Pergamon

Tetrahedron Letters, Vol. 38, No. 47, pp. 8279-8282, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)10167-8

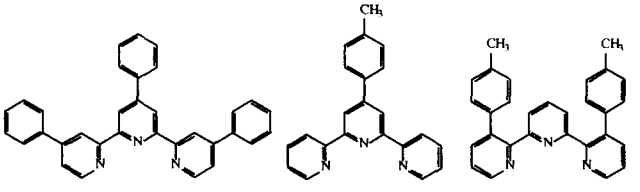
Building off the back of Chelators: Synthesis of 3,3"-*bis*(4-methylphenyl)-2,2':6',2"-Terpyridine

Andrew C. Benniston

Chemistry Department, University of Glasgow, Glasgow, G12 8QQ, U.K.

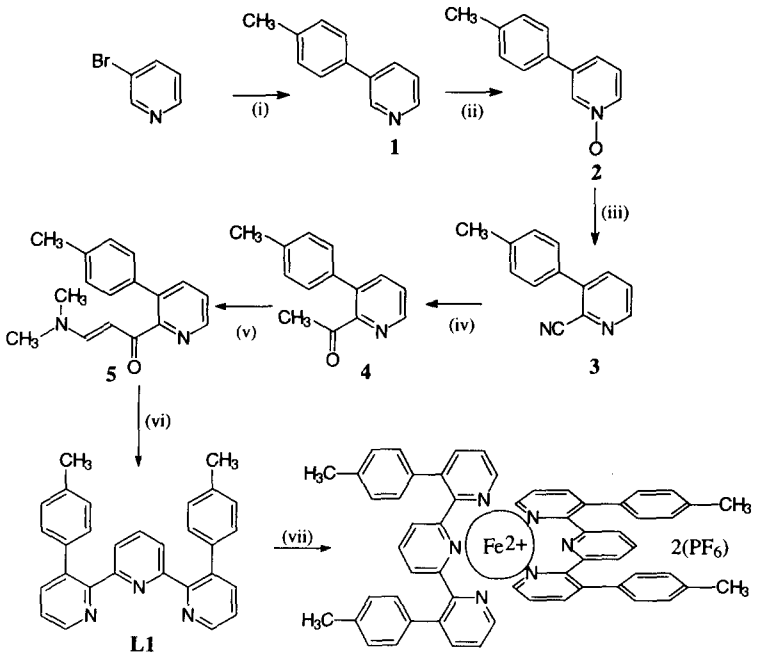
Abstract: Using an adaptation of the Jameson method for the synthesis of 2,2':6',2"-terpyridine (terpy), a ditolyl-functionalised ligand has been prepared in which the substituted groups are located in the highly unusual 3,3" position. The new ligand represents an attempt to develop terpy-based systems with di-functionality that emerges from the 'back side' of the chelator.

Derivatives of the versatile chelator 2,2':6',2"-terpyridine (terpy) are highly sought after commodities particularly in the field of metallosupramolecular chemistry,[1] and as building blocks in light-harvesting complexes.[2,3] The synthetic methodologies developed by Kröhnke,[4] Potts[5] and more recently Jameson[6] have been expanded to permit the incorporation of one, two or three (ttterpy) functional groups into specific locations on the pyridine rings. As a result, there are numerous examples of terpy-based ligands incorporating functional groups whereby substitution is performed at, for instance, the 4' position (tterpy) of the central ring, or 6,6" location of the two terminal pyridines. Despite this success, however, di-substituted derivatives using the 3,3" position as an anchor point are noticeably lacking,[7] which is surprising considering that such a location would allow construction from the rear of the chelator.



ttterpy tterpy L1

Herein, we accordingly describe the synthesis of a 3,3" tolyl-derivatised terpy chelator (**L1**) specifically designed to allow construction from its 'back side' of macrocyclic rings, and attachment of functional groups.[8] The procedure used in the synthesis of **L1** is depicted in Scheme 1 and represents an adaptation of that developed by Sauvage and Ward in the preparation of a terpy-based catenate.[9]



Scheme 1 Reagents and Conditions. (i) 4-bromotoluene, Mg, THF, 80 % yield, (ii) AcOH, H_2O_2, 83% yield, (iii) KCN, benzoyl chloride, recrystallisation Et_2O, 53% yield, (iv) MeMgI, benzene, hydrolysis, distillation 100 °C/0.05mm Hg, 80% yield, (v) excess *N,N'*-dimethylformamide dimethyl acetal, toluene, reflux, 70% yield, (vi) **4**, Bu^{t}OK, THF, NH_4OAc, 40% yield, (vii) $FeSO_4$, 80 % yield.

Using standard conditions, reaction of 3-bromopyridine with the *in-situ* generated Grignard reagent of 4-bromotoluene produced derivative **1**,[10] which was readily converted to the *N*-oxide **2**[11] in an overall yield for the two steps of 82%. In both cases no column chromatography was required and pure samples were obtained by simple trituration of the products with dry Et_2O followed by filtration. Subsequent reaction of **2** with potassium cyanide and benzoyl chloride produced the electronically favourable cyano derivative **3**,[12] which was easily separated from the lesser amount of 6-cyano isomer by simple recrystallisation from dry Et_2O. Conversion of **3** to the acetyl derivative **4**[13] proceeded smoothly using MeMgI in dry benzene at room temperature followed by careful hydrolysis. Following the procedure developed by Jameson, **4** was converted to the necessary enaminone **5**[14] though excess of *N,N'*-dimethylformamide dimethyl acetal was required and a longer reaction time (*ca.* 24h). Reaction of the readily generated anion of **4** with **5**, coupled with central pyridine formation from the generated dione produced crude **L1** which was accordingly purified from its iron complex as described in the literature.[15] Recomplexation of purified **L1**[16] with $FeSO_4$ produced the complex $[Fe(\mathbf{L1})_2](PF_6)_2$ which when recrystallised from CH_3CN/Et_2O produced a dark purple solid.[17]

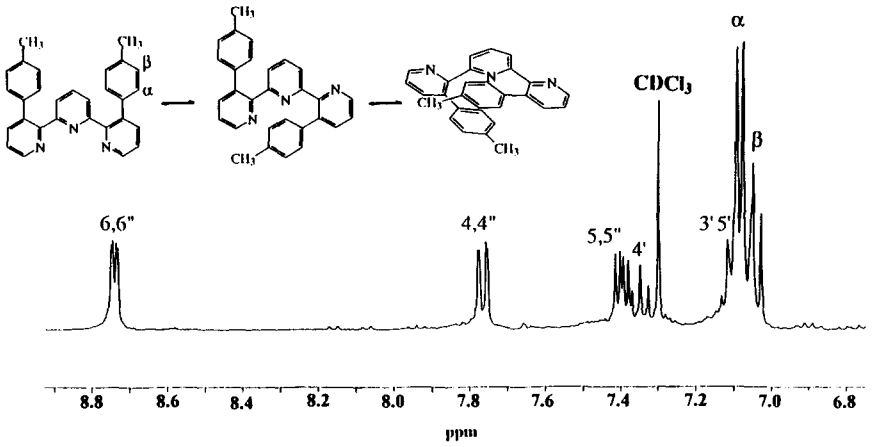


Figure 1

The ^{1}H NMR of **L1** in $CDCl_3$ is depicted in Figure 1, which also includes three possible ligand conformations that can be adopted in solution. It is well established for terpy, as well as its derivatives, that the nitrogens adopt the more thermodynamically favourable *trans-trans* orientation.[18] The adoption of a similar conformation by the 3,3"-derivatised ligand would in principal lead to a 'clash' of the two tolyl groups and a possible destabilisation of the *trans-trans* conformer. However, from molecular modelling calculations the eclipsing of the tolyl units at *ca.* 3.5Å apart is made favourable by the two aromatics forming a π–π stack. Overall, this weak secondary interaction leads to the ligand adopting a conformation (as shown) in which there is slight helical twist. A closer inspection of the ^{1}H NMR shifts for the tolyl α, β protons are also consistent with such secondary π–π interactions. Assuming the chemical shifts (δ_α = 8.16, δ_β = 7.50) in $CDCl_3$ for the appropriately 6,6" derivatised ligand **L2**[19] (Figure 2) represent two non-interacting tolyl groups, then the corresponding signals for **L1** are significantly shifted upfield by *ca.* 0.95 (CH_α) and 0.25 (CH_β) ppm, respectively. Such shifts are have been previously shown to indicate π-π interactions, particularly in complexes comprised of face-to-face donor-acceptor moieties.[20]

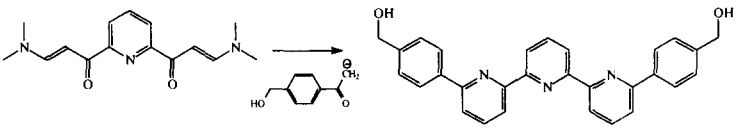


Figure 2 **L2**

In conclusion, a relatively simple synthetic procedure has been developed that allows the incorporation of two groups into the highly unusual 3,3" position of a tridentate chelator. The synthetic procedure also lends itself to be adapted to allow other groups to be incorporated at the 3,3" site. By further functionalisation of the methyl groups we expect to build off from the back of such chelators in a controlled manner so as to allow the construction of multidimensional molecular arrays.

Acknowledgement

This work was supported by the University of Glasgow. Preliminary work obtained by a Royal Society Fellowship (1991) with Dr Jean-Pierre Sauvage is also gratefully acknowledged.

REFERENCES AND NOTES

1. A. M. W. Cargill-Thompson *Coord. Chem. Rev.* **1997**, 160, 1-52.
2. A. C. Benniston, V. Grosshenny, A. Harriman, R. Ziessel, *Angew. Chem., Int. Ed. Engl.* **1994**, 33, 1884-1885.
3. M. Beley, S. Chodorowski-Kimmes, J-P. Collin, P. Lainé, J-P. Launay, J-P. Sauvage, *Angew. Chem., Int. Ed. Engl.* **1994**, 33, 1775-1778.
4. F. Kröhnke, *Synthesis*, **1976**, 1-24.
5. K. T. Potts, M. J. Cipullo, P. Ralli, G. Theodoridis, *J. Org. Chem.* **1982**, 47, 3027-3038.
6. D. L. Jameson, L. E. Guise, *Tetrahedron Lett.* **1991**, 32, 1999-2002.
7. A detailed search of the Beilstein database found only one other 3,3"-derivatised terpy ligand, see: M. Tingoli, M. Tiecco, L. Testaferri, R. Andrenacci, R. Balducci, *J. Org. Chem.* **1993**, 58, 6097-6102.
8. A. C. Benniston, P. R. Mackie, A. Harriman *Tetrahedron Lett.* **1997**, 38, 3577-3580.
9. J-P. Sauvage, M. Ward, *Inorg. Chem.* **1991**, 30, 3869-3874.
10. Analytical Data **1** ^{1}H NMR ($CDCl_3$, 200MHz): δ= 2.37 (s, 3H); 7.23-7.27 (d, 2H, J= 8.0Hz); 7.37-7.41 (d, 2H, J= 8.0Hz); 7.28-7.32 (d, 1H, J= 7.3Hz); 7-37-7.45 (t, 1H, J= 7.2Hz); 8.12-8.15 (d, 1H, J= 6.3Hz); 8.41 (s, 1H) EI-MS m/z = 169 $(M)^+$.
11. Analytical Data **2** ^{1}H NMR ($CDCl_3$, 200MHz): δ = 2.36 (s, 3H); 7.23-7.27 (d, 2H, J= 8.0Hz); 7.37-7.41 (d, 2H, J= 8.0Hz); 7.28-7.32 (d, 1H, J= 7.3Hz); 7-37-7.45 (t, 1H, J= 7.2Hz); 8.12-8.15 (d, 1H, J= 6.3Hz); 8.40 (s, 1H).
12. Analytical Data **3** ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.43 (s, 3H); 7.31-7.35 (d, 2H, J= 8.1Hz); 7.44- 7.48 (d, 2H, J= 8.1Hz); 7.52-7.59 (dd, 1H, J= 8.0Hz, J'= 4.7Hz); 7.82-7.87 (dd, 1H, J= 8.0Hz, J'= 1.5Hz); 8.65-8.68 (dd, 1H, J= 4.6Hz, J'= 1.5Hz). EI-MS m/z = 194 $(M)^+$.
13. Analytical Data **4** ^{1}H NMR ($CDCl_3$, 360MHz): δ = 2.39 (s, 3H); 2.53 (s, 3H); 7.15-7.25 (m, 4H); 7.40-7.44 (dd, 1H, J=7.8Hz, J'= 4.6Hz); 7.67-7.70 (d, 1H, J= 7.8Hz); 8.59-8.60 (d, 1H, J= 4.5 Hz). EI-MS m/z = 210 $(M-H)^+$; 196 $(M-CH_4)^+$; 168 $(M-CH_3CO)^+$.
14. Analytical Data **5** ^{1}H NMR ($CDCl_3$, 360MHz): δ = 2.34 (s, 3H); 2.79 (s, 3H); 3.02 (s, 3H); 5.5 (br, 2H); 7.15-7.17 (d, 2H, J= 7.9Hz); 7.27- 7.29 (d, 2H, J= 7.8Hz); 7.31- 7.33 (dd, 1H, J= 7.8Hz, J'= 4.7Hz); 7.65-7.67 (dd, 1H, J= 7.7Hz, J'= 1.0Hz); 8.53-8.54 (dd, 1H, J= 4.7Hz, J'= 1.5Hz). EI-MS m/z = 266 $(M)^+$; 251 $(M-CH_3)^+$; 223 $(M-N(CH_3)_2)^+$.
15. E. Constable, M. Ward, S. Corr, *Inorg. Chim. Acta.* **1988**, 141, 201-203.
16. Analytical Data **L1** ^{1}H NMR ($CDCl_3$, 360MHz): δ = 2.30 (s, 6H); 6.97- 7.00 (d, 2H, J=8.0Hz); 7.03-7.05 (2xd, 8H, J=8Hz); 7.27-7.29 (d, 1H, J= 8Hz); 7.32-7.35 (dd, 2H, J= 8Hz, J'= 5Hz); 7.69-7.72 (dd, 2H, J= 8Hz, J'= 1.4Hz); 8.68-8.69 (dd, 2H, J= 5Hz, J'= 1.4Hz). ^{13}C NMR ($CDCl_3$) 21.65 (2C); 123.59 (2C); 124.31 (2C); 129.50 (4C); 130.16 (4C); 135.91 (1C); 137.19 (2C); 138.89 (2C); 148.85 (2C); 156.80 (2C); 158.56(2C). EI-MS m/z = 413 $(M+H)^+$.
17. Analytical Data $[Fe(\mathbf{L1})_2](PF_6)_2$ ^{1}H NMR (d_6-acetone, 360 MHz): δ = 2.48 (s, 12H); 7.31-7.34 (t, 4H, J= 6.4Hz); 7.47-7.50 (m, 20H); 7.63-7.65 (d, 4H, J= 8.0Hz); 7.77-7.79 (d, 4H, J= 7.8Hz); 7.95-7.98 (t, 2H, J=6.5Hz). FABMS (NBA matrix) m/z = 1027 $(M-PF_6)^+$, 882 $(M-2PF_6)^+$. Elemental analysis: calculated for $C_{58}H_{46}N_6FeP_2F_{12}.7H_2O$ %C 53.61; %H 4.66; %N 6.47 found: %C 53.84, %H 4.06, %N 6.65.
18. E. C. Constable *Adv. Inor.Chem. Radiochem.* **1986**, 30 69-121.
19. Analytical Data **L2** ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 5.2 (s, 4H); 7.50-7.52 (d, 4H, J= 8.1Hz); 7.78-7.80 (d, 2H, J= 7.3Hz); 7.91-7.95 (t, 2H, J= 7.8Hz); 7.98-8.03 (t, 1H, J=7.9Hz); 8.16-8.19 (d, 4H, J= 8.1Hz); 8.60-8.63 (d, 2H, J= 7.5Hz); 8.66-8.69 (d, 2H, J= 7.8Hz). EI-MS m/z = 428 $(M-OH)^+$.
20. A. C. Benniston, A. Harriman, *J. Am. Chem. Soc.* **1994**, 116, 11531-11537.

(*Received in UK* 28 *August* 1997; *revised* 15 *September* 1997; *accepted* 19 *September* 1997)