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Synthesis of 6-phenyl-2,2′-bipyridine ligands bearing polyaromatic substituents

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Abstract—A simple protocol for the efficient preparation of substituted 6-phenyl-2,2′-bipyridine derivatives is described. An inverse Diels–Alder reaction between a 3-phenyl-5-pyridyl-1,2,4-triazine and an electron-rich ethynyl species at high temperature provides a mixture of two products easily separable by column chromatography. The most encumbered isomer is favoured, likely due to favourable π–π stacking interactions in the transition state. A variety of those ligands suitable for the synthesis of cyclo-metallated complexes have been produced.

Versatile synthetic strategies leading to novel ligands have been a major stimulus to recent developments in the chemistry of transition and lanthanide metals.[1,2] Intense interest in the particularly important family of oligopyridine ligands has been driven largely by the applications of their complexes in areas as diverse as biological analysis, photocatalysis and molecular electronics.[3–7] Current extensions of these applications include those in electroluminescent devices and in information storage and processing.[8,9]

Most prominent members of the oligopyridine group are 2,2′:6′,2″-terpyridine and 2,2′-bipyridine derivatives. These are chelating ligands which show particularly high affinities for transition metal ions and which frequently stabilise unusually low oxidation state species because of both dπ–pπ* back-bonding by the cations and their capacity to form ligated anion radicals. One deficiency is that, as neutral ligands, they give cationic complexes suited possibly to spin-coating techniques for film deposition but usually unsuited to vapour deposition from ultra-high vacuum. Neutral complexes derived from anionic ligands are generally better suited to such a procedure[10] and thus it is of interest to explore the use of oligopyridine analogues in which the replacement of pyridine rings by phenyl leads to the possibility of ortho-metallation and the generation thus of a formally anionic ligand.[11]Such anions are known to strongly stabilize d^8 or d^6 transition metals like Pt(II), Pd(II) and Ir(III), particularly well-known being phenylpyridine derivatives such as $Ir(C^\wedge N)_3$ ($C^\wedge N$ = 6-phenylpyridine),[12] although ortho-metallated Pt(II) and Pd(II) complexes of 6-phenyl-2,2′-bipyridine have also been described.[13,14]

In this contribution, we present the synthesis and some spectroscopic properties of 3 and 4-aryl 6-phenyl-2,2′-bipyridine ligands. Various aryl substituents have been attached, some of them bearing N or O atoms in the skeleton. To prepare these ligands, we developed a [4+2] cyclo-addition reaction between a 2,6-disubstituted-1,3,4-triazine and ethynyaryl reagents (Scheme 1). This protocol was inspired by well-known reverse Diels–Alder reactions of various electron-deficient dienes such as 1,2,4,5-tetrazines and 1,2,4-triazines.[15]

The target triazine was prepared in two steps from 2-cyanopyridine and hydrazine followed by condensation with phenylglyoxal (Scheme 1). Condensation of **1** with hydrazine hydrate was carried out as described in the literature.[16] Note that hydrazine should be handled with care due to its high toxicity and powerful reducing properties. Interestingly, condensation with 4-ethynyltoluene gave rise to two isomers, characterized by both NMR spectroscopy and X-ray diffraction. The slightly more polar species was the minor product (13% for the 4-substituted or *para* isomer **5**), whereas the 3-substituted derivative (*meta* isomer **4**) was the major one (42%).

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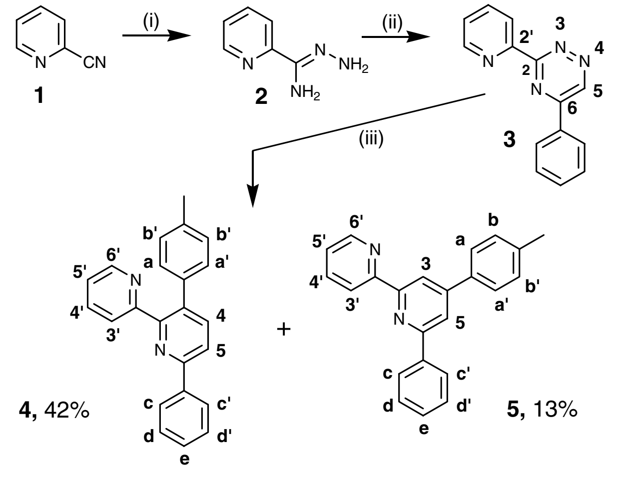


Scheme 1. Reagents and conditions: (i) N_2H_4 hydrate, EtOH; (ii) 2-phenyl glyoxal, EtOH, reflux; (iii) 4-ethynyltoluene, *o*-dichlorobenzene, 180 °C.

The proton NMR spectra (Fig. 1) provide "fingerprints" for these molecules.

The complete spectra of the two isomers could be unambiguously assigned. Protons 3 and 5 in the spectrum of the *para* isomer (**5**, top) protons 3 and 5 appear as two doublets (${}^4J = 1.5$ Hz) at 8.50 and 8.09 ppm, respectively, indicating that they are weakly coupled, whereas for the *meta* isomer (**4**, bottom) there is a stronger coupling of protons 4 and 5 ($J_{AB} = 8.1$ Hz, $\upsilon_0\delta = 12.7$ Hz), so that they appear as an obvious AB doublet pair (see Scheme 1 for labelling). These proton signals allow clear identification of the two isomers whatever be the substituents on the central pyridine ring. An interesting observation is that the doublet at 8.61 ppm assigned to the proton 3′ on the outer pyridine ring of the *para* isomer (**5**) is highly shifted (7.45 ppm) in the spectrum of the *meta* isomer (**4**), probably influenced by the proximity of the tolyl aromatic ring. This difference is also systematically observed in all cases.

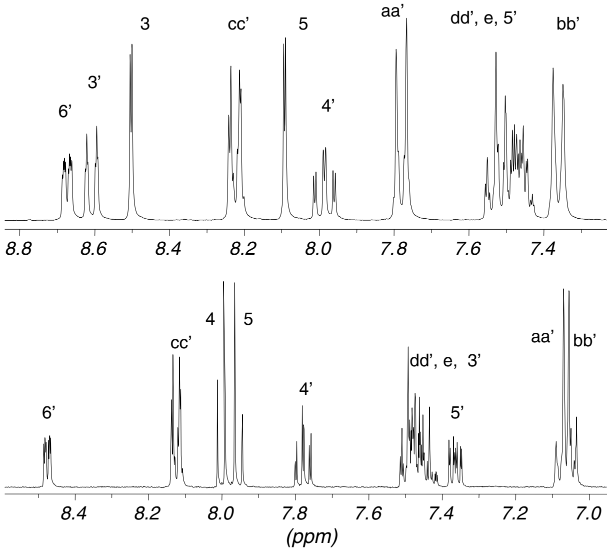
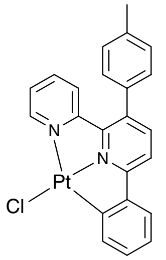


Figure 1. ${}^1H$ NMR (300 MHz, CD_3OD) of **5** (*para* isomer, top) and **4** (*meta* isomer, bottom).

The structures assigned spectroscopically (NMR) were confirmed by X-ray diffraction on single crystals (Fig. 2).

In both structures, the nitrogen atoms of the bipyridine unit lie in a *transoid* array, as usually observed for various oligopyridines.[17] However, while the two pyridine rings of the *para* isomer (**5**) are only slightly distorted with a small dihedral angle of 5.63° and 11.85° (two molecules in the asymmetric unit), they are strongly tilted by 67.06° and 60.86° in *meta* (**4**), as a direct result of the proximity of the tolyl ring. The latter is also more strongly tilted with respect to the central pyridine ring in the *meta* isomer (dihedral 53.90°) than in the *para* isomer (dihedral 30.92°).



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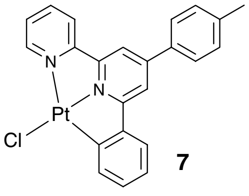

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In order to test the coordination abilities of both isomers towards Pt(II), we reacted them with K_2PtCl_4 in refluxing acetonitrile/water mixture. Both being stable,

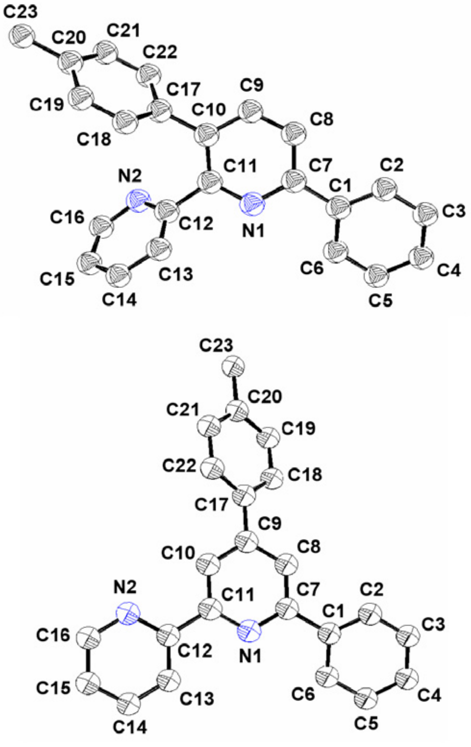


Figure 2. ORTEP view of ligands **4** (top) and **5** (bottom) with atom labeling. Probability displacement ellipsoids are shown at 50% level.

neutral complexes **6** and **7** were isolated in good yields (58 and 63%, respectively) and crystallized in a mixture of CH_2Cl_2 and cyclohexane. Their molecular structures determined by X-ray diffraction confirmed that the Pt(II) centres are square planar and that the first coordination sphere is completed by a ligated Cl anion (Fig. 3).

The tridentate cyclo-metallated ligand and the chlorine are arranged in a distorted square-planar geometry about the platinum atom. While in the *para* complex (**7**), the ligand unit is close to planar, with very small dihedral angles (3.06° with the pyridine; 2.00° with the phenyl) between the outer rings and the central pyridine, in the *meta* complex (**6**) there is a more significant distortion, resulting in a dihedral angle of 9.20° between both pairs. When compared to the respective uncomplexed ligands (**4** and **5**), the tilt between the tolyl substituent and the central pyridine is greater for the *meta* complex (**6**), with a dihedral angle of 64.28° and slightly lower for the *para* complex (**7**), with a dihedral angle of only 28.16°. The platinum–nitrogen bond lengths trans to the ortho-metallated-phenyl group [Pt(1)-N(1) 2.096 Å (**6**) and 2.109 Å (**7**)] are noticeably longer than those trans to the chlorine ligand [Pt(1)-N(2) 1.954 Å (**6**) and 1.952 Å (**7**)], which is consistent with the greater trans influence exerted by the phenyl substituent.

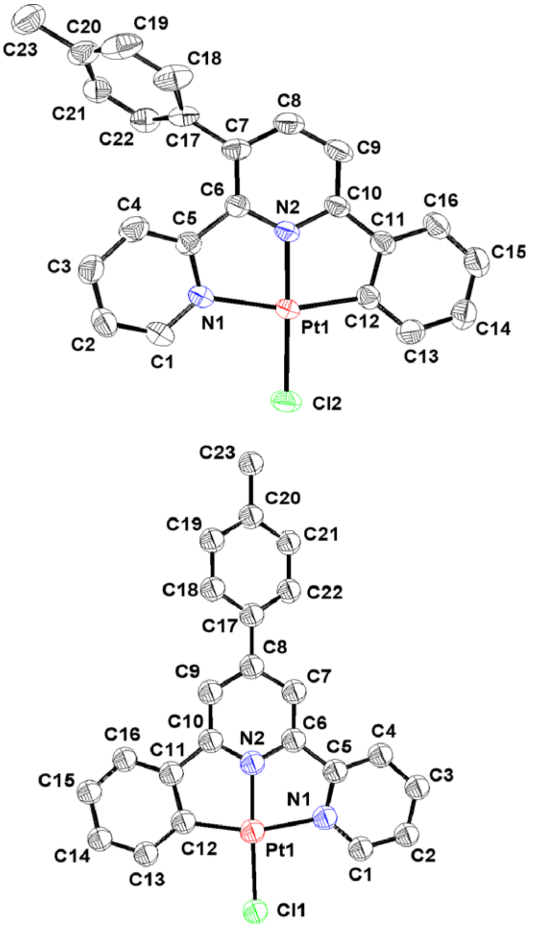
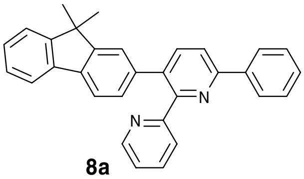
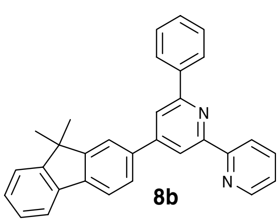


Figure 3. ORTEP view of complexes **6** (top) and **7** (bottom) with atom labeling. Probability displacement ellipsoids are shown at 50% level. Selected distances (Å) and angles (°) for **6**: Pt(1)–N(1) 2.096, Pt(1)–N(2) 1.954, Pt(1)–C(12) 1.983, Pt(1)–Cl(2) 2.309, N(1)–Pt(1)–N(2) 79.65, N(1)–Pt(1)–C(12) 162.42, N(2)–Pt(1)–Cl(2) 176.27; for **7**: Pt(1)–N(1) 2.109, Pt(1)–N(2) 1.952, Pt(1)–C(12) 1.988, Pt(1)–Cl(1) 2.305, N(1)–Pt(1)–N(2) 79.38, N(1)–Pt(1)–C(12) 161.28, N(2)–Pt(1)–Cl(1) 177.81.

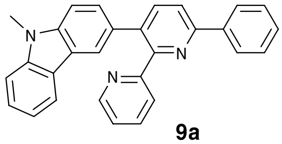
To further characterise the behaviour of the 2,6-disubstituted-1,3,4-triazine **3** and the regioselectivity of its reactions with monofunctionalised alkynes, 2-ethynyl-9,9-dimethylfluorene[18] and 3-ethynyl-9-methylcarbazole[19] were reacted with **3** at high temperature in *o*-dichlorobenzene. As found for 4-ethynyltoluene, the major products were the *meta* isomers **8a** and **9a** (isolated yields 33% and 43%), while the *para* isomers **8b** and **9b** were isolated in low yield (8% and 12%). For selected ^1H NMR data see Table 1.



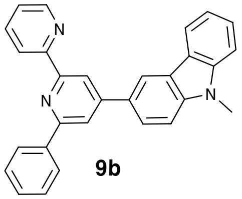
8a



8b

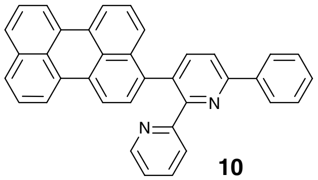


9a



9b

The use of even more electron-rich terminal alkynes, such as 3-ethynylperylene or 1-ethynylpyrene, provided almost exclusively the *meta* isomers **10** and **11**, identified by NMR spectroscopy (see Table 1).



10

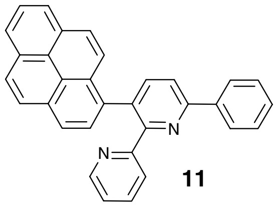


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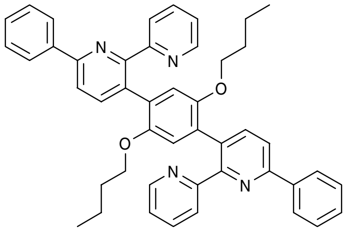
Table 1. Selected NMR data for the new ligands

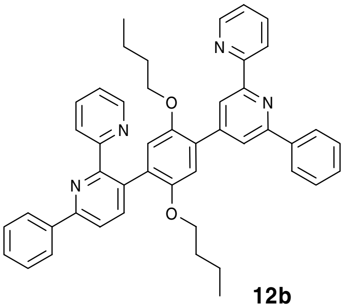
Compounds	Protons 4,5 (ppm) AB quartet (J_{AB}, $\upsilon_0\delta$, Hz)[a] For the *meta* isomer	Protons 3,5 (ppm) Doublet (J^4, Hz)[a] For the *para* isomer
8a	7.92 (8.1, 26.3)	—
8b	—	8.71 (1.5), 8.05 (1.3)
9a	7.93 (8.2, 33.0)	—
9b	—	8.57 (1.7), 8.12 (1.3)
10	7.92 (8.0, 6.8)	—
11	7.93 (7.7, 43.6)	—
12a	7.85 (8.1, 16.4)	—
12b	7.89 (8.2, 19.3)	8.60 (1.5), 8.09 (1.5)
12c	—	8.67 (1.5), 8.15 (1.5)

[a] ^1H NMR (300 MHz) spectra recorded in $CDCl_3$.

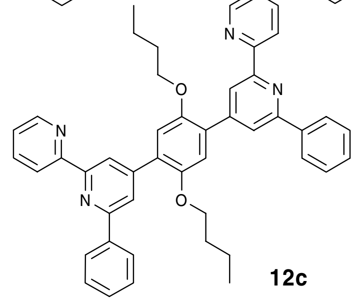
To broaden the synthetic scope of these reactions, we also tested a double condensation with a diethynyl derivative. 1,4-Diethynyl-3,6-dibutoxyphenyl was chosen due to its availability, good thermal stability, and relative solubility in *o*-dichlorobenzene. As anticipated, three products were separated by flash column chromatography. The *meta*/*meta* derivative **12a** was isolated in 21% yield, and the *meta*/*para* **12b** in 11%. The less favoured *para*/*para* isomer **12c** was formed in very low yield (3%).



12a



12b

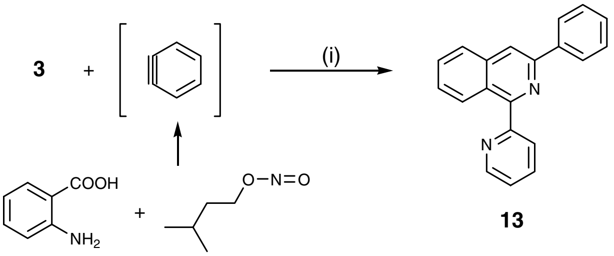


12c

Considering the possible mechanisms, we hypothesized that the *meta* isomer is favoured owing to favourable π–π* interaction in the transition state between the ethynylaryl and the pyridine ring. In the absence of such a stabilizing interaction, the *para* isomer should be favoured for steric reasons. In keeping with such a hypothesis is the fact that when *tert*-butylacetylene was used only the *para* isomer could be isolated. Here, the steric course of the reaction can be understood assuming that the reaction partners adopt an orientation in the transition state that minimizes unfavourable steric interaction between the bulky *tert*-butyl group and the pyridine substituent. Such regio-selectivity has previously been observed with stannane derivatives.[20]

Finally, in order to avoid isomer mixtures, we used benzyne as a synthetic equivalent of symmetrical acetylenic derivatives. This highly reactive reagent, prepared from anthranilic acid and isoamyl nitrite[21] was condensed *in situ* to provide the fused isoquinoline molecule **13** in low yield (Scheme 2).

Selected spectroscopic data are gathered for all compounds in Table 2. The absorption spectra of most compounds exhibit an intense band between 240 and 320 nm (ε in the range 16,000–44,000 M^{-1} cm^{-1}), which can be assigned to the spin-allowed π–π* transitions involving the pyridyl/phenyl/ancillary aryl rings. Such a band is slightly red-shifted for the fluorene and carbazole cases **8** and **9** because of the presence of additional aryl substituents. In compounds **10** and **11**, the increase of extinction coefficient is due to the strong and structured absorption of spin-allowed transitions involving the perylene and pyrene fragments, respectively. All the compounds exhibit a relatively intense emission (Table 2) in solution at room temperature. For **10** and **11** the intense fluorescence is due to the peripheral perylene and pyrene subunits. The emission spectrum is similar in shape and the emission is significantly red-shifted compared to the absorption spectrum, indicating a strong Stokes shift, which suggests a reorganization occurring in the excited state. Surprisingly, for the *para* derivatives a hypsochromic shift of about 30 nm is observed. Note that for complexes **6** and **7** the low energy absorption band corresponds to a metal-to-ligand charge transfer absorption band and the emission probably involves the same state.[22]



Scheme 2. (i) Anthranilic acid, *o*-dichlorobenzene, isoamyl nitrite in *o*-dichlorobenzene at 180 °C, 3 h.

In summary, a series of tridentate (C^N^N) ligands have been prepared and characterized by NMR spectroscopy and X-diffraction on single crystals in some key cases. The regioselectivity of the syntheses can be controlled by steric influences. The coordination potential of the ligands, as anionic species formed through ortho-metallation, has been tested by complexation with Pt(II). High solubility in apolar solvents can be ensured by the use of butoxy substituents. The synthetic strategy tolerates the

Table 2. Selected data for the new ligands

Compound	Yield (%)	FAB/MS *m/z* (relative intensity)[a]	λ_{max} (nm), ε (M^{-1} cm^{-1})[b]	λ_{em} (nm)[b]
4	42	323.1 (100)	289 (22,900)	—
5	13	323.1 (100)	264 (43,300)	362
6	58	516.1 (80)	433 (2,700)	575
7	63	552.1 (95)	436 (5,200)	567
8a	33	425.1 (100)	318 (33,000)	412
8b	8	425.1 (100)	318 (41,000)	380
9a	43	412.1 (100)	319 (20,500)	438
9b	12	412.2 (100)	320 (19,000)	405
10	9	483.1 (100)	450 (34,500)	470
11	20	433.1 (100)	349 (40,100)	425
12a	21	683.3 (100)	338 (sh, 17,600)	424
12b	11	682.3 (100)[c]	328 (sh, 18,500)	424
12c	3	682.3 (100)[c]	318 (23,000)	424
13	20	282.1 (100)	242 (16,500)	429

[a] FAB mass spectroscopy, the molecular peak corresponds to $[M+H]^+$ except for **6** and **7** where *m/z* accounts for $[M-Cl]^+$.

[b] Averaged value determined from at least two different solutions of non-degassed CH_2Cl_2 solution.

[c] EI-MS (70 eV) *m/z* (%) corresponding to M^+.

presence of tertiary amine fragments such as in the carbazole cases. Further work is directed towards the complexation of the perylene and pyrene ligands with Pt(II) and the substitution of the chloro ligand by alkyne derivatives, which should provide access to novel electroluminescent transition complexes.

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