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6-(Arylvinylene)-3-pyridinylboronic esters. Part 1: Versatile building blocks for conjugated chromophores via Suzuki cross-coupling

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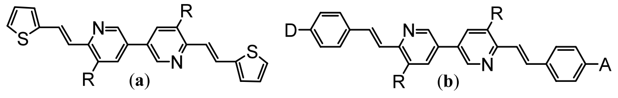
Abstract—This paper describes a general approach for the synthesis of conjugated 6,6′-disubstituted-3,3′-bipyridine chromophores. As preliminary results, 6-(4-hexyl-2-thienylvinylene)-5-methyl-3-bromopyridine, 6-(4-ethanol-2-thienylvinylene)-5-methyl-3-bromopyridine, and the corresponding 3-pyridinylboronic esters have been prepared. Coupled by Suzuki reaction, they gave the conjugated chromophores (**I**) and (**II**) in high yields and multigram scales.

π-Conjugated organic compounds have emerged as a promising class of materials for use in electronics and optoelectronics. Besides semi-conducting (conjugated) main-chain polymers used in light emitting devices (LEDs),[1] third-order nonlinear optics (NLO),[2,3] and photovoltaic cells,[4] are the side-chain polymers (SCPs) which have been investigated as active layers in LEDs,[5] and mainly as second-order NLO materials.[2,6] In these SCPs, active conjugated chromophores are covalently bound on a saturated polymer backbone as pendant groups.

In previous papers,[7–9] we have described a novel class of conjugated chromophores.



R = H, Me   D = OC_6H_{13}, $N(C_4H_9)_2$ A = CN, NO_2

These compounds are either symmetric molecules (**a**) or non-symmetric 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 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,[7,8] electrochemical,[7,8] photoluminescent,[7,8] and second-order NLO properties of the push–pull chromophores ((**b**) series).[8] We have also shown that symmetrical π-conjugated bridge on the one hand, and reduction of the ground-state aromatic character by incorporating thienyl ring as electron-rich moiety in the π-conjugated system on the other hand, enhanced the third-order NLO properties ((**a**) series).[9]

Considering all the above molecules as model compounds, the use of aldehydes bearing reactive functionalities (e.g., hydroxyl groups) at one end should offer the opportunity to synthesize reactive chromophores able to be grafted on a macromolecular chain, in order to obtain side-chain polymers exhibiting NLO and/or emitting properties. It should be noted that whatever the structure of parents (symmetric chromophores (**a**) or push–pull (**b**)), all the expected functionalized molecules are unsymmetrical. However, despite the above-mentioned attractive features, the previous two steps synthetic route, in the case of the non-symmetric chromophores, restricts the yield because of separation and purification difficulties, and consequently the potential 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.

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While synthetic approaches to 2,2′-bipyridines and its derivatives are well-established in the literature,[10a–c] there are few strategies leading to unsymmetrical disubstituted 2,2′-bipyridines.[10d,e] They are mainly based on palladium-catalyzed (Stille or Suzuki) cross-coupling reactions of pyridine rings. 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,[11] only, to our knowledge, the synthesis of 3-heteroarylpyridines,[12] and unsubstituted symmetric 3,3′-bipyridines,[13] 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.[14] In this context, it was a challenge to define a new, versatile and more efficient synthetic route, which allows the preparation of unsymmetrical functionalized π-conjugated 6,6′-disubstituted-3,3′-bipyridine derivatives.

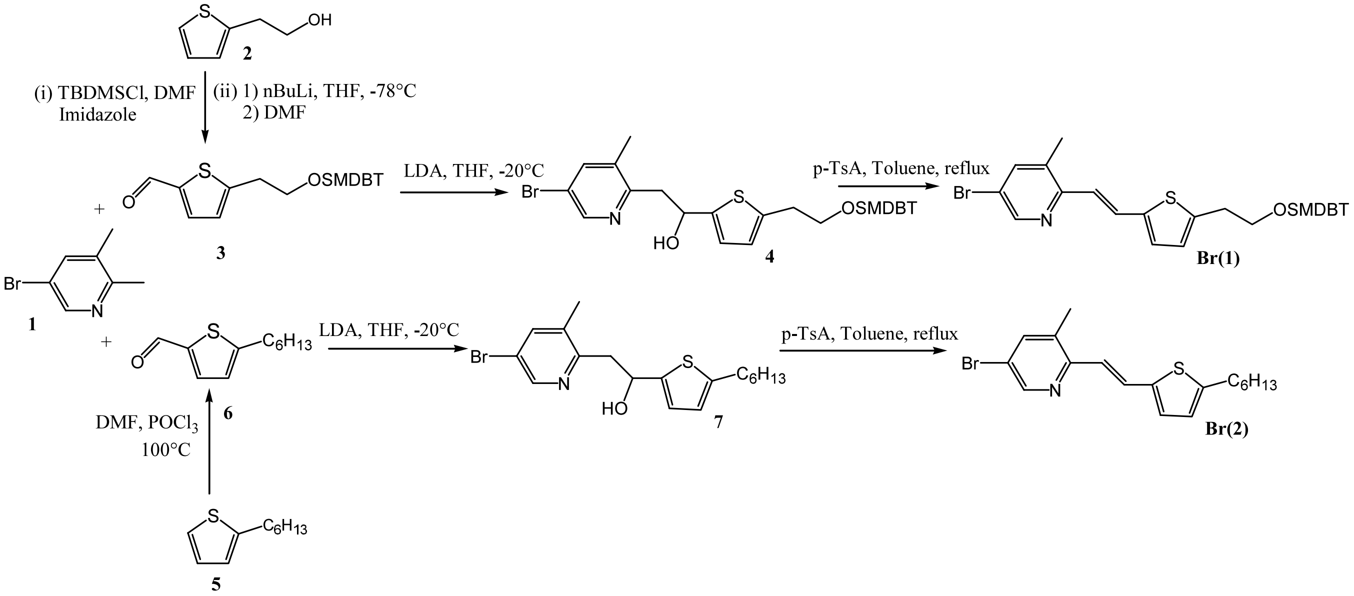
This new large-scale strategy is based on (i) the synthesis of a library of π-conjugated 6-substituted-3-bromopyridine building blocks (functionalized or not), (ii) their transformation to 6-substituted-3-pyridylboronic ester building blocks, and (iii) the cross-coupling by the metal-catalyzed Suzuki reaction. The main advantage of this synthetic pathway is the flexibility to combine 'tailor-made' building blocks depending on the expected mesogenic, electrochemical or optical properties of the chromophore. It should be noted that this route allows also the synthesis of symmetrical compounds.

This first contribution describes (i) the synthesis of π-conjugated 6-substituted-3-bromopyridine building blocks incorporating the electron-rich thienyl ring (Scheme 1), (ii) borylation of them by using a boronic diester, and (iii) the modular preparation of different (un)symmetrically 6,6′-disubtituted-3,3′-bipyridine chromophores by utilizing, for the first time at our knowledge, an non-symmetric 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 (Scheme 2).

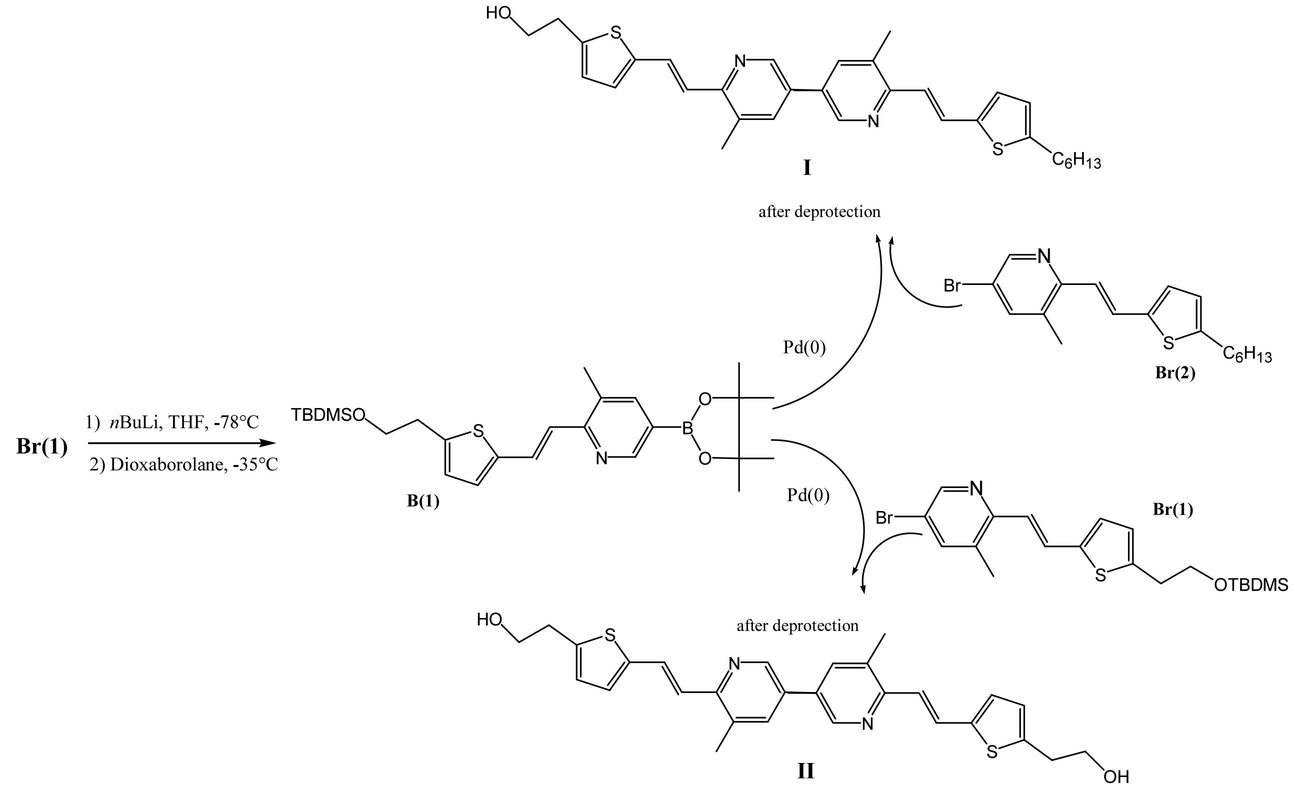
The starting materials, 2,3-dimethyl-5-bromopyridine (**1**), was prepared as described previously.[7] As reported in Scheme 1, the hydroxy functionalized derivative (**3**) was obtained by formylation, with *n*-butyllithium (*n*-BuLi) and DMF, of the protected 2-(2-thienyl)ethanol, whereas the 5-hexyl-2-thiophenecarboxaldehyde (**6**) was obtained by formylation (Vilsmeier–Haack reaction) of 2-hexylthiophene.

Since the Knoevenagel type condensation, under acidic conditions,[7] afforded building blocks with electron-rich ring (**Br(1)**, **Br(2)**) in poor yield, an alternative pathway, adapted from a procedure reported in the literature[15] for symmetrical 4,4′-disubstituted-2,2′-bipyridines, has been defined. Reaction of (**1**) with lithium diisopropylamide (LDA) generated the red-colored lithio-anion, which reacted with the appropriate aldehyde to give the corresponding alcohol (Scheme 1). Subsequent treatment with *p*-toluenesulfonic acid produced the respective π-conjugated 6-substituted-3-bromopyridine building blocks **Br(1)** and **Br(2)** in 80–85% yield on the 10–20 g scale. The presence exclusively of the *trans*-vinylene unit is clearly evidenced by the three bonds coupling constant ($^{3}J_{H,H} \approx 16$ Hz) in ^{1}H NMR spectra.

Because our synthetic approach is based on the non-symmetric Suzuki-type transition metal-catalyzed cross-coupling, previous building blocks needed to be functionalized (borylation) in a way that they can be used as building blocks in this reaction (Scheme 2). The incorporation of the coupling functionality (boronic



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



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

acid diester function) involves (i) the regiospecific lithiation at position 3 of appropriate 3-bromopyridine based building block followed by (ii) the introduction of boronic diesters. Recently, a two-steps synthesis of 3-pyridinylboronic esters has been reported,[12c] based on the preparation of the 3-pyridinylboronic acid, followed by the in situ transesterification with pinacol. By adapting standard procedures described for borylation of aryl halides, we have performed the obtention of the pyridinylboronic ester in a one-pot procedure.[16] As an example, TBDMS-protected hydroxy functionalized building block **Br(1)** has been converted to boronated building blocks **B(1)** upon reaction with n-BuLi and 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane in anhydrous THF. **B(1)** was isolated, after purification, as yellowish oil, in a 90% yield, and a 10 g scale. This compound is stable.

As our main aim was to use the palladium-catalyzed Suzuki cross-coupling for the preparation of various π-conjugated 6,6′-disubstituted-3,3′-bipyridine derivatives, two representative chromophores (**I**–**II**) have been synthesized.[17] As sketched in Scheme 2, the brominated building block **Br(1)** was coupled with various pyridylborane based building blocks (BrD1 and BrD2), giving, after deprotection, chromophores **I** and **II** respectively in 70–76% yield and multigram scale. After deprotection, chromophores **I** bearing a hydroxyl group could be graft as side-group, onto a polymer backbone, whereas **II** could be used as difunctional monomer and introduced in a main-chain polymer. All these compounds had spectral data consistent with the assigned structure.[18]

Preliminary linear optical measurements (i.e. absorption and emission spectra) have been performed in dichloromethane. **I** and **II** exhibited a strong and intense ($\varepsilon = 78000$ L mol^{-}1 cm^{-1}) low-lying absorption band (395 nm), which indicates a highly π-conjugated system, and intense fluorescence at 490 nm.

In summary, we have defined a strategy to synthesized symmetric and non-symmetric 6,6′-(disubstituted)-3,3′-bipyridine based conjugated chromophores. First we have described the synthesis of novel conjugated 6-substituted-3-bromopyridine and 6-substituted-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. Further experiments concerning the synthesis of push–pull chromophores by using this approach are currently under investigation. These results as well as more information about the photophysical properties will be published elsewhere.

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16. To a solution of compound **Br(1)** (9.62g, 22.6 mmol) in dry THF (170 mL) stirred at −78°C under argon was added dropwise a solution of *n*-BuLi 2.5 M in hexane (9.16 mL, 22.9 mmol). The mixture was stirred at −78°C for 20 min. Then the 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxoborolane (4.73 mL, 23.2 mmol) was added, the stirring was kept at −78°C for 2 h. The mixture was warm up slowly to −35°C and stirred at this temperature for 1 h. The mixture was pourrred into water. The aqueous layer was extracted with diethyl ether and the combinated diethyl ether layers were washed with distilled water and dried over Na_2SO_4. The solvent was removed under reduced pressure. The crude product was purified by filtration on silica (chlorform–ethyl acetat 9:1) yielding pure compound **B(1)** (9.97 g, 20.5 mmol) in a 91% yield as yellowish oil.
17. Typical procedure: dioxaborolane derivative **B(1)** (7.06 g, 14.6 mmol), bromide derivative **Br(2)** (5.3 g, 14.6 mmol) and $(PPh_3)_4Pd(0)$ (0.5–2.0 mol%) were dissolved in a mixture of THF ($[B(1)] = [Br(2)] = 0.4$ M) and aqueous 2M K_2CO_3 (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 Na_2SO_4. The solvent was removed under reduced pressure. The crude product was crystallized twice from hexane and acetonitrile, yielding compound **I**, protected (7.68 g, 12.2 mmol, 84%). Dimethyl-*tert*-butylsilyl 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** (5.8 g, 11 mmol, 76%).
18. Selected data for: **I**: mp = 143.4°C. ^{1}H NMR (DMSO d_6) δ [ppm]: 0.88–1.66 (m, 11H), 2.47 (s, 6H), 2.77 (t, 2H), 2.93 (t, 2H), 3.63 (t, 2H), 4.86 (t, 1H), 6.80 (d, 1H, $^3J_{H,H} = 3.29$ Hz), 6.84 (d, 1H, $^3J_{H,H} = 3.54$ Hz), 7.01 (dd, 2H, $^3J_{H,H} = 15.16$ Hz, $^4J_{H,H} = 4.03$ Hz), 7.17 (d, 1H, $^3J_{H,H} = 3.29$ Hz), 7.19 (d, 1H, $^3J_{H,H} = 3.29$ Hz), 7.82 (dd, 2H, $^3J_{H,H} = 15.16$ Hz, $^4J_{H,H} = 1.01$ Hz), 7.9 (d, 2H, $^4J_{H,H} = 2.02$ Hz), and 8.77 (d, 2H, $^4J_{H,H} = 2.02$ Hz). ^{13}C NMR (DMSO d_6) δ [ppm]: 14.4, 18.6, 22.5, 28.6, 30.1, 31.4, 34.1, 62.1, 122.1, 126, 126.7, 126.98, 127.02, 129.2, 129.4, 130.79, 130.83, 136, 140.1, 140.5, 143.5, 145.1, 146.7, and 152.3. **II**: mp = 198.3°C. ^{1}H NMR (DMSO d_6) δ [ppm]: 2.42 (s, 6H), 2.91 (t, 4H), 3.62 (d, 4H, $^3J_{H,H} = 4.8$ Hz), 4.85 (s, 2H), 6.83 (d, 2H, $^3J_{H,H} = 3.03$ Hz), 7.00 (d, 2H, $^3J_{H,H} = 15.15$ Hz), 7.17 (d, 2H, $^3J_{H,H} = 3.03$ Hz), 7.85 (d, 2H, $^3J_{H,H} = 15.41$ Hz), and 7.94 (s, 2H), 8.76 (s, 2H). ^{13}C NMR (DMSO d_6) δ [ppm]: 19.3, 40.7, 62.8, 122.8, 127.5, 127.8, 129.9, 131.6, 136.7, 141.2, 144.3, 145.9, 153.0.