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Synthesis and two-photon absorption of highly soluble three-branched fluorenylene-vinylene derivatives

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Abstract—Two new three-branched fluorenylene-vinylene derivatives were synthesized by triple Heck-type or Horner–Wadsworth–Emmons reactions. Their one-photon absorption and fluorescence as well as their two-photon absorption properties are reported. These compounds, which combine very high solubility in organic solvents, high fluorescence quantum yield and giant two-photon absorption cross-sections in the red-NIR region (up to 3660 GM, in the femtosecond regime) are promising candidates for both optical power limiting applications and two-photon laser scanning microscopy.

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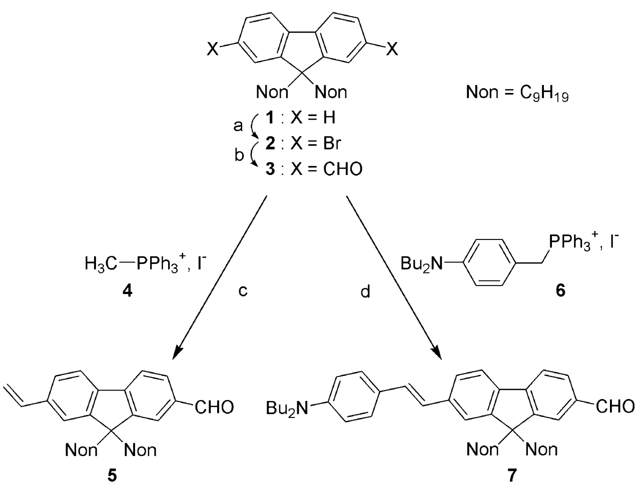
The numerous applications offered by molecular two-photon absorption (TPA), such as optical power limiting,[1,2] two-photon laser scanning fluorescence imaging,[3] microfabrication,[4] 3D optical data storage,[5] and photodynamic therapy,[6] require new, specifically engineered compounds. For instance, in the case of optical power limiting, candidate molecules should exhibit high solubility, high linear transmission at low intensities together with very large multiphoton absorptivities at the intensities delivered by high-power pulsed lasers. In the case of two-photon laser scanning microscopy, novel fluorophores combining high fluorescence quantum yields and TPA cross-sections orders of magnitude larger than endogenous chromophores in the red-NIR range (700-1200 nm) are required for biological imaging.[7]

The search for molecules endowed with large two-photon absorption cross-sections has mainly focussed on push–pull (D-π-A) molecules[2,8,9] as well as pull–pull (A-π-A), push–push (D-π-D) or quadrupolar molecules,[2,9–12] where D is an electron-donating group, A an electron-accepting group and π a conjugating moiety. It has more recently been shown that branched



Scheme 1. *Reagents and conditions:* (a) Br_2 (2 equiv.), CH_2Cl_2, 20°C, 15 h (97%); (b) *n*-BuLi (5 equiv.), benzene, 60°C, 4 h, then *N*-formylpiperidine, 20°C, 14 h (48%); (c) **4** (1.1 equiv.), NaH, THF, 20°C, 15 h (50%); (d) **6** (1 equiv), *t*-BuOK, CH_2Cl_2, 20°C, 16 h, then I_2 cat, h*ν*, Et_2O, 16 h (59%).

Keywords: nonlinear optics (NLO); two-photon absorption (TPA); two-photon-excited fluorescence (TPEF); fluorene; Heck coupling; Horner–Wadsworth–Emmons reaction.

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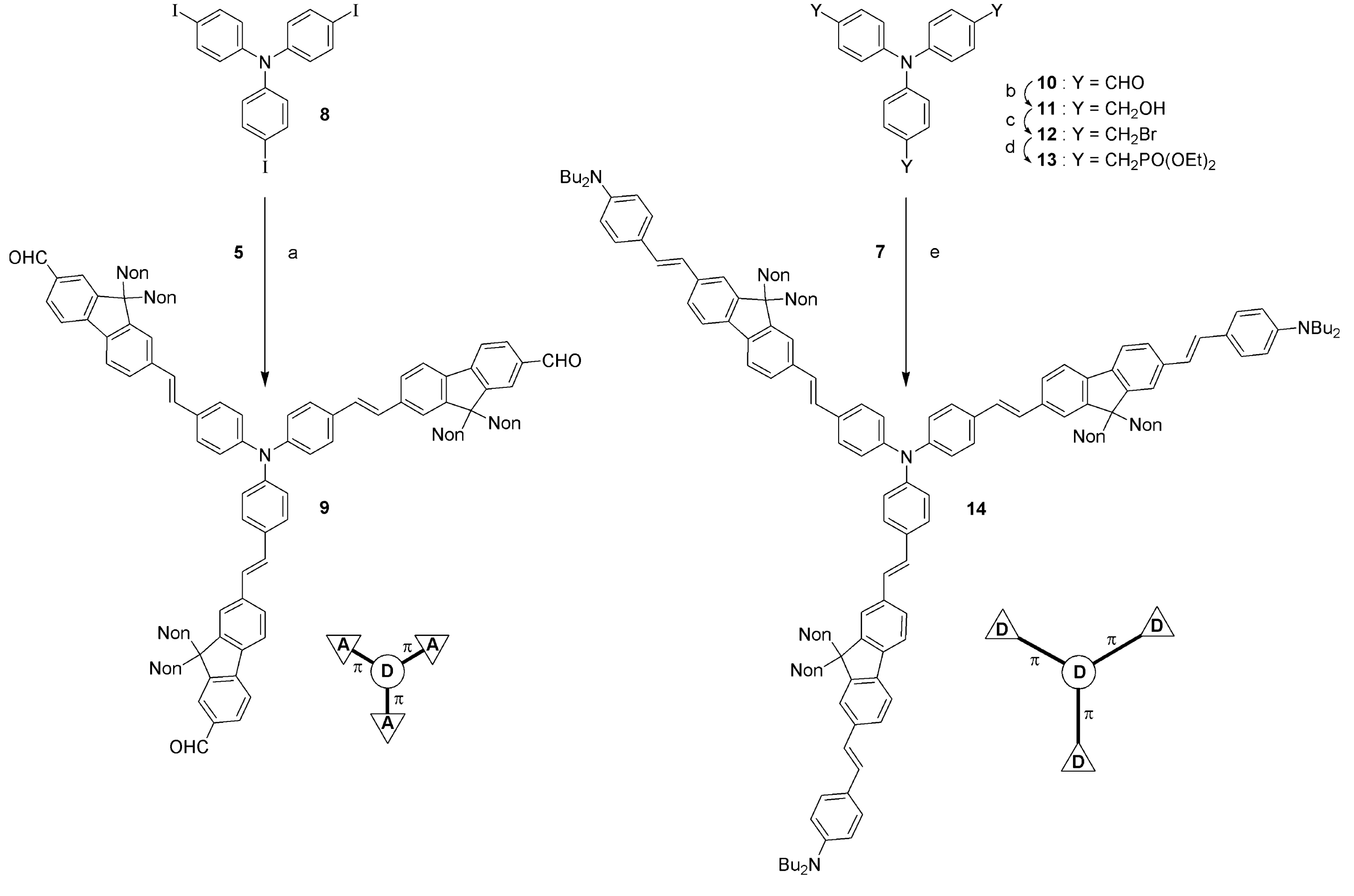
structures[13,14] and dendrimers[14] could also lead to compounds of interest for multiphoton absorption and optical limitation.

Within this context, we herein describe the synthesis as well as the one- and two-photon photophysical properties of two new three-branched fluorophores of D(-π-A)$_3$ and D(-π-D)$_3$ structural design. These molecules are based on the assembly of a triphenylamine ramification node acting also as donor group, fluorenylene-vinylene conjugated connectors and acceptor or donor peripheral groups. Long alkyl chains (*n*-nonyl) were added to the fluorene moieties to impart high solubility for such nanometric systems.

To achieve the synthesis of these fluorophores, two different strategies have been explored, involving triple Heck-type or Wittig-type condensations in the last step. The non-symmetrical fluorene-based connectors **5** and **7** were both obtained from 9,9-dinonylfluorene[12] **1** (Scheme 1). Bromination of **1** afforded the 2,7-dibromo derivative **2** in 97% yield. Treatment of **2** with *n*-BuLi in Et$_2$O or THF at various temperatures (between −60°C and room temperature), followed by addition of *N*-formylpiperidine, gave in our hands a complex mixture from which the expected bisaldehyde **3** could not be isolated in more than 27% yield. However the same halogen-metal exchange reaction conducted in benzene at 60°C for 4 h, followed by quenching of the precipitated dilithio intermediate with *N*-formylpiperidine, yielded 48% of **3**.[15] Wittig condensations between bisaldehyde **3** and a single equivalent of phosphonium salts **4** and **6**[16] afforded conjugated functionalized arms **5** and **7**, respectively. Compound **7** was obtained as a pure *E* stereoisomer, after treatment of the *Z*/*E* mixture resulting from the Wittig condensation with a catalytic amount of iodine under illumination with a 75 W tungsten lamp (Scheme 1).

The three-branch fluorophore **9** was prepared by means of a triple Heck-type coupling of tris(4-iodophenyl)amine[17] **8** with vinyl compound **5** under Jeffery's[18] conditions (Scheme 2). On the other hand, the synthesis of fluorophore **14** started from tris(4-formylphenyl)amine[19] **10**, which was converted to the trisphosphonate **13** in a three-step sequence (reduction, bromination and Michaelis-Arbuzov reaction). The triple Horner–Wadsworth–Emmons condensation of **13** with aldehyde **7** in the presence of sodium hydride finally afforded **14** (Scheme 2). All these derivatives have been fully characterized by NMR, HRMS and/or elemental analysis.[20] Nanometric fluorophores **9** and **14** (3.4 nm and 4.5 nm diameters, respectively) are extremely soluble in chlorinated solvents (typically



Scheme 2. *Reagents and conditions:* (a) **5** (5 equiv.), Pd(OAc)$_2$, PPh$_3$, *n*-Bu$_4$NCl, K$_2$CO$_3$, DMF, 90°C, 12 h (73%); (b) KBH$_4$, EtOH/CH$_2$Cl$_2$, 20°C, 5 h (92%); (c) conc. HBr, reflux, 5 h (85%); (d) P(OEt)$_3$, reflux, 72 h (59%); (e) **7** (4 equiv.), NaH, THF, reflux, 15 h (36%).

higher than 500 g L^{-1}) as well as in THF and toluene, which is of interest for optical limiting applications.

The one-photon absorption and fluorescence spectra of **9** and **14** in toluene and in chloroform are shown in Figure 1 and their comprehensive photophysical characteristics can be found in Table 1. Both compounds exhibit an intense absorption in the near UV/visible blue region (with very high extinction coefficient values) but maintain high transparency in the remaining range of the visible region. We observed that compound **14** showed an extinction coefficient more than twice that of compound **9**, whereas it showed a slightly lower fluorescence quantum yield and shorter fluorescence lifetime.

A slight bathochromic shift was observed for compound **9** in the absorption with increasing polarity of the solvent, while a significant positive solvatochromic shift was observed in the emission (Fig. 1). We noted a concomitant increase of the Stokes shifts and of the halfbandwiths of the emission bands with the solvent polarity. This distinct positive solvatochromic behavior suggests that significant charge redistribution takes place upon excitation leading to a highly polar excited state. This was corroborated by AM1 HOMO-LUMO calculations, which revealed a multidimensional intramolecular charge transfer from the triphenylamino donating core to the acceptor arms. In comparison, compound **14** showed less pronounced solvatochromic behavior: no noticeable absorption solvatochromic shift was observed and the emission red shift with increasing solvent polarity was smaller than for compound **9** (see Fig. 1). In addition compound **14** exhibited lower Stokes shifts than **9** (the difference increasing with increasing solvent polarity). These features are indicative of less pronounced charge redistributions occurring upon excitation. Indeed HOMO-LUMO calculations indicated that for compound **14**, intramolecular charge transfers take place from the central triphenylamino core and from the peripheral phenylamino donating groups to the fluorenylene-vinylene moieties upon excitation. The weaker solvatochromic behavior could thus possibly be related to the smaller extent of the charge transfer phenomenon and the larger size (and thus larger solvent cavity radius) of molecule **14** as compared to **9**.

The TPA spectra of fluorophores **9** and **14** between 735 and 960 nm were determined by studying their two-

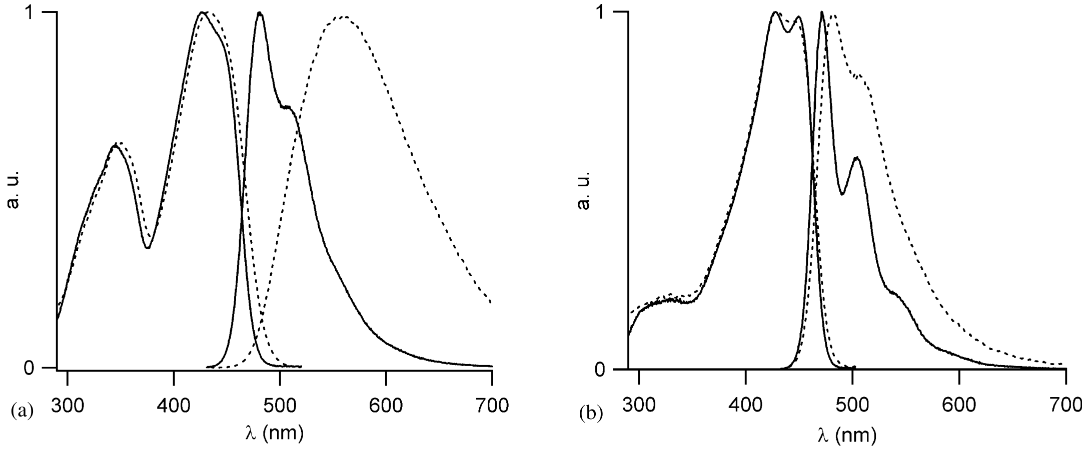


Figure 1. Normalized absorption and fluorescence emission spectra performed at $\lambda_{ex} = \lambda_{max}$ (abs) and $A_{\lambda ex} = 0.1$ for **9** (a) and **14** (b) in toluene (–) and $CHCl_3$ (--) at room temperature.

Table 1. One- and two-photon photophysical data of compounds **9** and **14**

Compd	λ_{abs} (nm)		ε^a (M^{-1} cm^{-1})	λ_{em} (nm)		$\Delta\nu^b$ (10^3 cm^{-1})	Stokes shift^c (10^3 cm^{-1})		ϕ^d	τ^e (ns)	λ_{TPA} (max)^a (nm)	$\sigma_2^{a,f}$ (GM)
	Toluene	$CHCl_3$		Toluene	$CHCl_3$		Toluene	$CHCl_3$				
9	426	430	119000	481	3.0	2.7	5.4	0.80	1.33	770	1265	
14	428	428	244000	471	482	0.5	2.1	2.6	0.74	0.85	740	3660

[a] In toluene.

[b] Emission solvatochromic shift = $1/\lambda_{em}$(toluene)–$1/\lambda_{em}$($CHCl_3$).

[c] Stokes shift = $(1/\lambda_{abs}-1/\lambda_{em})$.

[d] Fluorescence quantum yield determined in toluene relative to fluorescein in 0.1 N NaOH.

[e] Experimental fluorescence lifetime in toluene.

[f] TPA cross-section at λ_{TPA}(max); 1 GM = 10^{-50} cm^4 s $photon^{-1}$; TPEF measurements were performed using a mode-locked Ti:sapphire laser delivering 80 fs pulses at 80 MHz, calibrated with fluorescein.[21]

photon-excited fluorescence (TPEF) spectra, using femtosecond pulse excitation.[22] The TPA cross-sections (σ_2) are derived from the TPEF cross-sections ($\sigma_2\phi$). As shown in Figure 2 and Table 1, both compounds are efficient two-photon-absorbing molecules, with σ_2(max) values of 1265 and 3660 GM for **9** and **14**, respectively, which correspond to more than 30 and 100 times that of the standard fluorescein. Fluorophore **14** indeed shows one of the highest TPEF cross-sections[10,11e,11i,14c] measured in the femtosecond regime in the 700–1000 nm wavelength range, a spectral window of interest for biological applications.

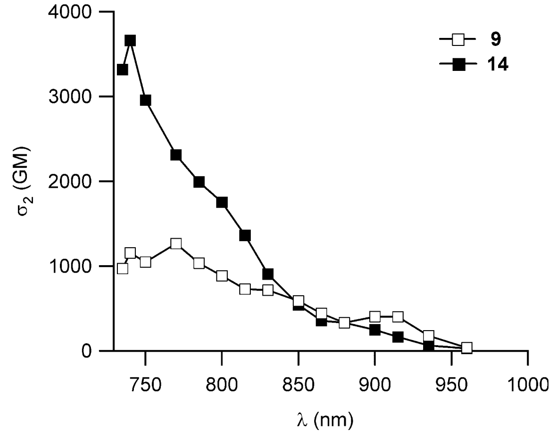


Figure 2. Two-photon excitation spectra of molecules **9** and **14** in 10^{-4} M toluene solutions, calibrated from that of fluorescein.

Interestingly, fluorophore **14** shows a σ_2(max) value about three times larger than that of **9**. Further comparison reveals that in the case of **14**, the TPA spectrum shows a sharp decline above its maximum at 740 nm, whereas **9** exhibits a red-shifted and broader TPA band, maintaining high values in the NIR (400 GM at 915 nm). Moreover, **9** is endowed with larger cross-sections than **14** above 850 nm. In summary, compounds **9** and **14**, which combine very high solubility in organic solvents, high fluorescent quantum yields, and exceptionally high TPA cross-sections in the red-NIR region are promising candidates for both optical power limiting applications in the red-NIR region and TPEF microscopy.

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20. Selected data for:
    9: mp 80–81°C; ^{1}H NMR (200.13 MHz, $CDCl_3$) δ 10.06 (s, 3H), 7.88 (d, $J=1.4$, 3H), 7.86 (dd, $J=8.3$, 1.4, 3H), 7.81 (d, $J=8.3$, 3H), 7.76 (d, $J=8.0$, 3H), 7.54 (d, $J=8.0$, 3H), 7.50 (s, 3H), 7.50 and 7.16 (AA′XX′, $J_{AX}=8.5$, 12H), 7.22 (d, $J=15.6$, 3H), 7.13 (d, $J=15.6$, 3H), 2.10–2.00 (m, 12H), 1.28–1.02 (m, 72H), 0.82 (t, $J=6.5$, 18H), 0.72–0.52 (m, 12H); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 192.3, 152.8, 151.7, 147.2, 146.7, 139.0, 138.2, 135.1, 132.2, 130.6, 128.4, 127.6, 127.5, 125.7, 124.3, 123.0, 121.2, 120.8, 119.8, 55.2, 40.2, 31.8, 29.9, 29.4, 29.21, 29.17, 23.7, 22.6, 14.0; HRMS (ES^{+}, CH_3OH/CH_2Cl_2: 95/5) calcd for $C_{120}H_{153}NO_3Na$ ([M+Na]$^{+}$) *m*/*z* 1679.1748, found 1679.1731. Anal. calcd for $C_{120}H_{153}NO_3$ (1657.55): C, 86.95; H, 9.30; N, 0.84. Found: C, 86.99; H, 9.32; N, 0.72.
    14: mp 109–110°C; ^{1}H NMR (200.13 MHz, $CDCl_3$) δ 7.64 (d, $J=7.8$ Hz, 3H), 7.62 (d, $J=7.8$ Hz, 3H), 7.51–7.34 (m, 24H), 7.14 (d, $J=8.3$ Hz, 6H), 7.14 (s, 6H), 7.10 (d, $J=16.4$ Hz, 3H), 6.96 (d, $J=16.4$ Hz, 3H), 6.64 (d, $J=9.1$ Hz, 6H), 3.30 (t, $J=7.3$ Hz, 12H), 2.06–1.94 (m, 12H), 1.67–1.52 (m, 12H), 1.37 (sext, $J=7.3$ Hz, 12H), 1.30–1.01 (m, 72H), 0.97 (t, $J=7.3$ Hz, 18H), 0.82 (t, $J=6.5$ Hz, 18H), 0.77–0.63 (m, 12H); ^{13}C NMR (50.32 MHz, $CDCl_3$) δ 151.4, 147.7, 146.5, 140.7, 139.6, 137.3, 136.1, 132.4, 128.2, 127.7, 127.3, 127.0, 125.4, 125.01, 124.96, 124.7, 124.3, 120.6, 120.1, 119.7, 119.6, 111.6, 54.9, 50.8, 40.5, 31.8, 30.1, 29.5, 29.4, 29.2, 23.7, 22.6, 20.4, 14.1, 14.0; ES^{+}-MS (CH_3OH/CH_2Cl_2: 10/90) *m*/*z* 2260.7 ([M+H]$^{+}$), 1130.9 ([M+2H]$^{2+}$), 754.4 ([M+3H]$^{3+}$); HRMS (ES^{+}, CH_3OH/CH_2Cl_2: 10/90) calcd for $C_{165}H_{224}N_4$ ([M+2H]$^{2+}$) *m*/*z* 1130.8826, found 1130.8835. Anal. calcd for $C_{165}H_{222}N_4$ (2261.62): C, 87.63; H, 9.89; N, 2.48. Found: C, 87.28; H, 10.13; N, 2.22.
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22. This allows ruling out excited-state absorption, which can lead to an artificially enhanced 'effective' TPA cross-section when experiments are conducted using nanosecond excitation pulses.