ELECTRONIC SUPPLEMENTARY INFORMATION

Promising two-photon probes for in-vivo detection of β amyloid deposits

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A. Computational details

The molecular structures of the three donor/acceptor group substituted phenyl polymethines are referred to as NIRF-0, NIRF-1 and NIRF-2 and were optimized using density functional theory with the B3LYP exchange-correlation functional together with the 6-311+g(d,p) basis set using the Gaussian09 package.[1] The geometry optimization was performed for the molecules in vacuo as well as in solution (dichloromethane). In the latter case, the PCM method was used. The one- and two-photon absorption spectra calculations in both vacuo and solution (on the respective geometries in vacuo and solution) were carried out using the CAM-B3LYP[2] functional and the TZVP[3] basis set employed for all atoms. For the calculations in solution the Polarizable Continuum Model[4] was used and the solute cavity was based on the UAHF model[5] The one- and two photon absorption properties were computed using linear and quadratic response theory within time-dependent density functional, respectively. All property calculations were performed using a locally modified version of the DALTON program[6].

The two-photon absorption cross section, $\sigma^{2\mathrm{PA}}(\omega)$ in Göppert-Mayer units was computed using the following expression:

$$\sigma^{2\mathrm{PA}}(2\omega) = \frac{4\pi^3\alpha a_0^5\omega^2}{c} g(2\omega)\delta^{2\mathrm{PA}} \tag{1}$$

where α is the fine structure constant, a_0 is the Bohr radius, c is the speed of light, ω is the energy of the photon, $g(2\omega)$ is the line shape function and $\delta^{2\mathrm{PA}}$ is the two-photon transition rate in atomic units. For the line shape function corresponding to a transition to a final state f, we assume a Lorentzian function:

$$g(2\omega) = \frac{1}{\pi}\frac{\frac{1}{2}\Gamma_f}{(\omega_f - 2\omega)^2 + (\frac{1}{2}\Gamma_f)^2} \tag{2}$$

In all calculations we used Γ_f=0.1 eV.[7]

B. Three-state model

A three-state model (TSM), which is a special case of a generalized few-state model suggested by Alam et al.[8,9], considers three electronic states: the ground ($|0\rangle$), intermediate ($|i\rangle$) and final ($|f\rangle$) states. The excited state $|f\rangle$ is also included as an intermediate in this model. The two-photon absorption probability corresponding to excitation from the ground to the final excited state is given by:

$$\delta_{3\mathrm{SM}}^{f\leftarrow 0} = \delta^{ii} + \delta^{ff} + 2\delta^{if} \tag{3}$$

where

$$\delta^{ii} = \frac{4}{15}\left(\frac{|\mu^{0i}||\mu^{if}|}{\omega_i - \frac{1}{2}\omega_f}\right)^2 (2\cos^2(\theta_{if}^{0i}) + 1) \tag{4}$$

$$\delta^{ff} = \frac{16}{15}\left(\frac{|\mu^{0f}||\mu^{ff}|}{\omega_f}\right)^2 (2\cos^2(\theta_{ff}^{0f}) + 1) \tag{5}$$

$$\delta^{if} = \frac{8}{15}\left(\frac{|\mu^{0i}||\mu^{0f}||\mu^{if}||\mu^{ff}|}{\omega_f(\omega_i - \frac{1}{2}\omega_f)}\right)(\cos\theta_{0f}^{ff}\cos\theta_{0i}^{if} + \cos\theta_{0f}^{0i}\cos\theta_{ff}^{if} + \cos\theta_{0f}^{if}\cos\theta_{0i}^{ff}) \,. \tag{6}$$

Here $\hbar\omega_i$ stands for the excitation energy from the ground state to the excited state $|i\rangle$, $\mu^{ij} = \langle i|\vec{\mu}|j\rangle$ and θ_{ij}^{kl} is the angle between (transition) dipole moments μ^{ij} and μ^{kl}.

C. Additional data

Table 1: Bond lengths (in Å) and BLA for NIRF-0, NIRF-1 and NIRF-2 in dichloromethane solvent. C1 refers to the polymethine carbon connected to the phenyl group while C7 refers to the carbon atom connected to the cyano groups and the intermediate carbons are labeled accordingly.

Probe ⇒	NIRF-0	NIRF-1	NIRF-2
Atom pairs ⇓			
C1-C2	1.4224	1.4279	1.4322
C2-C3	1.3836	1.3768	1.3737
C3-C4		1.4066	1.4122
C4-C5		1.3875	1.3807
C5-C6			1.4040
C6-C7			1.3894
N-C	1.3544	1.3577	1.3603
C-CCN	1.4202	1.4200	1.4195
	(1.4235)	(1.4190)	(1.4183)
BLA	0.04	0.07	0.10

Table 2: Ground and excited-state dipole moments (in Debyes) for NIRF-0 as obtained from CAM-B3LYP and RI-CC2 levels of theory using the TZVPP basis set. The calculations were carried out at the optimized gas phase geometry (B3LYP/6-311+G(d,p) level of theory). RI-CC2 calculations were performed using the TURBOMOLE 6.4 program.[10]

State	CAM-B3LYP	RI-CC2
0	11.16	10.82
1	15.16	17.83
2	12.09	11.41
3	16.36	17.07

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