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Synthesis of multifunctional ligands: a 2,9-diaryl-1,10-phenanthroline/2,2′:6′,2″-terpyridine conjugate

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Abstract—The synthesis of a ligand including a 1,10-phenanthroline and a 2,2′:6′,2″-terpyridine separated by a 1,3-phenylene spacer is presented. The different aromatic carbon–carbon bonds have been generated by reactions with organolithium compounds, and by Stille and Suzuki couplings.

Multifunctional ligands incorporating several coordination sites are of special interest in coordination chemistry because they are useful building blocks in the templated synthesis of multicomponent molecular assemblies,[1] including motors and machines,[1,2] or topological non-trivial compounds, like catenanes, rotaxanes and knots.[3,4] In particular, 1,10-phenanthroline and 2,2′:6′,2″-terpyridine moieties have been extensively used in the design of such ligands using either Cu(I) or Fe(II) as templating species.[5,6] We would now like to report a convenient directed synthesis of a dissymmetrical ligand containing two different chelates: a 1,10-phenanthroline and a 2,2′:6′,2″-terpyridine connected by a 1,3-phenylene spacer. In previous work, the *meta*-phenylene spacer has been shown to favour the formation of helical arrangements[7] and, when used as a bridge, to insure a significant level of electronic communication.[8]

The main difficulty of the synthesis of such a ligand is related to its unsymmetrical feature. The use of the non-symmetrical single synthon 5-bromo-2-chloropyridine **1**[9] (Fig. 1) associated with that of $NaSnMe_3$[10] appeared highly beneficial. Indeed, the key synthon **1** bears one bromine and one chlorine which differ strongly in reactivity. Due to this large difference of reactivity, only the bromine in the 5-position leads, by interconversion with butyllithium, to the 5-lithio-2-chloropyridine required for the preparation of boronic ester **2** (pathway A). This same bromine will be selectively involved in the Suzuki coupling reaction affording **4** (pathway B). Therefore, both intermediates **6** and **4** still bear an intact 2-chloro substituent and have been later converted into the trimethylstannanes **8** and **7**, respectively, required for the further C–C coupling reactions (routes C,D and D,E, respectively). Taking advantage of this striking difference of reactivity, we were able to build in both a parallel and convergent way the differently substituted phenanthroline and the immediate precursor to the terpyridine, which is only formed in the ultimate connection step (F). Our synthetic strategy, based on a cascade like successive formation of the different carbon–carbon bonds of ligand **10**, is depicted in Fig. 1.

Compound **1** was selectively lithiated at the 5 position with butyllithium in ether at −78°C; further treatment with $B(OMe)_3$ at −78°C and transesterification with 2,2-dimethylpropane-1,3-diol gave **2** in 74% yield.[11] Reaction of **2** with 1 equiv. of the 2,9-disubstituted phenanthroline **3**,[12] under Suzuki cross-coupling conditions,[13] afforded compound **6** in 55% yield. The chlorine of compound **6** was then converted into a trimethylstannyl group by reaction of a suspension of **6** with a solution of $NaSnMe_3$[10] in DME. A very short filtration over dry alumina gave stannane derivative **8** in 80% yield.

Reaction of **1** with 1 equiv. of the ester of *p*-methoxyphenylboronic acid,[14] under Suzuki cross-coupling conditions ($Pd[P(C_6H_5)_3]_4$ in toluene, aqueous Na_2CO_3, 60°C, 40 h), afforded pyridine derivative **4** in

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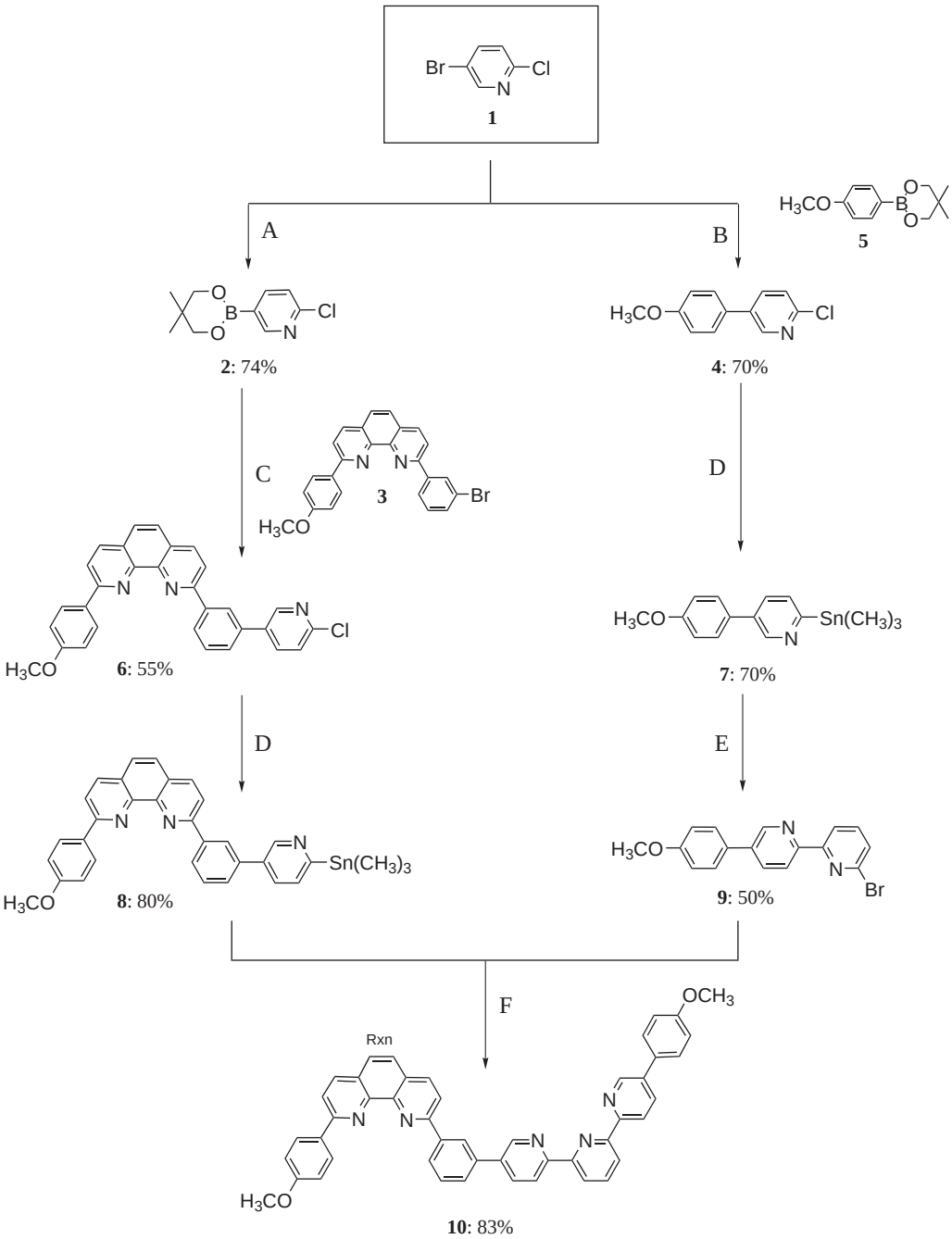

Figure 1. Conditions: (A) (1) BuLi, Et_2O, −78°C, 6 h, (2) $B(OMe)_3$, Et_2O, −78°C to rt, 12 h, (3) 2,2-dimethylpropane-1,3-diol, Et_2O, 1 h, 0°C, (4) methanesulfonic acid, Et_2O, 0°C, 30 min; (B) 2% $Pd[P(C_6H_5)_3]_4$, $C_6H_5CH_3$, 2 M Na_2CO_3, 60°C, 40 h; (C) 2% $Pd[P(C_6H_5)_3]_4$, $C_6H_5CH_3$, 2 M Na_2CO_3, 110°C, 7 h; (D) $NaSnMe_3$, DME, −13°C to rt, 15 h; (E) 2,6-dibromopyridine (1 equiv.), 1% $Pd[P(C_6H_5)_3]_4$, $C_6H_5CH_3$, 110°C, 15 h; (F) 2% $Pd[P(C_6H_5)_3]_4$, $C_6H_5CH_3$, 110°C, 15 h.

70% yield. Conversion of the chlorine of **4** into a trimethylstannyl group with $NaSnMe_3$ in DME gave stannane derivative **7** after a short column over alumina. The latter was reacted with 1 equiv. of 2,6-dibromopyridine to afford the bipyridine **9** in 50% yield.[15] In a final step, reaction of stannane **8** and bipyridine **9**, under Stille[16] cross-coupling conditions, afforded ligand **10**[17] in 83% yield.

In conclusion, we have developed a convenient synthesis of a functionalised bischelate ligand that can be obtained on a gram scale.

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9. (a) *Org. Synth.* Vol. 44, **1964**, 34–39; (b) *Org. Synth. Coll. Vol. II*, **1944**, 131. A typical procedure for the preparation of **1** is as follows: 2-amino-5-bromopyridine (6 g, 34.7 mmol) was dissolved in 35 mL of 37% HCl. A solution of $NaNO_2$ (2.43 g, 35.2 mmol) in 8 mL of water was then added at such a rate that the temperature was kept between −5 and 0°C. The white precipitate was poured on a freshly prepared suspension of CuCl at 70°C and the resulting mixture was stirred overnight at room temperature. After steam distillation and extraction with ether, **1** (2.5 g) was obtained in 40% yield.
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12. Compound **3** was synthesised by reaction of 1 equiv. of 2-*p*-methoxyphenyl-1,10-phenanthroline in THF (Dietrich-Buchecker, C. O.; Nierengarten, J. F.; Sauvage, J. P.; Armaroli, N.; Balzani V.; De Cola, L. *J. Am. Chem. Soc.* **1993**, *115*, 11237–11244) with 1 equiv. of the monolithio derivative of 1,3-dibromobenzene (Eisch, J. J.; King, R. B. *Organometallic Synthesis*; Academic Press: New York, 1981; Vol. 2, p. 93) at 0°C during 3.5 h followed by hydrolysis and rearomatisation with MnO_2.
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17. Compound **8**: ^{1}H NMR (200 MHz, $CDCl_3$, J in Hz): 0.43 (s, 9H), 3.94 (s, 3H), 7.14 (d, 2H, $J=9.1$), 7.63 (dd, 1H, $J=7.8$, $J=0.9$), 7.68–7.76 (m, 2H), 7.8 (s, 2H), 8.01 (dd, 1H, $J=7.6$, $J=2.5$), 8.12 (d, 1H, $J=8.4$), 8.20 (d, 1H, $J=8.6$), 8.29 (d, 1H, $J=8.4$), 8.35 (d, 1H, $J=8.6$), 8.40–8.50 (m, 1H), 8.49 (d, 2H, $J=9.1$), 8.88 (bs, 1H), 9.23 (dd, $J=2.3$, $J=0.9$). Compound **9**: mp 188°C; ^{1}H NMR (200 MHz, $CDCl_3$): 3.89 (s, 3H), 7.05 (d, 2H, $J=8.8$), 7.50 (dd, 1H, $J=7.9$, $J=0.7$), 7.60 (d, 2H, $J=8.8$), 7.69 (t, 1H, $J=7.8$), 7.98 (dd, 1H, $J=8.3$, $J=2.3$), 8.30–8.50 (m, 2H), 8.88 (dd, 1H, $J=2.5$, $J=0.7$). Compound **10**: mp 255°C; ^{1}H NMR (200 MHz, $CDCl_3$): 3.83 (s, 3H), 3.90 (s, 3H), 7.07 (d, 2H, $J=8.9$), 7.09 (d, 2H, $J=8.8$), 7.65 (d, 2H, $J=8.8$), 7.73 (t, 1H, $J=7.6$), 7.81 (s, 2H), 7.85 (m, 1H), 8.02 (t, 1H, $J=7.8$), 8.07 (dd, 1H, $J=8.2$, $J=2.3$), 8.13 (d, 1H, $J=8.6$), 8.25 (d, 1H, $J=8.6$), 8.30 (d, 1H, $J=8.6$), 8.35 (dd, 1H, $J=8.4$, $J=2.5$), 8.38 (d, 1H, $J=8.6$), 8.42 (m, 1H), 8.53 (d, 2H, $J=8.6$), 8.47–8.65 (m, 2H), 8.74 (d, 1H, $J=8.4$), 8.83 (d, 1H, $J=8.1$), 8.95 (d, 1H, $J=1.7$), 9.15 (bs, 1H), 9.24 (d, 1H, $J=1.7$). ES-MS: MH^+ (m/z) at 700.6 (calcd 700.8). Microanalysis calcd for $C_{47}H_{33}N_5O_2$: C, 80.67; H, 4.75; N, 10.01. Found: C, 80.77; H, 4.54; N, 9.82.