 4H), 7.53($J = 8$, *d*, 4H), 7.39($J = 8$, *d*, 4H), 7.06($J = 16$, *d*, 2H), 6.92($J = 16$, *d*, 2H), 6.68($J = 8$, *d*, 4H), 3.72-3.70(*m*, 8H), 3.67–3.64(*m*, 40H). ^{13}C NMR (100 MHz, $CDCl_3$, TMS)(Fig. S4): δ 147.58, 138.90, 137.17, 130.21, 127.84, 127.10, 126.90, 126.40, 123.62, 111.71, 70.81, 70.74, 68.72, 62.26, 62.19, 51.24. IR (KBr): 3038 (m), 1610 (m), 1491 (s), 1197 (s), 1122 (s). MS(ESI): 441.25 $[(M+2)/2]^+$. Anal. Calcd for $C_{52}H_{68}N_2O_{10}$: C, 70.88; H, 7.78; N, 3.18%. Found: C, 71.12; H, 7.53; N, 3.31%.

2.2.2.1. Linear absorption and single-photon excited fluorescence (SPEF). The photophysical properties of dyes 1 and 2 are summarized in Table 1. The linear absorption spectra (one-photon



Scheme 1. Preparation of the dyes 1 and 2.