Pergamon

Tetrahedron Letters 43 (2002) 4923–4925

TETRAHEDRON LETTERS

A new route to 6,6″-dicyano-2,2′:6′,2″-terpyridines and their complexes with Ni(II)

Dmitry N. Kozhevnikov,[a,*] Valery N. Kozhevnikov,[a,*] Tatiana V. Nikitina,[a] Vladimir L. Rusinov,[a] Oleg N. Chupakhin,[a] Igor L. Eremenko[b] and Grigory G. Aleksandrov[b]

[a]*Urals State Technical University, 620002 Ekaterinburg, Russia*
[b]*Institute of General and Inorganic Chemistry, Moscow, Russia*

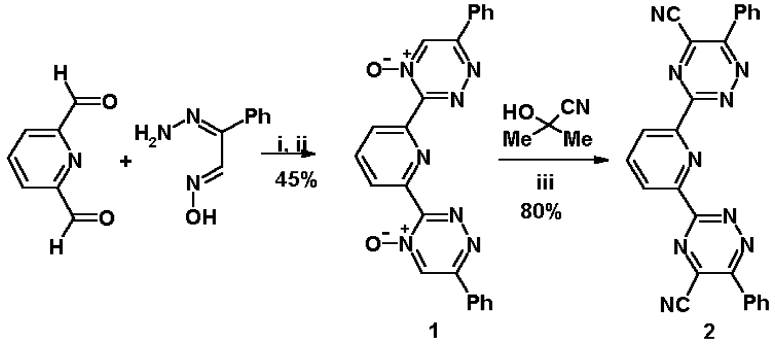
Received 26 March 2002; revised 7 May 2002; accepted 17 May 2002

Abstract—A new methodology for the synthesis of functionalised 2,2′:6′,2″-terpyridine systems is suggested: sequential synthesis of the heterocyclic assemblies based on the 1,2,4-triazine ring, direct introduction of the cyano group in the 1,2,4-triazine ring and the transformation of the latter to a pyridine ring via an aza-Diels–Alder reaction.

Organic molecules bearing the 2,2′:6′,2″-terpyridine moiety have a geometry is favourable for accepting various metal centres, therefore such molecules are used widely in coordination chemistry. Based on compounds of this series and their complexes, highly sensitive analytical reagents,[1] various sensor systems,[2] reagents for enantioselective synthesis,[3] and luminescent agents for labelled peptide synthesis[4] were created. Besides, 2,2′:6′,2″-terpyridines are attractive building blocks for supramolecular chemistry.[5]

The most common methods for the synthesis of the 2,2′:6′,2″-terpyridines are by means of combination of single pyridine blocks or formation of the central (rarely both terminal) pyridine rings starting from the corresponding open-chain intermediates (for a review see Ref. 6).

In the present paper we describe a new methodology for the synthesis of functionalised terpyridines, based on the direct introduction of substituents into a 1,2,4-triazine ring followed by transformation of the latter into the pyridine ring. In planning such an approach we proceeded from the following points: (a) 1,2,4-triazine 4-oxides are very electrophilic heterocycles, that allow the direct introduction to the 1,2,4-triazine ring of various nucleophiles including the formation of a new C–C bond;[7] (b) 1,2,4-triazines react relatively easier with electron rich dienophiles in an inverse electron demand aza-Diels–Alder reaction resulting in their transformation into pyridines.[8] In this situation, successful realisation of the suggested methodology depends on the synthesis of heterocyclic assemblies based on 1,2,4-triazines. To achieve this aim we used the method for the synthesis of the 1,2,4-triazine 4-



Scheme 1. *Reagents and conditions*: (i) EtOH, rt, 12 h; (ii) Pb_3O_4/AcOH, rt; (III) NEt_3, $CHCl_3$, reflux.

* Corresponding authors. Tel.: +7-3432-740458; fax: +7-3432-740458; e-mail: dnk@htf.ustu.ru

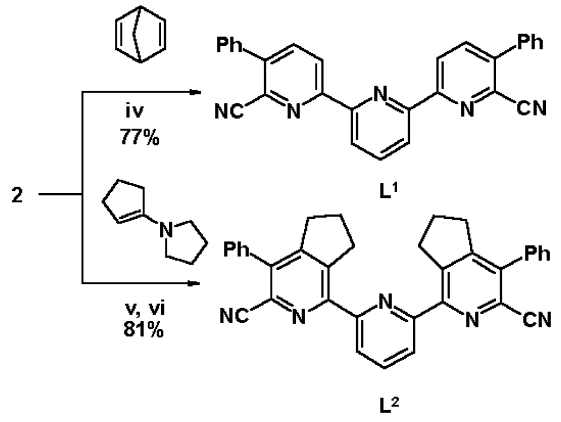
0040-4039/02/$ - see front matter
PII: S0040-4039(02)00951-6

oxides described earlier.[9] Thus, condensation of two molecules of the hydrazone of isonitrozoacetophenone with pyridine-2,6-dicarboxaldehyde in ethanol followed by oxidative aromatisation of the intermediate with Pb_3O_4 in acetic acid resulted in the formation of 2,6-bis(4-oxid-6-phenyl-1,2,4-triazin-3-yl)pyridine **1**.[10] The presence of the *N*-oxide group opens a way for functionalisation of the 1,2,4-triazine rings of **1** via nucleophilic substitution of hydrogen.[7] Cyanide anion was chosen as a nucleophile, since the introduction of the cyano group in the heterocycle allows further modifications of potential ligands via typical nitrile transformations. We decided not to use the cyanide ion itself in this reaction with **1**, but instead used its synthetic equivalent—acetone cyanohydrin in the presence of triethylamine,[11] affording 2,6-bis(5-cyano-6-phenyl-1,2,4-triazin-3-yl)pyridine **2** (Scheme 1).[12] The reaction proceeded in good yield, hence the 1,2,4-triazines seem to be useful building-blocks for the preparation of oligopyridine systems.

One characteristic feature increasing the attraction of 1,2,4-triazines is the possibility of their facile transformation into a pyridine ring in one step as result of the inverse electron demand Diels–Alder reaction.[8] Thus, refluxing dinitrile **2** with 2,5-norbornadiene in toluene yielded 6,6″-dicyano-5,5″-diphenyl-2,2′:6′,2″-terpyridine **L¹** (Scheme 2).[13]

It is appropriate to use in this reaction more electron-rich dienophiles such as enamines. For instance, treatment of dinitrile **2** with 1-pyrrolidinocyclopentene proceeded with loss of nitrogen resulting in an intermediate cycloadduct, which was aromatised without purification by the elimination of pyrrolidine by reflux in acetic acid to afford 2,6-bis(6-cyano-5-phenyl-3,4-cyclopentenopyridyl-2)-pyridine **L²** (Scheme 2).[14] The presence of two aliphatic rings in the molecule **L²** increases the solubility in comparison with terpyridine **L¹**, thereby facilitating the synthesis of complexes with transition metals.

Refluxing of ligand **L²** with $Ni(NO_3)_2 \cdot 6H_2O$ in acetonitrile led to the formation of a complex of molecular formula of this complex $\mathbf{L^2Ni(NO_3)_2}$.[15] The geometry was established by X-ray analysis (Fig. 1).[16] The Ni(II) atom adepts a strained octahedral environment formed by three nitrogen atoms of the ligand **L²** and three oxygen atoms of the nitrate anions with chelate and



Scheme 2. *Reagents and conditions*: (iv) toluene, reflux, 6 h; (v) toluene, reflux, 1 h; (vi) AcOH, reflux, 1 h.

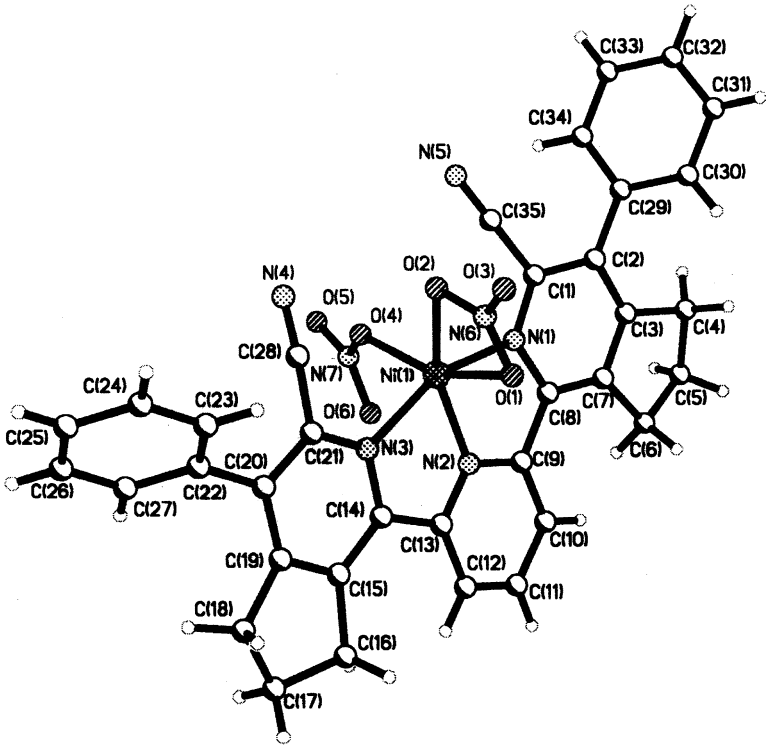


Figure 1. Geometry of the complex $\mathbf{L^2Ni(NO_3)_2}$.

terminal coordination. The terpyridine system is almost planar, and deviation of the metal atom from the average plane of the terpyridine is 0.047 Å. Torsion angles between the planes of the phenyl substituents and the terpyridine fragment are from 59.3 to 65.4°.

In conclusion, suggested methodology of sequential synthesis of the heterocyclic assemblies based on the 1,2,4-triazine ring, direct introduction of the cyano group via nucleophilic substitution of hydrogen and transformation of the 1,2,4-triazine rings into pyridine rings by way of the aza-Diels–Alder reaction is a convenient method for the synthesis of functionalised 2,2′:6′,2″-terpyridines. It has to be noted that such molecules are good acceptors for nickel atoms and, perhaps, for other d-block elements.

Acknowledgements

The authors thank the RFBR (grant no. 02-03-32635) and CRDF (project REC-005) for financial support.

References

1. Kröhnke, F. *Synthesis* **1976**, 1–24.
2. Keefe, M. H.; Benkstein, K. D.; Hupp, J. T. *Coord. Chem. Rev.* **2000**, *205*, 201–228.
3. Chelucci, G.; Cabras, M. A.; Saba, A. *J. Mol. Cat. A* **1995**, *95*, L7–L10.
4. Saha, A. K.; Kross, K.; Kloszewski, E. D.; Upson, D. A.; Toner, J. L.; Snow, R. A.; Black, C. D.; Decai, V. C. *J. Am. Chem. Soc.* **1993**, *115*, 11032–11033.
5. Ward, M. D. *Chem. Soc. Rev.* **1995**, 121–134.
6. Thompson, A. C. *Coord. Chem. Rev.* **1997**, *160*, 1–52.
7. Kozhevnikov, D. N.; Rusinov, V. L.; Chupakhin, O. N. *Russ. Chem. Rev.* **1998**, *67*, 633–648.
8. Neunhoeffer, H. In *Comp. Heterocycl. Chem. II*; Katrizky, A. R.; Rees, C. W.; Scriven, E. F. V., Eds.; Pergamon Press: Oxford, 1996; Vol. 6, pp. 507–574.
9. Kozhevnikov, D. N.; Kozhevnikov, V. N.; Rusinov, V. L.; Chupakhin, O. N. *Mendeleev Commun.* **1997**, 238–239.
10. 2,6-Bis(4-oxide-6-phenyl-1,2,4-triazin-3-yl)-pyridine **1**. Pyridine-2,6-dicarboxaldehyde (3.5 g, 26 mmol) and the hydrazone of isonitrosoacetophenone (8.5 g, 52 mmol) were dissolved in 50 ml of ethanol and kept overnight at room temperature. The crystals formed were filtered off, dried and suspended in 150 ml of acetic acid. Lead(IV) oxide (34.2 g, 50 mmol) was added to the resulting suspension. The reaction mixture was stirred for 3 h at room temperature. The crystals of the product were filtered off and recrystallised from DMF. Yield 5.6 g, 52%. Mp >270°C (dec.). ^{1}H NMR (DMSO-d_6) δ 7.6 (m, 6H), 8.25 (m, 7H), 9.43 (s, 2H); EI/MS (m/z) 421 (M^+, 10%). Anal. calcd for $C_{23}H_{15}N_7O_2$ (421.4): C, 65.55; H, 3.58; N, 23.26. Found C, 65.75; H, 3.39; N, 23.38%.
11. Chupakhin, O. N.; Rusinov, V. L.; Ulomsky, E. N.; Kozhevnikov, D. N.; Neunhoeffer, H. *Mendeleev Commun.* **1997**, 66–67.
12. 2,6-Bis(5-cyano-6-phenyl-1,2,4-triazin-3-yl)-pyridine **2**. Acetone cyanohydrine (3.9 ml, 43 mmol) and triethylamine (1.5 ml, 10 mmol) were added to a suspension of compound **2** (4.5 g, 10 mmol) in chloroform. After 30 min at reflux, followed by evaporation in vacuo, purification by column chromatography and recrystallisation from ethyl acetate the product **2** was obtained. Yield 2.7 g (58%). Mp 176–177°C. ^{1}H NMR (DMSO-d_6), δ: 7.75 (m, 6H), 8.15 (m, 4H), 8.48 (dd, 1H, J^3 7.8 Hz, J^3 7.8 Hz), 8.85 (d, 2H, J^3 7.8 Hz). EI/MS (m/z) 439 (M^+, 4%). Anal. calcd for $C_{25}H_{13}N_9$ (439.4): C, 68.33; H, 2.98; N, 28.69. Found C, 67.93; H, 2.71; N, 28.39%.
13. 5,5″-Diphenyl-6,6″-dicyano-2,2′:6′2″-terpyridine **L^1**. A mixture of compound **2** (680 mg, 1.5 mmol) and bicyclo[2.2.1]hepta-2,5-diene (1.3 ml, 12 mmol) in toluene (10 ml) were refluxed for 6 h. The crystals formed were filtered off and recrystallised from acetic acid to give 260 mg (40%) of the terpyridine **L^1**. Mp 296–297°C. ^{1}H NMR (DMSO-d_6), δ: 7.6 (m, 6H), 7.75 (m, 4H), 8.22 (dd, 1H, J^3 7.8 Hz, J^3 7.8 Hz), 8.3 (d, 2H, J^3 8.0 Hz), 8.5 (d, 2H, J^3 7.8 Hz), 8.93 (d, 2H, J^3 8.0 Hz); EI/MS (m/z) 435 (M^+, 100%). Anal. calcd for $C_{29}H_{17}N_5$ (435.5): C, 79.98; H, 3.93; N, 16.08. Found C, 79.60; H, 3.75; N, 16.35%.
14. 2,6-Bis(6-cyano-5-phenyl-3,4-cyclopentenopyridyl-2)-pyridine **L^2**. 1-Morpholinocyclopentene (0.1 ml, 1.16 mmol) was added to a solution of compound **2** (255 mg, 0.58 mmol) in toluene, the resulting mixture was kept at room temperature for 1 h, then refluxed additionally for 1 h. The solvent was removed in vacuo, and the residue was refluxed in 3 ml of acetic acid. The crystals formed were filtered off and recrystallised from DMF yielding 230 mg (77%) of the ligand **L^2**. Mp >300°C (dec.). ^{1}H NMR (DMSO-d_6), δ: 2.15 (m, 4H), 2.93 (t, 4H), 3.45 (t, 4H), 7.6 (m, 10H), 8.25 (m, 3H); EI/MS (m/z) 515 (M^+, 100%). Anal. calcd for $C_{35}H_{25}N_5$ (515.6): C, 81.53; H, 4.89; N, 13.58. Found C, 81.62; H, 4.81; N, 13.60%.
15. Complex **L^{2}Ni(NO$_3$)$_2$** was obtained as follows. A solution of $Ni(NO_3)_2 \cdot 6H_2O$ (84.4 mg, 0.29 mmol) in 3 ml of acetonitrile was added to a solution of ligand **L^2** (150 mg, 0.29 mmol) in acetonitrile (5 ml). The resulting mixture was refluxed for 15 min. The crystals formed after cooling were filtered off, redissolved in hot acetonitrile and kept at room temperature for 12 h resulting in green crystals, suitable for X-ray analysis. Yield 152 mg, 75%. Mp >300°C. Anal. calcd for $C_{35}H_{25}N_5^*Ni(NO_3)_2$ (698.3) C, 60.20; H, 3.61; N, 14.04. Found C, 59.33; H, 3.64; N, 13.82%.
16. CCDC 182870 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk