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Tetrahedron Letters 48 (2007) 4143–4146

Tetrahedron Letters

Synthesis of valuable terpyridine building blocks to generate a variety of metallodendrons by the convergent approach

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Received 16 March 2007; accepted 28 March 2007

Available online 3 April 2007

Abstract—Efficient strategies for the synthesis of three building-blocks 4′-(functionalized)-2,2′:6′,2″-terpyridine have been developed for the convergent synthesis of metallodendrons; these strategies provide a practical approach for the rational design of highly conjugated metallodendrimers.

In the early 1990s, Balzani's and Newkome's research groups extended the already active field of dendrimer chemistry by incorporation of metallic centres in highly branched macromolecules.[1] These metallodendrimers are of great interest because of their novel physicochemical properties (catalysis, optics, electrochemistry, photochemistry, etc.).[2] Newkome et al. distinguished four main classes of metallodendrimers depending on the position and the role played by the metallic centre M.[2] In the first one, metal cores bear organic dendritic branches.[2,3] In the second one, metals are located at the periphery of an organic dendritic core leading to surface functionalized metallodendrimers.[2,4] In the third class, metals act as branching centres. The $[M(diimine)_3]^{2+}$ unit has been often employed for this type of metallodendrimers as a consequence of its D_3 symmetry, favourable for the synthesis of dentritic structures, and also as a consequence of the facile functionalization of the bipyridine or the phenanthroline units.[2,5,6] In the last main class distinguished by Newkome et al., metals act as building-block connectors. The great majority of metallodendrimers of this family is built up from the $[M(4'\text{-(functionalized)-}2,2':6',2''\text{-terpyridine})_2]^{2+}$ fragment due to the high binding affinity of terpyridine with transition metals and also due to the facile functionalization of the 4′-position of terpyridine.[7] In all these systems, another distinction must be made according to the nature of the organic component. The organic part of the dendrimer either contains saturated carbon chains of variable length, bearing, for example, ether functions,[8] or is constituted by a fully conjugated system.[5,6] Such conjugated metallodendrimers are indeed tailored to potentially enhance electronic transfers between the metallic centres.

A large variety of approaches have been employed to synthesize metallodendrimers such as the so-called 'complexes as metals/complexes as ligands' strategy in which metal complexes are used as building blocks,[9] by pyrazine connection,[10] imidazole junction[11] or Suzuki coupling.[6] The Sonogashira cross-coupling reaction has already been used successfully to synthesize binuclear complexes[12] or star-shaped π-conjugated ligands providing a platform to generate new metallodendrimers.[13] The Sonogashira coupling,[14] which can be used to introduce the ethynyl group as a spacer between two aryl groups, has been commonly carried out using aryl bromides. However, it is now well established that the aryl halide reactivity follows the expected trend iodide > bromide ≫ chloride.[15]

In this Letter, we report the synthesis of three 4′-functionalized terpyridine derivatives, 4′-(4-iodophenyl)-2,2′:6′,2″-terpyridine (**1**),[16] 4′-(3,5-diiodophenyl)-2,2′:6′,2″-terpyridine (**2**) and 4′-(3,5-bis(ethynyl)phenyl)-2,2′:6′,2″-terpyridine (**3**), bearing one iodide, two iodides or two ethynyl pendant groups, respectively. The three derivatives were used to generate a ruthenium metallodendron of first generation. The efficient strategy reported here, in which the terpyridine iodide derivatives were submitted to the Sonogashira coupling reactions, can be easily tuned to synthesize a variety of symmetric and asymmetric metallodendrimers.

Keywords: Terpyridine; Ruthenium(II); Sonogashira coupling.

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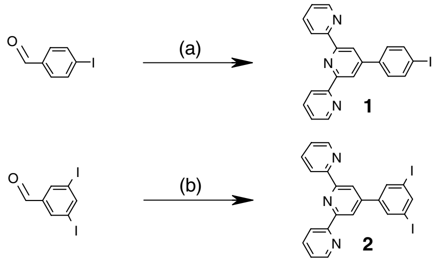
doi:10.1016/j.tetlet.2007.03.160



Scheme 1. Reagents and conditions: (a) 2-acetylpyridine, KOH, MeOH/NH_3 (30%); (b) (i) 2-acetylpyridine, KO*t*Bu, THF; (ii) NH_4OAc, MeOH.

Terpyridine iodide derivatives **1** and **2** were synthesized starting from 4-iodobenzaldehyde[17] and 3,5-diiodobenzaldehyde,[18] respectively. Two methods were used for the synthesis of each molecule **1** and **2**. The first method (Scheme 1, synthesis of **1**) was a one-pot procedure using 2-acetylpyridine and the appropriate benzaldehyde derivative in alkaline methanolic solution.[19a] In the second method (Scheme 1, synthesis of **2**), the first step afforded the 3-(functionalized)-1,5-di(pyridin-2-yl)-pent-2-ene-1,5-dione while the second step was a cyclization reaction generating the central pyridine by reaction with ammonium acetate in methanol.[19b] Compound **1** was obtained with similar yields (~63%) using both methods; nevertheless, using the first method, the pure product was easily recovered by direct precipitation from the reaction medium while the second method required a purification by chromatography. The one-pot method did not allow the synthesis of **2** due to rapid precipitation of 3-(3,5-diiodophenyl)-1-(pyridin-2-yl)-prop-2-en-1-one in the reaction medium. Compound **2** was isolated in 57% yield using the second method. Recrystallization from DMSO afforded colourless crystals suitable for single-crystal X-ray diffraction analysis (Fig. 1).[20]

Terpyridine derivative **3**, bearing two ethynyl pendant groups, was synthesized using two different strategies summarized in Scheme 2. In the first route, 3,5-bis-(ethynyl)benzaldehyde was prepared according to previously published procedures except that 3,5-diiodobenzaldehyde was used as the starting reagent instead of 3,5-dibromobenzaldehyde.[21] 3,5-Bis-(ethynyl)benzaldehyde was finally reacted with 2 equiv of 2-acetylpyridine and KO*t*Bu in THF to give **3** that was further purified by flash chromathography (45% yield). In the second route, the Sonogashira cross-coupling reaction of **2** and 2 equiv of trimethylsilylacetylene, in the presence of catalytic amounts of $Pd(PPh_3)_2Cl_2$ and CuI, gave 4′-(3,5-bis-(trimethylsilyl-ethynyl)-phenyl)-2,2′:6′,2″-terpyridine in 96% yield. The trimethylsilyl groups were removed in the final step with sodium hydroxide in THF to obtain **3** in 90% yield.

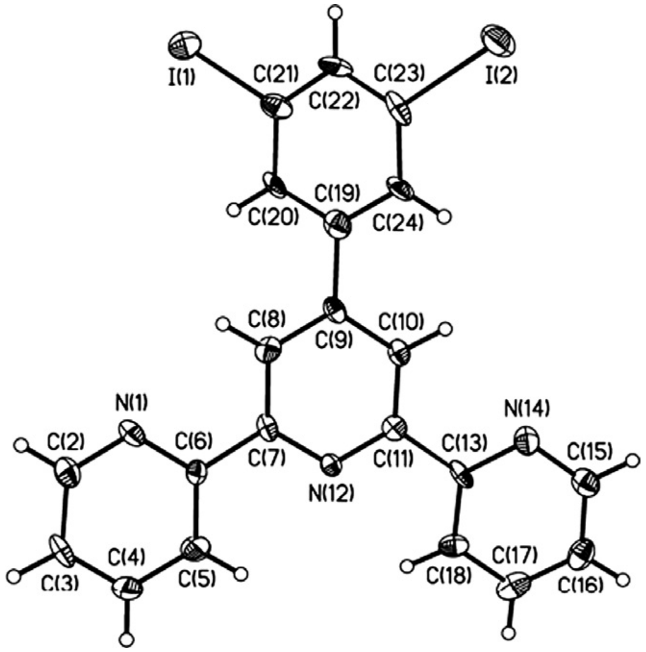
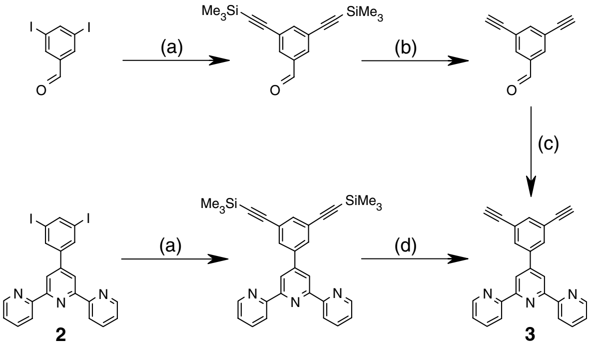
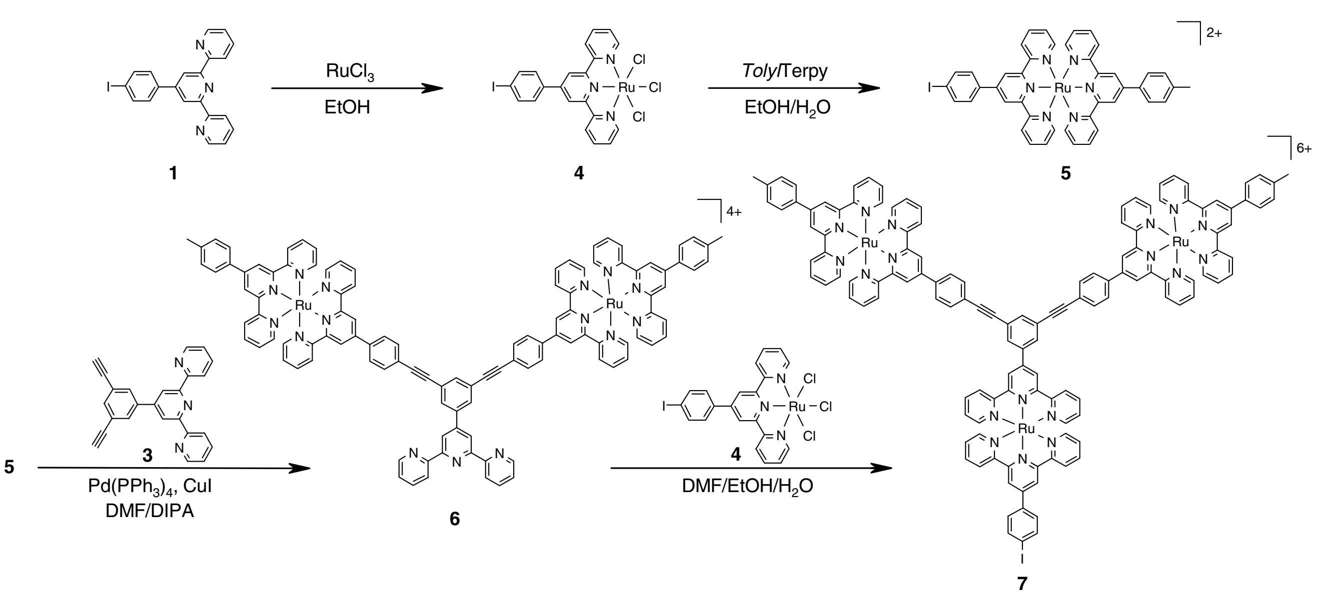


Figure 1. Structure of 4′-(3,5-diiodophenyl)-2,2′:6′,2″-terpyridine (**2**). Ellipsoids are at the 30% probability level.



Scheme 2. Reagents and conditions: (a) $Me_3Si–C{\equiv}CH$, $Pd(PPh_3)_2Cl_2$, CuI, DMF/Et_3N; (b) NaOH, THF; (c) (i) 2-acetylpyridine, KO*t*Bu, THF; (ii) NH_4OAc, MeOH; (d) NaOH, THF/MeOH.

The second part of this Letter is devoted to the synthesis of metallodendrons by using the above-described ligands. The so-called divergent and convergent methods have been described in the literature to generate metallodendrimers.[2] The divergent approach can be described as the sequential growth of branches starting from the core of the metallodendrimer while the convergent approach starts from the periphery and proceeds by iterative growth of the branches towards the core of the metallodendrimer. The metallodendrons and the method described thereafter, summarized in Scheme 3, are perfectly adapted to generate ruthenium- or mixed-metal-dendrimers using the convergent approach. Ruthenium complex **4** was obtained by reaction of **1** with an excess of $RuCl_3{\cdot}3H_2O$ in refluxing ethanol. Compound **4** was then reacted with 4′-(4-tolyl)-2,2′:6′,2″-terpyridine (denoted *Tolyl*Terpy) to give $[(\textit{Tolyl}\text{Terpy})\text{Ru}(\mathbf{1})]^{2+}$ (**5**) in 75% yield. The Sonogashira coupling in DMF of 2 equiv of the hexafluorophosphate salt of **5** with 1 equiv of **3** afforded the dinuclear complex **6**. Compound **6** was purified by column chromatography and its hexafluorophosphate salt isolated as a red solid in 50% yield. Compound **6** is a key intermediate complex bearing one pendant terpyridine group that can potentially react with a variety of metal ions to generate pentanuclear metallodendrimers of the general



Scheme 3. Synthesis of the metallodendrons.

formula $[M(\mathbf{6})_2]^{n+}$ (M = Fe, Zn, Ru, Os, Ir, etc.). In our study, **6** was reacted with 1 equiv of **4** to give the trinuclear metallodendron **7** in 69% yield. Compound **7** can be described as a first generation metallodendron possessing a single functional aryl iodide unit that could be further involved in a Sonogashira coupling reaction to build metallodendrimers of higher generation.

In summary, we synthesized and characterized three terpyridine derivative ligands bearing aryl iodide or ethynyl functional pendant units. These ligands have been used to prepare mono-, di- and tri-nuclear complexes of ruthenium. The ligands and the ruthenium complexes described in this Letter are very attractive building blocks for several reasons. They possess functional pendant groups that make them ideal candidates for the Sonogashira coupling reaction; they are therefore valuable building blocks to generate a variety of metallodendrons and metallodendrimers using the convergent method. The synthetic approach can also be easily tuned in order to obtain mixed-metal dendrons and dendrimers. The methodology presented in this Letter also allows the straightforward synthesis of fully conjugated metallodendrimers that could facilitate potential electronic transfer between the metallic centres. Moreover, this approach gives a potential access to a library of metallic complexes such as compound **6** that can be tailored to be grafted on metallic surfaces[22] or to functionalize preformed metallic nanoparticles bearing polypyridyl pendant groups.[23] An extensive study of the synthesis and the physico-chemical properties of fully conjugated metallodendrons and metallodendrimers obtained using the ligands and the method described in this Letter will be presented in due course.

Supplementary data

Supplementary data (experimental details, ESI-MS and NMR spectra) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.03.160.

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