A difluorenyl-carbo-cyclohexadiene: prospective chromophore for two-photon absorption

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For the purpose of outlining structure-property relationships for two-photon absorption (2PA), a "\( \sigma \)-locked" carbo-cyclohexadiene with two fluorenyl substituents has been envisaged for comparison with previously studied aromatic carbo-benzene and non-aromatic carbo-quinoid congeners. A representative where the C\textsubscript{10}-\( \pi \)-conjugated fluorenyl moieties are also connected by a C\textsubscript{8}-\( \pi \)-insulating 3,6-dimethoxy-3,6-bis(trifluoromethyl)octa-1,4,7-triyn-1,8-diyl edge has thus been synthesized in four steps from known C\textsubscript{8}F triyne and C\textsubscript{10} triynyldial, through a [8F+10] cyclization process. In spite of a relatively strong absorbance (\( \varepsilon = 84\ 800\ \text{L.mol}^{-1}.\text{cm}^{-1} \)) at 634 nm), the non-vanishing green fluorescence (at 533 nm) of the chromophore should allow measurements of the 2PA cross section by both the TPEF and Z-scan methods.

Introduction

87 Years after Maria Göppert-Mayer's seminal dissertation \[1a\], third-order non-linear optical (NLO) processes, and in particular two-photon absorption (2PA), attract a constantly renewed attention \[1b,c\]. Chromophores with large 2PA cross-sections (\( \sigma_{2PA} \)) can indeed find applications in diverse fields such as three-dimensional optical data storage \[2\], fluorescence microscopy \[3\], optical power limiting \[4\], photodynamic therapy \[5\] or microfabrication \[6\]. In the field of organic chromophores, many studies have highlighted the high 2PA efficiency of dipolar systems of the type D-\( \Pi \)-A \[7\], and quadrupolar counterparts of the type D-\( \Pi \)-D or D-A-D \[8\], where D and A denote \( \pi \)-electron donating and accepting moieties, respectively, and \( \Pi \) a \( \pi \)-conjugating bridge. Aromatic macrocycles can also be
envisioned as bridging cores $\Pi$: after the $C_{20}N_4$ pentacycle of porphyrines [5,9], the $C_{18}$ monocycle of *carbo*-benzenes was recently reported to act as an efficient $\Pi$ core in quadrupolar 2PA chromophores [10]. Using the $Z$-scan technique, a 2PA cross section $\sigma_{2PA} = 656$ GM was indeed measured for the *carbo*-benzene 1b upon femtosecond excitation at 800 nm (Figure 1). More recently, preliminary $Z$-scan measurements performed on the *carbo*-quinoid 2 [11] indicated that the non-aromatic $C_{18}$ core at stake tends to provide higher 2PA than the aromatic *carbo*-benzene version ($\sigma_{2PA} = 765$ GM at 800 nm) [12].

![Figure 1](image_url)

**Figure 1.** Previously studied *carbo*-meric 2PA chromophores.

As both the *carbo*-quinoid and *carbo*-benzene cores possess two parallel $C_8 \pi$-conjugating paths, results suggested the design of *carbo*-chromophores with a single $C_8 \pi$-conjugating path in a rigid planar environment. In order to benefit from sufficient stability and solubility [13], the 3,6-dimethoxy-3,6-bis(trifluoromethyl) octa-1,4,7-triyne moiety was selected as the rigidifying $C_8 \pi$-insulating path: the preparation of the trifluoromethylated difluorenyl-*carbo*-cyclohexadiene 3 was thus envisaged by extension of synthetic procedures previously developed for analogous targets [13].

**Experimental part**

**Material and methods**

THF and diethyl ether were dried and distilled over sodium/benzophenone, pentane and dichloromethane over P$_2$O$_5$. All other reagents were used as commercially available. In particular, commercial solutions of $n$-BuLi were 2.5 M in hexane, solutions of HCl were 2 M in diethylether. All reactions were carried out under nitrogen or argon atmosphere using Schlenk and vacuum line techniques. Column chromatography was carried out on silica gel (60 P, 70-200 mm). Silica gel thin–layer chromatography plates (60F254, 0.25 mm) were revealed by treatment with an ethanolic solution of phosphomolybdic acid (20 %). The following analytical instruments were used. $^1$H and $^{13}$C NMR: Bruker DPX 300, Avance 300, Avance 400, Avance 400WB or Avance 500 spectrometers. Mass spectrometry: Quadrupolar Nermag R10-10H spectrometer. UV-vis absorption: Perkin-Elmer Win-Lab Lambda 35
spectrometer. UV-vis fluorescence: HORIBA Jobin Yvon Fluoromax-4 spectrofluorometer. Most of the NMR spectra were recorded in CDCl$_3$ solutions. NMR chemical shifts $\delta$ are in ppm, with positive values to high frequency relative to the tetramethylsilane reference; coupling constants $J$ are in Hz.

**Synthesis**

3-[10-(9,9-dihexyl-9H-fluoren-3-yl)-13,16-dimethoxy-4,7-diphenyl-13,16-bis(trifluoromethyl)cyclooctadeca-1,2,3,7,8,9-hexaen-5,11,14,17-tetrayn-1-yl]-9,9-dihexyl-9H-fluorene 3. To a solution of HMDS (hexamethyldisilazane: 0.12 mL, 0.57 mmol) in THF (7 mL) under stirring at -78 °C was added $n$-BuLi (0.216 mL, 0.54 mmol). The mixture was stirred for 30 minutes at -78 °C before addition of a solution of 4 (27 mg, 0.09 mmol) in THF (3 mL). The reaction mixture was stirred for 30 minutes at -78 °C before dilution with THF (25 mL). This solution and a solution of 5 (90 mg, 0.09 mmol) in THF (35 mL) were then slowly syringed simultaneously into a round bottom flask filled with THF (250 mL) under stirring at -78 °C. The temperature of the resulting mixture was allowed to slowly increase up to room temperature, and the stirring was maintained overnight before treatment with a saturated aqueous solution of NH$_4$Cl. The aqueous layer was extracted with Et$_2$O and the combined organic layers were washed with brine, dried over MgSO$_4$ and concentrated under reduced pressure. The residue containing the poorly stable [6]pericyclynediol 6 was directly used in the subsequent reduction step without further purification (HRMS-control: HRMS (MALDI-DCTB): $m/z$ calcd for C$_{86}$H$_{90}$O$_6$F$_6$ [M]$^+$: 1332.6642, found: 1332.6598).

To a solution of the residue in dry DCM (30 mL) under stirring at -78 °C were added SnCl$_2$ (190 mg, 1.0 mmol) and then HCl•Et$_2$O (1.0 mL, 2.0 mmol). The temperature was slowly increased up to 0 °C over 3 hours. Aqueous 1 M NaOH (2.1 mL, 2.1 mmol) was then added to the mixture. The aqueous layer was extracted with DCM and the combined organic layers were washed with brine, dried over MgSO$_4$ and concentrated under reduced pressure. The residue was purified by silica gel chromatography (DCM:pentane 1:9) to give 3 (mixture of isomers) as a dark solid with 29 % yield over two steps (32 mg). $R_t$ (DCM: pentane 1:9) ≈ 0.15. A pure fraction of one of the diastereoisomers could be separated (8 mg).

Atom numbering in the fluorenyl substituents ("Fluo") for NMR assignment:

![Atom numbering diagram]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.02 (d, $J = 7.8$ Hz, 4 H, $o$-Ph), 7.86 – 7.72 (m, 8 H, $H9,H10,H12,H13$(Fluo)), 7.59 (t, $J = 7.9$ Hz, 4 H, $m$-Ph), 7.53 – 7.39 (m, 8 H, $p$-Ph, $H6,H7,H8$(Fluo)), 3.76 (s, 6 H, OCH$_3$), 2.10 – 1.95 (m, 8 H, (Fluo)(CH$_2$)$_2$), 1.19 – 0.54 (m, 44 H, (CH$_2$)$_{4n}$-CH$_3$). $^{13}$C{${^1}$H} NMR (101 MHz,
To a solution of 9 (195 mg, 0.35 mmol) in DCM (40 mL) under stirring at 0 °C was added solid MnO₂ (550 mg, 6 mmol), and the mixture was stirred for 1 hour at 0 °C, then 3 hours at room temperature. The mixture was filtered through Celite®, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel chromatography (EtOAc:pentane 1:9) to give 5 as a light solid with 52 % yield (100 mg). M.p. 53 °C.

**1,10-dione 5.** To a solution of 8 (340 mg, 0.82 mmol) in THF (20 mL) under stirring at -78 °C was added n-BuLi (308 μl, 0.77 mmol). The mixture was stirred for 1 hour at -78 °C before addition of a solution of 7 (130 mg, 0.35 mmol) in THF (5 mL). The temperature was allowed to slowly increase up to -20 °C over 3 hours, before addition of a saturated aqueous NH₄Cl solution. The aqueous layer was extracted with Et₂O and the combined organic layers were washed with brine, dried over MgSO₄ and concentrated to dryness under reduced pressure. The residue was purified by silica gel chromatography (EtOAc:pentane 2:8) to give 9 as a light oil with 54 % yield (195 mg). Rf (EtOAc:heptane 2:8) = 0.20.
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.87 – 7.81 (m, 2 H- H(Fluo)), 7.75 – 7.65 (m, 4 H, o-Ph), 7.59 – 7.48 (m, 4 H, m-Ph), 7.46 – 7.30 (m, 14H, H(Fluo), p-Ph), 5.70 (s, 2 H, CH$_2$-OH, 3.60 (s, 6 H, OCH$_3$), 2.48 (bs, 2 H, OH), 1.96 (m, 8 H, (Fluo)(C$_2$H$_2$)$_2$), 1.19 – 0.62 (m, 44 H, (C$_2$H$_2$)$_4$-C$_3$H$_3$)).

$^{13}$C{$_^1$H} NMR (101 MHz, CDCl$_3$) $\delta$ 151.3, 151.0 (C$_2$, C$_5$(Fluo)), 141.6, 140.5, 139.9, 138.9 (i-Ph, C$_3$,C$_4$,C$_{11}$(Fluo)), 128.9, 128.5, 127.3, 126.8, 126.5, (o-,m-,p-Ph, C$_7$,C$_8$(Fluo)), 125.5, 122.9, 121.2, 119.9, 119.8 (C$_6$,C$_9$,C$_{10}$,C$_{12}$,C$_{13}$(Fluo)), 87.2, 84.6, 83.9 (-C=C-), 72.0 (C-OMe), 65.0 (C-OH), 55.1 (C$_1$(Fluo)), 53.4 (OCH$_3$), 40.3 ((CH$_2$)-Fluo)), 31.5, 29.7, 23.7, 22.6 ((CH$_2$)$_4$), 14.0 (CH$_3$). MS (MALDI-TOF/DCTB): m/z: 1061.6 [MNa]$^+$. HRMS (MALDI-DCTB): m/z calcd for C$_{74}$H$_{86}$O$_4$Na [MNa]$^+$: 1061.6424, found: 1061.6449.

Results and discussion

Among the two main synthetic procedures previously developed for the preparation of carbo-1,3-cyclohexadienes [13b], the strategy based on a [8F+10] macrocyclization step between the bis-trifluoromethylated C$_8$F triyne dinucleophile 4 and the C$_{10}$ diketone dielectrophile 5 was selected for the synthesis of the [6]pericyclediiodol precursor 6 (Scheme 1) [14]. The known C$_{8F}$ triyne 4 was obtained in five steps and 37 % overall yield from triisopropylsilylacetylene and ethyl trifluoroacetate [13b,15]. The phenyl-substituted diketone 5 was prepared in two steps from the known dialdehyde 7 [16]. Both 4 and 5 were obtained as statistical mixtures of diastereoisomers. As previously devised for the carbo-benzenes 1a and 1b, C9-dialkylated fluorenyl substituents were used with the view to ensure sufficient solubility of the carbo-cyclohexadiene target 3. The 2-bromo-9,9-dihexyfluorene 8 precursor was thus prepared from 2-bromofluorene according to a known procedure [17]. Two equivalents of the lithiated reagent of 8 were added to the dialdehyde 7, to give the corresponding diol 9, which was isolated with 54 % yield. After MnO$_2$-mediated oxidation of 9, the C$_{10}$ diketone product 5 was involved in a [8F+10] macrocyclization step with the C$_{8F}$ triyne 4, in the presence of LiHMDS as base. The resulting poorly stable [6]pericyclediiodol 6 was not isolated in the pure state, and was directly treated with SnCl$_2$ and HCl in DCM to give the carbo-cyclohexadiene 3, which was isolated as a dark blue solid with 29 % yield over two steps. During the purification by chromatography, a fraction (8 mg) of one of the two diastereoisomers of 3 was isolated, giving unique $^1$H and $^{19}$F NMR singlet signals at 3.76 ppm and −78.73 ppm, corresponding to the two C$_2$- or C$_5$-equivalent CH$_3$ and CF$_3$ groups, respectively (Figure 2; pairs of singlet signals are observed for the mixture of diastereoisomers).

Figure 2. Aromatic and methoxy region of the $^1$H NMR spectrum (CDCl$_3$) of one pure diastereoisomer of 3.

In the absence of single crystals suitable for X-ray diffraction analysis, the cis (meso) or trans (dl) configuration of the isolated pure diastereoisomer of 3 could not be assigned.

The absorption properties of the blue carbo-chromophore 3 were studied in a chloroform solution (Figure 3). The UV-visible absorption spectrum of 3 exhibits several bands, with a maximum absorption wavelength at 634 nm, which is the highest $\lambda_{max}$ value ever observed among known carbo-cyclohexadienes [13b]. The classical two-bands shape of the absorption spectra of carbo-cyclohexadienes is not observed for 3, which presents four main bands, the one at 289 nm corresponding to the absorption of the fluorenyl moieties. The molar extinction
coefficient of 3 ($\varepsilon = 84,800 \text{ L.mol}^{-1}.\text{cm}^{-1}$) is however in the classical range for a carbo-cyclohexadiene, and much lower than those of related carbo-benzenes ($\varepsilon$ values above 300 000 L.mol$^{-1}$.cm$^{-1}$ were reported for the bis-fluorenyl-carbo-benzenes 1a and 1b)[10].

Fluorescence spectra of the fluorophore-substituted carbo-cyclohexadiene 3 were found to display a weak emission at $\lambda = 533$ nm upon excitation at 470 nm. This result meets previous observations of poor emission properties of carbo-chromophores, even those bearing fluorophore substituents, the fluorescence quenching being correlated with their high absorbance [18].

Figure 3. UV-visible absorption spectrum of 3 (CHCl$_3$).

Conclusion

The difluorenyl-carbo-cyclohexadiene 3 was prepared as a stable and soluble bis-trifluoromethylated carbo-chromophore, and completes the fluorenly-substituted C$_{18}$ core series of carbo-mers comprising the two carbo-benzenes 1a and 1b, and the carbo-quinoid 2.

The weak but non-zero fluorescence of 3 should allow the measurement of its 2PA cross-section by the TPEF method. Otherwise, Z-scan measurements of the 2PA cross-section could also be performed. These experiments will be carried out soon. Comparison of the values with those of 1a and 2 (independently from the C$_2$ elongation effect in 2b vs 2a) should allow delineation of a qualitative structure-property relationship in a structurally homogeneous series, at least regarding the number of $\pi$-conjugating paths and aromaticity of a rigid monocyclic C$_{18}$ core in a pseudo-quadrupolar environment.

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