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Synthetic protocol for the preparation of new ([2,2′:6′,2″-terpyridin]-4′-yl)naphthalene derivatives

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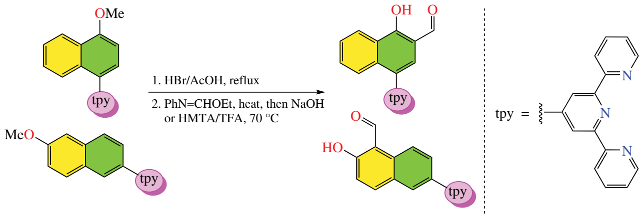
An effective synthesis of new functionalized ([2,2′:6′,2″-terpyridin]-4′-yl)naphthalenes involves demethylation in NaphthOMe group followed by formylation with PhN=CHOEt reagent. The obtained compounds containing aromatic hydroxy and formyl groups can be of interest as ligands for transition metals or as building blocks for the synthesis of polytopic ligands.



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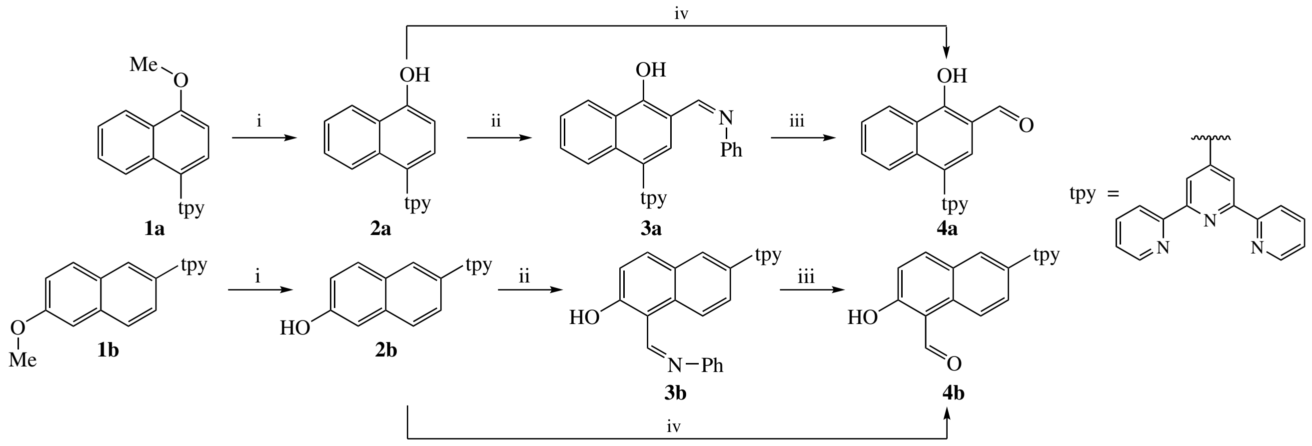
Terpyridines are a well-known family of compounds which are referred to multidentate nitrogen-donor ligands.[1] Their complex coordination chemistry and strong binding affinity towards transition metals have gained significant attention across various disciplines such as catalysis, optoelectronics, pharmacy, supramolecular chemistry and materials science.[2–6] The properties of terpyridines strongly depend on the nature of the substituents, their size, and the presence of additional coordinating fragments.[7–9] 2,2′:6′,2″-Terpyridines featuring three nitrogen coordination sites and acting as an NNN-type pincer ligand enable them to tightly chelate various metal cations while maintaining a nearly planar structure.[1,2,6,10] The literature, however, includes examples where the terpyridines act either as monotopic or ditopic ligands, with κ^{2}N-bidentate coordination mode, which is a type of hypodentate non-classical coordination.[11,12] Of particular interest are terpyridines with additional coordination centers separated from the terpyridine core by linker. This approach to the design of terpyridines allows one to increase stability of the related complexes and enables fine-tuning of the reactivity and selectivity of active centers through their steric and electronic properties.[13,14] However, these compounds are usually difficult to access and require expensive approaches such as using cross-coupling reactions for their synthesis.[15,16] In this paper, we propose efficient synthetic means toward 4-([2,2′:6′,2″-terpyridin]-4′-yl)-1-hydroxy-2-naphthaldehyde and 6-([2,2′:6′,2″-terpyridin]-4′-yl)-2-hydroxy-1-naphthaldehyde, which seem promising building blocks for the synthesis of polytopic ligands.

The terpyridine core was assembled by the Krohnke method using commercially available 4-methoxy-1-naphthaldehyde, 6-methoxy-2-naphthaldehyde, and 2-acetylpyridine.[17] The resulting terpyridine-containing methoxynaphthalenes **1a**,**b** had



Scheme 1 *Reagents and conditions*: i, Py·HCl, 140 → 210 °C for 6 h, then BBr$_3$, CH$_2$Cl$_2$, 0 °C, 30 min, then HBr, AcOH, reflux, 4 h; ii, PhN=CHOEt, 140 → 210 °C, 6 h; iii, 5% aq. NaOH, reflux, 2 h; iv, (CH$_2$)$_6$N$_4$, CF$_3$CO$_2$H, 70 °C, 72 h, then 100 °C, 4 h.

Table 1 Demethylation reaction of compounds **1a**,**b** under various conditions.

Entry	Starting ether	Demethylation agent	Product	Yield (%)
1	**1a**	Py · HCl	**2a**	73
2	**1a**	BBr_3	**2a**	83
3	**1a**	HBr	**2a**	93
4	**1b**	Py · HCl	**2b**	69
5	**1b**	BBr_3	**2b**	72
6	**1b**	HBr	**2b**	78

to be preliminarily demethylated, as their formylation did not lead to the desired products (Scheme 1). It was shown that using HBr as a demethylating agent was the most preferred, since it is the most accessible method and resulted in higher yields (Table 1, entry 3). Several approaches were examined to obtain naphthaldehydes. The first one was based on the reaction of compounds **2a**,**b** with PhN=CHOEt under heating with formation of imines **3a**,**b** in almost quantitative yields, however significant losses were observed during further hydrolysis of imines **3a**,**b** into aldehydes **4a**,**b**. The second approach involved the direct formylation of naphthols **2a** and **2b** with hexamethylenetetramine $(CH_2)_6N_4$ in CF_3CO_2H medium *via* the Duff reaction;[18] this provided higher yields, especially in the case of compound **4a**.

The structure of the obtained compounds was confirmed by ^{1}H and ^{13}C NMR spectroscopy, HRMS spectrometry as well as X-ray study for compounds **2a**,**b** (Figure 1).[†] The ^{1}H NMR spectra contain a characteristic signal for the OH group at ~10 ppm in the case of **2a**,**b** and ~12 ppm for **4a**,**b** (DMSO-d_6). The aldehydic proton appears in the range of 10.2–10.8 ppm. According to X-ray diffraction data, the terpyridine unit of **2a**,**b** anticipated *trans*,*trans*-conformation with typical bond lengths and angles. The aromatic rings are twisted with respect to each other. In the case of **2a**, twist angles between planes of rings containing N(1) and N(2), N(1) and N(3) are 19.84° and 0.06°, respectively. In the case of **2b**, these values are 3.53° and 18.58°. The plane of the naphthalene fragment and the pyridine ring containing N(1) for **2a** are almost perpendicular to each other, with a twist angle of 72.69° and slightly twisted for **2b**, with a twist angle of 13.69°.

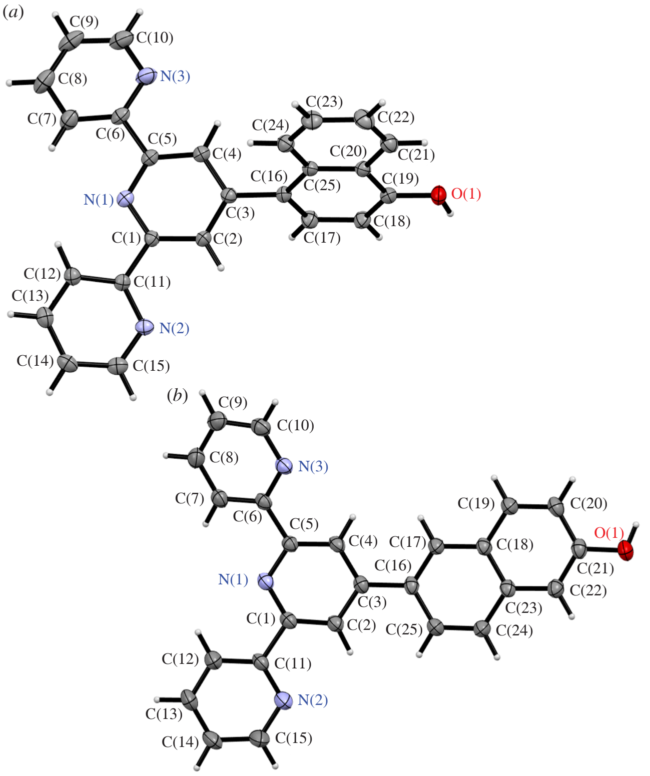


Figure 1 Molecular structure of (*a*) compound **2a** and (*b*) compound **2b** according to X-ray diffraction data with the atom numbering used in the crystallographic analysis.

In conclusion, six new ([2,2′:6′,2″-terpyridin]-4′-yl)naphthalene derivatives were synthesized. These derivatives can be of interest as transition metal ligands; moreover, terpyridine-containing hydroxy aldehydes **4a**,**b** can be used as building blocks for the synthesis of multidentate ligands with extra functional groups.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.71267/mencom.7579.

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[†] *Crystal data for* **2a**. $C_{25}H_{17}N_3O$ ($M = 375.41$ g mol^{-1}), orthorhombic, space group $Pna2_1$ (no. 33), $a = 8.7581(3)$, $b = 16.1319(4)$ and $c = 12.8091(4)$ Å, $V = 1809.73(10)$ Å^3, $Z = 4$, $T = 100.00(10)$ K, μ(MoKα) = 0.086 mm^{-1}, $d_{\text{calc}} = 1.378$ g cm^{-3}, 24971 reflections measured ($5.05 \leqslant 2\theta \leqslant 67.918$), 6431 unique ($R_{\text{int}} = 0.0432$, $R_{\text{sigma}} = 0.0395$) which were used in all calculations. The final R_1 was 0.0462 [$I > 2\sigma(I)$] and wR_2 was 0.1217 (all data).

Crystal data for **2b**. $C_{25}H_{17}N_3O$ ($M = 375.41$ g mol^{-1}), orthorhombic, space group $P2_12_12_1$ (no. 19), $a = 4.8933(2)$, $b = 15.7625(9)$ and $c = 23.8086(10)$ Å, $V = 1836.37(15)$ Å^3, $Z = 4$, $T = 100.01(11)$ K, μ(MoKα) = 0.085 mm^{-1}, $d_{\text{calc}} = 1.358$ g cm^{-3}, 27165 reflections measured ($5.168 \leqslant 2\theta \leqslant 68.094$), 7055 unique ($R_{\text{int}} = 0.0584$, $R_{\text{sigma}} = 0.0658$) which were used in all calculations. The final R_1 was 0.0597 [$I > 2\sigma(I)$] and wR_2 was 0.1401 (all data).

Colorless prism of **2a** and block of **2b** were grown by slow evaporation of a MeCN solution of the compounds. The X-ray diffraction data set was recorded on an Agilent SuperNova diffractometer using a microfocus X-ray radiation source with copper anode and Atlas S2 two-dimensional CCD detector. The reflections were collected, unit cell parameters determined and refined using the specialized CrysAlisPro software suite (Rigaku Oxford Diffraction, 2015).[19] The structures were solved using the ShelXT program (Sheldrick, 2015)[20] and refined with the ShelXL program (Sheldrick, 2015).[21] Molecular graphics and presentation of structures for the publication were performed with the Olex2 ver. 1.5 software suite.[22]

CCDC 2371441 (**2a**) and 2371447 (**2b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* https://www.ccdc.cam.ac.uk.

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