Synthesis and characterisation of push–pull flavin dyes with efficient second harmonic generation (SHG) properties†

Nabeel Mohammed,†a Alan A. Wiles,†ab Michael Belsley,†ab Sara S. M. Fernandes,c Michele Cariello,a Vincent M. Rotello,†bd M. Manuela M. Raposo†cd and Graeme Cooke†a

Organic compounds displaying second-order non-linear optical properties are key materials for optoelectronics. Here, three push–pull flavin derivatives (FLA–A–C) have been synthesised and their optical, redox and second harmonic generation (SHG) properties have been investigated. In particular, we describe the role differing electron donor units (N,N-dimethylaniline–, N,N-diphenylaniline– and ferrocenyl–) attached through the C(8) position of the flavin unit have on the optical and redox properties of the latter. Hyper-Rayleigh scattering in dioxane solutions using a fundamental wavelength of 1064 nm was employed to evaluate their second-order nonlinear optical properties. Our experiments have indicated that their first hyperpolarisabilities (γ) are influenced by the electronic nature and strength of the donor groups. N,N-dimethylaniline–functionalised derivative FLA–A exhibited the largest first hyperpolarisability (γ = 9550 × 10⁻³⁰ esu, using the T convention) and high decomposition temperature (Td = 312 °C), thus indicating its potential application as a useful material for incorporation into non-linear optical devices.

Introduction

Nonlinear optical (NLO) materials represent one of the principal branches of optoelectronics. Applications of NLO materials encompass a range of scientific sub-disciplines including medicine (e.g. second harmonic generation (SHG)-imaging, high-resolution optical microscopy for biological imaging) and materials science (e.g. frequency conversion of lasers, waveguides and electro-optic modulators, optical transistors, fibres and lenses). Organic NLO chromophores possess several advantages over their inorganic brethren including convenient synthesis, tunability, straightforward processability, ultrafast response times, lower dielectric constants and enhanced NLO responses. Accordingly, during the last four decades, extensive progress has been made in the improvement of the SHG properties of organic donor–acceptor π-conjugated systems.

Organic push–pull NLO chromophores are promising materials, and typically comprise of a strong electron donor (D) (e.g. arylamino groups) and strong electron acceptor (A) group (e.g. cyano, nitro, di- or tricyanovinyl) linked through a π-bridge (aromatic or heterocyclic) (D–π–A). This D–π–A arrangement promotes efficient intramolecular charge-transfer (ICT) between the D and A groups and generates dipolar push–pull systems possessing an intense, low-energy CT absorption, and the propensity to display strong molecular SHG. The NLO response correlates strongly with the strength of the attached D and A groups as well as the electronic nature and length of the π-conjugated spacer.

Amines (NR₂), such as 4-N,N-dimethylaniline- or 4-N,N-diphenylaniline–, are commonly used donor groups in NLO chromophores. The latter moieties tend to have a lower electron donating ability due to the partial delocalisation of the nitrogen nonbonding lone pair to the conjugated phenyl units that are usually organised in a nonplanar fashion. On the other hand, N,N-diarylaniline moieties usually impart significantly higher thermo- and photostabilities compared to their N,N-dialkylaniline analogues. Consequently, chromophores featuring N,N-dialkylaniline donor groups tend to show much higher nonlinearities compared to their N,N-dialkylaniline brethren, although they generally have much lower thermostabilities. Organometallic’ groups such as ferrocene have also been utilised as D moieties in NLO chromophores. More recently, electron-rich (e.g. thiophene and pyrrole) and electron-poor (e.g. azoles and diazines) five-membered heterocycles have also been
used as efficient “non-conventional” electron donor or acceptor moieties, respectively, due to their auxiliary D–A heterocycle effect.

Flavins are electron deficient heterocycles and are important cofactors in a range of flavoenzymes. Synthetic flavin derivatives due to their convenient synthesis, photostability and tunable optical and redox properties have found application in a diverse range of areas including: supramolecular chemistry and photonics such as solvatochromic probes and photon-induced energy and charge transfer systems. However, their application as A units in NLO materials has not been widely reported. For example, Stanley and co-workers have reported that a push–pull flavin moiety was achieved through condensation of 4a–c with alloxan monohydrate to give the flavin-based dyes FLA-A–C.

Results and discussion

Synthesis

The three push–pull flavins (FLA-A–C) have been synthesised from 5-chloro-2-nitroaniline 1 through a simple 4-step route in moderate to high yields (Scheme 1). Firstly, compound 1 was acetylated to give compound 2 in high yield. The differing donor moieties were then added to this building block using either Suzuki (compounds 3a and 3b) or Sonogashira (compound 3c) coupling methodologies. Simultaneous reduction of both the carbonyl- and nitro-moieties with LiAlH4 gave compounds 4a–c. Finally, formation of the flavin moiety was achieved through condensation of 4a–c with alloxan monohydrate to give the flavin-based dyes FLA-A–C.

Optical properties

The UV-vis spectra of the three flavin dyes were recorded to determine their optical properties and solvatochromic behaviour, as the latter has been shown to have strong correlation to the ability of compounds to display SHG properties. The absorption bands of FLA-A show the highest absorbance at 536 nm (3066 L mol$^{-1}$ cm$^{-1}$) and 517 nm (4009 L mol$^{-1}$ cm$^{-1}$) nm, respectively. On the other hand, FLA-C shows a highest absorbance at 545 nm (2657 L mol$^{-1}$ cm$^{-1}$) nm and a weaker but longer wavelength absorption at 566 nm (873 L mol$^{-1}$ cm$^{-1}$), which we assign as π-LUMO and metal-LUMO bands, respectively. Investigation of the influence solvent polarity has on the absorbance of dyes FLA-A–C (Fig. 2) has revealed that significant solvatochromic behaviour exists for this series of dyes. In accordance with previously reported data for a related push–pull flavin derivative, the $\lambda_{max}$ values for FLA-A–B did not display a linear correlation with solvent polarity (dielectric constant or $E_r(30)$), suggesting that solute–solvent interactions are occurring. Interestingly, the position of the metal-LUMO absorption bands of FLA-C are in broad correlation with the dielectric constants for the different solvents.

Scheme 1. Synthesis of flavin based dyes. Reagents and conditions: (i) isobutyryl chloride, triethylamine, THF, DMAP, rt, 3 h; (ii) 4-(N,N-dimethylamino)phenylboronic acid, K$_2$CO$_3$, NaCl, 1,4-dioxane, reflux, $N_2$, 24 h; (iii) 4-(N,N-diphenylamino)phenylboronic acid, K$_2$CO$_3$, NaCl, 1,4-dioxane, reflux, $N_2$, 24 h; (iv) ethynylferrocene, 10% Pd/C, SPhos, K$_2$CO$_3$, DMA, 110 °C, $N_2$, 2 h; (v) LiAlH$_4$, dry-THF, rt, $N_2$, 24 h; (vi) alloxan monohydrate, boric anhydride, acetic acid, rt, $N_2$, 24 h.
NLO properties

The molecular first hyperpolarisabilities $\beta$ of flavin derivatives FLA-A–C were measured by the hyper-Rayleigh scattering (HRS) method at a fundamental wavelength of 1064 nm and the data are summarised in Table 1. It is clear that the electronic donor ability of the moieties attached at the position C(8) of the flavin derivative for compounds FLA-A–C modulates the red-shifted absorption maxima and nonlinearities as anticipated from the donor strengths of the substituents (ferrocenyl- $<$ 4-N,N-diphenylnalanine- $<$ 4-N,N-dimethylaniline-). These results are not unexpected bearing in mind the Hammett $\sigma_p$ constants of N,N-dimethylaniline ($\sigma_p = -0.83$), N,N-diphenylnalanine ($\sigma_p = -0.56$) and ferrocenyl ($\sigma_p = -0.18$), donor groups as well as data provided in several earlier studies. Therefore, 4-N,N-dimethylaniline, being the strongest electron-donor group, gives rise to a higher $\beta$ value for compound FLA-A. On the other hand, the ferrocenyl derivative FLA-C exhibits the lowest hyperpolarisability ($\beta = 355 \times 10^{-30}$ esu) compared to FLA-A and B ($\beta = 9550$ and $8660 \times 10^{-30}$ esu, respectively).

Thermal stabilities

In order to be readily incorporated into efficient optoelectronic devices, organic NLO-phores should exhibit large molecular quadratic hyperpolarisability, good optical transparency and excellent thermal and chemical stabilities. Derivatives that feature alkyl- and aryl-ammonio moieties as their donor units have been shown to possess these important properties. The thermal stability of chromophores FLA-A–C was studied by thermogravimetric analysis (TGA) and by differential scanning calorimetry (DSC) (see Fig. S1–S3, ESI†). FLA-A–C exhibit high decomposition temperatures of 312, 329 and 319 °C respectively. Comparison of the thermal stability of N,N-dimethylaniline derivative FLA-A with flavin FLA-B shows that the N,N-diphenylnalanine-substitution results in an enhanced thermal stability which is in agreement with previous findings.

Theoretical calculations

To further our understanding of the properties of these dyes and establish a comparative computational basis for this series, density functional theory (DFT) calculations were undertaken. The HOMO and LUMO maps of FLA-A–C were computed in

Table 1 UV-vis absorptions, $\beta$ and $\beta_0$ values and $T_d$ data for flavin derivatives FLA-A–C

<table>
<thead>
<tr>
<th>Comp.</th>
<th>Donor</th>
<th>$\lambda_{\text{max}}$ (nm)</th>
<th>$\epsilon_{\text{max}}$ (M$^{-1}$ cm$^{-1}$)</th>
<th>$\beta ^{\text{a}}$ (10$^{-30}$ esu)</th>
<th>$\beta_0 ^{\text{b}}$ (10$^{-30}$ esu)</th>
<th>$T_d ^{\text{c}}$ (°C)</th>
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<tr>
<td>FLA-A</td>
<td>DMA</td>
<td>487</td>
<td>22 087</td>
<td>9550</td>
<td>1220 ± 120</td>
<td>309</td>
</tr>
<tr>
<td>FLA-B</td>
<td>TPA</td>
<td>473</td>
<td>25 520</td>
<td>8660</td>
<td>1460 ± 180</td>
<td>329</td>
</tr>
<tr>
<td>FLA-C</td>
<td>Fc</td>
<td>449</td>
<td>12 720</td>
<td>355</td>
<td>85 ± 15</td>
<td>310</td>
</tr>
<tr>
<td>pNA</td>
<td></td>
<td>352</td>
<td>—</td>
<td>40.1</td>
<td>20.1</td>
<td>—</td>
</tr>
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</table>

*a* Experimental first hyperpolarisabilities $\beta$ and spectroscopic data measured in dioxane solutions are reported using the T convention. *b* All compounds are transparent at the 1064 nm fundamental wavelength. *c* Data corrected for resonance enhancement at 532 nm using the two-level model with $\beta_0 = \beta [1 - (\lambda_{\text{max}}/1064)^2] [1 - (\lambda_{\text{max}}/532)^2]$; damping factors not included 1064 nm. *d* Decomposition temperature ($T_d$) measured at a heating rate of 10 °C min$^{-1}$ under a nitrogen atmosphere, obtained by thermogravimetric analysis (TGA).
Table 2: Computational result summary of FLA-A–C hyperpolarizability calculations

<table>
<thead>
<tr>
<th>Comp.</th>
<th>Donor</th>
<th>( \mu ) (D)</th>
<th>( \beta_{\text{tot}} ) (10^{-30} esu)</th>
<th>( \beta_{\text{H}} ) (10^{-30} esu)</th>
<th>HOMO (eV)</th>
<th>LUMO (eV)</th>
</tr>
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<tr>
<td>FLA-A</td>
<td>DMA</td>
<td>17.01</td>
<td>804</td>
<td>477</td>
<td>-5.64</td>
<td>-3.14</td>
</tr>
<tr>
<td>FLA-B</td>
<td>TPA</td>
<td>14.30</td>
<td>1448</td>
<td>870</td>
<td>-5.57</td>
<td>-3.24</td>
</tr>
<tr>
<td>FLA-C</td>
<td>Fe</td>
<td>13.66</td>
<td>615</td>
<td>370</td>
<td>-5.89</td>
<td>-3.36</td>
</tr>
</tbody>
</table>

**Experimental**

**General methods**

All reactions were undertaken under inert atmosphere. Solvents were purified using a Pure Solv™ solvent purifier system. Reagents were purchased from Sigma Aldrich, and were used without further purification. NMR spectra were obtained with either a Bruker AVIII 400 MHz or a Bruker AVIII 500 MHz spectrometer (relative to TMS). UV-vis spectra were recorded on a Perkin Elmer Lambda 25 instrument. Optical band gaps \( E_{G,OPT} \) were estimated using the onset of the longest wavelength absorption (\( \lambda \)) using \( E_{G,OPT} (eV) = (1240/\lambda) \) (nm).

**Synthesis**

**Compound 2.** Isobutyryl chloride (1.84 mL, 17.4 mmol) and triethylamine (2.43 mL, 17.4 mmol) were added drop-wise to a solution of 5-chloro-2-nitroaniline \( 1 \) (2.00 g, 11.6 mmol) and 4-(dimethylamino)pyridine (0.14 g, 1.74 mmol) dissolved in THF (100 mL). The mixture was stirred overnight at reflux, and the solvents were then removed under reduced pressure. The crude product was then purified by flash chromatography (petroleum ether/ethyl acetate; 95:5) and then recrystallised from hot ethanol to yield title compound 2 as yellow needles (2.69 g, 95%). Mp 91–92 °C; \( \delta_{H} \) (500 MHz, CDCl₃, TMS) 10.56 (1H, s), 8.96 (1H, d, \( J = 2.3 \)), 8.18 (1H, d, \( J = 9.0 \)), 7.13 (1H, dd, \( J = 9.0, 2.3 \)), 2.66 (1H, sept, \( J = 6.9 \)), 1.31 (6H, d, \( J = 6.9 \)); \( \delta_{C} \) (125 MHz, CDCl₃, TMS) 176.3, 143.0, 136.3, 134.5, 127.1, 123.4, 121.9, 37.8, 19.4; HRMS (EI⁺, m/z): [M⁺]⁺ found, 242.0455; calc. for \( (C_{16}H_{12}ClN_{2}O_{3})^+ \), 242.0458.

**Compound 3a.** Compound 2 (1.00 g, 4.13 mmol), 4-(dimethylamino)phenylboronic acid (1.36 g, 8.26 mmol), NaCl (0.425 g, 4.13 mmol) and \( K_{2}CO_{3} \) (2.28 g, 16.5 mmol) were dissolved in 1,4-dioxane (35 mL) and the solution was degassed for 30 minutes with \( N_2 \). PdCl₂(PPh₃)₂ (68.3 mg, 83.0 μmol) was added and the solution was left to stir at reflux. After 24 hours the mixture was allowed to cool to room temperature, poured into water (200 mL) and extracted with \( Et_{2}O \) (4 × 200 mL). The

**Table 3: Computational study of FLA-A–C in different solvents**

<table>
<thead>
<tr>
<th>Comp.</th>
<th>Donor</th>
<th>( \mu ) (D)</th>
<th>( \mu_{\text{H}} ) (D)</th>
<th>( \mu_{\text{tot}} ) (D)</th>
<th>( \beta_{\text{tot}} ) (10^{-30} esu)</th>
<th>( \beta_{\text{H}} ) (10^{-30} esu)</th>
<th>HOMO (eV)</th>
<th>LUMO (eV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLA-A</td>
<td>DMA</td>
<td>17.0152</td>
<td>17.2402</td>
<td>20.2001</td>
<td>21.4030</td>
<td>5.64</td>
<td>-3.14</td>
<td></td>
</tr>
<tr>
<td>FLA-C</td>
<td>Fe</td>
<td>13.6595</td>
<td>13.8190</td>
<td>15.7836</td>
<td>16.5851</td>
<td>5.89</td>
<td>-3.36</td>
<td></td>
</tr>
</tbody>
</table>

\( \mu \): dipole moment, \( \beta \): hyperpolarizability, \( HOMO \) and \( LUMO \): highest occupied and lowest unoccupied molecular orbitals, respectively.
combined organic extracts were dried over MgSO₄, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (dichloromethane/petroleum ether; 80:20) affording 3a as an orange solid (2.08 g, 65%). Mp 182–183 °C; δ H (500 MHz, CDCl₃, TMS) 10.75 (1H, s), 9.12 (1H, d, J 2.0), 8.24 (1H, d, J 8.9), 7.64–7.63 (2H, m), 7.35 (1H, dd, J 8.9, 2.0), 6.77–6.74 (2H, m), 3.02 (6H, s), 2.68 (1H, sept, J 6.9), 1.33 (6H, d, J 6.9); δ C (125 MHz, CDCl₃, TMS) 176.5, 151.4, 149.2, 136.1, 133.7, 128.5, 126.6, 123.4, 120.1, 118.0, 112.5, 40.4, 37.8, 19.6; HRMS (ESI⁺, m/z): [M + Na]⁺ found, 350.1475; calc. for (C₁₂H₁₆N₄Na₂O₄), 350.1481.

**Compound 3b.** Compound 2 (1.00 g, 4.13 mmol), 4-(diphenylmethyl)phenylboronic acid (1.99 g, 5.37 mmol), NaCl (0.425 g, 4.13 mmol) and K₂CO₃ (0.248 g, 1.65 mmol) were dissolved in dry THF (7 mL mmol) and acetic acid (2 mL mmol) was added. A Nd:YAG laser operating at a 10 Hz repetition rate with approximately 10 mJ of energy per pulse and a pulse duration (FWHM) averaged 8.25 (1H, d, J 8.9), 7.57–7.53 (2H, m), 7.35 (1H, dd, J 8.9, 2.0), 7.32–7.27 (4H, m), 7.15–7.06 (8H, m), 2.68 (1H, sept, J 6.9), 1.32 (6H, d, J 6.9); δ C (100 MHz, CDCl₃, TMS) 176.5, 149.3, 148.7, 147.1, 136.0, 134.4, 131.5, 129.6, 128.5, 126.6, 125.2, 123.9, 122.9, 120.8, 119.3, 37.8, 19.6; HRMS (ESI⁺, m/z): [M + Na]⁺ found, 474.1799; calc. for (C₂₂H₂₃N₄Na₂O₄), 474.1794.

**Compound 3c.** Compound 2 (2.00 g, 8.26 mmol), 4-(diphenylmethyl)phenylboronic acid (2.60 mg, 12.4 mmol) and K₂CO₃ (0.153 g, 0.372 mmol) were dissolved in dry THF (7 mL mmol) and acetic acid (2 mL mmol) was added. A Nd:YAG laser operating at a 10 Hz repetition rate with approximately 10 mJ of energy per pulse and a pulse duration (FWHM) averaged 6.7); δ C (125 MHz, CDCl₃, TMS) 176.5, 151.4, 149.2, 136.1, 133.7, 128.5, 126.6, 123.4, 120.1, 118.0, 112.5, 40.4, 37.8, 19.6; HRMS (ESI⁺, m/z): [M + Na]⁺ found, 350.1475; calc. for (C₁₂H₁₆N₄Na₂O₄), 350.1481.

**Flash column chromatography (FLA-A).** A dark purple red solid (0.195 g, 38%), from 3a (0.408 g, 1.00 mmol). Mp > 300 °C; δ H (400 MHz, CDCl₃, TMS) 8.40 (1H, s), 8.26 (1H, d, J 8.7), 7.86 (1H, dd, J 8.7, 1.8), 7.68 (1H, d, J 1.8), 7.66–7.62 (2H, m), 6.86–6.82 (2H, m), 4.70 (2H, bs), 3.09 (6H, s) 2.51(1H, sept, J 6.7), 1.09 (6H, d, J 6.7); δ C (100 MHz, CDCl₃, TMS) 159.9, 155.3, 151.7, 151.5, 149.4, 135.2, 135.1, 134.1, 133.8, 128.7, 125.5, 125.5, 112.8, 111.1, 51.4, 40.3, 27.8, 20.3; HRMS (ESI⁺, m/z): [M + H]⁺ found, 390.1922; calc. for (C₂₂H₂₃N₄O₂), 390.1925.

**Flash column chromatography (FLA-B).** A dark purple red solid (0.132 g, 42%), from 3b (0.275 g, 0.610 mmol). Mp > 300 °C; δ H (400 MHz, CDCl₃, TMS) 8.37 (1H, s), 8.31 (1H, d, J 8.6), 7.85 (1H, dd, J 8.6, 1.7), 7.71 (1H, s), 7.58–7.54 (2H, m), 7.36–7.31 (4H, m), 7.20–7.12 (8H, m) 4.70 (2H, bs), 2.51 (1H, sept, J 6.7), 1.09 (6H, d, J 6.7); δ C (100 MHz, CDCl₃, TMS) 159.6, 155.1, 151.5, 150.0, 148.7, 146.9, 136.0, 135.3, 133.9, 130.8, 129.8, 128.9, 125.8, 125.7, 124.5, 122.2, 113.2, 51.5, 27.8, 20.3; HRMS (ESI⁺, m/z): [M + H]⁺ found, 514.2249; calc. for (C₂₂H₂₃N₄O₂), 514.2238.

**Flash column chromatography (FLA-C).** A green solid (0.268 g, 34%), from 3c (0.683 g, 1.65 mmol). Mp > 300 °C; δ H (500 MHz, CDCl₃, TMS) 8.50 (1H, s), 8.22 (1H, d, J 8.5), 7.65 (1H, dd, J 8.5, 1.4), 7.62 (1H, d, J 1.4), 4.65 (2H, bs), 4.62 (2H, t, J 1.9), 4.40 (2H, t, J 1.9), 4.30 (5H, s), 2.49 (1H, sept, J 6.9), 1.09 (6H, d, J 6.9); δ C (125 MHz, CDCl₃, TMS) 170.2, 154.9, 151.5, 135.2, 133.6, 133.4, 132.6, 129.9, 117.4, 113.2, 98.8, 72.3, 70.4, 70.3, 63.1, 51.5, 31.1, 27.7, 20.2; HRMS (ESI⁺, m/z): [M + H]⁺ found, 479.1176; calc. for (C₂₂H₂₃N₄O₂Fe₂O₄), 479.1171.

Nonlinear optical measurements using the hyper-Rayleigh scattering (HRS) method

Hyper-Rayleigh scattering (HRS) was used to measure the angle-averaged first hyperpolarisability β response of the molecules studied. The experimental set-up for hyper-Rayleigh measurements has previously been described in detail. A Q-switched Nd:YAG laser operating at a 10 Hz repetition rate with approximately 10 mJ of energy per pulse and a pulse duration (FWHM) close to 12 ns is used to excite hyper-Rayleigh scattering with an incident wavelength of 1064 nm. The hyper-Rayleigh signal was normalized at each pulse by using a small fraction of the laser pulse to generate a second harmonic signal from a KDP crystal to compensate for fluctuations in the temporal profile of the laser pulses due to longitudinal mode beating. Dioxane was used as the solvents.
used as a solvent, and the $\beta$ values were calibrated using a reference solution of p-nitroaniline (pNA) also dissolved in dioxane at a concentration of $1 \times 10^{-2}$ mol dm$^{-3}$ (external reference method). The hyperpolarisability of pNA dissolved in dioxane is known from EFISH measurements carried out at the same fundamental wavelength. We have chosen to report our values using the so-called $T$ (Taylor expansion) convention in which the $\beta_{313}$ of pNA in dioxane at 1064 nm is $40 \times 10^{-30}$ esu. This value includes a correction factor of 1.88 that accounts for the most recent measurement of the CCl$_4$ hyper-Rayleigh scattering signal which was used as a reference. All solutions were filtered (0.2 $\mu$m porosity) to avoid spurious signals from suspended impurities. The small hyper Rayleigh signal that arises from dioxane was taken into account. We took particular care to avoid reporting artificially high hyperpolarisabilities due to a possible contamination of the hyper-Rayleigh signal by molecular fluorescence near 532 nm. Measurements were carried out using two different interference filters with different transmission pass bands centred near the second harmonic at 532 nm allowing us to estimate and correct for any fluorescence emitted near 532 nm.

**TGA/DSC**

Thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) were performed using a TA Instruments SDT Q-600 series thermal analyser. Gas flow was 100 mL min$^{-1}$. The DSC curves show exotherms as up and endotherms as down.

**Theoretical calculations**

Gaussian 09 (ref. 25) was used to estimate solvent dependence and hyperpolarisability factors of the chromophores. The geometry of each dye was initially obtained semi-empirically (PM6). These hyperpolarisability factors of the chromophores. The geometry of each dye was initially obtained semi-empirically (PM6). These geometries were then re-optimised at DFT level using the hybrid B3LYP level by employing the 6-31+G** basis set using polarizable continuum model (keyword: scf = solvent). Frequency calculations were performed to ensure the absence of negative frequencies. Hyperpolarisability factors were estimated using an incident wavelength of 1064 nm (keywords: freq = raman, cphf = rdfreq, polar) and with a polarized solvent continuum using dioxane as the solvent (Table 2).

**Conclusions**

In conclusion, flavins FLA-A-C were readily synthesised from 5-chloro-2-nitroaniline using a simple 4-step synthetic route in moderate to high yields. Evaluation of the first hyperpolarisabilities of FLA-A-C using the hyper-Rayleigh scattering technique showed that derivatives FLA-A and FLA-B bearing stronger donor groups exhibit the higher hyperpolarisabilities ($\beta = 8660$–$9550 \times 10^{-30}$ esu) and higher thermal stabilities thereby indicating their potential future application in NLO devices. The convenient synthesis, good thermal stability and efficient SHG properties of this class of flavin derivatives suggest that related molecules may prove to be interesting candidates for further development. Moreover, the well-documented ability to accurately predict the physical properties of flavins using linear free energy relationships and, as we have shown here DFT calculations, will help ensure that push–pull flavin derivatives of this type, once embedded into acenitric structures, will become an important class of NLO materials with predictable properties.

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**References**


