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Short Note

4′-(*N*-(Propargyl)pyrrol-2-yl)-2,2′:6′,2″-terpyridine

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Abstract: A new terpyridine molecule, bearing a *N*-propargylated pyrrole, was prepared and characterized. Its synthesis was based on a Krohnke-type reaction between 2-acetylpyridine and *N*-propargylpyrrole-2-carboxaldehyde in a basic medium. An allene-containing terpyridine was also obtained as a by-product.

Keywords: alkyne derivatives; *N*-donor ligands; oligopyridines; pyrrole derivatives

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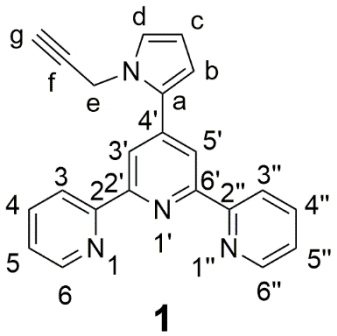
1. Introduction

Owing to their ability to form a broad range of complexes with metals, 2,2′:6′,2″-terpyridine derivatives have been widely studied. Terpyridines and their complexes can find applications in many fields ranging from medicinal chemistry to functional materials [1,2]. In particular, terpyridine derivatives which contain an additional pyrrole heterocycle (named hereafter pyrrole-terpys) are interesting compounds because they can be deposited as thin films onto surfaces via electropolymerization [3]. The so-obtained polymeric materials can be used, for example, as an active layer in a sensor device [4]. Additionally, pyrrole-terpys can find applications in other fields such as catalysis [5] or as photosensitizers [6,7], just to name a few. Consequently, the synthesis of new pyrrole-terpys could be of interest for a broad range of scientific fields. In particular, the introduction of an alkyne moiety onto a pyrrole-terpy could be interesting since it offers the possibility to "click" the terpyridine onto various materials or biomolecules [8–10] via the Huisgen reaction [11] and allows the preparation of hetero-polymetallic complexes through complexation of both the terpyridine and alkyne parts of the molecule [12]. This paper describes the preparation and characterization of the new 4′-(*N*-(propargyl)pyrrol-2-yl)-2,2′:6′,2″-terpyridine **1** (Figure 1).



1

Figure 1. Structure and atom labeling of 4′-(*N*-(propargyl)pyrrol-2-yl)-2,2′:6′,2″-terpyridine **1**.

2. Results and Discussion

A tentative synthesis of **1** through *N*-propargylation of 4′-(pyrrol-2-yl)-2,2′:6′,2″-terpyridine is already reported in the literature [13]. The synthetic pathway that was explored relies on the *N*-alkylation of the pyrrole ring with propargyl bromide in a strong

basic medium [14]. Nevertheless, this approach failed in providing **1**, and only isomeric 4′-(*N*-(propan-1,2-dienyl)pyrrol-2-yl)-2,2′:6′,2″-terpyridine **2** was obtained (Figure 2). This can be explained by the strong basic conditions (potassium hydroxide in dimethylsulfoxide is a superbase [15]) of the reaction which result in isomerization of the triple bond. Therefore, another synthetic strategy was developed in the present research to obtain compound **1**.

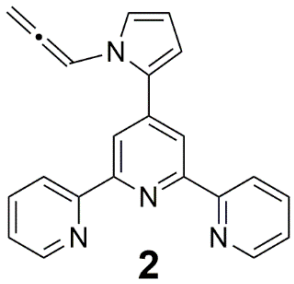


Figure 2. Structure of 4′-(*N*-(propan-1,2-dienyl)pyrrol-2-yl)-2,2′:6′,2″-terpyridine **2**.

Many synthetic protocols are available for the preparation of terpyridines [16–18], most of them being based on Krohnke's method [19]. Here, the reaction between 2-acetylpyridine and *N*-propargylpyrrole-2-carboxaldehyde [20] in the presence of potassium hydroxide and aqueous ammonia in ethanol [21] was selected (Figure 3).

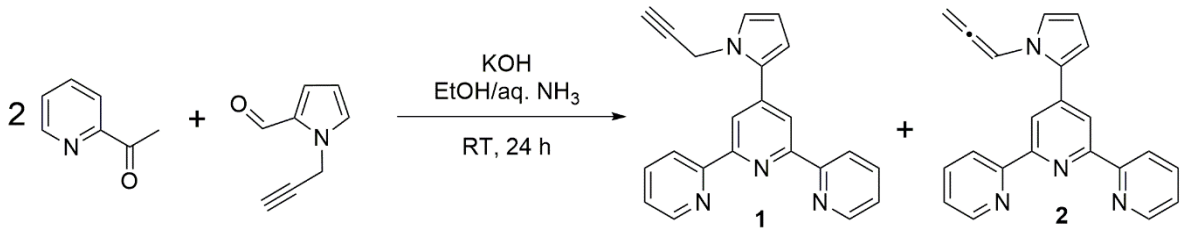


Figure 3. Reaction scheme.

Although the reaction is also conducted in a basic medium, it was expected that the basicity of potassium hydroxide would be lower in the present solvent system (aqueous ethanol) than in dimethylsulfoxide (vide supra), thus minimizing the formation of compound **2**. In fact, after 24 h of reaction, a mixture of **1** and **2** was obtained. The two products were separated by flash chromatography over neutral alumina (Figure 4). The main product was the awaited terpyridine **1** which was obtained in 9.4% yield, while compound **2** was obtained in 2.8% yield.

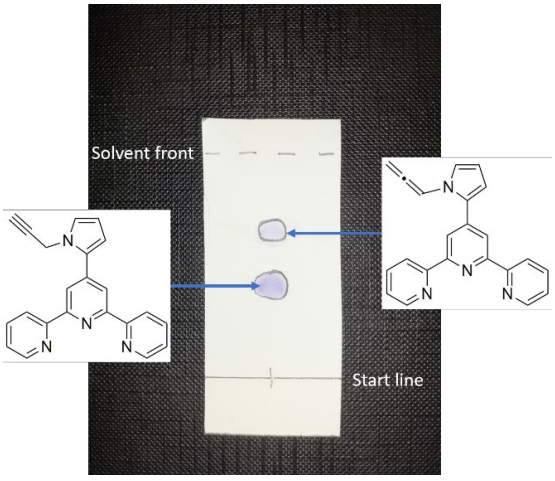


Figure 4. TLC onto alumina (cyclohexane/ethyl acetate 9:1 *v*/*v*) of the crude mixture after staining with an aqueous solution of Mohr's salt.

The molecular structure of compound **1** was unambiguously confirmed by different analytical techniques. First, the ^{1}H-NMR spectrum (Supplementary Material) exhibits the typical signals for the terpyridine and pyrrole sub-units as reported for other pyrrole-terpys [6,13,14,22,23]. Moreover, the acetylenic protons were characterized by a triplet and a doublet (J = 2.6 Hz) centered at 2.45 and 4.91 ppm, respectively. These chemical shifts and/or multiplicities also agree with those previously reported for other *N*-propargylated pyrroles [24,25]. The ^{13}C-NMR spectrum exhibits 15 peaks, which fully agree with the proposed structure for **1**.

Additionally, the infrared spectrum exhibits the characteristic ≡C-H stretching signal for the terminal alkyne at 3174 cm^{-1} as well as the -C≡C- stretching signal at 2114 cm^{-1} (Supplementary Material). Finally, the recorded mass spectra of compound **1** agree with the proposed structure since the molecular peak $[M + H]^+$ (m/z = 337.14436) as well as the isotopic distribution fits with the calculated spectrum (Supplementary Material).

To reduce the amount of undesired compound **2**, one experiment was carried out using an even weaker base. For this, *N*-propargylpyrrole-2-carboxaldehyde was reacted with 2-acetylpyridine and basic alumina under solventless conditions as already described for the preparation of other terpyridine derivatives [26]. Unfortunately, no trace of a terpyridine product was noticed under these conditions (Figure 5).

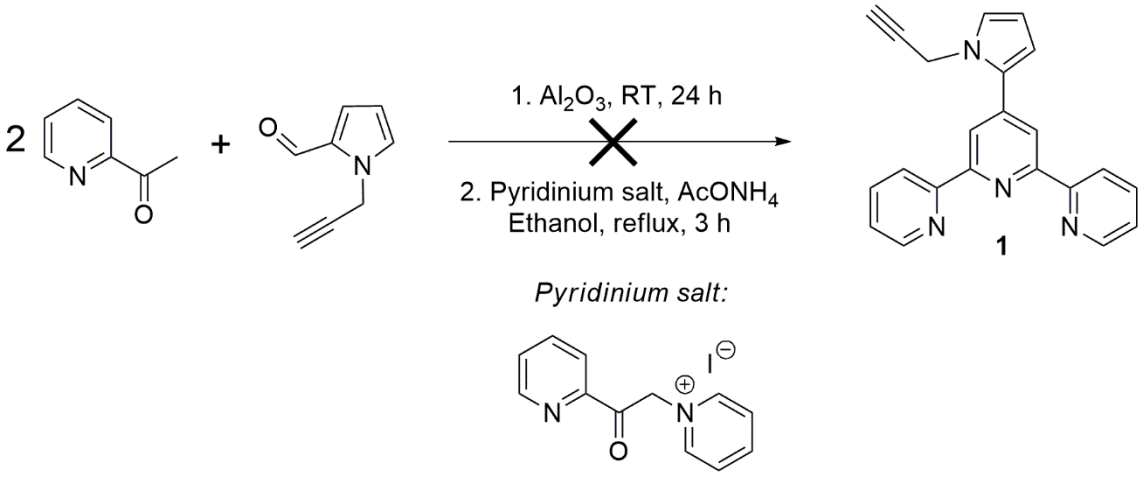


Figure 5. Tentative attempt to obtain compound **1** with an alternative synthetic protocol.

3. Materials and Methods

All reagents were purchased from commercial suppliers and used as received. The starting pyrrole aldehyde was prepared according to the literature [20]. Flash chromatography was carried out on a Combiflash Rf+ Lumen (Teledyne ISCO, Lincoln, NE, USA) using a PuriFlash 220 g neutral alumina cartridge (Interchim, Montluçon, France) with a hexane/ethyl acetate mixture (100:0 to 90:10 *v*:*v*) as an eluent. ^{1}H and ^{13}C-NMR spectra were recorded on a Brucker AC 400 (Bruker, Wissembourg, France) at 400 and 100 MHz, respectively, using $CDCl_3$ as a solvent. Infrared spectra were recorded on an Alpha II spectrometer (Bruker, Wissembourg, France) as KBr discs. Melting points were recorded with a Stuart SMP 10 melting point apparatus (Bibby Sterilin, Stone, UK) and were uncorrected. HR-MS was recorded at Sayens SATT, Dijon, France.

4′-(N-(Propargyl)pyrrol-2-yl)-2,2′:6′,2″-terpyridine (**1**) and *4′-(N-(propan-1,2-dienyl)pyrrol-2-yl)-2,2′:6′,2″-terpyridine* (**2**): *N*-Propargylpyrrole-2-carboxaldehyde (4.69 g; 35 mmol), 85% potassium hydroxide pellets (5.43 g; 82 mmol) and 25% aqueous ammonia solution (102 mL) were successively added to a solution of 2-acetylpyridine (8.53 g; 70 mmol) in absolute ethanol (180 mL). The reaction mixture was stirred at room temperature for 24 h. The precipitated solid was collected by filtration and washed with ice-cold 50% ethanol until washings were colorless. The crude product was air dried and purified by flash chromatography over neutral alumina (eluent: cyclohexane/ethyl acetate 100:0 to 90:10

v/*v*). This afforded compound **1** as a white solid (1.11 g; 9.4%) Mp = 136 °C together with compound **2** (0.33 g; 2.8%) as a white solid Mp = 128 °C.

Compound **1**: ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm): 8.71 (m, 2H H6, 6″), 8.65 (d, 2H, H3, 3″, *J* = 8.0 Hz), 8.57 (s, 2H, H3′, 5′), 7.87 (td, 2H, H4, 4″, *J* = 7.6 Hz, *J* = 1.8 Hz), 7.34 (ddd, 2H, H5, 5″, *J* = 7.5 Hz, *J* = 4.8 Hz, *J* = 1.1 Hz), 7.07 (dd, 1H, Hd, *J* = 2.7 Hz, *J* = 1.8 Hz), 6.62 (dd, 1H, Hb, *J* = 3.7 Hz, *J* = 1.8 Hz), 6.32 (dd, 1H, Hc, *J* = 3.7 Hz, *J* = 2.9 Hz), 4.91 (d, 2H, He, *J* = 2.6 Hz), 2.45 (t, 1H, Hg, *J* = 2.6 Hz). ^{13}C-NMR ($CDCl_3$, 100 MHz), δ (ppm): 156.2, 155.8, 149.2, 142.1, 136.8, 132.1, 124.5, 123.8, 121.3, 119.6, 111.9, 109.4, 78.4, 73.9, 37.5. HR-MS: calc. for $[C_{22}H_{16}N_4 + H]^+$ 337.14477, found 337.14436. IR (KBr disc): n_{max} (cm^{-1}): 3174, 3049, 3013, 2114.

Compound **2**: The physical and spectroscopic properties agree with those reported in the literature [13].

4. Conclusions

The new terpyridine ligand 4′-(*N*-(propargyl)pyrrol-2-yl)-2,2′:6′,2″-terpyridine was prepared and characterized. Future work will emphasize incorporating this ligand into new complexes and functional materials.

Supplementary Materials: ^{1}H- and ^{13}C- NMR, IR spectra and HR-MS (full report) of terpyridine **1**.

Author Contributions: J.H. conceived and carried out the experiments, analyzed data and prepared the manuscript. L.G. analyzed data and contributed to the manuscript preparation. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement: The data from this study are available in this paper and in its Supplementary Materials.

Conflicts of Interest: The authors declare no conflict of interest.

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