Towards fluorescent indolyl-*carbo*-benzenes

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The C_{18} macro-aromatic *carbo*-benzene core is a strong chromophoric unit resembling the porphine ring which is prone to quench the emission of fluorophoric substituents. Within the aim of preparing fluorescent *carbo*-benzenes (and *carbo*-cyclohexadiene parents) for measurement of their two-photon absorption cross-section by the TPEF method, several indole derivatives were devised and anchored to the C_{18} macrocycle either directly, *p*-phenylogously or ethynylogously. Synthesis methodology and spectroscopical measurements are presented in a comparative prospect.

Introduction

Most recent efforts in *carbo*-mer chemistry[1] focused on the synthesis of *p*-disubstituted *carbo*-benzenes[2], essentially because of promising theory-predicted third-order non-linear optical (NLO) properties, and more particularly Two-Photon Absorption (TPA) properties which can be more generally anticipated for generic quadrupolar π-extended systems[3]. As the measurement of TPA cross-section is classically performed by the Two-Photon Excited Fluorescence (TPEF) method applicable to fluorescent molecules only, the synthesis of fluorophore-*p*-disubstituted *carbo*-benzenes was envisaged. The *p*-dianisyl-*carbo*-benzene **1**[2a], which is the central ring *carbo*-mer of the terphenyl fluorophore **2**[4], was first targeted and synthesized, but appeared to exhibit almost no fluorescence (Figure 1). Anchoring of indolyl fluorophores to a *carbo*-benzene core was then envisaged, either directly, or through different conjugated linkers. The synthesis and properties of such *p*-bis-indolyl-*carbo*-benzenes are described hereafter. The influence of both the linker (simple bond, *p*-phenylene or ethynylene), and the anchoring atom in the indole unit (N or C_3) on the

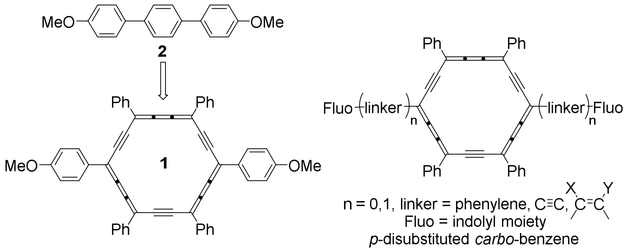
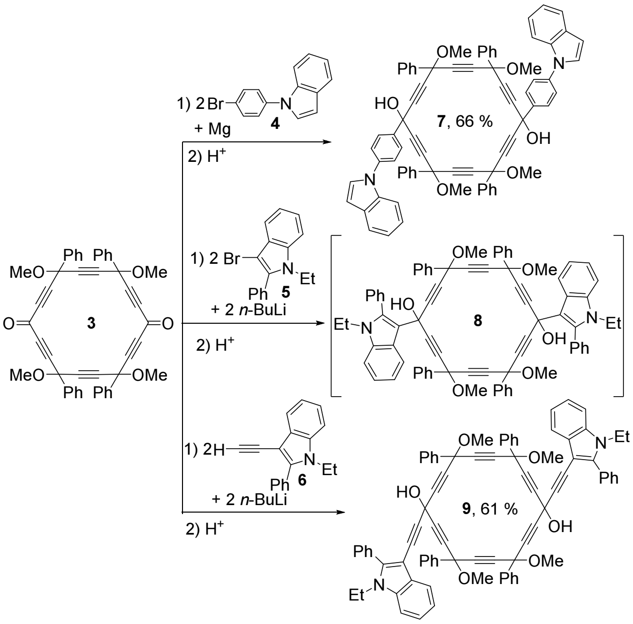


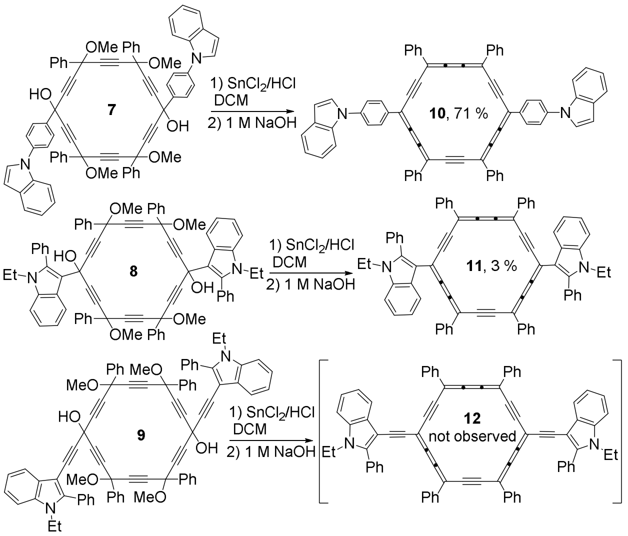
Figure 1. Targeted fluorophore-*p*-disubstituted *carbo*-benzenes.

spectroscopic and optical properties of the *carbo*-chromophores are then considered.

Results and discussion

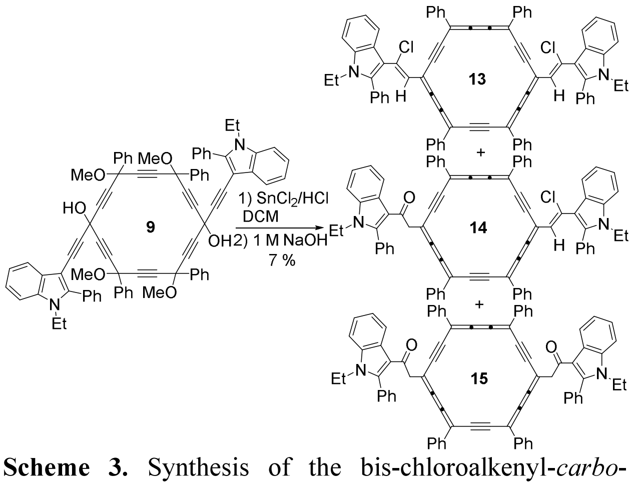


Scheme 1. Double nucleophilic addition of indolyl substituents to the [6]pericyclynedione **3**.



Scheme 2. Reductive aromatization of the bis-indolyl-[6]pericyclynediol substrates **7-9** (Scheme 1).

The synthesis of fluorophore-*p*-disubstituted *carbo*-benzenes was performed from a common [6]pericyclynedione key precursor **3** (Scheme 1), whose preparation in 9 steps and 7 % overall yield had been optimized[5]. The Grignard reactant of commercially available *p*-bromophenyl-N-indole **4** and the lithium derivatives of the 3-bromoindole **5**[6] and indol-3-ylacetylene **6**[7] were added to the same [6]pericyclynedione **3**. The obtained [6]pericyclynediol products **7**, bearing *p*-N-indolylphenyl substituents, and **9**, bearing C-indolylacetylene substituents, could be isolated in 66 and 61 % yield respectively, while the bis-C-indolyl-substituted macrocycle **8** was found to be poorly stable and could not be purified[8]. In view of performing the macro-aromatization step to the bis-indolyl-*carbo*-benzene targets, the [6]pericyclynediols **7-9** were then treated with SnCl$_2$/HCl in DCM, followed by aqueous NaOH. The bis-indolyl precursors **7** and **8** thus gave the expected *carbo*-benzenes **10** (in 71 % yield from **7**) and **11** (in 3 % yield from **3** over 2 steps) respectively, but the bis-alkynyl-substituted substrate **9** did not furnish the expected *carbo*-benzene **12** upon such acidic reductive conditions (Scheme 2). Indeed, the process of reductive aromatization of **9** appeared to be poorly selective, giving three highly colored spots on TLC plates of the reaction mixture, and after treatment, none of the chromophoric products were found to correspond to the targeted bis-alkynyl-*carbo*-benzene **12**. The main product isolated by flash chromatography was the bis-chloroalkenyl-*carbo*-benzene **13** resulting from the regio- and stereo-selective addition of HCl onto the two external triple bonds of **9**, likely induced by the combined π-donor effect of both the electron-rich C_{18} ring and the adjacent indole moieties (Scheme 3). This situation has been termed as a "π-frustration" between facing π-electron rich moieties in a given molecule[2c,7b]. The *carbo*-chromophore **13** was found to react with traces of water on silicagel to give two other *carbo*-benzenes **14** and **15**. These two products result from mono- and di-hydrolysis of one or both the chloroalkenyl groups of **13**, respectively, during purification on silicagel. The sensitivity of the chloroalkenyl groups of **13**, giving methylene ketone motifs in the presence of traces of acids, can be ascribed again to the combined π-donor effects, or π-frustration, of the neighboring indole and C_{18} aromatic rings. Hydrolysis of chloroalkenes into methylene ketones indeed generally requires the use of much harsher conditions[9].



Scheme 3. Synthesis of the bis-chloroalkenyl-*carbo*-benzene **13** and its hydrolysis products **14** and **15**.

The three *carbo*-benzenes **13-15** were obtained in a global 7 % yield from **9** and, in spite of their low stability, could be well characterized by MS and NMR spectroscopy. Full NMR studies (including 2D experiments) allowed confirmation of the proposed structures[7b]. It is noteworthy that the ethylenic protons of **13** and **14**, resonating at 8.4 and 8.5 ppm respectively in ^{1}H NMR, are quite deshielded because of their proximity with the strong diatropic ring current of the aromatic macrocycle. The structures of the *carbo*-benzenes **11** and **13** were confirmed by X-ray diffraction analysis of single crystals deposited from DCM solutions (Figure 2).

As compared to the bis-indolylphenyl-*carbo*-benzene **10**, the poor stability of the bis-chloroalkenyl-*carbo*-benzene **13** (where the indole moieties are separated from the C_{18} ring by conjugated bridges of similar lengths) was explained by an enhanced π-frustration in **13** resulting from the more efficient conjugation through the linear ethylenic linkers of **13** than through the cyclic, aromatic, and thus insulating, phenylene linkers of **10**[7b]. The two hydrolyzed *carbo*-benzenes **14** and **15** also appeared to be poorly stable despite the loss of direct conjugation between the indole moieties and the macrocycle through methylene ketone linkers. A possible explanation for this sensitivity could be the persistence of a conjugation (and so of a π-frustration) through the enolic form of the methylene ketone groups, and/or the enhanced reactivity of the oxygen

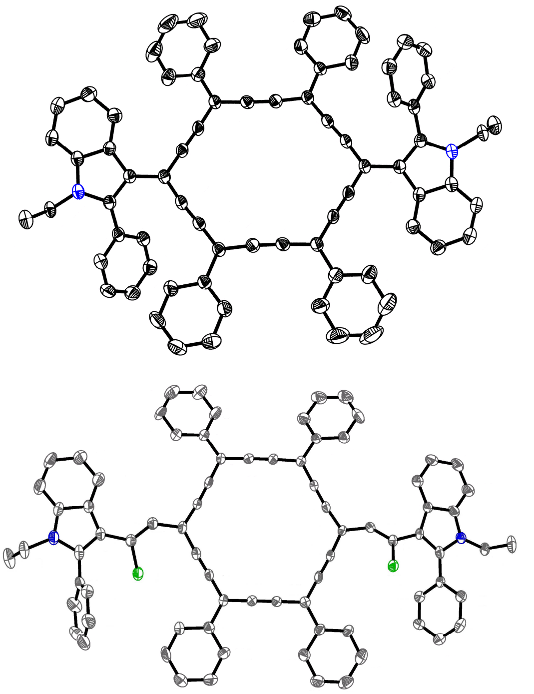


Figure 2. XRD molecular views of **11** (*top*) and **13** (*bottom*).

atom due to the π-donor effect of the adjacent indole unit. Alternatively, a prototropic rearrangement of the acidic methylene groups and adjacent butyne/butatriene edges of the *carbo*-benzene ring, leading to a conjugated keto group, could initiate the de-aromatization and degradation of the former.

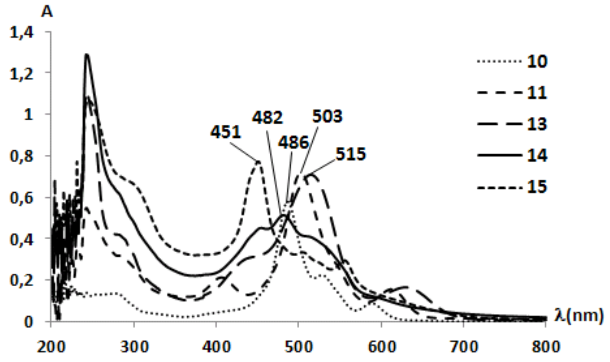


Figure 3. UV-vis absorption spectra of indolyl-substituted *carbo*-benzenes **10**, **11**, **13-14** (in $CHCl_3$).

The absorption spectra of the five indolyl-substituted *carbo*-benzenes **10**, **11**, **13-15** were recorded in chloroform solutions (Figure 3)[10]. By comparing the *carbo*-benzenes **10** and **13** having the same conjugation extent, and the largest in the series, one can see that the λ_{max} value of **13** (515 nm) is much higher than that of **10** (486 nm, $\Delta\lambda_{max}$ = 29 nm), thus showing that the conjugation through a linear ethylenic linker is more efficient than through a cyclic and aromatic phenylene linker. The *carbo*-benzene **13**, having a large and efficient conjugation path, displays the highest λ_{max} value of the whole series. Upon hydrolysis of a chloroalkenyl group (first from **13** to **14**, then from **14** to **15**), a 30 nm hypsochromic shift of the λ_{max} value was observed, likely due to the loss of conjugation between the indole and the *carbo*-benzene moieties, when passing from a chloroalkene linker to a methylene ketone linker (even if a residual conjugation should occur in the enolic form). Finally, the *carbo*-benzene **11**, where the indolyl substituents are directly connected to the aromatic macrocycle by the C_3-atom, exhibits the expected hypsochromic shift of the λ_{max} value (503 nm). This is due to the shorter conjugation extent in **11** as compared to **13** (λ_{max} = 515 nm, $\Delta\lambda_{max}$ = 12 nm) bearing the same C_3- connected indolyl motifs, but here separated from the macrocycle by chloroalkene linkers.

The poor stability of the bis-indolyl-*carbo*-benzenes **13-15** prevented the determination of their emission properties. Nevertheless, emission spectra of the two stable representatives of the series (**10** and **11**) were recorded and were found to display quite different patterns. Indeed, while the *p*-N-indolylphenyl-substituted *carbo*-benzene **10** was reported to be very weakly fluorescent, exhibiting a unique small emission band at 595 nm, assigned to the residual fluorescence of the *carbo*-benzene core[2c], the *p*-bis-C-indolyl-*carbo*-benzene **11** was found to be strongly emitting at 305 nm upon excitation at 242 nm, this emission being assigned to the fluorescence of the indole moieties. A weak emission at 603 nm was also detected upon excitation at 503 nm and could be attributed to the *carbo*-benzenic core fluorescence (Table 1, Figure 3). So, the emission of the indole units is quenched in **10** (while its [6]pericyclynic precursor **7** strongly emits at 333 nm), but persists in **11**. Such a quenching of the fluorescence was also recently observed in fluorene-substituted *carbo*-benzenes without *p*-phenylene linkers[11], but this phenomenon could not be clearly explained to date.

[6]pericyclynediols			*Carbo*-benzenes		
#	$\lambda_{\mathrm{maxAbs}}$	$\lambda_{\mathrm{Em}}/\lambda_{\mathrm{exc}}$	#	$\lambda_{\mathrm{maxAbs}}$	$\lambda_{\mathrm{Em}}/\lambda_{\mathrm{exc}}$
7	268(302)	333(481)/302	**10**	486	595/297
8	–	–	**11**	503(242)	305/242 603/503

Table 1. Absorption ($\lambda_{\mathrm{maxAbs}}$) and emission ($\lambda_{\mathrm{Em}}$) wavelengths of stable *p*-bis-indolyl-*carbo*-benzenes and precursors (in $CHCl_3$, in nm, secondary bands in brackets).

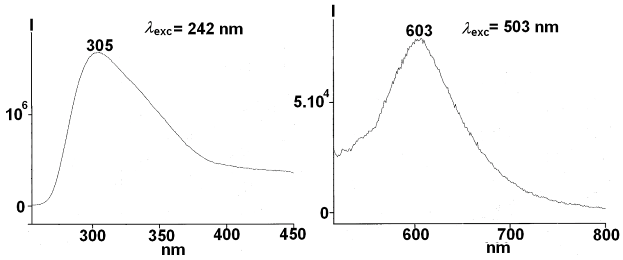


Figure 3. Emission spectra of **11** in $CHCl_3$ upon excitation at 242 nm (l*eft*) and at 503 nm (*right*: 500 times magnified vertical scale).

An interpretation could be a color quenching (re-absorption of the emitted photons by a strongly colored environment) in **10** due to its very large extinction coefficient (ε = 350 000 $L.mol^{-1}.cm^{-1}$) while that of **11** is much smaller (ε = 41 000 $L.mol^{-1}.cm^{-1}$).

Conclusions

A series of *p*-bis-indolyl-*carbo*-benzenes, where the indole moieties are connected to the C_{18} macrocycle by different atoms of the fluorophore and through different linkers have been prepared, and their relative stability was interpreted by the proposition of the π-frustration concept. The absorption and emission properties of the most stable representatives were studied and compared. The *carbo*-benzene **11**, bearing indole units directly connected to the aromatic macrocycle by their C_3 atom, appears as the first example of fluorescent *carbo*-benzene.

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