Pergamon

Tetrahedron Letters 42 (2001) 4705–4707

TETRAHEDRON LETTERS

4′-Functionalized 2,2′:6′,2″-terpyridines as building blocks for supramolecular chemistry and nanoscience

Ulrich S. Schubert,[a,b,*] Christian Eschbaumer,[a,b] Oliver Hien[b] and Philip R. Andres[a]

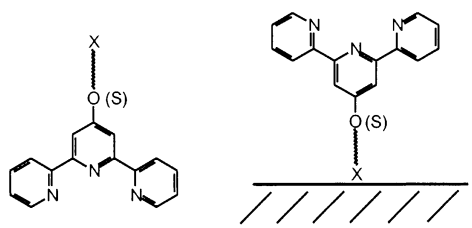
[a]*Laboratory of Macromolecular and Organic Chemistry, Eindhoven University of Technology, PO Box 513, 5600 MB Eindhoven, The Netherlands*

[b]*Lehrstuhl für Makromolekulare Stoffe, Technische Universität München, Lichtenbergstrasse 4, 85747 Garching, Germany*

Received 19 March 2001; accepted 11 May 2001

Abstract—Different mono- and bis-terpyridines were synthesized utilizing nucleophilic substitution of 4′-chloro-2,2′:6′,2″-terpyridine. In the case of the mono-functionalized ligands, different functional groups opposite to the metal binding site could be introduced; with the bis-functionalized ligands building blocks for metal-containing polymers with a tailored alkyl-chain length were accessible. As examples, a functionalized terpyridine cadmium(II) complex as well as a fullerene derivative were prepared.

Since Morgan and Burstall first described the synthesis of 2,2′:6′,2″-terpyridine in 1932[1] there have been many investigations of this metal-complexing ligand, its complexes and derivatives. These studies concerned complex formation, photochemical properties and most recently the use as building blocks for novel supramolecular structures such as double helicates,[2] dendrimers[3] or ordered architectures on surfaces.[4] A biochemical application is the use of (terpyridine)Cu(II) as a RNA hydrolysis agent in ribozyme mimetics.[5] Bis-functionalized ligands are of special interest due to their ability to serve as bridging ligands in metal-containing polymers, possibly allowing materials with tailored physical properties.[6–10] Applications also seem possible in nanotechnology such as the formation of ordered architectures or the introduction of metal binding sites onto colloids or nano-particles, in order to gain access to materials with new properties (Scheme 1).



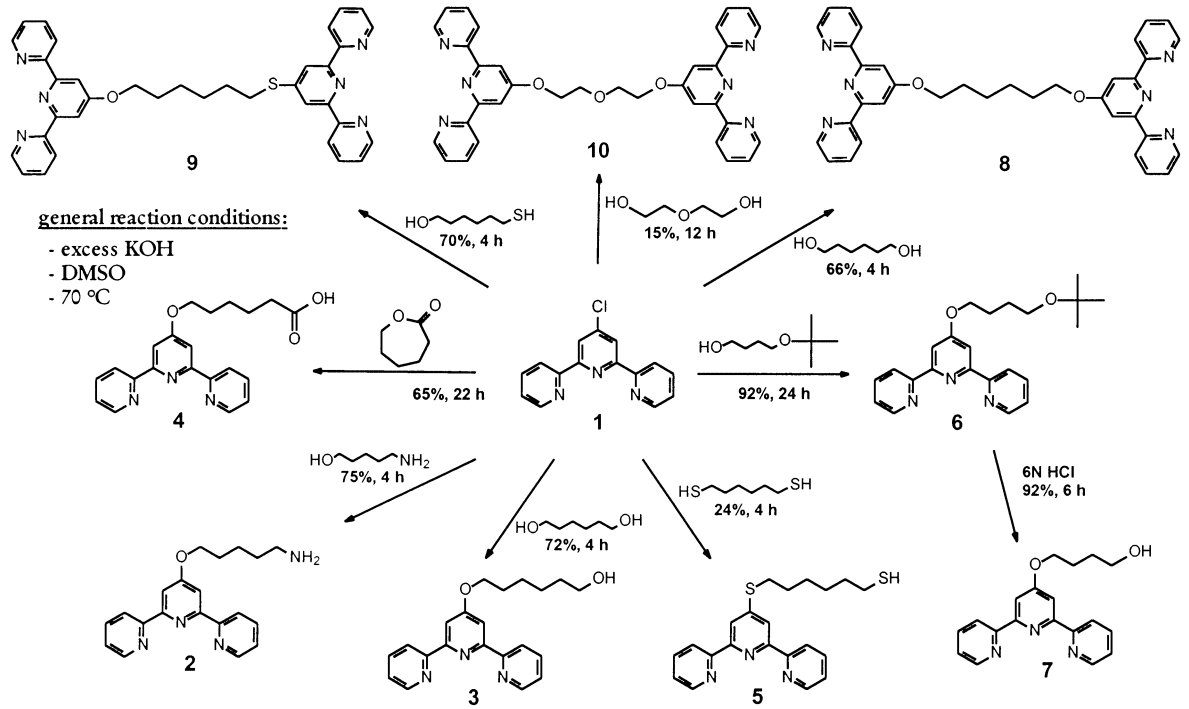
Scheme 1.

* Corresponding author. Fax: +31 40 2474186; e-mail: u.s.schubert@tue.nl

However, for all such purposes suitable functional groups (X in Scheme 1) such as SH, COOH, NH_2 or OH, have to be introduced in reasonable yields. Here we present the synthesis of different 2,2′:6′,2″-terpyridines, functionalized in the 4′-position, as well as some bis-terpyridine terminated systems. The mono-terpyridines were synthesized according to a modified procedure first described by Newkome et al.[11] (Scheme 2). All of the products were obtained by nucleophilic substitution of 4′-chloro-2,2′:6′,2″-terpyridine **1**[12] utilizing an excess of KOH and dry DMSO as solvent.[13] Different thiolates and alkoxides also containing another functional group were used as nucleophiles. Starting with 5-amino-1-pentanol, the already described aminofunctionalized terpyridine **2** could be synthesized in a multi-gram scale in 75% yield using a simple precipitation procedure for purification (however, to obtain completely pure products, column chromatography or recrystalization should also be applied).

Even better results were obtained using 4-*tert*-butyloxybutanol as nucleophile.[14] The corresponding *tert*-butyloxy-terminated terpyridine **6** could be isolated in 92% yield. After deprotection the hydroxy-terminated ligand **7** is accessible in 92% yield. Furthermore, the direct preparation of hydroxy or thiol-terminated terpyridines is possible utilizing a ten-fold excess of bis-hydroxy or bis-thiol-functionalized starting material. In this way compounds **3** and **5** could be prepared in 72 and 24% yields, respectively. The rather low yield in the thiol case is due to purification problems. However, the latter ligand represents a very useful compound for the

0040-4039/01/$ - see front matter
PII: S0040-4039(01)00796-1



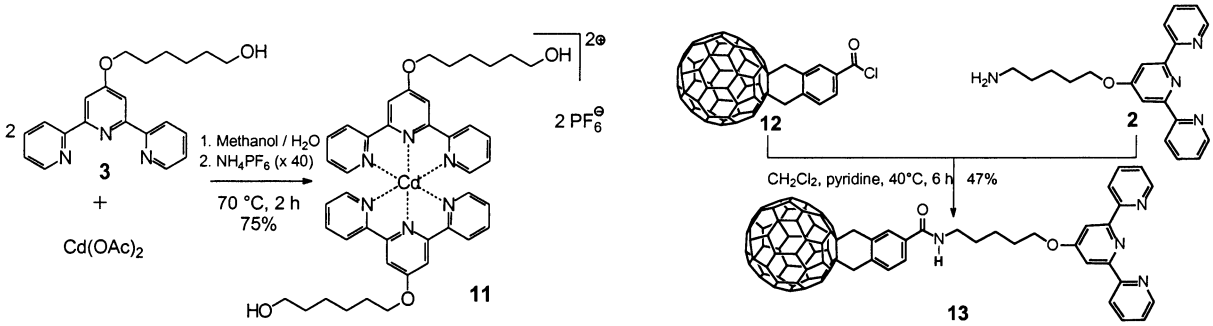
Scheme 2.

preparation of terpyridine coated gold substrates and particles. The carboxy-terminated terpyridine **4** could be prepared in 65% yield using in situ ring-opening of ε-caprolactone. In order to synthesize bis-terpyridine terminated systems, the same basic procedure, as in the case of the mono-terpyridines only with equimolar amounts of the reactants, was applied[15] (for other routes to functionalized terpyridine ethers and thioethers see, e.g. Ref. 16 and for other bridging ligands see, e.g. Ref. 17). Utilizing 6-mercapto-1-hexanol and 1,6-hexanediol the corresponding bis-terpyridine terminated ligands **8** and **9** could be obtained in 66 and 70% yield, respectively. Furthermore, ethylene glycol derivatives could be utilized, providing a route to highly soluble systems such as **10**.

Selected data for the mono-terpyridine ligands **2** to **5** are given in Table 1. The characterization of the ligands was carried out using NMR spectroscopy and MALDI-TOF mass spectrometry, as well as elemental analysis. In particular, ^{1}H NMR spectroscopy was very useful for the characterization of the described compounds. The successful nucleophilic substitution can be easily detected by a characteristic shift of the 3′,5′-proton signals in the ^{1}H NMR spectra depending on the kind of nucleophile used. A shift of the ^{1}H NMR signals

Table 1. Comparison of some of the mono-terpyridine ligands: reaction conditions and yields

No.	X	Reagent	Time (h)	Temp. (°C)	Mp (°C)	3′,5′ (ppm)	Yield (%)
2	NH_2	5-Amino-1-pentanol[11]	4	80	104	8.03	75
3	OH	1,6-Hexanediol[16]	4	80	111	8.01	72
4	COOH	ε-Caprolactone	22	80	187	7.99	65
5	SH	1,6-Dimercaptohexane	4	80	87	8.33	24



Scheme 3.

from δ 8.48 ppm for the 4′-chloro-terpyridine **1** to 8.03 ppm in the case of the hydroxy-based nucleophile **2** or to 8.33 ppm in the case of the thiol-based nucleophile **5** can be observed. Both signals appear in the spectra of both the oxo-ether and thio-ether containing compound **9**. For the compounds with higher mass, the existence of the desired products could be proved by MALDI-TOF-MS measurements. The prepared terpyridine derivatives represent very interesting building blocks for attachment to polymers, surfaces or biological systems, as well as for direct use in metal complexation. The latter direction would lead to new interesting metallo-supramolecular building blocks. As a first example concerning complexation in functionalized metallo-supramolecular units, we reacted hydroxy-functionalized terpyridine with cadmium(II) acetate.[18] The corresponding octahedral metal complex **11** was formed in a methanol/water mixture and could be isolated in 75% yield after anion exchange utilizing a large excess of ammonium hexafluorophosphate. Furthermore, a fullerene carboxylic acid chloride **12**[19] was reacted with **2**. The resulting unit **13** was isolated after size exclusion chromatography in 47% yield (Scheme 3).[20]

The synthetic route described yields a variety of different mono-functionalized terpyridines as well as bis-terpyridine compounds in gram to multi-gram quantities. As first applications a bis-hydroxy-functionalized terpyridine cadmium(II) complex and a fullerene derivative were prepared. Studies on the incorporation of such ligands and supramolecular building blocks into polymers with special photochemical properties as well as attachment to metal surfaces and nanoparticles are currently in progress.

Acknowledgements

This study was supported by the Bayerisches Staatsministerium für Unterricht, Kultus, Wissenschaft und Kunst, the Stiftung Stipendien-Fonds des Verbandes der Chemischen Industrie and the Deutsche Forschungsgemeinschaft (SFB 266, Teilprojekt B 15, SFB 486 Teilprojekt A 8).

References

1. Morgan, S. G.; Burstall, F. H. *J. Chem. Soc.* **1931**, 20.
2. Lehn, J.-M. *Supramolecular Chemistry, Concepts and Perspectives*; VCH: Weinheim, 1995.
3. (a) Newkome, G. R.; He, E.; Godinez, L. A. *Macromolecules* **1998**, *31*, 4382; (b) Schubert, U. S.; Weidl, C. H.; Moorefield, C. N.; Baker, G. R.; Newkome, G. R. *Polym. Prepr.* **1999**, *40*, 940.
4. (a) Salditt, T.; An, Q. R.; Plech, A.; Eschbaumer, C.; Schubert, U. S. *Chem. Commun.* **1998**, 2731; (b) Schubert, U. S.; Eschbaumer, C.; An, Q.; Salditt, T. *J. Incl. Phenom.* **1999**, *32*, 35.
5. Daniher, A. T.; Bashkin, J. K. *Chem. Commun.* **1998**, 1077.
6. Constable, E. C. *Macromol. Symp.* **1995**, *98*, 503.
7. Kelch, S.; Rehahn, M. *Macromolecules* **1999**, *32*, 5818.
8. Schütte, M.; Kurth, D. G.; Linford, M. R.; Cölfen, H.; Möhwald, H. *Angew. Chem.* **1998**, *110*, 3058; *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2891.
9. (a) Schubert, U. S.; Eschbaumer, C. *Polym. Prepr.* **1999**, *40*, 1070; (b) Schubert, U. S.; Hien, O.; Eschbaumer, C. *Macromol. Rapid Commun.* **2000**, *21*, 1156.
10. Schwab, P. F. H.; Levin, M. D.; Michl, J. *Chem. Rev.* **1999**, *99*, 1863.
11. Newkome, G. R.; He, E. *J. Mater. Chem.* **1997**, *7*, 1237.
12. Constable, E. C.; Ward, M. D. *J. Chem. Soc., Dalton Trans.* **1990**, 1405.
13. *Mono-terpyridines* ***2–6***: General synthetic strategy: To a stirred suspension of powdered KOH (11.6 g, 206 mmol) in dry DMSO (180 ml) at 80°C, the alcohol (43.0 mmol) was added. After 30 min, 4′-chloro-2,2′:6′,2″-terpyridine was added (11.5 g, 43.0 mmol) and the mixture was stirred for 4 h at 70°C and then poured into 2 l of distilled water. The aqueous phase was extracted with CH_2Cl_2 (3×200 ml). The combined organic phases were dried over Na_2SO_4 and evaporated in vacuo, and the residue was recrystallized from ethyl acetate or purified by column chromatography (CH_2Cl_2/MeOH). **7**: **6** (3.01 g, 8 mmol) was dissolved in dry dioxane (200 ml). Hydrochloric acid (4N, 50 ml) was added dropwise and the mixture was refluxed for 6 h. After removal of the dioxane, aqueous $NaHCO_3$ (260 ml, 1 M) was added and the mixture was extracted with CH_2Cl_2 (3×200 ml). The combined organic phases were dried over Na_2SO_4 and the solvent was removed in vacuo yielding 2.35 g of **7** (92%) as a white solid.
14. See, e.g. Eisenbach, C. D.; Göldel, A.; Terskan-Reinold, M.; Schubert, U. S. *Macromol. Chem. Phys.* **1995**, *196*, 1077.
15. General synthetic strategy: The same route was used as described in Ref. 11 only with equimolar amounts of the reactants.
16. Sampath, U.; Putnam, W. C.; Osiek, T. A.; Touami, S.; Xie, J.; Cohen, D.; Cagnolini, A.; Droege, P.; Klug, D.; Barnes, C. L.; Modak, A.; Bashkin, J. K.; Jurisson, S. S. *J. Chem. Soc., Dalton Trans.* **1999**, 2049.
17. Khatyr, A.; Ziessel, R. *J. Org. Chem.* **2000**, *65*, 3126.
18. To a solution of **3** (191 mg, 0.55 mmol) in distilled methanol (19 ml) cadmium(II)-acetate hydrate (627 mg, 0.27 mmol) was added and refluxed for 2 h. Ammonium hexafluorophosphate (3.90 g, 23.9 mmol) in distilled water (3 ml) was added and the mixture was stirred for 10 minutes. The precipitate was filtered off and washed with water (3×20 ml), methanol (3×20 ml) and diethyl ether (3×20 ml). The white solid was recrystallized from diethyl ether/acetone yielding 225 mg (75%) of **11** as a white solid.
19. **12** was directly used after formation (FD-MS characterization). Harth, E. Dissertation, Mainz, 1998.
20. See also: Schubert, U. S.; Weidl, C. H.; Cattani, A.; Eschbaumer, C.; Newkome, G. R.; He, E.; Harth, E.; Müllen, K. *Polym. Prepr.* **2000**, *41*, 229.