Organic & Biomolecular Chemistry

Cite this: *Org. Biomol. Chem.*, 2011, **9**, 1608

www.rsc.org/obc

PAPER

Synthesis and NLO properties of new *trans* 2-(thiophen-2-yl)vinyl heteroaromatic iodides†

Cosimo Gianluca Fortuna,*[a] Carmela Bonaccorso,[a] Fadi Qamar,[b] Anu Anu,[b] Isabelle Ledoux[b] and Giuseppe Musumarra[a]

Received 26th April 2010, Accepted 22nd November 2010
DOI: 10.1039/c0ob00046a

The synthesis and characterisation of new *trans* 2-(thiophen-2-yl)vinyl pyridinium, imidazolium and quinoilinium iodides is reported together with their solvatochromic shifts and EFISH characterization. 2-{(*E*)-2-[5′-(dibutylamino)-2,2′-bithien-5-yl]vinyl}-1-methyl pyridinium and quinolinium iodides display high $\mu.\beta_{vec}$ values up to 1200×10^{-48} esu. The promising non-linear optical (NLO) properties of this new family of chromophores, which can be further improved by the design of highly efficient systems exploiting the donor and acceptor properties of both heteroaromatic rings and substituents, make them suitable candidates for second harmonic generation imaging with interesting biological applications.

Introduction

For more than a decade our research group has synthesised and characterised new *trans* 1,2-diheteroaryl ethylenes, investigating their basicity,[1] their photochemical behaviour and their interaction with DNA[2,3] in view of potential applications as antitumour agents. Indeed several *trans* 2-heteroaryl-vinyl-pyridinium, imidazolium and quinolinium iodides exhibited interesting *in vitro* antiproliferative activities[4–6] which could be rationalised and improved by molecular modelling approaches based on physicochemical and pharmacokinetic properties.[4,5] The biological activity of the above compounds relies on an optimal balance between hydrophilic and hydrophobic character in these molecules, due to the peculiarities of the heteroaromatic rings linked to the ethylene moiety, a positively charged pyridinium, imidazolium or quinolinium cation and a five membered heterocycle. However, the above structures belong to the class of the so called push–pull (donor–acceptor, D–A) molecules due to the electron donating and electron withdrawing abilities of the heteroaromatic rings linked by a transmitting ethylene moiety. Therefore potential non linear optical applications can be envisaged and the solvatochromic shifts exhibited by new *trans* 1-indolyl-2-(1-methyl pyridinium and quinolinium-2-yl) ethylene iodides[6] highlighted these new push–pull heteroaromatics as promising candidates for NLO applications.

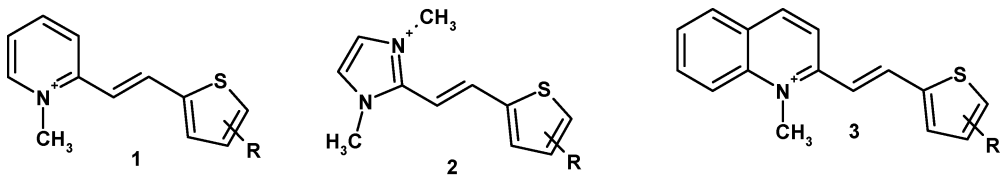
Molecular materials for second-order NLO[7] are now well-recognized as promising solutions to develop a new generation of low cost optoelectronic devices.[8] A wide choice of NLO molecules, designed according to well-established molecular engineering rules, have been proposed and synthesized.[9–12] More recently, NLO molecules have been used as molecular markers of biologically active molecules, as they may help to image, by multiphotonic interactions such as 2-photon fluorescence (TPF)[13] or second harmonic generation (SHG),[14] targeted structures of cells and membranes. In particular, SHG studies provide specific, complementary to that offered by TPF, valuable information about symmetry properties of these structures.[15] Combining therapeutic properties with NLO responses is of particular interest to localize and characterize the biological sites interacting with drugs. Directly tracking these drug molecules by NLO techniques is therefore of great interest for a better understanding of the biological processes underlying their therapeutic activity.

The aim of this work is to provide evidence of significant NLO response of 2-(thiophen-2-yl)vinyl heteroaromatic iodides with potential therapeutic properties. We do not propose here an entirely novel and comprehensive molecular engineering scheme to maximize non linear molecular hyperpolarizabilities, but we report on the evidence of significant quadratic NLO responses of therapeutic molecules, offering an interesting perspective for optical tracking of drugs and the related improved knowledge of therapeutic mechanisms of these structures. From this perspective, we focused our work on molecular NLO properties only, optimization at the material level not being relevant in the context of molecular markers and drugs, where biological affinity and compatibility are the most critical issues for a proper use of NLO molecules in this context.

The optimization of NLO dipolar dyes is related to the molecular factor of merit $\mu.\beta_{vec}$. This parameter is the scalar

[a]*Dipartimento di Scienze Chimiche, Università di Catania, Viale A. Doria, 6, 95125, Catania, Italy. E-mail: cg.fortuna@unict.it*
[b]*Laboratoire de Photonique Quantique et Moleculaire, Institut d'Alembert - Ecole Normale Superieure de Cachan, 1 avenue du President Wilson, 94235, Cachan, France*

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c0ob00046a



DESIGNATION
a: R=4-phenyl
b: R=5-phenyl
c: R=5-(thiophene-2'-yl)
d: R=5-(5'-N,N-dibutylamino-thiophene-2'-yl)

Scheme 1

product of the molecular dipole moment μ and the vector part of the quadratic hyperpolarizability tensor β_{vec}. The best factors of merits result from a sophisticated molecular design corresponding to $\mu.\beta_{vec} = 35000 \times 10^{-48}$ esu[16] for highly conjugated chromophores for telecommunications.

Here we report on lower NLO performances, but with a good potential for significant improvement, and that are compatible with molecular biological activity

Due to their charged character, zwitterions and cations have not been widely investigated for quadratic NLO applications. However, there are some reports evidencing the possibility to measure their $\mu.\beta_{vec}$ values in chloroform[17,18] using a technique called Electric-field induced second harmonic (EFISH) .[19] It has been shown that the application of a DC field on a zwitterion dissolved in a non-polar solvent does not dissociate the ionic moieties and result in large $\mu.\beta_{vec}$ values.[17,18] In the present work we will revisit these investigations on push–pull chromophores by using heterocyclic conjugated moieties and various ionic nitrogen-containing heterocycles as strong electron acceptors.

In this context we herein report the solvatochromic shifts and EFISH characterization of *trans* 2-(thiophen-2-yl)vinyl heteroaromatic iodides **1–3** (**a,b,c**), including more efficient systems exploiting the donor and acceptor properties of both heteroaromatic rings and substituents designated as **d** (Scheme 1).

Results and discussion

The synthesis of *trans* 2-(thiophen-2-yl)vinyl heteroaromatic iodides **1–3** (**a,b,c**) is straightforward and can be easily achieved by condensation of 1,2-dimethyl pyridinium iodide, or 1,2-dimethyl quinolinium iodides with heteroaromatic aldehydes. As expected, the pyridinium and quinolinium α methyls are quite reactive due to the strong electron withdrawing effect of the positively charged nitrogen ring.

Under appropriate conditions, outlined in the experimental section, pure *trans* isomers **1–3** (**a,b,c**) were obtained, as evidenced by the ethylenic protons *J* coupling constants in the NMR spectra. Compounds **1–3** (**a,b,c**) possessing electron donating moieties connected by a vinyl linker to a strong electron withdrawing moiety are expected to exhibit significant solvatochromic shifts. The solvatochromic shifts of cations **1–3** (**a,b,c**), reported in Table 1, encouraged us to perform Electric-field induced second harmonic generation (EFISH)[19] characterization at 1.9 μm on the above molecules. Unfortunately, EFISH measurements could not be performed on the quinolinium cations **3** due to the low solubility of these compounds. On the another hand, compound **2d** was obtained as a mixture of *cis–trans* forms. The β value of the cis-form was not being easily accessible, as it would require low-yield separation procedures from the *trans* form. Moreover, the resulting *cis* isomer was not expected to be not highly stable at room temperature.

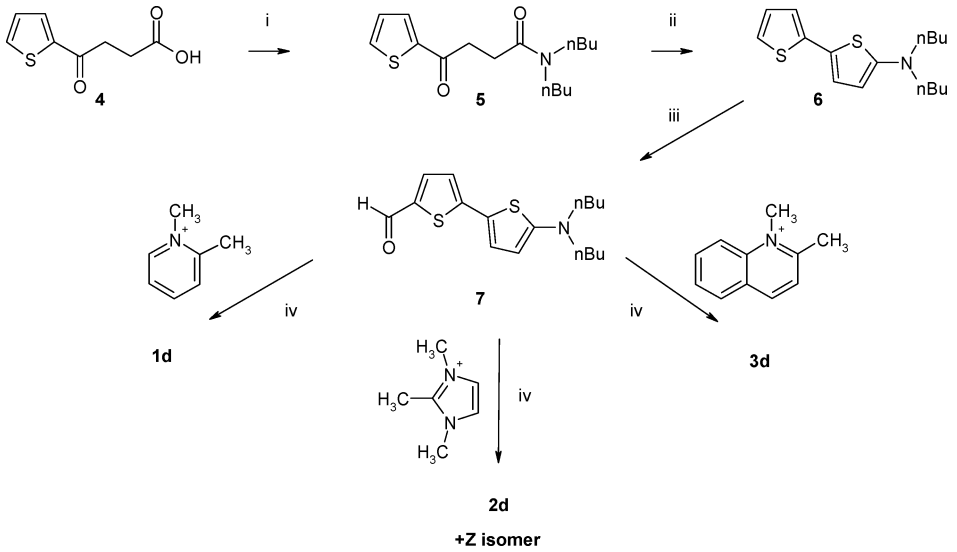
Table 1 Solvatochromic shifts and $\mu.\beta_{vec}$ values of cations **1–3**

Compounds	λ_{max} $CHCl_3$ (nm)	λ_{max} H_2O (nm)	$\Delta\lambda_{max}$ (nm)	$\mu.\beta_{vec}$[a] (10^{-48} esu)
1a	400	380	20	180
2a	354	342	12	236
3a	440	410	40	n.d.
1b	420	400	20	213
2b	429	359	70	243
3b	480	430	50	n.d.
1c	450	417	33	307
2c	383	360	23	353
3c	500	460	40	n.d.
1d	625	533	92	1240
3d	718	604	114	1250

[a] Experimental errors do not exceed 6%.

From Table 1 we can infer some information about the electron accepting character of the ionic nitrogen heterocycles investigated here. Comparison of $\mu.\beta_{vec}$ values between pyridinium salts **1** on one hand, and imidazolium salts **2** on the other hand, clearly highlights the better electron accepting character of the imidazolium cations as compared to the pyridinium cation. This results in a higher $\mu.\beta_{vec}$ value when imidazolium is used as an electron acceptor. Furthermore, comparison between molecules **1c** and **2c** on the one hand, and **1b** and **2b** on the other hand, shows the higher electron donating character of the bis-thiophene moiety as compared with the phenyl-thiophene moiety. However, $\mu.\beta_{vec}$ remains modest, as these moieties do not induce a significant intramolecular charge transfer towards the ionic heterocycles through the conjugated path.

The above results point out that the bisthiophene derivatives designated as **c** display valuable NLO properties and show that both solvatochromic shifts and $\mu.\beta_{vec}$ values can be modulated varying the electronic parameters in both the donor and acceptor heteroaromatic moieties. In fact, as reported in literature, in general β increases with increasing donor and acceptor strength and with increasing separation as long as there is strong



Scheme 2

electronic coupling through the conjugated bridge,[7–12] although some exceptions might occur.[20] There is still active interest in the design of more efficient donors, acceptors and conjugating units. In this context, we decided to introduce a dialkylamino substituent in the *alpha* position of the terminal thiophene ring increasing the electron donating character of the donor group, with the aim of improving the solvatochromic shifts and the EFISH performances.[21]

In order to support this hypothesis β_0 for compounds **1c** and **1d** were calculated at the Hartree–Fock level of theory (See ESI† for details). When adding the *N*,*N*-dimethylamino substituent into the 5′ position of the thiophene moiety the β_0 (au) value is more than three times higher, increasing from 15768 to 49772 au.

The (*n*-butyl)amino derivatives **1d** and **3d** were obtained according to the synthetic strategy outlined in Scheme 2, similar to that adopted for the synthesis of other dialkylamino aldehydes.[22,23]

Direct amidation of the acid **4** with the amine was obtained through a DCC-BtOH catalysed reaction (**i**);[22] subsequent treatment of the amide (**5**) with Lawesson's reagent (**ii**) afforded the corresponding aminobithiophene **6**. The synthesis of the formyl derivative **7** was achieved by metallation, using *n*-BuLi, followed by quenching with DMF[23] (**iii**). Actually the synthesis of the aldehyde **7** in 6.5% yield adopting a different synthetic pathway has recently been reported.[24] However, the present synthetic procedure involving formylation of *N*,*N*-dibutyl-2,2′-bithiophen-5-amine **6** provides a significantly better yield. Compounds **1d** and **3d** were obtained by condensation of the heteroaromatic aldehyde **7** with the corresponding iodide salt in the presence of piperidine as the base (**iv**). Condensation of **7** with imidazolium iodide provided a mixture of *E* and *Z* isomers **2d** in low yields.

As expected, *N*,*N*-di-*n*-butylamino bisthiophene derivatives **1d** and **3d** exhibit significantly higher solvatochromic shifts with respect to the corresponding unsubstituted compounds **1c** and **3c**. This is paralleled by high $\mu.\beta_{vec}$ values up to 1200×10^{-48} esu for compounds **1d** and **3d** confirming the necessity to introduce strong dialkylamino groups to induce a high quadratic molecular NLO response. These values are in agreement with those reported in the literature for similar structures.[25,26] The experimental $\mu.\beta_{vec}$ value for **1d** is four times higher than that of **1c**, in agreement with the trend already indicated by theoretical calculations.

It is well known that observation of second harmonic generation (SHG) phenomena[27] is essential to envisage applications in the field of non linear optical biomedical imaging. Recent advances in diode-pumped solid state (DPSS) lasers have made near-IR lasers extremely compact and affordable, with green laser pointers (532 nm) the most common product utilizing DPPS laser (1064 nm) through an SHG process. Both **1d** and **3d** exhibit a significant absorbance at 532 nm, making them suitable for SHG excited DPPS lasers. This preliminary investigation of a new family of chromophores for NLO can be extended by designing structures bearing increased conjugation lengths and more efficient donor and acceptor substituents and undergo a more complete characterization of their tensor properties by using Harmonic Light Scattering[28,29] experiments to infer the octupolar component of their β tensor.

Conclusion

We have synthesized and characterized *trans* 2-(thiophen-2-yl)vinyl heteroaromatic derivatives and evidenced their interest for quadratic nonlinear optics. Choosing organic cationic species does not prevent an accurate and reliable determination of their molecular factor of merit $\mu.\beta_{vec}$. The straightforward synthesis of the above compact heterocyclic structures, their strong non linear optical properties and their absorption peaks around 532 nm, make them promising probes for second harmonic generation imaging with interesting biological applications.

Experimental section

The values of $\mu.\beta_{vec}$ for the chromophores were measured using the electric-field induced second harmonic generation (EFISH) technique. A Nd^{3+}:YAG laser at 1.06 μm pumps a hydrogen Raman cell so as to obtain a larger wavelength (1.907 μm) for which both the fundamental and harmonic frequencies are far away from the resonance of the investigated molecule. A Schott RG 1000 filter

was used to filter out any remaining visible light from the laser flash lamp. Suitable neutral density filters were used to control the power of the incident beam and a half wave plate and polariser were used to set the incident polarisation along the direction of the applied electric field. In addition, a band pass filter was mounted on the front of the detection PMT along with a filter to remove any remaining radiation at the fundamental wavelength. A high voltage was applied across the EFISH cell containing the solution. The EFISH cell consisted of a stainless steel container with two quartz optical windows, which were glued to form a wedge shaped cavity within the cell. The electrode was connected to the high voltage supply *via* an isolated stainless steel rod situated above the wedge shaped cavity. The interelectrode distance was 2 mm, giving a static electric field of around 40 kVcm. The cell was mounted on an electrically isolated translation stage. The whole cell was then translated horizontally relative to the incident beam to produce fringes at the second harmonic wavelength. Every measurement was referenced separately to the fringes of the pure solvent that was used to dissolve the chromophore to take into account fluctuations in laser power. An in-house computer program was used to calculate the interfringe distance together with the fringe amplitude. These data were then used to calculate the $\mu.\beta_{vec}$ of the chromophore, taking the pure solvent (chloroform) as the reference solution.

In principle, EFISH is precluded in the case of ionic species, due to ion migration towards poling electrodes and a related cancellation of the poling field. Here, we have adapted the EFISH technique to $\mu.\beta_{vec}$ measurements of ionic chromophores by i) using a short (1 μs) DC poling field, provided that ion mobility in chloroform is not high enough to permit ion migration towards electrodes within the short time duration of the DC pulse, ii) operating in a solvent of low polarity stabilizing undissociated ion pairs. Consequently, EFISH experiments were carried out in chloroform (ε_r = 4.7) and at 1.907 nm (provided by a hydrogen Raman cell pumped by a Nd^{3+}:YAG laser in order to avoid absorption of the second harmonic. Reproducible β values (with a variation of ± 6%) were obtained. Concentrations did not exceed 1×10^{-3} mol L^{-1}, and no significant influence of the chromophore concentration on β values could be noticed in the 1×10^{-4}–1×10^{-3} mol L^{-1} concentration range.

All calculations in this work were carried out using the GAUSSIAN 03 package. The geometrical structures for the model compounds were obtained at the density functional theory (DFT) B3LYP/6-311+G(d,p) level; after the minimization process, the vibrational spectra have been evaluated to check that no imaginary frequencies are present. The static first hyperpolarizabilities (β_0) were evaluated by the coupled perturbed Hartree Fock (CPHF) approach at the Hartree–Fock level with 6-311+G(d,p) basis set for all the atoms. Solvation effects were taken into account using the Polarizable Continuum Model.[30]

^{1}H NMR spectra were recorded at 27 °C using a Varian Inova 500 spectrometer. Chemical shifts (δ) are expressed in ppm and referenced to residual undeuterated solvent. NMR data were processed using MestReC software (http://www.mestrec.com). Two-dimensional (2D) NMR experiments (gCOSY; gHSQCAD; gHMBCAD) were carried out on all new compounds using the pulse sequences from the Varian user library. On the basis of 2D-NMR analyses, complete assignments of ^{1}H and ^{13}C signals were obtained (see ESI†).

Electron Spray Ionization mass spectra were recorded on a Thermo Finnigan LCQ Deca mass spectrometer equipped with an ESI source.

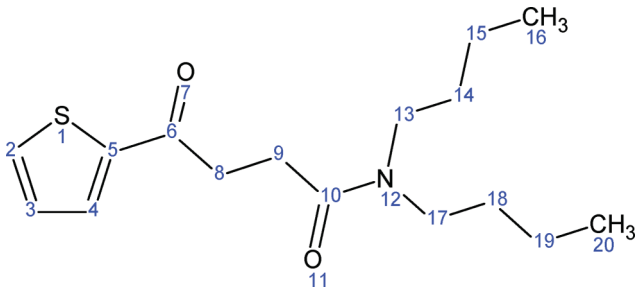
General procedure for the synthesis of compounds 1–3 (a,b,c)

Heteroaromatic carboxaldehydes were Aldrich commercial products.

2-Heteroaryl thiophene derivatives, all iodide salts, were obtained by refluxing equimolar amounts of 1,2,3-trimethylimidazolium iodide in ethanol, or 1,2-dimethylpicolinium iodide or 1,2-dimethylquinolinium iodide and the appropriate heteroaromatic aldehyde in the presence of few drops 20% NaOH or piperidine. The resulting precipitate was recrystallized from ethanol.

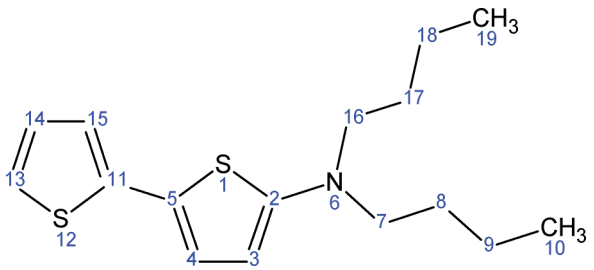
Details on the synthetic conditions and products characterization have been reported.[31]

Synthesis of compounds 5–7; 1d and 3d



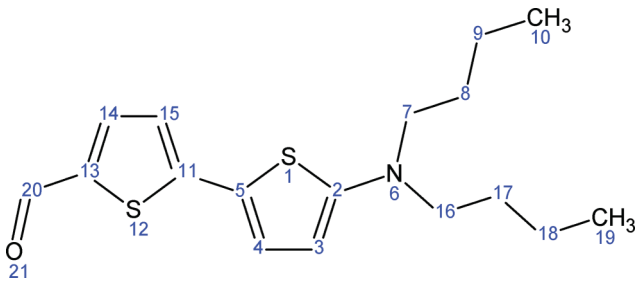
***N*,*N*-dibutyl-4-oxo-4-(2-thienyl)butanamide (5).** 1,3-Dicyclohexylcarbodiimide (DCC) (3350 mg, 16.3 mmol) and 1-hydroxybenzotriazole (BtOH) (2.50 g, 16.3 mmol) were added to a stirred solution of the acid (**4**) (2500 mg, 13.6 mmol) in dichloromethane (100 mL) at 0 °C. The mixture was stirred for 30 min at rt after which the amine (2.29 mL, 13.6 mmol) was added and the mixture was stirred overnight. The by-products formed were separated by filtration to give a pale brown solution. This organic solution was extracted with a solution of citric acid 5% (4 × 100 mL), a solution of sodium bicarbonate (5%) (2 × 100 mL), dried over $MgSO_4$ and evaporated to give an oily brown residue. The product was purified by chromatography on silica gel (eluent: hexane\ethylacetate) and gave pure (**5**) as an orange oil (2010 mg, 6,78 mmol, 51%)

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 7.81 (dd, $^3J(H,H)_1$ = 3.8 Hz, $^3J(H,H)_2$ = 1.1 Hz, 1H; 4-ArH), 7.62 (dd, $^3J(H,H)_1$ = 5.0, Hz, $^3J(H,H)_2$ = 1.1 Hz, 1H; 2-ArH), 7.13 (dd, $^3J(H,H)_1$ = 5.0 Hz, $^3J(H,H)_2$ = 3.8 Hz, 1H; 3-ArH), 3.32 (m, $^3J(H,H)$ = 6.9 Hz, 4H; NCH_2), 3.30 (t, $^3J(H,H)$ = 6.7 Hz, 2H; $ArCOCH_2$), 2.77 (t, $^3J(H,H)$ = 6.7 Hz, 2H; $NCOCH_2$), 1.63–1.47 (m, 4H; NCH_2CH_2), 1.39–1.25 (m, 4H; $NCH_2CH_2CH_2$), 0.98–0.89 (t, $^3J(H,H)$ = 6.9 Hz, 6H; CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 192.29 (Ar*C*O), 170.88 (*C*ON), 144.08 (5 C_{Ar}), 133.34 (2 C_{Ar}), 132.01 (4 C_{Ar}), 128.07 (3 C_{Ar}), 47.71 (13 CH_2), 45.98 (17 CH_2), 34.48 (8 CH_2), 31.06 (14 CH_2), 29.90 (18 CH_2), 27.17 (9 CH_2), 20.26 (15 CH_2), 20.16 (19 CH_2), 13.86 (16 CH_3), 13.83 (20 CH_2). ESI-MS: *m*/*z* (%): 612.8 (95) [2M+Na^+], 296.2 (100) [M+H^+].



***N*,*N*-dibutyl-2,2′-bithiophen-5-amine (6).** A mixture of Lawesson's reagent (1250 mg, 3.1 mmol) and the amide (**5**) (890 mg, 3 mmol) was heated in toluene (15 mL) for 60 min. The mixture was cooled and the solvent was evaporated under reduced pressure to give the crude bithiophene (**6**) as an oil. Chromatography purification on silica gel (eluent: hexane\dichloromethane) gave pure (**6**) as yellow oil (757,2 mg, 2.57 mmol, 83%).

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 7.05 (dd, $^3J(H,H)_1$ = 3.8 Hz, $^3J(H,H)_2$ = 1.1 Hz, 1H; 13-ArH), 6.95 (dt, $^3J(H,H)_1$ = 3.8 Hz, $^3J(H,H)_2$ = 1.1 Hz, 1H; 14-ArH), 6.93 (dd, $^3J(H,H)_1$ = 3.8 Hz, $^3J(H,H)_2$ = 1.1 Hz, 1H; 15-ArH), 6.86 (d, $^3J(H,H)$ = 3.8 Hz, 1H; 4-ArH), 5.77 (bs, 1H; 3-ArH)), 3.21 (t, $^3J(H,H)$ = 6.9 Hz, 4H; NCH_2), 1.61 (m, 4H; NCH_2CH_2), 1.36 (m, 4H; $NCH_2CH_2CH_2$), 0.95 (t, $^3J(H,H)$ = 7.2 Hz, 4H; CH). ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 156.93 (2 CAr), 139.01 (11 CAr), 127.47 (14 CAr), 123.69 (4 CAr), 121.68 (13 CAr), 120.62 (15 CAr), 120.13 (5 CAr), 101.78 (3 CAr), 53.55 (16–7 CH_2), 29.17 (17–8 CH_2), 20.27 (18–9 CH_2), 13.90 (19–10 CH_3). ESI-MS: *m*/*z* (%): 585.3 (95) $[2M+H]^+$, 294.3 (100) $[M+H]^+$.



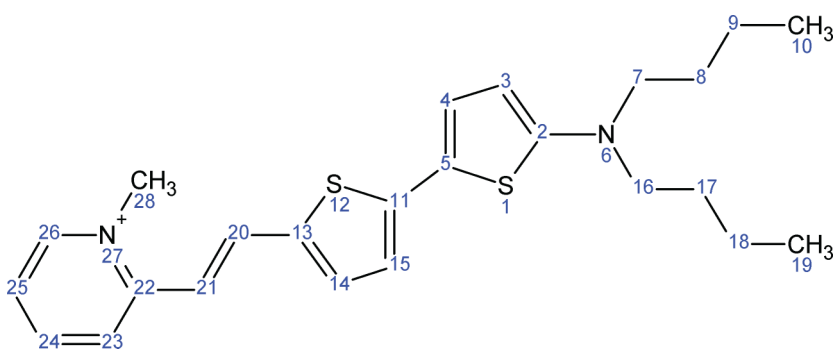
5′-(dibutylamino)-2,2′-bithiophene-5-carbaldehyde (7). This compound, recently reported,[24] was synthesized adopting a different procedure providing a better yield with respect to the literature one (6.5%). A 2.5 M solution of BuLi in hexane (0.8 mL, 2.0 mmol) was dropped at 10 °C to a stirred solution of bithiophene (**6**) (0.30 g, 1.0 mmol) in anhydrous ether (2 mL). After 30 min DMF (0.13 mL, 1.5 mmol) was slowly added, and the mixture was allowed to react for 50 min. The mixture was poured into water (10 mL) and extracted with (3 × 25 mL) of ethyl acetate. The whole organic phase was washed with water (100 mL), dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure to give the crude 5-formyl-bithiophene (**7**) as a dark oil. Chromatography on silica gel (eluent: exane\dichloromethane) gave pure (**7**) as a red solid (183.7 mg, 5.7 × 10^{-1} mmol, 57%). The ^{1}H- and ^{13}C-NMR spectra (500 MHz, $CDCl_3$) and the mass spectrum were coincident with those reported in the literature[24]

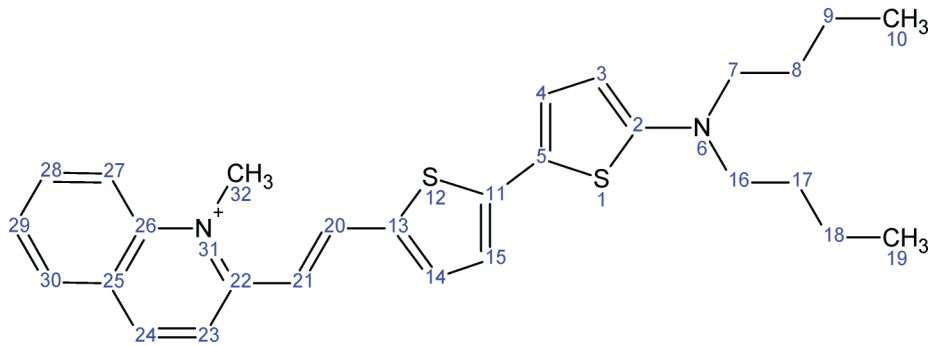
2-{(*E*)-2-[5′-(dibutylamino)-2,2′-bithien-5-yl]vinyl}-1-methyl-pyridinium iodide (1d). 1,2-Dimethyl-pyridinium iodide (47 mg, 0.2 mmol) was added to a solution of aldehyde **7** (67 mg, 0.2 mmol) in 2 mL ethanol and in the presence of few drops of piperidine; the mixture was stirred for 6 h at 50 °C. The solvent was removed under reduced pressure to give (**1d**) as a dark oil. Chromatography purification on silica gel (eluent: dichloromethane\methanol) gave pure (**1d**) as dark solid (46.06 mg, 1.12 × 10^{-1} mmol, 56%).

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 9.11 (d, $^3J(H,H)$ = 6.3 Hz, 1H; 26-ArH), 8.26 (d, $^3J(H,H)$ = 8.0 Hz, 1H; 23-ArH), 8.19 (t, $^3J(H,H)$ = 7.9 Hz, 1H; 24-ArH), 7.94 (d, $^3J(H,H)$ = 15.2 Hz, 1H; 21-ArH), 7.57 (dt, $^3J(H,H)_1$ = 6.4 Hz, $^3J(H,H)_2$ = 1.2 Hz, 1H; 25-ArH), 7.42 (d, $^3J(H,H)$ = 3.9 Hz, 1H; 14-ArH), 7.09 (d, $^3J(H,H)$ = 4.2 Hz, 1H; 4-ArH), 6.85 (d, $^3J(H,H)$ = 3.9 Hz, 1H; 15-ArH), 6.65 (d, $^3J(H,H)$ = 15.2 Hz, 1H; 20-ArH), 5.79 (d, $^3J(H,H)$ = 4.2 Hz, 1H; 3-ArH), 4.45 (s, 3H; 28-CH_3), 3.29 (t, $^3J(H,H)$ = 7.6 Hz, 4H; NCH_2), 1.65 (m, 4H; NCH_2CH_2), 1.38 (m, 4H; $NCH_2CH_2CH_2$), 0.99 (t, $^3J(H,H)$ = 7.6 Hz, 4H; CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 159.83 (2 C_{Ar}), 152.56 (22 C_{Ar}), 146.94 (11 C_{Ar}), 145.66 (26 C_{Ar}), 142.93 (24 C_{Ar}), 137.45 (21 C_{Ar}), 136.67 (14 C_{Ar}), 134.28 (13 C_{Ar}), 127.88 (4 C_{Ar}), 123.78 (23 C_{Ar}), 122.81 (25 C_{Ar}), 120.85 (15 C_{Ar}), 117.63 (5 C_{Ar}), 109.52 (20 C_{Ar}), 101.91 (3 C_{Ar}), 53.47 (7,16 CH_2), 46.63 (28 NCH_3), 29.25 (8,17 CH_2), 20.08 (9,18 CH_2), 13.82 (9,18 CH_3). ESI-MS: *m*/*z* (%): 411.3 (100) $[M^+]$.

2-{(*E*)-2-[5′-(dibutylamino)-2,2′-bithien-5-yl]vinyl}-1-methyl-quinolinium iodide (3d). 1,2-Dimethyl-quinolinium iodide (55 mg, 0.2 mmol) was added to a solution of aldehyde **7** (67 mg, 0.2 mmol) in 2 mL ethanol and in the presence of few drops of piperidine; the mixture was stirred for 6 h at 50 °C. The solvent was removed under reduced pressure to give (**3d**) as a dark oil. Chromatography purification on silica gel (eluent: dichloromethane\methanol) gave pure (**3d**) as a dark solid (37.82 mg, 8.2 × 10^{-2} mmol, 41%).

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.64 (d, $^3J(H,H)$ = 9.3 Hz, 1H; 24-ArH), 8.59 (d, $^3J(H,H)$ = 14.9 Hz, 1H; 21-ArH), 8.36 (d, $^3J(H,H)$ = 9.3 Hz, 1H; 23-ArH), 8.05 (d, $^3J(H,H)$ = 8.8 Hz, 1H; 27-ArH), 7.83 (dt, $^3J(H,H)_1$ = 7.9 Hz, $^3J(H,H)_2$ = 1.3 Hz, 1H;





29-ArH), 7.78 (dd, $^3J(H,H)_1$ = 7.9 Hz, $^3J(H,H)_2$ = 1.1 Hz, 1H; 30-ArH), 7.71 (d, $^3J(H,H)$ = 4.2 Hz, 1H; 14-ArH), 7.51 (t, $^3J(H,H)$ = 7.7 Hz, 1H; 28-ArH), 7.06 (d, $^3J(H,H)$ = 4.2 Hz, 1H; 4-ArH), 6.88 (d, $^3J(H,H)$ = 15.2 Hz, 1H; 20-ArH), 6.57 (d, $^3J(H,H)$ = 4.2 Hz, 1H; 15-ArH), 5.79 (d, $^3J(H,H)$ = 4.2 Hz, 1H; 3-ArH), 4.49 (s, 3H; 32-CH_3), 3.31 (t, $^3J(H,H)$ = 7.7 Hz, 4H; NCH_2), 1.68 (m, 4H; NCH_2CH_2), 1.42 (m, 4H; $NCH_2CH_2CH_2$), 1.02 (t, $^3J(H,H)$ = 7.3 Hz, 6H; CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 160.91 (2 C_{Ar}), 155.22 (22 C_{Ar}), 149.20 (11 C_{Ar}), 141.77 (24 C_{Ar}), 141.20 (23 C_{Ar}), 139.74 (14 C_{Ar}), 139.31 (25 C_{Ar}), 135.32 (13 C_{Ar}), 133.91 (29 C_{Ar}), 129.71 (30 C_{Ar}), 129.38 (4 C_{Ar}), 127.43 (26 C_{Ar}), 126.73 (28 C_{Ar}), 121.39 (21 C_{Ar}), 121.34 (15 C_{Ar}), 117.86 (27 C_{Ar}), 117.76 (5 C_{Ar}), 110.87 (20 C_{Ar}), 102.72 (3 C_{Ar}), 53.54 (7,16 CH_2), 40.41 (32 NCH_3), 29.23 (8,17 CH_2), 20.24 (9,18 CH_2), 13.92 (9,18 CH_3). ESI-MS: m/z (%): 461.3 (100) [M^+].

References

1 A. Ballistreri, L. Gregoli, G. Musumarra and A. Spalletti, *Tetrahedron*, 1998, **54**, 9721.
2 L. Giglio, U. Mazzucato, G. Musumarra and A. Spalletti, *Phys. Chem. Chem. Phys.*, 2000, **2**, 4005–4012.
3 E. Marri, U. Mazzucato, C. G. Fortuna, G. Musumarra and A. Spalletti, *J. Photochem. Photobiol., A*, 2006, **179**, 314–316.
4 F. P. Ballistreri, V. Barresi, P. Benedetti, G. Caltabiano, C. G. Fortuna, M. L. Longo and G. Musumarra, *Bioorg. Med. Chem.*, 2004, **12**, 1689–1695.
5 C. G. Fortuna, V. Barresi, G. Berellini and G. Musumarra, *Bioorg. Med. Chem.*, 2008, **16**, 4150–4159.
6 C. G. Fortuna, V. Barresi, N. Musso and G. Musumarra, *Arkivoc*, 2009, **(viii)**, 222–229.
7 J. Zyss, *Molecular Nonlinear Optics: Materials Physics and Devices;* Academic Press: Boston, 1994.
8 Y. Shi, W. Lin, D. J. Olson, J. H. Bechtel, H. Zhang, W. H. Steier, C. Zhang and L. R. Dalton, *Appl. Phys. Lett.*, 2000, **77**, 1.
9 S-H Jang and A. K-Y Jen, Polymeric Second-Order Nonlinear Optical Materials and Devices, in *Introduction to Organic Electronic and Optoelectronic Materials and Devices*, edited by Sam-Shajing Sun and Larry R. Dalton, CRC Press, p. 467, 2008.
10 H. S. Nalwa, S. Miyata, *Nonlinear Optics of Organic Molecules and Polymers;* CRC Press: New York, 1997.
11 T. Verbiest, S. Houbrechts, M. Kauranen, K. Clays and A. Persoons, *J. Mater. Chem.*, 1997, **7**, 2175.
12 J. E. Reeve, H. A. Collins, K. De Mey, M. M. Kohl, K. J. Thorley, O. Paulsen, K. Clays and H. L. Anderson, *J. Am. Chem. Soc.*, 2009, **131**, 2758–2759.
13 W. Denk, J. H. Strickler and W. W. Webb, *Science*, 1990, **248**, 73–76.
14 L. Moreaux, O. Sandre, M. Blanchard-Desce and J. Mertz, *Opt. Lett.*, 2000, **25**, 3220–3222.
15 P. Yan, A. C. Millard, M. Wei and L. M. Loew, *J. Am. Chem. Soc.*, 2006, **128**(34), 11030–11031.
16 Y. Q. Shi, C. Zhang, H. Zhang, J. H. Bechtel, L. R. Dalton, B. H. Robinson and W. H. Steier, *Science*, 2000, **288**, 119–122.
17 H. Kang, A. Facchetti, H. Jiang, E. Cariati, S. Righetto, R. Ugo, C. Zuccaccia, A. Macchioni, C. L. Stern, Z. F. Liu, S. T. Ho, E. C. Brown, M. A. Ratner and T. J. Marks, *J. Am. Chem. Soc.*, 2007, **129**, 3267–3286.
18 V. Alain, M. Blanchard-Desce, I. Ledoux-Rak and J. Zyss, *Chem. Commun.*, 2000, 353.
19 B. F. Levine and C. G. Bethea, *Appl. Phys. Lett.*, 1974, **24**, 445–447.
20 M. González, J. L. Segura, C. Seoane, N. Martín, J. Garín, J. Orduna, R. Alcalá, B. Villacampa, V. Hernández and J. T. López Navarrete, *J. Org. Chem.*, 2001, **66**, 8872–8882.
21 I. Ledoux, J. Zyss, E. Barni, C. Barolo, N. Diulgheroff, P. Quagliotto and G. Viscardi, *Synth. Met.*, 2000, **115**, 213–217.
22 M. M. M. Raposo and G. Kirsch, *Heterocycles*, 2001, **55**(8), 1487–1498.
23 M. M. M. Raposo and G. Kirsch, *Tetrahedron*, 2003, **59**, 4891–4899.
24 P. Yan, A. Xie, M. Wie and L. M. Leow, *J. Org. Chem.*, 2008, **73**, 6587–6594.
25 A. G. Jiang, Y. G. Liu and D. Y. Huang, *THEOCHEM*, 2000, **499**, 203–206.
26 A. Carella, A. Castaldo, R. Centore, A. Fort, A. Sirigu and A. Tuzi, *J. Chem. Soc., Perkin Trans. 2*, 2002, 1791–1795.
27 P. Yan, A. C. Millard, M. Wei and L. M. Loew, *J. Am. Chem. Soc.*, 2006, **128**, 11030.
28 R. W. Terhune, P. D. Maker and C. M. Savage, *Phys. Rev. Lett.*, 1965, **14**, 681–684.
29 K. Clays and A. Persoons, *Phys. Rev. Lett.*, 1991, **66**, 2980–2983.
30 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. G. Johnson, W. Chen, M. W. Wong, C. Gonzalez and J. A. Pople, *GAUSSIAN 03 (Revision E.01)*, Gaussian, Inc., Wallingford, CT, 2004.
31 C. G. Fortuna, V. Barresi and G. Musumarra, *Bioorg. Med. Chem.*, 2010, **18**, 4516–4523.