



Tetrahedron Letters 44 (2003) 5883-5887

TETRAHEDRON LETTERS

6-(Arylvinylene)-3-pyridinylboronic esters. Part 2: Versatile building blocks for push-pull nonlinear optical chromophores

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Received 2 June 2003; revised 3 June 2003; accepted 3 June 2003

Abstract—This paper describes a general approach for the synthesis of push–pull 6,6'-disubstituted-3,3'-bipyridine chromophores. As examples, 6-(4-ethanol-2-thienylvinylene)-5-methyl-3-bromopyridine, 6-(4-hydroxy-phenylvinylene)-5-methyl-3-bromopyridine, and the corresponding 3-pyridinylboronic esters have been prepared as building blocks end-capped with electron donor groups (D). 6-(4-Cyano-phenylvinylene)-5-methyl-3-bromopyridine, and 6-(4-cyano-phenylvinylene)-3-bromopyridine have been synthesized as building blocks end-capped with electron acceptor groups (A). $\{A \times D\}$ type cross-couplings via Suzuki reaction gave the push–pull chromophores (I) and (II) in high yields and multigram scales. © 2003 Elsevier Ltd. All rights reserved.

Organic second-order nonlinear optical (NLO) polymeric materials have been intensively studied for many years.^{1,2} In these systems NLO noncentrosymmetric chromophores are either covalently attached to the backbone as side-groups, or are made part of the polymer backbone itself. A typical NLO chromophore consists of an electron-accepting group and an electrondonating group connected by a π -conjugated bridge (push-pull structure). The structure-property relationships of the molecular NLO property (β) of these one-dimensional dipolar chromophores have been theoretically and experimentally established.^{3–5}

In previous papers,^{6–9} we have described a novel class of conjugated molecules.



These compounds are either symmetric molecules (a) or asymmetric push-pull molecules (b). They were prepared by a one-step ((a) series) or a two-steps ((b) series) Knoevenagel type condensation, under acidic conditions, of 6,6'-dimethyl-3,3'-bipyridine derivatives

0040-4039/\$ - see front matter © 2003 Elsevier Ltd. All rights reserved. doi:10.1016/S0040-4039(03)01427-8

with corresponding aromatic aldehydes: thienyl ring as donor group, or benzene ring para-substituted with electron-donor (D) or electron-acceptor (A) groups. By lateral substitutions of the π -conjugated bridge and by varying the nature of the acceptor/donor pair, we were able to tune the mesogenic,^{6,7} electrochemical,^{6,7} photoluminescent,^{6,7} and second- as well as third-order NLO properties of the chromophores.^{7–9} However, despite the above-mentioned attractive features, the previous two-step synthetic route, in the case of the nonsymmetric chromophores, restricts the yield because of separation and purification difficulties. Consequently, it was difficult to access many combinations of donor/acceptor pairs. This is the reason why it was necessary to define a new more efficient synthetic route to obtain such unsymmetrical conjugated chromophores. Moreover, we were interested in synthesizing chromophores with reactive functionalities (e.g. hydroxyl groups) at one end to covalently couple the chromophores to a polymer backbone.

Concerning substituted 3,3'-bipyridines, few general routes have been described whatever the symmetry of the molecule: besides the synthesis of symmetrical 6,6'-disubstituted-3,3'-bipyridines by a Ni(0)-coupling of 3-halopyridines,¹⁰ only, to our knowledge, the synthesis of 3-heteroarylpyridines,¹¹ and unsubstituted symmetric 3,3'-bipyridines,¹² by Pd(0)-catalyzed cross-coupling of 3-stannylpyridines or 3-pyridylboranes with heteroaryl halides or 3-bromopyridine respectively, have been reported in the literature.

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We have recently described a new general route to access to 6,6'-(disubstituted)-3,3'-bipyridine based conjugated chromophores.¹³ This new large-scale strategy was based on (i) the synthesis of a library of π -conjugated 6-substituted-3-bromopyridine building blocks (functionalized or not), (ii) their transformation to 6substituted-3-pyridylboronic ester building blocks, and (iii) the cross-coupling by the metal-catalyzed Suzuki reaction. As an example, we have reported on the synthesis of novel conjugated 6-substituted-3-bromopyridine and 6-substituted-3-pyridylboronic diester building blocks incorporating the electron-rich thienyl ring (Br(1) and B(1) respectively as reported in Schemes 1 and 2), and successfully demonstrated that such blocks can be homo- and cross-coupled in high yields and multigram scales, leading to $\{Br(1) \times B(1)\}$ type chromophores.

The goal of the present paper is to extend this strategy to push-pull chromophores, highlighting the main advantage of the synthetic pathway, that is the flexibility to combine 'tailor-made' building blocks depending on the expected mesogenic, electrochemical or optical properties of the chromophore. This second contribution describes (i) the synthesis of π -conjugated 6-substituted-3-bromopyridine building blocks incorporating or an electron donor group (**Br(2**)) either an electron attractor group (**Br(3**)) (Scheme 1), (ii) borylation of some of them by using a boronic diester (**B(2**)), and (iii) the modular preparation of different unsymmetrically 6,6'-disubstituted-3,3'-bipyridine chromophores (Scheme 2) by utilizing, for the first time to our knowledge, a nonsymmetric Suzuki-type palladium-catalyzed cross-coupling of a conjugated 6-substituted-3-pyridylborane based building block with a conjugated 6-substituted-3-bromopyridine based building block. To illustrate the versatility of this pathway, the cross-coupling of **Br(3)** with **B(1)**, and of **Br(3)** with **B(2)** have been tested, giving (I) and (II) as $\{Br(3) \times B(1)\}$ and $\{Br(3) \times B(2)\}$ type chromophores respectively. Moreover, as shown in Schemes 1 and 2, the lateral substitution of the pyridinic ring was also a parameter of the cross-coupling.

The key materials, 2,3-dimethyl-5-bromopyridine (1a) and 2-methyl-5-bromopyridine (1b), were prepared as described previously.⁶ The hydroxyl group of (5) was protected with TBDMS, which is chosen because it can tolerate later lithiation. The hydroxy functionalized derivative (3) was obtained by formylation, with *n*-butyllithium (*n*-BuLi) and DMF, of the protected 2-(2-thienyl)ethanol, as shown in Scheme 1. The detailed procedure has been reported previously.¹³

Two different routes were used for the synthesis of the conjugated 6-substituted-3-bromopyridine building blocks, depending on the electron-donor or electron-attractor character of the substituent. We have previously defined a two-step procedure to access the building block with electron-rich ring (**Br(1**)). This route has been adapted for the synthesis of the building block bearing the protected p-hydroxybenzaldehyde as



Scheme 1. Obtention of bromo building blocks Br(1), Br(2) and Br(3).



Scheme 2. Obtention of boronic esters building blocks B(1)-B(2), and chromophores I-II.

donor group. In this general procedure, reaction of (1a) with lithium diisopropylamide (LDA) generated the red-colored lithio-anion, which reacted with the appropriate aldehyde to give the corresponding alcohol (Scheme 1a). Subsequent treatment with *p*-toluenesulfonic acid produced the respective π -conjugated 6-substituted-3-bromopyridine building blocks in 80-85% yield on the 10–20 g scale: Br(1), previously described,¹³ and the new molecule Br(2). On the other hand, because the presence of the cyano electron acceptor group precludes the use of this general procedure in the case of the aldehyde (8), an alternative route has been used,¹⁴ as reported in Scheme 1b. Thus, the building blocks end-capped with the cyano substituent (Br(3a) and Br(3b)) have been obtained in reasonable yield (31%) on the multigram scale from the one-step Knoevenagel type condensation reaction, in acidic medium, of 1a and 1b respectively, with the *para*-cyanobenzaldehyde (8). The three novel compounds Br(2), Br(3a) and **Br(3b)** have been characterized by NMR spectroscopy. Whatever the synthetic sequence, the presence exclusively of the *trans*-vinylene unit was clearly evidenced by the three bonds coupling constant $({}^{3}J_{H,H} \approx 16 \text{ Hz})$ in ¹H NMR spectra.

Because our synthetic approach is based on the nonsymmetric Suzuki-type transition metal-catalyzed crosscoupling, previous building blocks needed to be functionalized (borylation) in a way that they can be used as building blocks in this reaction (Scheme 2). We have previously reported on a one-pot procedure for the incorporation of the coupling functionality (boronic acid diester function).¹³ It involves (i) the regiospecific lithiation at position 3 of appropriate 3-bromopyridine based building block followed by (ii) the introduction of boronic diesters. As examples, TBDMS-protected hydroxy functionalized building block **Br(1)** and **Br(2)** has been converted to boronated building blocks **B(1)** and **B(2)** upon reaction with *n*-BuLi and 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in anhydrous THF. The new compound **B(2)** was isolated, after purification, in a 90% yield, and a multigram scale. As **B(1)**, this compound is stable. However, it should be noted that this route is not available for building blocks bearing the electron-withdrawing cyano-group, because of the sensitivity of this one towards *n*-BuLi.

As our main aim was to use the palladium-catalyzed Suzuki cross-coupling for the preparation of various push–pull chromophores, two representative chromophores (I–II) have been synthesized.¹⁵ As sketched in Scheme 2, the brominated building block **Br(3)** was coupled with the pyridylborane based building blocks (**B1** and **B2**), giving, after deprotection, chromophores I and II respectively in 75% yield and on the gram scale. Chromophores I and II bearing a hydroxyl group could be grafted as side-groups, onto a polymer backbone. All these compounds had spectral data consistent with the assigned structure.¹⁶

Because linear optical properties of **II** have been reported elsewhere, only the absorption and emission characteristics of **I** in solution have been measured. As illustrated in Figure 1, **II** exhibits an intense absorption band in the UV-blue range ($\lambda_{abs} = 383$ nm), whatever the solvent, which indicates that no noticeable solvatochromic shift is observed. This is a feature of this series of chromophores, in contrast to typical NLO ones. The value of λ_{abs} lies near the one of **I** (373 nm). On the other hand, an evolution of the position of the



Figure 1. Normalized absorption and fluorescence emission spectra of I in dioxane, CH_2Cl_2 and DMF.

emission maximum is observed according to the solvent polarity. A large shift (2600 cm⁻¹) is observed when dioxane is replaced with DMF. This large solvatochromic behavior observed for the new molecule I is attributed to an intramolecular charge transfer (ICT) state involving charge separation within the whole molecule, inducing consequently a large dipole moment for the excited state, and NLO properties as observed for the other push–pull chromophores of this series.⁷ Because the thienyl group is a weak donor group, the NLO properties should be relatively low, similar to the ones measured previously for II ($\mu\beta \sim 20 \times 10^{-48}$ esu). It should be noted that the goal of this work was not to synthesize chromophores with large molecular nonlinearities, but to test a synthetic strategy.

In summary, we have defined a combinatorial strategy to synthesized symmetric,¹³ and nonsymmetric 6,6'-(disubstituted)-3,3'-bipyridine based conjugated chromophores. First we have described the synthesis of novel conjugated 6-substituted-3-bromopyridine and 6substituted-3-pyridylboronic diester building blocks. Second, we have successfully demonstrated, for the first time, that such blocks can be homo- and cross-coupled in high yields and multigram scales under standard Suzuki-type conditions. This versatile approach opens up the way to develop this family of reactive chromophores for optoelectronics, and more particularly to obtain new chromophores with enhanced NLO performances by using stronger electron-donor and -acceptor groups.

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- 14. 2,3-Dimethyl-5-bromopyridine (1b) (4.255 g, 22.9 mmol), 4-cyanobenzaldehyde (2) (3 g, 22.9 mmol) and p-toluenesulfonic acid (0.805 g, 4.58 mmol) were blended. The mixture was then stirred at 160°C. After 36 h, the mixture was cooled to room temperature and washed with brine. The aqueous layer was extracted with dichloromethane. The resulting organic layer was washed with distilled water and dried over Na2SO4. The solvent was removed under reduced pressure. The crude product was purified by three washings with acetone. 2.14 g (7.16 mmol) of clear powder was obtained (Yield: 31%). ¹H NMR (CDCl₃) δ [ppm]: 2.45 (s, 3H), 7.35 (d, 1H, ${}^{3}J_{H,H}$ =15.7 Hz), 7.65 (m, 5H), 7.79 (d, 1H, ${}^{3}J_{H,H} = 15.7$ Hz), and 8.52 (d, 1H, ${}^{4}J_{\text{H,H}} = 2.3$ Hz). 13 C NMR (CDCl₃) δ [ppm]: 17.8, 110.7, 118.1, 118.7, 125.7, 126.7, 126.9, 127.1, 131.6, 132.1, 139.6, 140.0, 140.5, 147.3, 147.7 and 150.4.
- 15. Typical procedure: Dioxaborolane derivative B(1) (1.518 g, 3.2 mmol), bromide derivative Br(3a) (0.90 g, 3.2 mmol) and (PPh₃)₄Pd(0) (0.5-2.0 mol%) were dissolved in a mixture of THF ([B(1)] = [Br(3a)] = 0.4 M) and aqueous 2 M K₂CO₃ (1:1.5 THF). The solution was first put under argon atmosphere and was heated at 80°C with vigorous stirring for 48 h. After extraction, the aqueous layer was extracted with dichloromethane and the combined dichloromethane layers were washed with distilled water and dried over Na₂SO₄. The solvent was removed under reduced pressure. The crude product was crystallized twice from hexane and acetonitrile, yielding compound I, protected (1.39 g, 2.62 mmol, 82%). Dimethyl-tertbutylsilyl ethers are cleaved rapidly to alcohols by treatment with fluoride acid (10 equiv.) in tetrahydrofuran at room temperature for 5 h. Then the mixture was poured into ammoniac solution. The two phases were separated. The aqueous phase was extracted with dichloromethane and the combinated organic phases were washed with

distilled water and dried over Na_2SO_4 . The crude product was precipitated from dichloromethane solution into hexane solution, yielding pure chromophore I (1.06 g, 2.37 mmol, 74%).

16. Selected data for I: ¹H NMR (CDCl₃) δ [ppm]: 2.49 (s, 3H), 2.91 (t, 2H), 3.62 (m, 2H), 4.85 (s, 1H), 6.77 (d, 1H, ³J_{H,H}=3.5 Hz), 7.05 (d, 1H, ³J_{H,H}=3.8 Hz), 7.06 (d, 1H, ³J_{H,H}=15.2 Hz), 7.30 (d, 1H, ³J_{H,H}=16.2 Hz), 7.49 (d, 1H, ${}^{3}J_{\rm H,H}$ = 7.8 Hz), 7.67 (s, 4H), 7.68 (d, 1H), 7.71 (d, 1H, ${}^{3}J_{\rm H,H}$ = 14.2 Hz), 7.91 (dd, ${}^{3}J_{\rm H,H}$ = 8 Hz, ${}^{4}J_{\rm H,H}$ = 2.5 Hz), 7.93 (d, 1H, ${}^{3}J_{\rm H,H}$ = 15.9 Hz), 8.70 (d, 1H, ${}^{4}J_{\rm H,H}$ = 2.3 Hz) and 8.89 (d, 1H, ${}^{4}J_{\rm H,H}$ = 2 Hz). 13 C NMR (CDCl₃) δ [ppm]: 18.9, 40.7, 63.8, 111.4, 118.8, 121.5, 122.8, 124.7, 126.1, 127.5, 128.3, 130.5, 130.6, 130.7, 130.9, 131.9, 132.5, 134.4, 134.6, 135.6, 135.9, 137.9, 140.68, 141.0, 142.6, 144.3, 144.4, 145.1, 147.9, 148.0, 153.3, 153.7, 153.8 and 154.7.