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Segmented multitopic ligands constructed from bipyrimidine, phenanthroline, and terpyridine modules

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Abstract—Starting from bromo-substituted 2,2′-bipyrimidine or 1,10-phenanthroline building blocks, the preparation in a first step of ethynyl grafted molecules allows the production in a second step of multitopic ligands by cross-coupling with difunctionalised chelating molecules. Various combinations allow the interconnection of bipyrimidine to terpyridine, pyrene, or phenanthroline fragments. When two alkyne functions are present, a simple protocol gives a large variety of linear or bent ligands with an increasing number of nitrogen atoms. It was also possible to construct a linear complex capped at the periphery by ruthenium(II) centers and retaining an uncomplexed phenanthroline fragment in its core.

The engineering of new acetylene substituted molecules has gained increasing attention due to their use in the construction of carbon rich scaffolds,[1] supramolecular systems,[2] molecular materials,[3] nanoelectronic architectures,[4] and liquid crystalline matter.[5] One of the key issue concerns how best to interconnect and interlock the various modules into ordered arrays that allow control of physical factors such as orientation of the binding vectors and electrical dipoles, electric and electronic conductivity, and amphipatic character of the molecules. Our own research into functionalised waveguides[6,7] led us to consider whether functionalised bipyrimidine and phenanthroline targets could be adapted in the synthesis of such elaborated molecules. The availability of families of molecules based on bipyridine and terpyridine ligands allow to establish firm structure/property relationship and to conclude that ethynyl spacing units are among the most interesting tools to introduce directionality and versatility in sophisticated structures. Furthermore, such acetylenic tethers offer an excellent control of the distance between the chromophoric centers due to its linearity and rigidity, and concomitantly provide a synthetic handle for further elaboration of sophisticated molecular structures. One possible feature to induce electronic directionality is reducing the redox potential of the bridge. Bipyrimidine is well known to be easier reducible than its oligopyridinic partners but could also be doubly reduced within a given potential windows.[8] It was consequently tempting to introduce such electron reservoir as spacer between two chromophoric fragments.

Following the precedent of our recent work with ethynylated polyaromatic and oligopyridinic derivatives,[9] we envisaged preparing a series of new ethynylated bipyrimidine and phenanthroline ligands with various surrounding scaffolds such as pyrenes, terpyridines, and bipyridines. The most prevalent method we found suitable for the alkynylation of oligopyridines involves Sonogashira coupling reactions between a terminal alkyne and an oligopyridinic bromide or triflate. In some cases we found this protocol to be sensitive to the reaction conditions but also to the stability of the ethynylpyridinic frameworks. In our hands, one way to avoid the formation of side-products was to apply a one-pot deprotection/cross-coupling protocol under phase transfer conditions.[10]

Access to bipyrimidine-based platforms first requires producing the key starting materials **2** and **5** with good yields (Scheme 1). Stimulated by our previous success in the large scale preparation of 5- and 5,5′-dibromo substituted 2,2-bipyridine,[11] we tested 2,2′-bipyrimidine under the same experimental conditions (pressurised vessel containing derivative **1** as a solid with neat bromine at 150–180 °C). Note that such sealed tubes must

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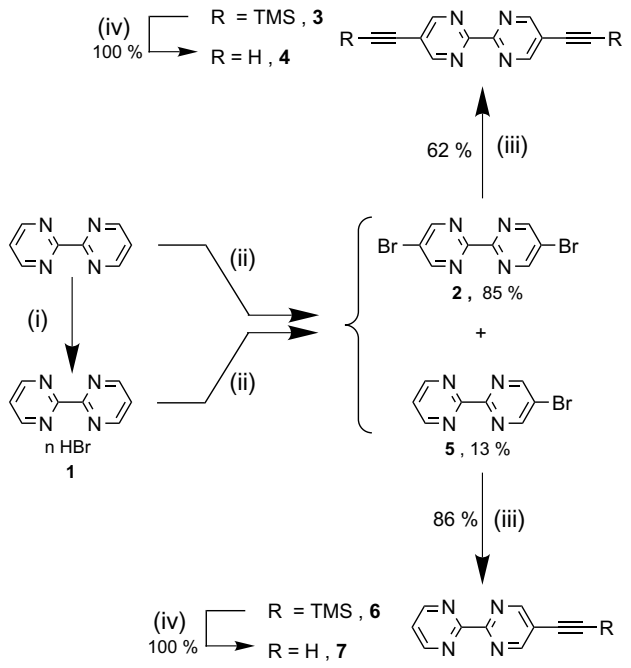


Scheme 1. (i) HBr(g), EtOH; (ii) Br_2, 150 °C; (iii) HC≡CTMS, $[PdCl_2(PPh_3)_2]$ 10 mol%, CuI 20 mol%, $^iPr_2NH$, THF; (iv) KF, MeOH, rt.

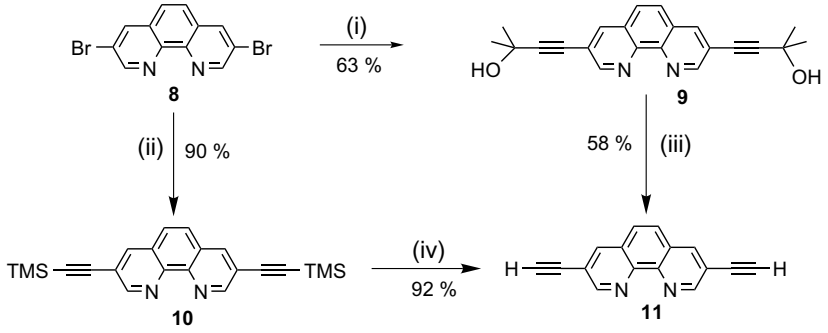
be contained in a Bomben Rohr during the heating process. As indeed expected, 5,5′-dibromo-2,2′-bipyrimidine was isolated as the main product (85% isolated yield), whereas 5-bromo-2,2′-bipyrimidine was obtained as side product (13%), in the presence of 2 equiv of bromine. Surprisingly, in this case the prior protonation of the bipyrimidine is not mandatory to obtain a good yield contrary to the bipyridine case where a mixture of compounds was obtained in the absence of protonation.[11] Note that the use of 0.8 equiv of bromine and a lower temperature (130 °C) gave rise to compound **5** in 44% yield along with unreacted starting material. Despite the fact that the reaction is difficult to monitor, the harsh conditions do not induce any degradation or formation of other brominated derivatives. This is consistent with previous observations made with protonated bipyridine derivatives.[11] Recently, 5-bromo and 5,5′-dibromo bipyrimidine derivatives have been produced in low yield in solution under severe experimental conditions.[12] In the light of our previous findings,[9] conversion of derivatives **2** and **5** into the corresponding alkynylated species **3** and **6** is straightforward and does not require special conditions (Scheme 1). Deprotection is quantitative with KF in a protic solvent leading to the key compounds **4** (FAB^+/MS: $m/z = 207.1$) and **7** (FAB^+/MS: $m/z = 193.1$).

Unfortunately, the preparation of similar phenanthroline targets by a conceptionally similar approach did not proceed. As foreseen, the presence of the double bond bridging both pyridines is detrimental for the bromination procedure. Indeed, 3-bromo-, and 3,8-dibromo-1,10-phenanthroline were prepared according to the literature procedure.[13] Standard Sonogashira coupling of **8** with trimethylsilyl acetylene or propargylic alcohol yielded after standard deprotection the desired compound **11** in fair yields (Scheme 2). Notice that the propargylic route is less efficient but significantly cheaper compared to the use of preformed trimethylsilylacetylene.

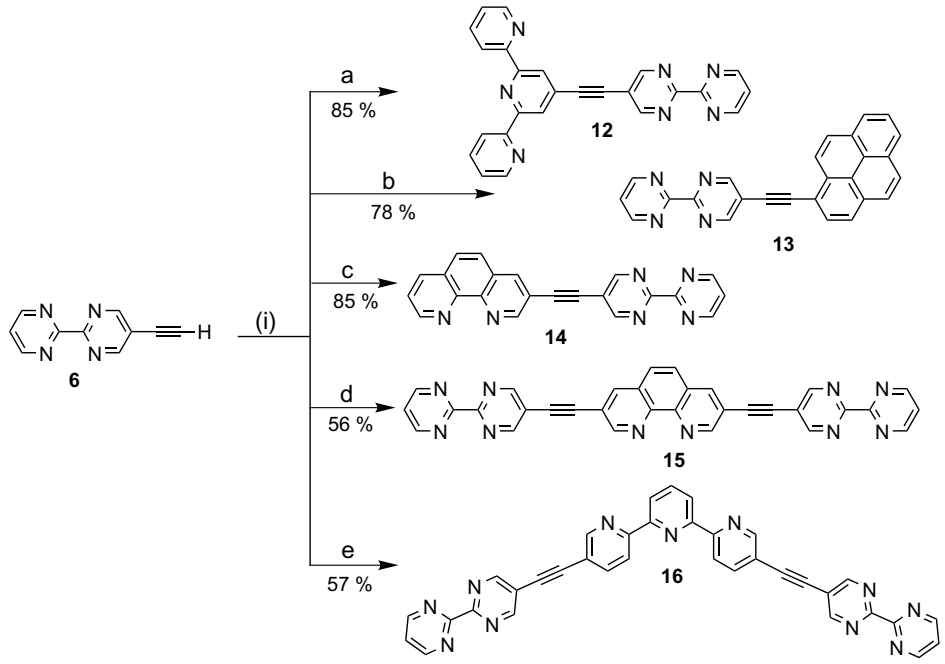
In an attempt to test the reactivity of the monoethynyl bipyrimidine we succeeded in producing, in fair yields, the mono substituted derivative **12** to **14** in a single step via a Sonogashira–Hagihara reaction promoted by low valent palladium(0), as sketched in Scheme 3.[14]

Subjecting 5-ethynyl-2,2′-bipyrimidine **6** (2 equiv) to similar coupling conditions with disubstituted 3,8-dibromo-1,10-phenanthroline or 5,5″-dibromo-2,2′: 6′,2″-terpyridine resulted in the formation of ligands **15** and **16** equipped with two bipyrimidine auxiliaries. Here the yields are significantly lower due to the intermediate formation of the mono-substituted derivatives, which are less reactive towards ethynylation owing to the withdrawing effect induced by the first ethynyl fragment.

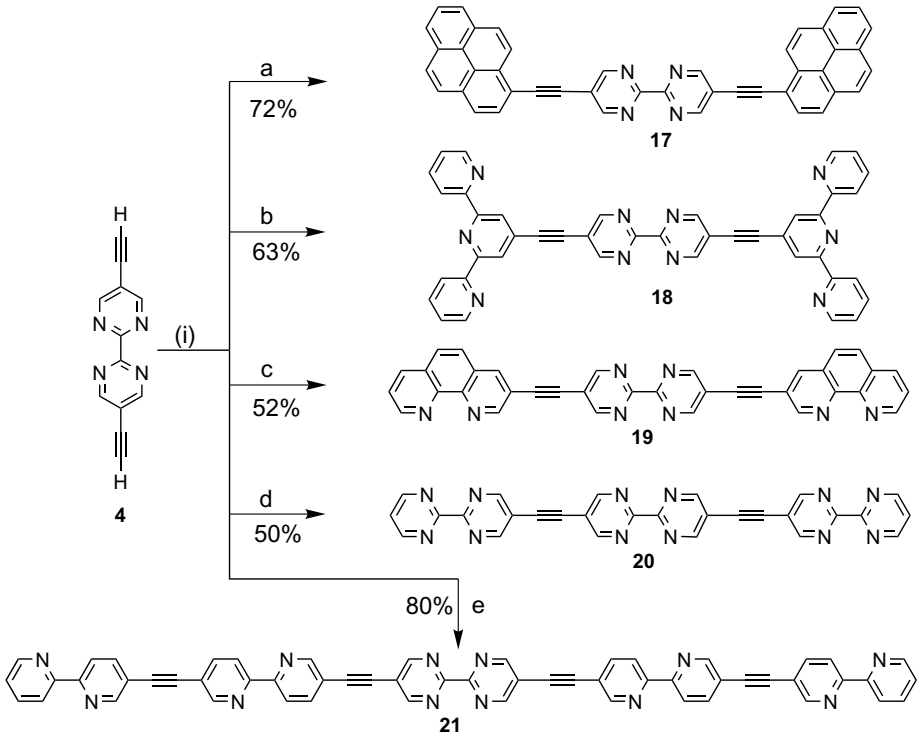
In the context of screening new potential ligands displaying multiple complexation sites linked by unsaturated spacers it can be easily imagined that other peripheral entities can be introduced as their acetylene derivatives in the same fashion from 5,5′-diethynyl-2,2′-bipyrimidine. This is a convenient and versatile method because the required ligands (Scheme 4) precipitate during the reaction and could be recovered by centrifugation and adequate purification. During these reac-



Scheme 2. (i) $HC{\equiv}CC(CH_3)_2OH$, $[Pd(PPh_3)_4]$ (6 mol%), benzene, $^nPrNH_2$, 60 °C; (ii) HC≡CTMS, $[Pd(PPh_3)_2Cl_2]$ (6 mol%), CuI (12 mol%), THF, $^iPr_2NH$, rt; (iii) KOH, toluene, 100 °C; (iv) KF, MeOH, rt.



Scheme 3. Reagents and conditions: (i) $[Pd(PPh_3)_4]$ (3 mol%), benzene, $^iPr_2NH$, 80 °C; (a) 4′-{[(trifluoromethyl)sulfonyl]oxy}-2,2′: 6′,2″-terpyridine (1 equiv), (b) 1-bromopyrene (1 equiv), (c) 3-bromo-1,10-phenanthroline (1 equiv), (d) 3,8-dibromo-1,10-phenanthroline (0.5 equiv), (e) 5,5″-dibromo-2,2′:6′,2″-terpyridine (0.5 equiv).



Scheme 4. Reagents and conditions: (i) $[Pd(PPh_3)_4]$ (3 mol%), benzene, $^iPr_2NH$, 80 °C; (a) 1-bromopyrene (2 equiv), (b) 4′-{[(trifluoromethyl) sulfonyl]oxy}-2,2′:6′,2″-terpyridine (2 equiv), (c) 3-bromo-1,10-phenanthroline (2 equiv), (d) 3-bromo-2,2′-bipyrimidine (2 equiv), (e) 5-bromo-5′-(5-ethynyl-2,2′-bipyridine-yl)-2,2′-bipyridine (2 equiv).

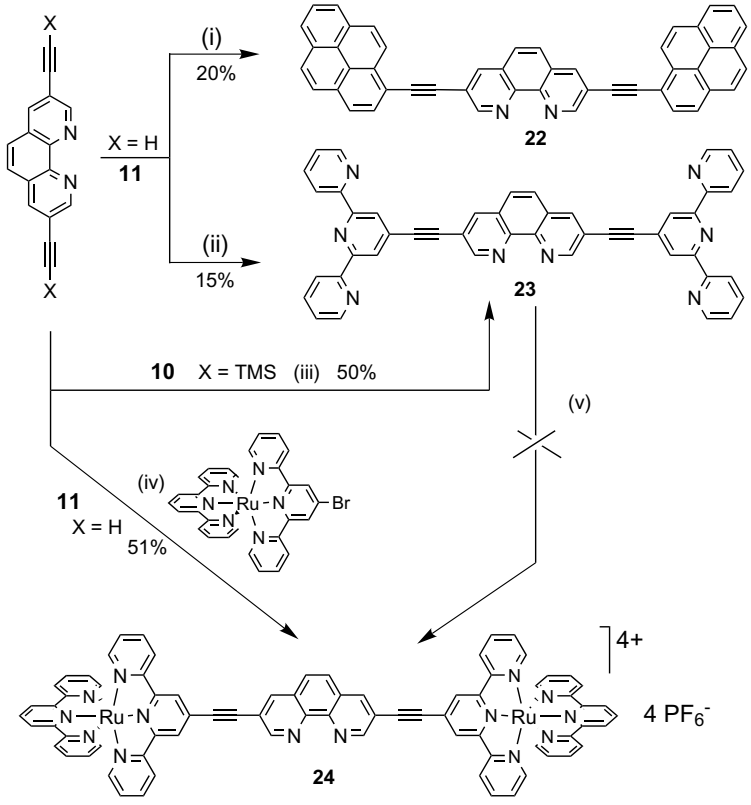
tions it was soon established by thin layer chromatography that the mono-substituted derivatives are preferentially formed at the early stage of the reaction. The use of lower temperature (ca. 50 °C) favors the precipitation of the mono-substituted compound and inhibits partly the second substitution process, a situation, which is not targeted in this context but auspicious for the potential engineering of molecules bearing different coordination sites. Interestingly, around 80 °C the mono-derivative is soluble and reactive towards further

substitution leading to compounds **17**, **18**,[15] **19**, and **20**[16] in acceptable yields. We also noticed that under these conditions the chemical stability of the diethynyl derivative **4** is poor affording side products. Cross linking of 5-bromo-5′-(5-ethynyl-2,2′-bipyridine-yl)-2, 2′-bipyridine[17] with **4**, very efficiently provides the hexatopic ligand **21**.

Similarly, reaction of 3,8-diethynyl-1,10-phenanthroline **11** provides some additional ligands (Scheme 5). The low yields found for derivatives **22** and **23** are probably due to the high reactivity and detrimental decomposition of the starting material **11**. After some experimentation we were pleased to find that in situ deprotection of 3,8-di(trimethylsilylacetylene)-1,10-phenanthroline **10** could be performed in a biphasic mixture using benzene and aqueous sodium hydroxide and 10 mol% of a quaternary ammonium salt favoring the phase transfer (Scheme 5). The cross-coupling reaction between the resulting 3,8-diethynyl-1,10-phenanthroline **11** and 4′-{[(trifluoromethyl)sulfonyl]oxy}-2,2′:6′,2″-terpyridine occurs in the organic phase and is promoted by Pd(0). The nascent acid is quenched in the aqueous basic solution by phase transfer. According to previous studies[18,19] and because the reaction requires mild heating it is believed that the deprotection step is relatively slow while the cross coupling reaction would be much faster under the phase transfer conditions. This procedure, not yet optimised seems to be well adapted for the synthesis of derivative **23** were the isolated yields could be improved to 50% (Scheme 5).

Finally, an elegant way to smoothly prepare molecules bearing at the periphery metal complexes with an additional recognition center able to trap specific analytes was realized by cross-coupling reaction 3,8-diethynyl-1,10-phenanthroline **11** with an adequate metallo-synthon grafted with a reactive bromine function. Complex **24**[20] could be isolated pure in 51%, when all attempts to prepare the same species by a more classical pathway, using metal free ligand **23** and *cis*-[Ru(terpy)(DMSO)Cl_2][21] as metal precursor, failed (Scheme 5).

In summary, we have prepared new-segmented ligands bearing a controlled number of chelating fragments by a rational approach, using transition metal-catalyzed coupling reactions. The next phase of this work is to complex the empty coordination sites in a controlled manner with specific transition metal salts and to study their optical and redox properties. It is foreseen that the triple bond will serve as an efficient conduit for shuttling the electron. The development of these photosensitisers would expand the opportunities for applications in the field of sensors and bipolar electroluminescent materials. The study of these scaffoldings is currently underway and the results will be disclosed in the near future.



Scheme 5. Reagents and conditions: (i) [$Pd(PPh_3)_4$] (3 mol%), benzene, $^iPr_2NH$, 80 °C, 1-bromopyrene (2 equiv); (ii) [$Pd(PPh_3)_4$] (3 mol%), benzene, $^iPr_2NH$, 80 °C, 4′-{[(trifluoromethyl)sulfonyl]oxy}-2,2′:6′,2″-terpyridine (2 equiv); (iii) phase transfer conditions; [$Pd(PPh_3)_2Cl_2$] 6 mol%, CuI 10 mol%, benzene, water, NaOH, Et_3BzNCl, 4′-{[(trifluoromethyl)sulfonyl]oxy}-2,2′:6′,2″-terpyridine (2 equiv), 60 °C; (iv) [$PdCl_2(PPh_3)_2$] 6 mol%, CuI 10 mol%, $^iPr_2NH$, THF, rt; (v) *cis*-[Ru(terpy)(DMSO)Cl_2] (2 equiv), $AgBF_4$ (2.2 equiv), MeOH, CH_2Cl_2 (1/1, v/v), 50 °C.

Acknowledgements

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14. Tritopic ligand **12**: Isolated yield 85%. ^{1}H NMR ($CDCl_3$) $\delta = 9.09$ (s, 2H), 9.01 (d, $^3J = 4.8$ Hz, 2H), 8.72 (d, $^3J = 4.8$ Hz, 2H), 8.64 (d, $^3J = 8.0$ Hz, 2H), 8.55 (s, 2H), 7.92 (td, $^3J = 7.9$ Hz, $^4J = 1.8$ Hz, 2H), 7.42 (ddd, $^3J = 5.0$ Hz, $^3J = 4.8$ Hz, $^4J = 1.2$ Hz, 2H), 7.53 (t, $^3J = 4.8$ Hz, 1H). FAB$^+$ (*m*-NBA) *m*/*z* (relative intensity in %) 414.2 ($[M+H]^+$, 100), 232.2 (20). IR (KBr, cm^{-1}) 3425, 2147 (w), 1585, 1456, 1392, 1264, 1093, 1037, 878. Anal. Calcd for $C_{25}H_{15}N_7$ ($M_r = 413.43$): C, 72.63; H, 3.66; N, 23.72. Found: C, 72.37; H, 3.29; N, 23.34.
15. Tetratopic ligand **18**: Isolated yield: 63%. Ligand too insoluble to run NMR spectrosocpies. FAB$^+$ (*m*-NBA) *m*/*z* (relative intensity in %) 669.2 ($[M]^+$, 100), 478.2 (20). IR (KBr, cm^{-1}) 3404, 1584, 1566, 1467, 1446, 1425, 1392, 1156, 1090, 1046, 799. Anal. Calcd for $C_{42}H_{24}N_{10}$ ($M_r = 668.73$): C, 75.44; H, 3.62; N, 20.95. Found: C, 75.29; H, 3.39; N, 20.75.
16. Hexatopic ligand **20**: Isolated yield: 50%. ^{1}H NMR (d_7-DMF) $\delta = 9.06$ (s, 4H), 9.08 (s, 4H), 8.99 (d, $^3J = 5.0$ Hz, 4H), 7.47 (t, 2H, $^3J = 5.0$ Hz). FAB$^+$ (*m*-NBA) *m*/*z* (relative intensity in %) 519.2 ($[M+H]^+$, 100), 338.2 (20). IR (KBr, cm^{-1}) 3418, 2976, 2163, 1578, 1523, 1507, 1423, 1236, 876. Anal. Calcd for $C_{28}H_{14}N_{12}$ ($M_r = 518.49$): C, 64.86; H, 2.72; N, 32.42. Found: C, 64.45; H, 2.56; N, 32.05.
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20. Dinuclear Complex **24**: Isolated yield: 51%. ^{1}H NMR (CD_3CN) $\delta = 9.49$ (d, 2H, $^3J = 2,0$ Hz), 8.99 (s, 4H), 8.84 (d, 2H, $^3J = 2.0$), 8.78 (d, 4H, $^3J = 8.4$), 8.41–8.59 (m, 10 H), 8.19 (s, 2H), 7.90–8.02 (m, 8H), 7.38–7.43 (m, 8H), 7.15–7.25 (m, 8H). ESI-MS *m*/*z* (nature of the peak, relative intensity in %) 1795.2 ($[M-PF_6]^+$, 100), 825.2 ($[M-2PF_6]^{2+}$, 40), 501.8 ($[M-3PF_6]^{3+}$, 10). IR (KBr, cm^{-1}) 3420, 1604, 1449, 1424, 840, 788, 768, 557. UV–vis (CH_3CN) λ_{max}, nm (ε, M^{-1} cm^{-1}) 495.0 (94,500), 307.0 (16,900), 272.0 (14,900). Anal. Calcd for $C_{76}H_{48}N_{14}P_4F_{24}Ru_2$ ($M_r = 1939.32$): C, 47.07; H, 2.49; N, 10.11. Found: C, 47.09; H, 2.43; N, 10.49.
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