Jérôme Husson* and Laurent Guyard

Synthesis of new 4′-(*N*-alkylpyrrol-2-yl)-2,2′:6′,2″-terpyridines via *N*-alkylation of a pyrrole moiety

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Abstract: New 4′-(*N*-alkylpyrrol-2-yl)-2,2′:6′,2″-terpyridines were synthesized by *N*-alkylation of a pyrrole substituent with alkyl halides in dimethyl sulfoxide.

Keywords: alkylation; polymer functionalization; pyrrole; terpyridine.

Introduction

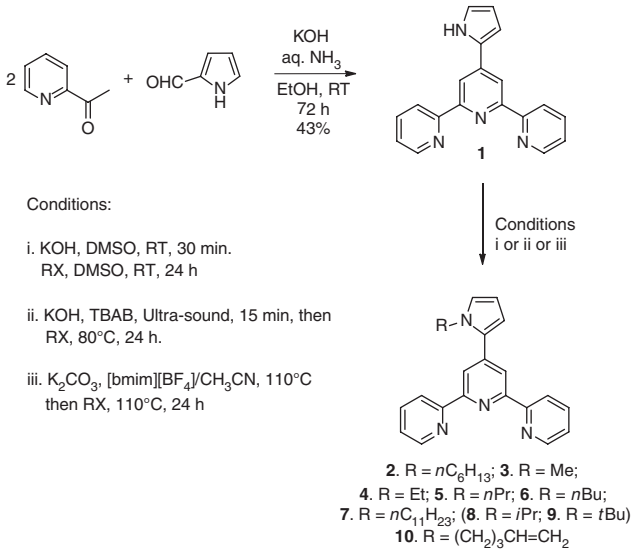
2,2′:6′,2″-Terpyridines (terpyridines) are ligands that have been widely studied owing to their capability to form complexes with many metals [1, 2]. Alkyl-functionalized terpyridines and their complexes find many applications such as sensitizers for photovoltaic devices [3, 4], as ligands for the removal of actinides from nuclear wastes [5, 6], or as catalysts [7], to name a few. Synthesis of such alkyl-containing terpyridines is of interest in view of the above-mentioned applications. This article describes the preparation of new alkyl-functionalized terpyridines through the *N*-alkylation of a pyrrole moiety attached to the terpyridine scaffold. This methodology was selected owing to the fact that terpyridines containing five-membered heterocycles are easily prepared [8, 9] and the pyrrole ring can be easily modified at the *N*-atom [10].

Results and discussion

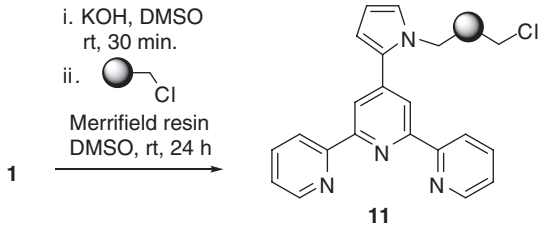
The synthesis started with the preparation of the pyrrole-functionalized terpyridine **1** [11–13] from 2-acetylpyridine and pyrrole-2-carboxaldehyde. Among the methods available [14, 15], a simple and efficient one-pot two steps method was employed [16] (Scheme 1).

With **1** in hand, three different methods were tested for the *N*-functionalization of the pyrrole ring. The first one (method *i*) relies on the use of potassium hydroxide as a base in the aprotic polar solvent dimethyl sulfoxide (DMSO) [17] and has been already used in our laboratory [18]. The second one (method *ii*) is a solvent-less procedure with a phase transfer reagent [19] that has a 'green' advantage because solvent is not used. The final method (method *iii*) uses an ionic liquid as a medium [20]. Ionic liquids are generally considered green solvents because they are non-volatile and recyclable [21]. To determine which method would be the most adequate, a series of experiments were carried out on the alkylation of **1** with hexyl bromide (Scheme 1) to obtain compound **2**. Method *ii* failed in providing the desired pure compound. Thin layer chromatography (TLC) analysis showed that the crude mixture contained many polar compounds that were inseparable by chromatography as well as large amount of the remaining starting material. Method *iii* provided the desired product but with a low yield. Additionally, recovery of the ionic liquid was not possible, resulting in the loss of the 'green' advantage of the method. The best result in the preparation of compound **2** was achieved using the classical method *i*. Subsequently, this method was successfully used in the preparation of other pyrrole-containing terpyridines **3**–**7** and **10** by alkylation of **1** with the corresponding halides. Unfortunately, the attempted alkylation of **1** with isopropyl or *t*-butyl bromide failed to produce the respective products **8** and **9**, apparently for steric reasons. Quite low yields were obtained for **5** and **10** with large amount of starting material remaining. It is nevertheless interesting to note that this protocol tolerates the presence of double bonds. Thus, efforts are in progress to improve the yield of **10** because this ethylenic derivative could be valuable for further functionalization of terpyridines. Although the use of primary alkyl chlorides resulted in the preparation of the corresponding alkylpyrroles in low yields, a notable exception was the alkylation of the polymeric Merrifield resin. The reaction of the chloromethyl

***Corresponding author: Jérôme Husson,** Institut UTINAM UMR CNRS 6213, Université de Franche-Comté, 16 Route de Gray, 25030 Besançon cedex, France, e-mail: jerome.husson@univ-fcomte.fr
Laurent Guyard: Institut UTINAM UMR CNRS 6213, Université de Franche-Comté, 16 Route de Gray, 25030 Besançon cedex, France



Scheme 1



Scheme 2

groups of the resin with **1** enabled a partial functionalization of the polymer to provide the polymeric material **11** (Scheme 2). Functionalization of the polymer matrix was evidenced by elemental analysis, and the degree of functionalization was estimated to be 0.15 mmol/g of the material.

Conclusions

New alkyl-functionalized pyrrolyl-substituted terpyridines were prepared by *N*-alkylation of the pyrrole ring with primary alkyl halides in the presence of potassium hydroxide in DMSO. The protocol is also suitable for the functionalization of the Merrifield resin.

Future work will focus on integrating these new terpyridines in metal complexes, developing applications for the Merrifield-terpyridine resin, and the synthesis of further functionalized terpyridines.

Experimental

All reagents were obtained from commercial suppliers and used as received. For *N*-alkylation, potassium hydroxide pellets (85%) were powdered with an IKA A11 analytical mill, and the powder was stored under reduced pressure over P_2O_5. Anhydrous DMSO and Merrifield polymer resin (2% cross-linked with divinylbenzene, 2.8–3.2 mmol Cl/g, 200–400 mesh) were purchased from Acros Organics. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in $CDCl_3$ on a Bruker Avance 300 spectrometer. Elemental analysis was obtained at Service d'Analyse Elementaire (Vandoeuvre-les-Nancy, France).

4′-(Pyrrol-2-yl)-2,2′:6′,2″-terpyridine (1)

2-Acetylpyridine (13.43 g; 0.11 mol), ethanol (250 mL), pyrrole-2-carboxaldehyde (5.27 g; 0.055 mol), 85% potassium hydroxide pellets (8.56 g; 0.13 mol), and 25% aqueous ammonia (170 mL) were placed in a round-bottom flask, and the mixture was stirred at room temperature for 72 h. The resultant precipitate was filtered, washed with ice-cold 50% aqueous ethanol until washings were colorless, and dried under reduced pressure. Compound **1** was obtained as a light yellow solid and used in the next step without further purification. Physical and spectroscopic properties are in agreement with those reported [10–12].

Preparation of 4′-(*N*-alkylpyrrol-2-yl)-2,2′:6′, 2″-terpyridines 2–7 and 10

A suspension of powdered potassium hydroxide (0.44 g; 6.7 mmol) in DMSO (35 mL) was stirred at room temperature under argon for 30 min, then treated with compound **1** (1.00 g; 3.35 mmol), and the resultant red solution was stirred at room temperature under argon for 30 min. The appropriate alkyl halide (3.35 mmol) was added, and the mixture was stirred at room temperature under argon for 24 h. It was then poured onto water (100 mL), and a small amount of brine was added for an easy decantation. The aqueous layer was extracted with dichloromethane (4×25 mL). Organic layers were combined, washed with brine (100 mL), dried over sodium sulfate, and concentrated under reduced pressure. The residue was subjected to flash chromatography on neutral alumina (8 g), eluting initially with *n*-hexane followed by *n*-hexane/ethyl acetate (4:1).

4′-(*N*-Hexylpyrrol-2-yl)-2,2′:6′,2″-terpyridine (2) Light yellow oil; yield 59% from hexyl iodide; ^{1}H NMR: δ 0.81 (t, 3H, J = 7 Hz), 1.27 (m, 6H), 1.77 (t, 2H, J = 7 Hz), 4.15 (t, 2H, J = 7 Hz), 6.28 (t, 1H, J = 3.4 Hz), 6.61 (dd, 1H, J = 1.8 Hz and J' = 3.4 Hz), 6.87 (t, 1H, J = 1.8 Hz), 7.32 (t, 2H, J = 7 Hz), 7.85 (td, 2H, J = 1.8 Hz and J' = 8 Hz), 8.56 (s, 2H), 8.66 (d, 2H, J = 8 Hz), 8.71 (d, 2H, J = 3.4 Hz); ^{13}C NMR: δ 14.0, 22.5, 26.3, 31.3, 31.7, 48.0, 108.4, 111.3, 119.5, 121.2, 123.7, 124.7, 131.8, 136.8, 142.9, 149.2, 155.6, 156.3. Anal. Calcd for $C_{25}H_{26}N_4$: C, 78.50; H, 6.85; N, 14.65. Found: C, 78.34; H, 6.74; N, 14.40.

4′-(*N*-Methylpyrrol-2-yl)-2,2′:6′,2″-terpyridine (3) White solid; mp 125–127°C; yield 38% from methyl iodide; ^{1}H NMR: δ 3.89 (s, 3H), 6.26 (t, 1H, J = 4 Hz), 6.66 (dd, 1H, J = 1.8 Hz and J' = 4.0 Hz), 6.81 (m, 1H), 7.34 (t, 2H, J = 6 Hz), 7.86 (td, 2H, J = 1.8 Hz and J' = 8.0 Hz),

8.55 (s, 2H), 8.65 (d, 2H, J = 8.0 Hz), 8.71 (d, 2H, J = 4 Hz); ^{13}C NMR: δ 35.9, 108.4, 111.3, 119.2, 121.3, 123.7, 126.1, 132.2, 138.8, 142.5, 149.2, 155.6, 156.3. Anal. Calcd for $C_{20}H_{16}N_4$: C, 76.90; H, 5.16; N, 17.94. Found: C, 76.70; H, 5.13; N, 17.56.

4′-(*N*-Ethylpyrrol-2-yl)-2,2′:6′,2″-terpyridine (4) White solid; mp 144–146°C; yield 39% from ethyl iodide; ^{1}H NMR: δ 1.41 (t, 3H, J = 7.2 Hz), 4.21 (q, 2H, J = 7.2 Hz), 6.28 (t, 1H, J = 3.3 Hz), 6.58 (dd, 1H, J = 1.5 Hz and J' = 3.3 Hz), 6.89 (m, 1H), 7.34 (dd, 2H, J = 4.2 Hz and J' = 7.2 Hz), 7.86 (td, 2H, J = 1.5 Hz and J' = 8.0 Hz), 8.53 (s, 2H), 8.65 (d, 2H, J = 8.0 Hz), 8.71 (d, 2H, J = 4.2 Hz); ^{13}C NMR: δ 16.8, 42.6, 108.6, 111.3, 119.6, 121.3, 123.7, 123.8, 131.7, 136.8, 142.9, 149.2, 155.6, 156.3. Anal. Calcd for $C_{21}H_{18}N_4$: C, 77.28; H, 5.56; N, 17.17. Found: C, 77.49; H, 5.64; N, 16.80.

4′-(*N*-Propylpyrrol-2-yl)-2,2′:6′,2″-terpyridine (5) White solid; mp 109–111°C; yield 9% from propyl iodide, 6% from propyl chloride; ^{1}H NMR: δ 0.85 (t, 3H, J = 7.2 Hz), 1.77 (q, 2H, J = 7.2 Hz), 4.13 (t, 2H, J = 7.2 Hz), 6.26 (s, 1H), 6.59 (m 1H), 6.87 (s, 1H), 7.33 (dd, 2H, J = 5.0 Hz and J' = 6.3 Hz), 7.86 (t, 2H, J = 7.2 Hz), 8.53 (s, 2H), 8.66 (d, 2H, J = 7.2 Hz), 8.71 (d, 2H, J = 5.0 Hz); ^{13}C NMR: δ 11.1, 24.9, 49.6, 108.4, 111.4, 119.5, 121.2, 123.7, 124.7, 131.8, 136.8, 142.9, 149.2, 155.6, 156.3. Anal. Calcd for $C_{22}H_{20}N_4$: C, 77.62; H, 5.92; N, 16.46. Found: C, 77.34; H, 5.87; N, 16.23.

4′-(*N*-Butylpyrrol-2-yl)-2,2′:6′,2″-terpyridine (6) Light yellow oil; yield 37% from butyl iodide, 1.8% from butyl chloride); ^{1}H NMR: δ 0.87 (t, 3H, J = 7.2 Hz), 1.28 (q, 2H, J = 7.5 Hz), 1.75 (q, 2H, J = 7.5 Hz), 4.17 (t, 2H, J = 7.2 Hz), 6.29 (t, 1H, J = 3 Hz), 6.63 (dd, 1H, J = 1.5 Hz and J' = 3 Hz), 6.88 (s, 1H), 7.31 (dd, 2H, J = 3 Hz and J' = 7.2 Hz), 7.84 (td, 2H, J = 1.5 Hz and J' = 7.5 Hz), 8.58 (s, 2H), 8.67 (d, 2H, J = 7.5 Hz), 8.71 (d, 2H, J = 3 Hz); ^{13}C NMR: δ 13.7, 19.8, 33.8, 47.8, 108.5, 111.4, 119.5, 121.2, 123.7, 124.7, 131.8, 136.8, 142.9, 149.2, 155.6, 156.3. Anal. Calcd for $C_{23}H_{22}N_4$: C, 77.94; H, 6.26; N, 15.81. Found: C, 77.68; H, 6.26; N, 15.43.

4′-(*N*-Undecylpyrrol-2-yl)-2,2′:6′,2″-terpyridine (7) Light yellow oil; yield 42% from undecyl bromide; ^{1}H NMR: δ 0.87 (t, 3H, J = 6.9 Hz), 1.22 (m, 14H), 1.77 (t, 2H, J = 6.9 Hz), 4.15 (t, 2H, J = 7.5 Hz), 6.28 (t, 1H, J = 4 Hz), 6.61 (dd, 1H, J = 1.5 Hz and J' = 4 Hz), 6.87 (s, 1H), 7.33 (dd, 2H, J = 5 Hz and J' = 7.5 Hz), 7.86 (td, 2H, J = 1.5 Hz and J' = 7.5 Hz), 8.56 (s, 2H), 8.67 (d, 2H, J = 7.5 Hz), 8.71 (d, 2H, J = 4 Hz); ^{13}C NMR: δ 14.1, 22.7, 29.1, 29.3, 29.4, 29.5, 29.5, 29.6, 31.9, 48.0, 108.5, 111.3, 119.5, 121.2, 123.7, 124.6, 131.9, 136.7, 142.9, 149.2, 155.6, 156.3. Anal. Calcd for $C_{29}H_{34}N_4$ C, 79.41; H, 7.81; N, 12.77. Found: C, 80.09; H, 8.09; N, 12.25.

4′-(*N*-Pent-5-enylpyrrol-2-yl)-2,2′:6′,2″-terpyridine (10) Light yellow oil; yield 2% from 5-bromo-1-pentene; ^{1}H NMR: δ 1.86 (m, 2H), 2.02 (m, 2H), 4.17 (t, 2H, J = 7.5 Hz), 4.90 (d, 1H, J = 10.2 Hz), 4.96 (dd, 1H, J = 1.5 Hz and J' = 17.1 Hz), 5.74 (tdd, 1H, J = 6 Hz, J' = 10.2 Hz and J'' = 17.1 Hz), 6.27 (t, 1H, J = 3 Hz), 6.61 (t, 1H, J = 1.5 Hz), 6.87 (s, 1H), 7.34 (t, 2H, J = 6 Hz), 7.87 (td, 2H, J = 1.5 Hz and J' = 7.8 Hz), 8.53 (s, 2H), 8.66 (d, 2H, J = 7.8 Hz), 8.71 (d, 2H, J = 3 Hz); ^{13}C NMR: δ 30.6, 30.7, 47.3, 108.5, 111.5, 115.5, 119.4, 121.2, 123.7, 124.7, 131.8, 136.8, 137.4, 142.8, 149.2, 155.6, 156.3. Anal. Calcd for $C_{24}H_{22}N_4$ C, 78.66; H, 6.05; N, 15.29. Found: C, 78.76; H, 6.13; N, 15.22.

Preparation of terpyridine-functionalized Merrifield resin (11)

A suspension of powdered potassium hydroxide (2.09 g) in DMSO (50 mL) was stirred at room temperature under argon for 30 min. Then, 4′-(pyrrol-2-yl)-2,2′:6′,2″-terpyridine (**1**, 4.78 g) was added, and the resultant red solution was stirred at room temperature under argon for 30 min followed by addition of Merrifield resin (5.00 g). The suspension was stirred at room temperature for 72 h. The resin was filtered, washed with water and ethanol, and then extracted for 24 h in a Soxhlet apparatus with dichloromethane. After drying under a reduced pressure over phosphorus pentoxide, the product was obtained as a dark solid (5.40 g). Elemental analysis (C, 76.01; H, 6.13; N, 0.86) indicates a degree of functionalization of 0.15 mmol/g.

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