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A convenient method of producing thiophene linked bipyridine oligomers

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Abstract—A series of soluble polybipyridine ligands comprising one to five bipyridine modules sandwiched between rigid carbon–carbon triple bonds substituted by 3,4-dibutylthiophene repeating units was synthesized. Two different protocols have been explored with the idea to use a divergent/convergent approach starting from bisymmetrically and symmetrically substituted bipyridine modules. At each stage of the iteration two bipy/thiophene modules are connected. The use of triethylsilylacetylene and 2-methylbut-3-yn-2-ol insures an easy entry to pivotal building blocks, which could be selectively deprotected from the TES or 2-hydroxyprop-2-yl sites. All cross-coupling reactions are promoted with palladium(0) tetrakistriphenylphosphine under mild conditions.

The design and tailoring of new molecules with special electrochemical and/or optical properties for application in the fields of supramolecular chemistry,[1] molecular materials[2] and nanoelectronic architectures,[3] has received considerable attention over the past several years. Such systems may play crucial roles in the areas of light emitting materials for displays,[4] sensors in environmental chemistry,[5] photocatalysis[6] and energy supply systems.[7] Following a lot of successful examples of luminescent transition metals complexes[8] it is still highly challenging to achieve the preparation of segmented multitopic ligands in which each compartment is connected to its neighbour via an unsaturated linker. To achieve such a conjugation our particular interest has been directed at the development of alkyne and alkene connectors.[9,10] We have recently reported that heterotopic ligands constructed from a large variety of oligopyridines are easily produced in good yields. Whereas this approach seems promising for efficient CC couplings, the prospects seem less hopeful for the selective complexation sequence.[10] This is due to the high reactivity of the metal precursors and the lack of selectivity of the incoming bi- or tridentate ligand fragment. Therefore, we decided to start a programme for the construction of homotopic ligands in which each bipyridine module is connected to a 3,4-dibutyl-2,5-diethynylthiophene fragment and end-capped by a 3,4-dibutyl-2-ethynylthiophene fragment. Such features will insure that each unit lies in the same electronic and topological environment. These sophisticated molecular structures should allow to shed more light on multinuclear transition metal systems with the aim of studying light harvesting and energy conversion systems. In these respects, we examined different synthetic strategies for the step-by-step construction of homopolypyridine architectures. The representative targets are sketched in Chart 1.

The choice of thiophene is motivated by the prominent role it plays in *plastic electronics*[11] whereas the ethynyl and butyl functions will, respectively, insure a good

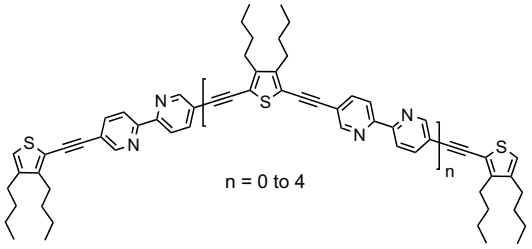

Chart 1.

Keywords: Segmented ligands; Thiophene; Bipyridine; Triple bonds; Palladium.
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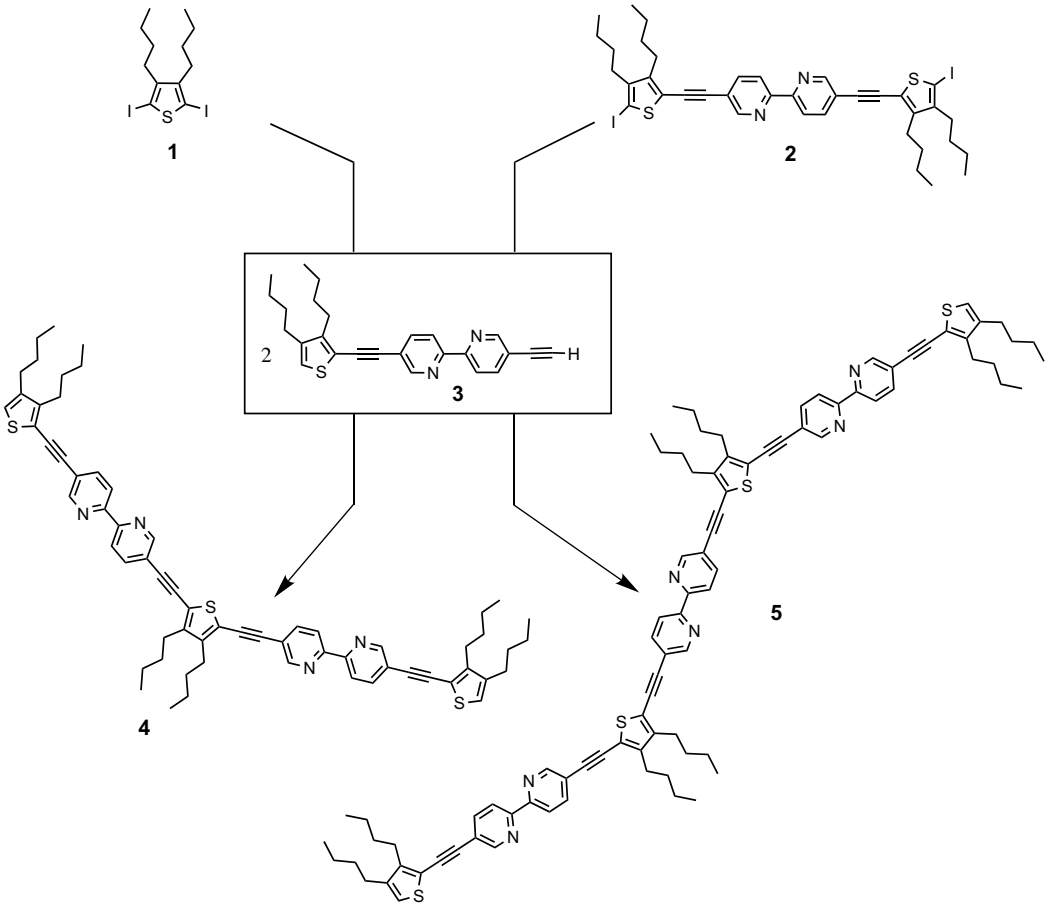
electronic connectivity and solubility of the oligomers. From a general point of view bipyridine and thiophene have been associated in molecular[12] or polymeric structures.[13] Firstly, we examined the simplest route for the synthesis of the dimer and trimer using, as shown in Scheme 1, a common building block **3**.

The first trial is to prepare the starting material **3** (Scheme 2). As foreseen, the mono-substitution of 5,5′-dibromo-2,2′-bipyridine using a single acetylene source in sub-stoichiometric conditions failed due to the very difficult separation step induced by the close polarity of the resulting products. After some experimentation we were pleased to find that access to derivative **3** first requires the dissymmetrization of the bipyridine framework by a palladium promoted reaction with two different acetylene sources displaying different polarities. We succeeded to produce the pivotal intermediate (TES or TMS/2-hydroxyprop-2-yl alcohol) in 33% isolated yield by the mean of a facile chromatographic separation from the less-polar bis-TES or TMS derivatives and the most polar bis-2-hydroxyprop-2-yl derivative (Scheme 2). These side products could be used in the production of symmetrically substituted bipyridine synthons.

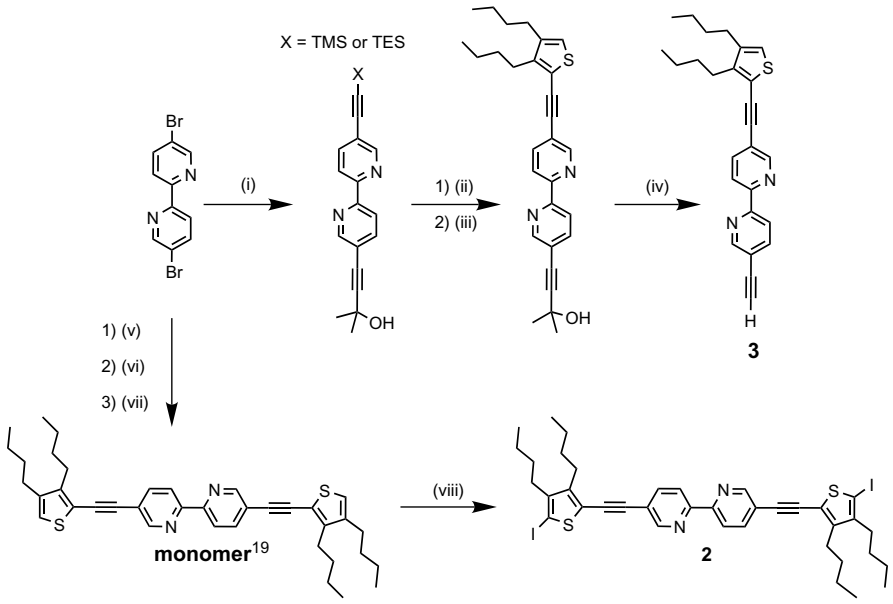
As previously reported subjecting 5,5′-dibromo-2,2′-bipyridine to 2 equiv of TMS–acetylene followed by deprotection of the TMS is straightforward and effective under mild conditions.[14] Reaction of 5,5′-diethynyl-2,2′-bipyridine with 3,4-dibutyl-2-iodothiophene[15] gives the dithienyl compounds, which is readily metallated with LDA at low temperature. Subsequent reaction with iodine afforded compound **2** in fair yield. With these two starting materials in hands it was easy to produce the dimer and trimer by cross-coupling half an equivalent of 3,4-dibutyl-2,5-diiodothiophene[15] or compound **2** with 2 equiv of compound **3** in the presence of low valent palladium(0) complexes (Scheme 1).[16] The dimer[17] and trimer[18] were produced in, respectively, 70% and 86% isolated yields. The monomer[19] was synthesized in 71% yield according to a three-step protocol sketched in Scheme 2.

Unfortunately, both dimer and trimer remain unreactive towards metallation and iodation sequence of reactions and consequently this drastically limits the engineering of the higher oligomers by implementation with building block **3**. However, these ligands are themselves interesting scaffolds for the complexation of luminescent transition metals.

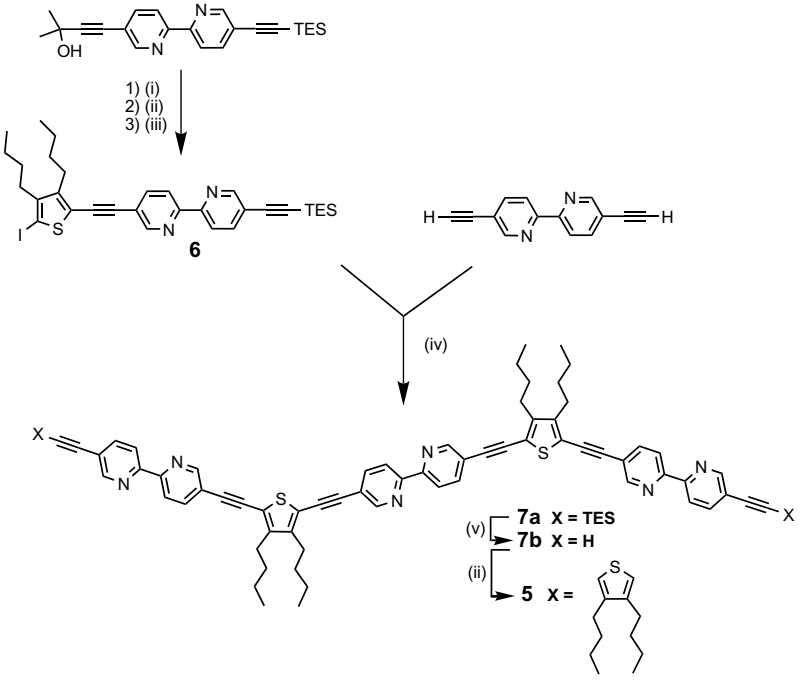
One elegant way to circumvent this lack of reactivity is to suggest a protocol where the pivotal building block carries an iodothiophene group on one side and a kinetically stable and protected acetylene function on the



Scheme 1.



Scheme 2. Reagents and conditions: (i) $[PdCl_2(PPh_3)_2]$, CuI, THF, *i*-Pr_2NH, rt, HC≡CX, then HC≡CMe_2OH, for X = TMS: 33%, for X = TES: 31%; (ii) For X = TMS: KF, MeOH, THF, 96%; (iii) 3,4-dibutyl-2-iodothiophene, $[Pd(PPh_3)_4]$, *n*-$PrNH_2$, 60 °C, 98%; (iv) NaOH, toluene, 130 °C, 97%; (v) $[PdCl_2(PPh_3)_2]$, CuI, THF, *i*-Pr_2NH, rt, acetylene TMS, 77%; (vi) KF, MeOH, THF, 97%; (vii) 3,4-dibutyl-2-iodothiophene, $[Pd(PPh_3)_4]$, benzene, Et_3N, 60 °C, 95%; (viii) LDA, I_2, THF, −78 °C, 83%.



Scheme 3. Reagents and conditions: (i) NaOH, anhydrous toluene, 130 °C, 97%; (ii) 3,4-dibutyl-2-iodothiophene, $[Pd(PPh_3)_4]$, benzene, Et_3N, 60 °C, compound **6**: 86%, compound **5**: 86%; (iii) LDA, NIS, THF, −78 °C, 80%; (iv) $[Pd(PPh_3)_4]$, benzene, Et_3N, 60 °C, 93%; (v) K_2CO_3, MeOH, THF, 90%.

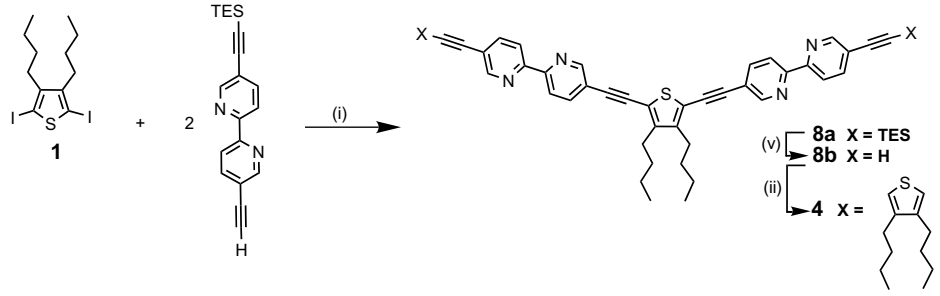
other side. This approach would lead to oligomers with TES acetylene end groups, which might be easily deprotected and able to react smoothly with 3,4-dibutyl-2-iodothiophene. Indeed, the key derivative **6** is prepared as sketched in Scheme 3 from the dissymmetrically substituted TES/2-hydroxyprop-2-yl bipyridine moiety by a sequence of reactions including: (i) a selective deprotection of the 2-hydroxyprop-2-yl with NaOH in refluxing anhydrous toluene,[20] (ii) a cross-coupling reaction with 3,4-dibutyl-2-iodothiophene and finally (iii) a metallation with LDA at −78 °C followed by a reaction with iodine. A double cross-coupling reaction with 5,5′-diethynyl-2,2′-bipyridine provides the TES protected trimer **7a**, readily deprotected to **7b**. Finally, trimer **5** is likely synthesized by double cross-coupling of compound **7b** with 3,4-dibutyl-2-iodothiophene.

We next turned our attention to the dimer **4**, which could be conveniently produced in a similar fashion by a double cross-coupling of the 3,4-dibutyl-2,5-diiodothiophene with a dissymmetrically substituted TES/2-hydroxyprop-2-yl bipyridine synthon, followed by deprotection and end-capping with 3,4-dibutyl-2-iodothiophene (Scheme 4). In the latter synthetic scheme the choice of a TES versus TMS protecting group is motivated by its good chemical stability.

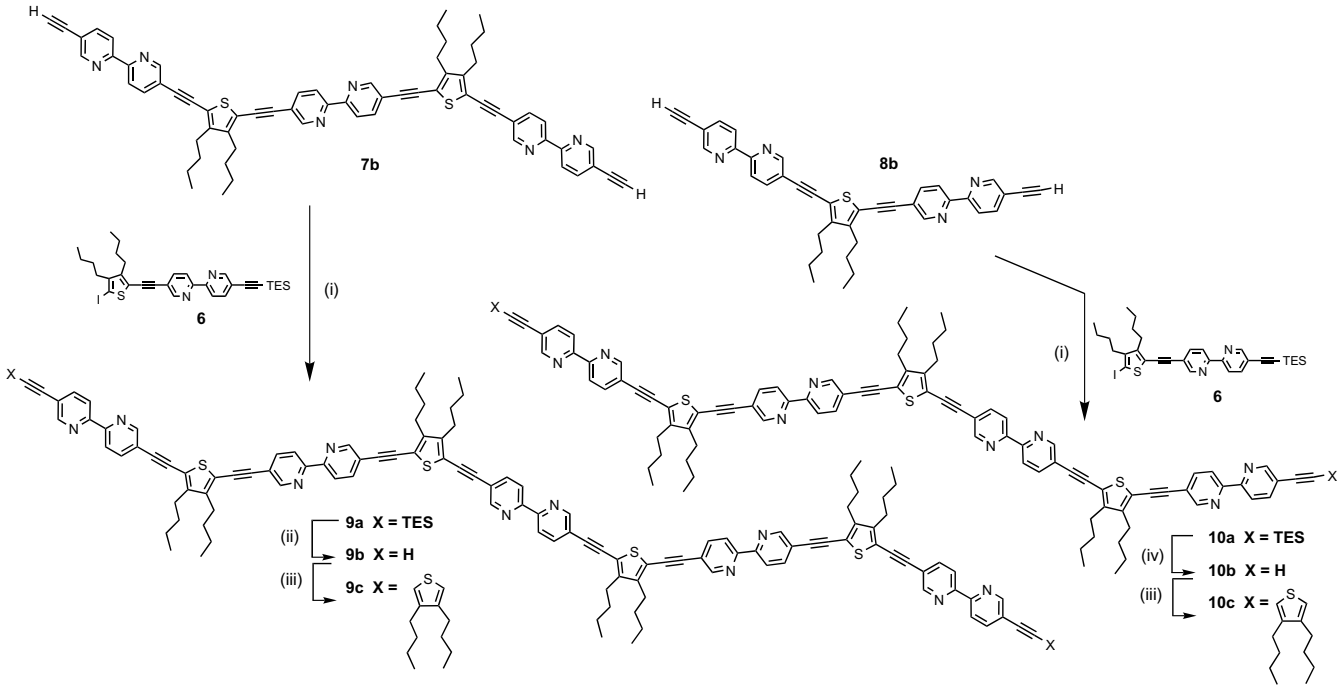
Interestingly, derivatives **7b** and **8b** are useful platforms for the preparation of the larger oligomers. For instance, reaction of intermediates **7b** and **8b** with compound **6** affords the opportunity to increase the molecular size by adding two supplementary bipy/thiophene modules. The pentamer and tetramer precursors **9a** and **10a** could be end-capped by subsequent deprotection and reaction with 3,4-dibutyl-2-iodothiophene leading to the target ligand **9c**[21] and **10c**[22] (Scheme 5).

The ^{1}H NMR allows us to properly characterize the five ligands. We can notice that the size of the ligands has no influence on the chemical shift values of any protons of the molecules. For each of them, we found three signals at 8.78, 8.43 and 7.90 ppm for the bipyridine protons, one singlet at 6.92 ppm for thiophene protons and two signals for the CH_2, in α-position of the thiophenes at 2.75 and 2.53 ppm. This second signal is a triplet, integrating for four protons corresponding to the α-CH_2 of the two external chains on the two 'end' thiophene rings. These observations confirm that each unit (bipyridine/C≡C triple bond/3,4-dibutylthiophene/C≡C triple bond) lies in the same electronic and topological environment.

In summary, we have outlined linear multistep protocols for the synthesis of symmetrically and unsymmetrically substituted bipyridine synthons from readily available precursors. These molecules were used to prepare



Scheme 4. Reagents and conditions: (i) $[Pd(PPh_3)_4]$, benzene, Et_3N, 60 °C, 53%; (ii) K_2CO_3, MeOH, THF, 96%; (iii) 3,4-dibutyl-2-iodothiophene, $[Pd(PPh_3)_4]$, benzene, Et_3N, 60 °C, 70%.



Scheme 5. Reagents and conditions: (i) $[Pd(PPh_3)_4]$, benzene, Et_3N, 60 °C, compound **9a**: 86%, compound **10a**: 87%; (ii) KF, THF, MeOH, 80%; (iii) 3,4-dibutyl-2-iodothiophene, $[Pd(PPh_3)_4]$, benzene, Et_3N, 60 °C, compound **9c**: 38%, compound **10c**: 33%; (iv) K_2CO_3, THF, MeOH, 81%.

new-segmented ligands bearing a controlled number of chelating fragments in a convergent manner by a rational approach using palladium catalyzed CC bond formation reactions. Notice that each bipyridine unit is from an electronic point of view in the same environment and that such a protocol may serve as a useful handle for further manipulation. Work is currently in progress in order to further define the overall scope of the sequence and to complex the free sites with luminescent metals. The results of these findings will be reported in the due course.

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17. Spectral data for dimer **4**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.78 (m, 4H), 8.43 (m, 4H), 7.89 (m, 4H), 6.92 (s, 2H), 2.75 (m, 8H), 2.53 (m, 4H), 1.53 (m, 24H), 0.98 (m, 18H); FAB^+ *m/z* (nature of the peak, relative intensity) 989.5 ($[M+H]^+$, 100).
18. Spectral data for trimer **5**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.78 (m, 6H), 8.43 (m, 6H), 7.89 (m, 6H), 6.92 (s, 2H), 2.72 (m, 12H), 2.53 (m, 4H), 1.52 (m, 32H), 0.98 (m, 24H); FAB^+ *m/z* (nature of the peak, relative intensity) 1385.6 ($[M+H]^+$, 100).
19. Spectral data of monomer: ^{1}H NMR (200 MHz, DCl_3): δ 8.77 (d, ^4J = 2.1 Hz, 2H), 8.41 (d, ^3J = 8.1 Hz, 2H), 7.88 (dd, ^3J = 8.1 Hz, ^4J = 2.1 Hz, 2H), 6.92 (s, 2H), 2.75 (m, 4H), 2.53 (m, 4H), 1.50 (m, 32H), 0.98 (m, 6H), 0.96 (m, 6H); FAB^+ *m/z* (nature of the peak, relative intensity) 593.3 ($[M+H]^+$, 100).
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22. Spectral data for tetramer **10c**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.78 (m, 8H), 8.43 (m, 8H), 7.90 (m, 8H), 6.92 (s, 2H), 2.75 (m, 16H), 2.53 (m, 4Hz), 1.53 (m, 40H), 0.99 (m, 30H); FAB^+ *m/z* (nature of the peak, relative intensity) 1782.7 ($[M+H]^+$, 100).