Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron Letters
Tetrahedron Letters 47 (2006) 3471–3473

Synthesis of a novel ditopic ligand incorporating directly bonded 1,10-phenanthroline and 2,2′:6′,2″-terpyridine units

Pablo Gaviña* and Sergio Tatay

Instituto de Ciencia Molecular, Universidad de Valencia, Polígono de la Coma s/n, 46980 Paterna (Valencia), Spain

Received 26 January 2006; revised 15 February 2006; accepted 3 March 2006
Available online 30 March 2006

Abstract—The synthesis of a rigid ditopic ligand incorporating a 1,10-phenanthroline directly connected through its 3-position to the 5-position of a 2,2′:6′,2″-terpyridine is described. The synthesis is based on a series of palladium(0)-catalyzed cross-coupling reactions (Stille and Suzuki couplings) starting from 1,10-phenanthroline and bromo-substituted pyridines.

Oligopyridine-based linear ligands incorporating several coordination sites are fundamental building blocks in metallosupramolecular chemistry, particularly in the construction of molecular helicates, racks and grids[1] or transition metal-based rotaxanes, catenanes and knots.[2] Among the different binding subunits, 2,2′-bipyridine, 2,2′:6′,2″-terpyridine and 1,10-phenanthroline moieties are by far the most widely used.[3] The development of modern palladium(0) cross-coupling based methodologies for the direct C–C bond formation has made possible the design of many symmetrical oligopyridines and oligophenanthrolines where the pyridine or phenanthroline units are directly bonded or connected through different bridging ligands, like ethynyl or phenylene spacers.[4] In some cases these ligands are also functionalized with ending groups which can be covalently incorporated into larger structures.[5] However, unsymmetrical ligands containing both, a terpyridine and a phenanthroline chelate are not as common,[6] and as far as we know, a linear ditopic ligand containing a terpyridine unit *directly bonded* to a phenanthroline moiety was still a challenge. Such ligand would be of great interest in the field of molecular motors, as a rigid linear fragment in the construction of bistable transition metal-based rotaxanes.[2]

We would like to report herein the synthetic route leading to the first 3,5-connected phenanthroline/terpyridine conjugate. Ligand **1** (depicted in Fig. 1) is characterized by the presence of two different coordination sites: a 2,2′:6′,2″-terpyridine (*terpy*) tridentate ligand and a 1,10-phenanthroline (*phen*) bidentate moiety. The main feature of this ligand is that the *phen* and *terpy* units are *directly connected to one another* (the 3-position of the *phen* to the 5-position of the *terpy*), without any bridging ligand in between. Compound **1** also possesses two different substituents at the ends of the string which can be further functionalized.

Our synthetic approach for compound **1** relies on the preparation of two asymmetrically substituted *phen* and *terpy* ligands, **2** and **3** (see Fig. 1), bearing each one a bromine atom at the appropriate position. The final step would be a palladium(0)-catalyzed cross-coupling reaction between one or both ligands and the organoboron or organotin derivative from the other one.

As one would expect, the main difficulty for the synthesis of such ligands is related to their unsymmetrical nature. 3-Bromo-8-(*p*-anisyl)-1,10-phenanthroline (**2**) was easily prepared in 50% isolated yield from 3,8-dibromo-1,10-phenanthroline (**4**)[7] and 1 equiv of *p*-anisylphenylboronic ester **5** under Suzuki cross-coupling conditions ($Pd(PPh_3)_4$, aq Na_2CO_3, toluene, reflux) (Scheme 1). Some unreacted **4** and the symmetrically disubstituted phenanthroline were also isolated (ca. 15–20%). The synthesis of the *terpy* fragment **3** was accomplished by two consecutive cross-coupling reactions involving different tributylstannyl pyridine derivates. It is worth mentioning that we also tried to prepare the less toxic and environmental friendly boron derivatives instead of the tin compounds to carry out

* Corresponding author. Tel.: +34 963544421; fax: +34 963543273; e-mail: pablo.gavina@uv.es

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.03.025

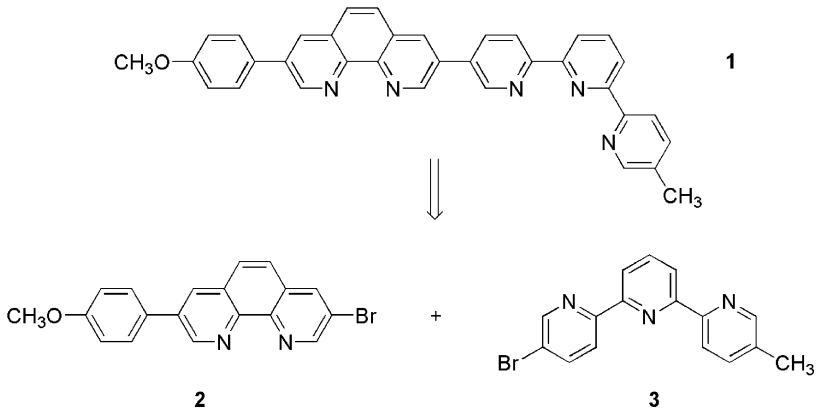
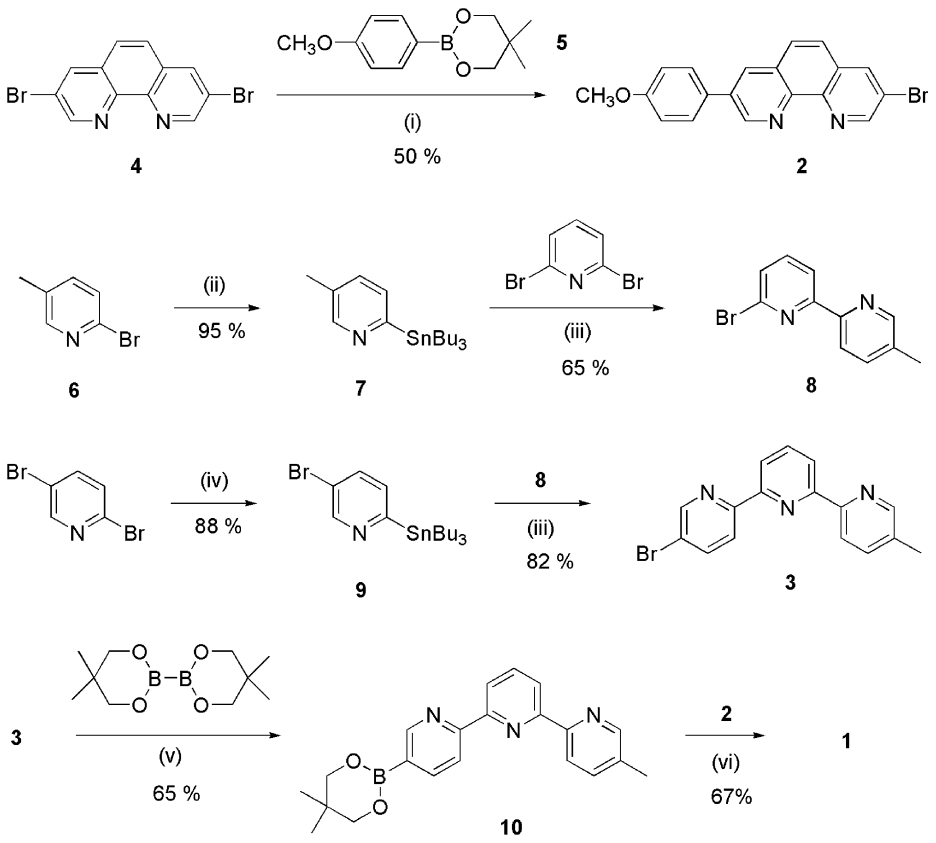


Figure 1. Ditopic ligand **1** and key building blocks **2** and **3**.



Scheme 1. Reagents and conditions: (i) $Pd(PPh_3)_4$, Na_2CO_3, toluene–H_2O, reflux; (ii) (1) BuLi, THF, −78 °C; (2) Bu_3SnCl; (iii) $Pd(PPh_3)_4$, toluene, reflux; (iv) (1) BuLi, toluene, −78 °C; (2) Bu_3SnCl; (v) $Pd(dppf)Cl_2$, KOAc, DMSO, 80 °C; (vi) $Pd(PPh_3)_4$, K_2CO_3, DMF–H_2O.

cross-coupling reactions under Suzuki conditions, but we were unsuccessful probably due to deboronation side reactions.[8]

The synthesis of 5-bromo-5″-methyl-2,2′:6′,2″-terpyridine (**3**) is schematically depicted in Scheme 1. Starting from commercially available 2-amino-5-methylpyridine, 2-bromo-5-methylpyridine (**6**) was synthesized by a diazotation/bromination sequence with bromine, HBr and sodium nitrite. 2-Tributylstannyl-5-methylpyridine (**7**) was prepared in 95% yield from **6** by Br–Li exchange with butyllithium at −78 °C followed by stannylation with tributyltin chloride.[9] Stille-type cross-coupling of **7** with 1.5 equiv of 2,6-dibromopyridine in toluene, in the presence of $Pd(PPh_3)_4$ afforded 6-bromo-5′-methyl-2,2′-bipyridine (**8**) in 65% yield after chromatographic purification. Here every attempt to use the lithiation/stannylation protocol to obtain a tin derivative of **8** was unsuccessful. However, some preliminary results suggested the possibility of coupling **8** with the bromostannyl derivative **9**, taking advantage of the higher reactivity of the bromine atom at the 6-position of the bipyridine to overcome possible undesired homocoupling side reactions. 5-Bromo-2-(tributylstannyl)pyridine (**9**) was prepared by a selective monolithiation of 2,5-dibromopyridine at the 2-position with butyllithium

in toluene at −78 °C,[10] followed by in situ addition of tributyltin chloride. Compound **9** could thus be isolated in 88% yield after a short column chromatography on alumina. Finally, reaction of **9** with the bromobipyridine **8** under Stille cross-coupling conditions (refluxing toluene in the presence of a catalytic amount of $Pd(PPh_3)_4$) afforded the monobromo substituted terpyridine **3** in 82% yield.[11]

At this point, we tried to obtain either a boron or tin derivative of the precursors **2** or **3** using classical metal–halogen exchange methodologies with very poor results. We could finally manage to obtain a boronic ester derivative of the *terpy* ligand **3** by using the palladium catalyzed Miyaura cross-coupling reaction.[12] Thus, **3** was reacted with bis(neopentyl glycolato)diboron in DMSO in the presence of potassium acetate and a catalytic amount of $Pd(dppf)Cl_2$. Pure 5-(neopentyl glycolatoboron)-5″-methyl-2,2′:6′,2″-terpyridine (**10**) was isolated as a white solid after recrystallization from $EtOH/CH_2Cl_2$ in 65% yield. The desired ditopic ligand **1** could be finally obtained in 67% yield by a Suzuki cross-coupling reaction between boronic ester **10** and the bromophenanthroline **2**.[13]

In conclusion, the synthesis of a novel ditopic ligand in which a *phen* moiety is directly bonded through its 3-position to the 5-position of a *terpy* unit is described. This ligand will be used as a linear thread in the construction of bistable metallic rotaxanes.[2] In addition complexation studies of this ligand with different transition metals are currently in progress. Particularly, we expect that the photophysical properties of the ruthenium(II) bis-terpyridine complex will be of special interest.[14]

Acknowledgements

This work has been supported by the Spanish Ministerio de Educación y Ciencia (MAT2004-03849). P.G. acknowledges the Spanish Government for a Ramón y Cajal contract, and S.T. for a Ph.D. fellowship.

References and notes

1. (a) Lehn, J.-M. *Supramolecular Chemistry: Concepts and Perspectives*; VCH: Weinheim, 1995; (b) *Comprehensive Supramolecular Chemistry*; Sauvage, J.-P., Hosseini, W., Eds.; Pergamon, 1996; (c) Hanan, G. S.; Arana, C. R.; Lehn, J.-M.; Fenske, D. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1122–1124; (d) Schmittel, M.; Kalsani, V.; Bats, W. *J. Inorg. Chem.* **2005**, *44*, 4115–4117; (e) Ruben, M.; Rojo, J.; Romero-Salguero, F. J.; Uppadine, L. H.; Lehn, J.-M. *Angew. Chem., Int. Ed.* **2004**, *43*, 3644–3662.
2. (a) *Molecular Catenanes, Rotaxanes and Knots*; Dietrich-Buchecker, C., Sauvage, J.-P., Eds.; Wiley-VCH: Weinheim, 1999; (b) Collin, J.-P.; Dietrich-Buchecker, C.; Gaviña, P.; Jiménez-Molero, M. C.; Sauvage, J.-P. *Acc. Chem. Res.* **2001**, *34*, 477–487.
3. Schubert, U. S.; Eschbaumer, C. *Angew. Chem., Int. Ed.* **2002**, *41*, 2892–2926.
4. Some representative examples: (a) Constable, E. C.; Ward, M. D. *J. Chem. Soc., Dalton Trans.* **1990**, 1405–1409; (b) Cárdenas, D. J.; Sauvage, J.-P. *Synlett* **1996**, 916–918; (c) Ziessel, R.; Stroh, C. *Tetrahedron Lett.* **2004**, *45*, 4055–4501; (d) Dietrich-Buchecker, C.; Colasson, B.; Jouvenot, D.; Sauvage, J.-P. *Chem. Eur. J.* **2005**, *11*, 4374–4386; (e) Zong, R.; Thummel, R. P. *Inorg. Chem.* **2005**, *44*, 5984–5986; (f) Zong, R.; Wang, D.; Hammitt, R.; Thummel, R. P. *J. Org. Chem.* **2006**, *71*, 167–175.
5. (a) Lehmann, U.; Henze, O.; Schlüter, A. D. *Chem. Eur. J.* **1999**, *5*, 854–859; (b) Benaglia, M.; Ponzini, F.; Woods, C. R.; Siegel, J. S. *Org. Lett.* **2001**, *3*, 967–969.
6. (a) Gaviña, P.; Sauvage, J.-P. *Tetrahedron Lett.* **1997**, *38*, 3521–3524; (b) Belfrekh, N.; Dietrich-Buchecker, C.; Sauvage, J.-P. *Tetrahedron Lett.* **2001**, *42*, 2779–2781; (c) Jiménez-Molero, M.-C.; Dietrich-Buchecker, C.; Sauvage, J.-P. *Chem. Eur. J.* **2002**, *8*, 1456–1466; (d) Champin, B.; Sartor, V.; Sauvage, J.-P. *New J. Chem.* **2006**, *30*, 22–25.
7. Saitoh, Y.; Koizumi, T.; Osakada, K.; Yamamoto, T. *Can. J. Chem.* **1997**, *75*, 1336–1339.
8. For a recent synthesis of halopyridin-2-yl-boronic esters, see: Bouillon, A.; Lancelot, J.-C.; Santos, J. S. O.; Collot, V.; Bovy, P. R.; Rault, S. *Tetrahedron* **2003**, *59*, 10043–10049.
9. Schubert, U. S.; Eschbaumer, C.; Hochwimmer, G. *Synthesis* **1999**, 779–782.
10. Wang, X.; Rabbat, P.; O'Shea, P.; Tillyer, R.; Grabowski, E. J. J.; Reider, P. J. *Tetrahedron Lett.* **2000**, *41*, 4335–4338.
11. Compound **3**: ^1H NMR ($CDCl_3$, 300 MHz): δ 8.73 (d, $J = 2.3$ Hz, 1H), 8.55–8.50 (m, 2H), 8.47 (d, $J = 8.1$ Hz, 1H), 8.43 (dd, $J = 7.8$ and 0.9 Hz, 1H), 8.39 (dd, $J = 7.8$ and 0.9 Hz, 1H), 7.96 (dd, $J = 8.5$ and 2.3 Hz, 1H), 7.94 (s, $J = 7.8$ Hz, 1H), 7.66 (dd, $J = 8.1$ and 1.77 Hz, 1H), 2.42 (s, 3H). HRMS (EI): calcd for $C_{16}H_{12}N_3Br$ 325.021, found 325.023.
12. Ishimira, T.; Murata, M.; Miyaura, N. *J. Org. Chem.* **1995**, *60*, 7508–7510.
13. Ligand **1**: ^1H NMR ($CDCl_3$, 300 MHz): δ 9.5 (d, $J = 2.3$ Hz, 1H), 9.44 (d, $J = 2.3$ Hz, 1H), 9.12 (d, $J = 2.0$ Hz, 1H), 8.82 (d, $J = 8.3$ Hz, 1H), 8.59–8.43 (m, 5H), 8.37 (d, $J = 2.3$ Hz, 1H), 8.26 (dd, $J = 8.3$ and 2.4 Hz, 1H), 7.99 (t, $J = 7.8$ Hz, 1H), 7.92 (s, 2H), 7.74 (d, $J = 8.7$ Hz, 2H), 7.70 (s, 1H), 7.10 (d, $J = 8.7$ Hz, 2H), 3.91 (s, 3H) 2.44 (s, 3H). HRMS(FAB): calcd for $C_{35}H_{25}N_5O_1$ 531.206, found 531.205.
14. Bolink, H. J.; Cappelli, L.; Coronado, E.; Gaviña, P. *Inorg. Chem.* **2005**, *44*, 5966–5968.