A Facile Route to Sterically Hindered and Non-Hindered 4′-Aryl-2,2′:6′,2″-Terpyridines

Jianhua Wang, Garry S. Hanan*

Département de Chimie, Université de Montréal, Montreal, Québec H3T 1J4, Canada
Fax +1(514)3437586; E-mail: garry.hanan@umontreal.ca

Received 11 February 2005

Abstract: A facile one-pot synthesis of 4′-aryl-2,2′:6′,2″-terpyridines from aryl aldehydes and 2-acetylpyridine is presented. The synthesis of terpyridines incorporating sterically hindered aryl groups, such as the 9-anthryl group, can also be readily synthesized using this method.

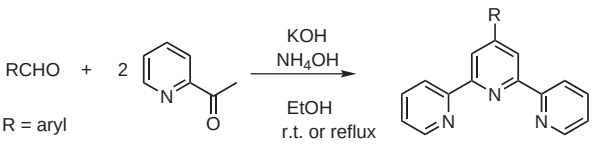
Key words: nitrogen ligands, heterocycles, substituted terpyridines, one-pot reactions

Transition metal complexes of polypyridyl ligands have long been a target in coordination chemistry due to their potential utility in a range of applications, such as luminescent chemosensors, photocatalysts, components of devices for the conversion of light into electrical energy, and new electroluminescent materials.[1–3] The prototypical 2,2′-bipyridine (bpy) and 2,2′:6′,2″-terpyridine (tpy) ligands have been employed in a large number of these studies, usually binding as bidentate and tridentate ligands, respectively. The advantage of the latter ligand is that structurally simple achiral bis-tpy complexes are obtained with octahedrally coordinating metal ions, which can in turn be used to build up stereochemically discrete polynuclear arrays, as opposed to the racemic mixtures derived from bpy. Moreover, the achirality of tpy complexes is retained upon the chemical modification of the tpy by introducing functional groups into its 4′-position, which necessarily arranges them in a *trans* configuration along a C2 axis.

Introducing aryl substituents at the 4′-position of tpy can also have a profound influence on the photophysical properties of bis-tpy metal complexes and this effect has been investigated in some detail.[4] More recently, the photophysical properties of uncomplexed terpyridines have also begun to attract interest due to their potential application in photophysical devices.[5–8] Strategies for the incorporation of aryl substituents into the 4′-position of the terpyridine core are of considerable interest with respect to many of the applications discussed above.

The classical approach to 4′-aryl-tpy are based on the synthesis of a pyridine, involving the condensation of two equivalents of 2-acetylpyridine with the appropriate aryl aldehyde, with formation of the central pyridine ring from the reaction of the diketone intermediate with ammonia (or a source thereof) at elevated temperatures.[9] A number of variations have been reported, some involving isolation of the intermediate enone or diketone, others employing mild or solvent-free conditions for parts of the synthesis, but almost all relying on a common step in which the central pyridine ring is formed.[10] In particular, the approach involving the reaction of 2-pyridyl enaminone and 2-acetylpyridine with a strong base, *t*-BuOK, has been widely employed for the synthesis of the parent tpy ligand. Distinctly different synthetic approaches, in which all three pyridine rings are present in the starting materials, include the reaction of 2,2′-bipyridine with 2-pyridyl-lithiums, the Stille coupling of 2,6-dibromopyridines with 2-trialkylstannyl pyridines,[11] and the Suzuki cross-coupling of 4′-bromo-tpy with aryl-boronic acid/ester.[12] However, these approaches feature relatively long reaction times, harsh conditions and the necessity to purify the products by column chromatography. As part of our research with Ru(II) complexes of tridentate tpy ligands, a mild and efficient synthesis of a variety of 4′-aryl-tpy ligands was required.[13] Herein we report the facile one-step synthesis of a variety of tpy-based ligands with aromatic substituents in their 4′-position, which greatly improves the one-pot synthesis for 4′-aryl-tpy ligands previously reported.[14]

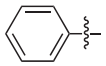
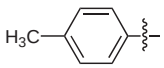
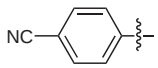
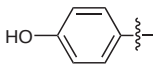
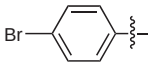
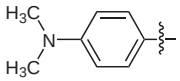
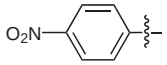
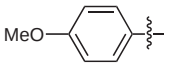
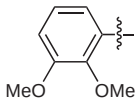
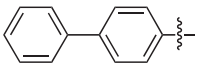
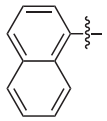
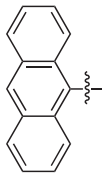
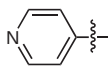
Our optimization of the one-step reaction started from readily available aryl aldehydes[15] and 2-acetylpyridine (Scheme 1). The reaction conditions and yields of the various ligands are gathered in Table 1. The enolate of 2-acetylpyridine can be generated by KOH under mild conditions. The following aldol condensation and Michael addition proceeded smoothly at room temperature. The soluble diketone intermediate was then allowed to form the central pyridine ring with an aqueous ammonia nitrogen source. The synthesis of the phenyl-based tpy ligands, **1**–**9**, was very straightforward using these mild conditions. Typically, the ligands precipitated from the reaction mixture as finely dispersed solids, which were easily separated by filtration. For **4**, after 24 hours reaction, the ligand was separated from the reaction mixture by acidification with AcOH, extraction with CH_2Cl_2 and recrystallization from EtOH.



Scheme 1 Facile one-pot synthesis of 4′-aryl-2,2′:6′,2″-terpyridine

SYNLETT 2005, No. 8, pp 1251–1254
Advanced online publication: 21.04.2005
DOI: 10.1055/s-2005-868481; Art ID: S01605ST

Table 1 Reaction Conditions and One-Step Yields of 4′-Aryl-2,2′:6′,2″-terpyridines as Compared with Previously Reported Methods[a]

Ligand	R	Reaction time (h), yield (%)[b]	Reported yield (%),[c] (steps)[d]
1		2, (53)	<5, (4)[6e]
2		2, (49)	19, (4)[5]; 46 (1)[13]
3		4, (42)	36, (5)[6e]
4		12, (43)	40, (2)[17]
5		2, (56)	70, (2)[5]
6		12, (25)	17, (4)[5]; 29, (4)[6e]
7		4, (51)	65, (2)[5]; 34, (5)[6e]
8		12, (20)	20, (4)[5]
9		24, (27)	New
10		4, (48)	42, (1)[6f]
11		4, (32)	No yield available[18]
12		24,[g] (27)	59, (2)[4c]
13		4, (24)	69, (2)[19]
14		4, (42)	69, (2)[20]

[a] Reaction conditions: 1.0 equiv aryl aldehyde, 2.0 equiv 2-acetyl pyridine, 2.0 equiv KOH, 2.5 equiv NH_4OH, EtOH, r.t.
[b] Isolated yield of first crop of precipitate in our work.
[c] Isolated overall yields as previously reported.
[d] Number of reaction steps from commercially available starting materials.
[e] In ref.[6], from 4′-TfO-2,2′:6′,2″-terpyridine (TfO-tpy, 45% overall yield over 3 steps) or 4′-bromo-2,2′:6′,2″-terpyridine (45% overall yield over 4 steps).
[f] Starting from 4′-*p*-bromophenyl-2,2′:6′,2″-terpyridine.
[g] Reaction conditions: 1.0 equiv 9-anthryl aldehyde, 2.0 equiv 2-acetyl pyridine, 2.0 equiv KOH, 2.5 equiv NH_4OH, EtOH, reflux, 24 h.

The encouraging results for the synthesis of ligands **1**–**9** led us to apply these mild conditions to introduce organic chromophores into the tpy moiety, which is a critical step to prolong the room temperature luminescence lifetime of $Ru(tpy)_2^{2+}$ complexes by the bichromophore approach.[16] The 4′-biphenyl and 1-naphthyl groups were introduced into 4′-position of tpy to give ligand **10** and **11** by stirring at room temperature for four hours. However, the syn-

thesis of ligand **12** with the bulkier 9-anthryl group was problematic due to the insolubility of the intermediate, 2-[1-(9-anthryl)-3-oxo-3-prop-2-enyl] pyridine, in EtOH. Treatment of the same starting materials at reflux kept the enone intermediate in solution leading to a one-step synthesis of 4′-(9-anthryl)-tpy. It is noteworthy that this is the first example of a one-step synthesis of tpy-based ligands with bulky substituents in the 4′-position.

To survey the scope of the reaction conditions for heteroatom aromatic aldehydes, the 2-furyl-tpy (**13**) and 4-pyridyl-tpy (**14**) were also synthesized in moderate yield.

In conclusion, we have developed mild reaction conditions for the synthesis of 4′-aryl and 4′-heteroaryl substituted tpys. These reaction conditions are compatible with various functional groups and provide an efficient route to tridentate 2,2′:6′,2″-terpyridine-based ligands.

Representative Procedure for Ligands 1–11, 13–16
Synthesis of 1

2-Acetylpyridine (4.84 g, 40 mmol) was added into a solution of benzaldehyde (2.12 g, 20 mmol) in EtOH (100 mL). KOH pellets (3.08 g, 85%, 40 mmol) and aq NH_3 (58 mL, 29.3%, 50 mmol) were then added to the solution. The solution was stirred at r.t. for 4 h. The off-white solid was collected by filtration and washed with EtOH (3 × 10 mL). Recrystallization from $CHCl_3$–MeOH afforded white crystalline solid **1** (3.24 g, 10.5 mmol, 53%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 (s, 2 H, $H_{3',5'}$), 8.74 (d, *J* = 6.5 Hz, 2 H, $H_{6,6''}$), 8.68 (d, *J* = 8.0 Hz, 2 H, $H_{3,3''}$), 7.92 (d, *J* = 6.9 Hz, 2 H, H_{Ph}), 7.90 (t, *J* = 7.5 Hz, 2 H, $H_{4,4''}$), 7.52 (t, *J* = 6.9 Hz, 2 H, $H_{Ph2,6}$), 7.46 (t, *J* = 6.9 Hz, 1 H, $H_{Ph3,5}$), 7.37 (dd, *J* = 7.5, 5.0 Hz, 2 H, $H_{5,5''}$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.5, 156.2, 150.8, 149.4, 138.8, 137.4, 129.5, 129.3, 127.8, 124.3, 121.9, 119.4. Anal. Calcd for $C_{21}H_{15}N_3$: C, 81.53; H, 4.89; N, 13.58. Found: C, 81.15; H, 4.98; N, 13.50.

4′-(2,3-Dimethoxyphenyl)-2,2′:6′,2″-terpyridine (9)

Yield 27%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.72 (dt, *J* = 6.7, 0.7 Hz, 2 H, $H_{6,6''}$), 8.70 (s, 2 H, $H_{3',5'}$), 8.68 (d, *J* = 8.0 Hz, 2 H, $H_{3,3''}$), 7.88 (td, *J* = 7.7, 1.7 Hz, 2 H, $H_{4,4''}$), 7.34 (ddd, *J* = 7.4, 4.8, 0.8 Hz, 2 H, $H_{5,5''}$), 7.18–7.16 (m, 2 H, $H_{Ph5,6}$), 7.02 (m, 1 H, H_{Ph4}), 3.95 (s, 3 H, H_{CH3}), 3.73 (s, 3 H, H_{CH3}). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.8, 155.8, 153.5, 149.6, 148.7, 147.3, 137.2, 134.2, 124.6, 124.1, 122.8, 122.0, 121.7, 113.3, 61.5, 56.4. FAB-MS: 370.4 $[M + 1]^+$. Anal. Calcd for $C_{23}H_{19}N_3O_2$: C, 74.78; H, 5.18; N, 11.37. Found: C, 74.26; H, 5.15; N, 11.09.

4′-(1-Naphthyl)-2,2′:6′,2″-terpyridine (11)

Yield 32%. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.76 (d, *J* = 7.8 Hz, 2 H, $H_{3,3''}$), 8.71 (d, *J* = 3.7 Hz, 2 H, $H_{6,6''}$), 8.68 (s, 2 H, $H_{3',5'}$), 8.01–7.90 (m, 5 H, $H_{4,4'',nap}$), 7.63–7.49 (m, 4 H, H_{nap}), 7.37 (t, *J* = 5.6 Hz, 2 H, $H_{5,5''}$). ^{13}C NMR (100 MHz, CD_3Cl): δ = 156.7, 155.9, 151.3, 149.6, 138.4, 137.3, 134.1, 131.4, 129.1, 128.8, 127.5, 127.0, 126.4, 126.0, 125.7, 124.3, 122.8, 121.8. FAB-MS: 359.1 $[M]^+$. Anal. Calcd for $C_{25}H_{17}N_3$: C, 83.54; H, 4.77; N, 11.69. Found: C, 83.27; H, 4.79; N, 11.61.

4′-(9-Anthryl)-2,2′:6′,2″-terpyridine (12)
Ligand 12

2-Acetylpyridine (0.61 g, 5.0 mmol) was added into a solution of 9-anthraldehyde (0.52 g, 2.5 mmol) in EtOH (25 mL). KOH pellets (0.39 g, 85%, 5.0 mmol) and aq NH_3 (7.5 mL, 29.3%, 6.3 mmol) were then added to the solution. The solution was heated at reflux for 24 h. After cooling down to ambient temperature, the solution was evaporated to dryness under reduced pressure. Recrystallization of the residue from $CHCl_3$–MeOH afforded a yellow crystalline solid (0.28 g, 0.68 mmol, 27%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.82 (d, *J* = 7.9 Hz, 2 H, $H_{3,3''}$), 8.66 (d, *J* = 0.3 Hz, 2 H, $H_{6,6''}$), 8.63 (s, 2 H, $H_{3',5'}$), 8.57 (s, 1 H, H_{An10}), 8.09 (d, *J* = 8.7 Hz, 2 H, $H_{An1,8}$), 7.95 (t, *J* = 7.5 Hz, 2 H, $H_{4,4''}$), 7.73 (d, *J* = 8.7 Hz, 2 H, $H_{An2,7}$), 7.49 (t, *J* = 7.2 Hz, 2 H, $H_{An3,6}$), 7.39–7.36 (m, 4 H, $H_{5,5'',An4,5}$). ^{13}C NMR (100 MHz, CD_3Cl): δ = 156.5, 156.0, 150.0, 149.6, 137.4, 134.7, 131.6, 129.9, 128.8, 127.8, 126.8, 126.3, 125.6, 124.3, 124.3, 121.9. FAB-MS: 409.5 $[M]^+$. Anal. Calcd for $C_{29}H_{19}N_3$: C, 85.06; H, 4.68; N, 10.26. Found: C, 85.27; H, 4.65; N, 10.08.

Acknowledgment

The authors thank the Natural Sciences and Engineering Research Council (NSERC) of Canada and the Université de Montréal for financial support.

References

(1) (a) Demas, J. M.; DeGra, B. A. *Coord. Chem. Rev.* **2001**, *211*, 317. (b) For a recent example: Kimura, M.; Takahashi, A.; Sakata, T.; Tsukahara, K. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1839. (c) Péchy, P.; Rotzinger, F. P.; Nazeeruddin, M. K.; Kohle, O.; Zakeeruddin, S. M.; Humphry-Baker, R.; Grätzel, M. *J. Chem. Soc., Chem. Commun.* **1995**, 65. (d) Baldo, M. A.; Thompson, M. E.; Forrest, S. R. *Nature* **2000**, *403*, 750. (e) Ziessel, R. J. *Inclusion Phenom. Macrocyclic Chem.* **1999**, *35*, 369.

(2) Constable, E. C.; Cargill Thompson, A. M. W.; Tocher, D. A.; Daniels, M. A. M. *New J. Chem.* **1992**, *16*, 855.

(3) Sauvage, J.-P.; Collin, J.-P.; Chambron, J.-C.; Guillerez, S.; Coudret, C.; Balzani, V.; Barigelletti, F.; De Cola, L.; Flamigni, L. *Chem. Rev.* **1994**, *94*, 993.

(4) (a) Maestri, M.; Armaroli, N.; Balzani, V.; Constable, E. C.; Cargill Thompson, A. M. W. *Inorg. Chem.* **1995**, *34*, 2759. (b) Hammarström, L.; Barigelletti, F.; Flamigni, L.; Indelli, M. T.; Armaroli, N.; Calogero, G.; Guardigli, M.; Sour, A.; Collin, J.-P.; Sauvage, J.-P. *J. Phys. Chem. A* **1997**, *101*, 9061. (c) Albano, G.; Balzani, V.; Constable, E. C.; Maestri, M.; Smith, D. R. *Inorg. Chim. Acta* **1998**, *277*, 225.

(5) Mutai, T.; Cheon, J.-D.; Arita, S.; Araki, K. *J. Chem. Soc., Perkin Trans. 2* **2001**, 1045.

(6) Goodall, W.; Williams, J. A. G. *Chem. Commun.* **2001**, 2514.

(7) Roberto, D.; Tessore, F.; Ugo, R.; Bruni, S.; Manfredi, A.; Quici, S. *Chem. Commun.* **2002**, 846.

(8) Alcock, N. W.; Barker, P. R.; Haider, J. M.; Hannon, M. J.; Painting, C. L.; Pikramenou, Z.; Plummer, E. A.; Rissanen, K.; Saarenketo, P. *J. Chem. Soc., Dalton Trans.* **2000**, 1447.

(9) A comprehensive review of methods up to 1995 is provided by: Cargill Thompson, A. M. W. *Coord. Chem. Rev.* **1997**, *160*, 1.

(10) (a) Kröhnke, F. *Synthesis* **1976**, 1. (b) Constable, E. C.; Ward, M. D.; Corr, S. *Inorg. Chim. Acta* **1988**, *141*, 201. (c) Frank, R. L.; Riener, E. F. *J. Am. Chem. Soc.* **1950**, *72*, 4182. (d) Korall, P.; Börje, A.; Norrby, P.-O.; Åkermark, B. *Acta Chem. Scand.* **1997**, *51*, 760. (e) Cave, G. W. V.; Raston, C. L. *Chem. Commun.* **2000**, 2199.

(11) (a) Cardenas, D. J.; Sauvage, J.-P. *Synlett* **1996**, 916. (b) Hanan, G. S.; Schubert, U. S.; Volkmer, D.; Riviere, E.; Lehn, J.-M.; Kyritsakas, N.; Fisher, J. *Can. J. Chem.* **1997**, *75*, 169. (c) Fallahpour, R.-A.; Neuberger, M.; Zehnder, M. *New J. Chem.* **1999**, *23*, 53. (d) Fallahpour, R.-A. *Eur. J. Inorg. Chem.* **1998**, 1205.

(12) Goodall, W.; Wild, K.; Arm, K. J.; Williams, J. A. G. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1669.
(13) During the preparation of this paper, a similar approach to synthesize 4′-*p*-tolyl-2,2′:6′,2″-terpyridine was reported: Vaduvescu, S.; Potvin, P. G. *Eur. J. Inorg. Chem.* **2004**, 1763.
(14) Collin, J.-P.; Guillerez, S.; Sauvage, J.-P.; Barigelletti, F.; De Cola, L.; Flamigni, L.; Balzani, V. *Inorg. Chem.* **1991**, *30*, 4230.
(15) Most of the starting aryl aldehydes were purchased from Aldrich. Aldehydes that were not commercial available were synthesized from the corresponding aryl bromides by lithiation and then formylation with dimethylformamide.
(16) Wang, J.; Hanan, G. S.; Loiseau, F.; Campagna, S. *Chem. Commun.* **2004**, 2068.
(17) Yoo, D.-W.; Yoo, S.-K.; Kim, C.; Lee, J.-K. *J. Chem. Soc., Dalton Trans.* **2002**, 3931.
(18) Michalec, J. F.; Bejune, S. A.; Cuttell, D. G.; Summerton, G. C.; Gertenbach, J. A.; Field, J. S.; Haines, R. J.; McMillin, D. R. *Inorg. Chem.* **2001**, *40*, 2193.
(19) Husson, J.; Beley, M.; Kirsch, G. *Tetrahedron Lett.* **2003**, *44*, 1767.
(20) Persaud, L.; Barbiero, G. *Can. J. Chem.* **1991**, *69*, 315.