Tetrahedron: Asymmetry Vol. 4, No. 1, pp. 39-42, 1993
Printed in Great Britain

0957-4166/93 $6.00+.00

Efficient and Short Synthesis of New Camphor Sultam Based Chiral Bipyridines and Phenanthrolines

Christof Kandzia[a], Eberhard Steckhan*[a], and Falk Knoch[b]

a Institut für Organische Chemie und Biochemie der Universität Bonn, Gerhard-Domagk-Straße 1, W-5300 Bonn 1, Germany
b Institut für Anorganische Chemie II der Universität Erlangen-Nürnberg, Egerlandstraße 1, W-8520 Erlangen, Germany

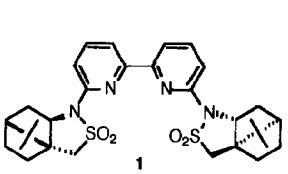
(*Received in UK 25 November* 1992)

Abstract: Starting from bromo substituted bipyridines or phenanthrolines new camphor sultam (10,10-dimethyl-4-aza-3,3-dioxo-thiatricyclo[5.2.1.$0^{1,5}$]decane) based chiral chelating ligands are synthesized by copper catalyzed aromatic nucleophilic substitution. Another class of ligands having a methylene linker between the camphor sultam and the heterocycle is established by use of the corresponding bromo methyl derivatives as precursors.

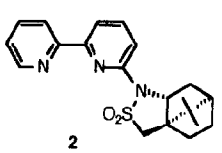
Bipyridines are effectively used as chiral ligands in metal catalyzed reactions such as the enantioselective hydrosilylation of aromatic ketones[1], the alkylation of aldehydes by diethylzinc[2], and the cyclopropanation of styrene[3].

For those purposes, different chiral bipyridines have been synthesized. However, the synthesis of those ligands is sometimes rather complicated because numerous steps are involved[3,4], the reagents are difficult to handle[2], or even resolution of antipodes is necessary[5].

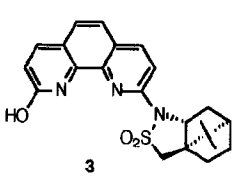
We are interested in easily accessible chiral bipyridines and phenanthrolines, which have to be stable under oxidative and anodic conditions. So we decided to involve camphor sultam in the design of such chiral ligands. Sultams are known to be extremly stable towards anodic oxidation[6], while on the other hand camphor sultam is configurationally stable and therefore often used as an excellent stereodifferentiating auxiliary[7]. Besides, it is commercially available or prepared in few steps from naturally occuring D-(+)-camphor[8].



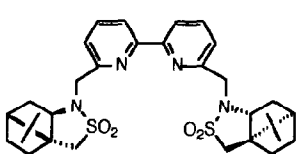
1



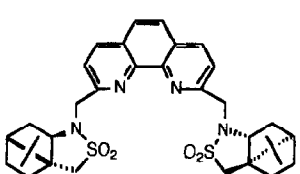
2



3



4

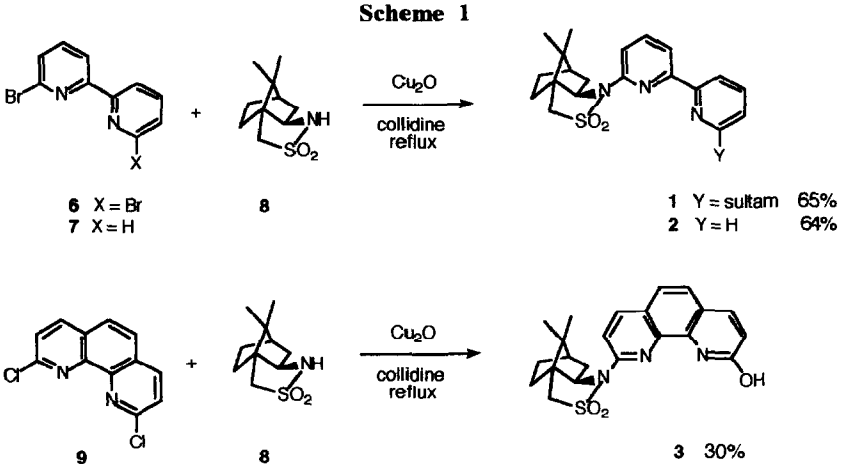


5

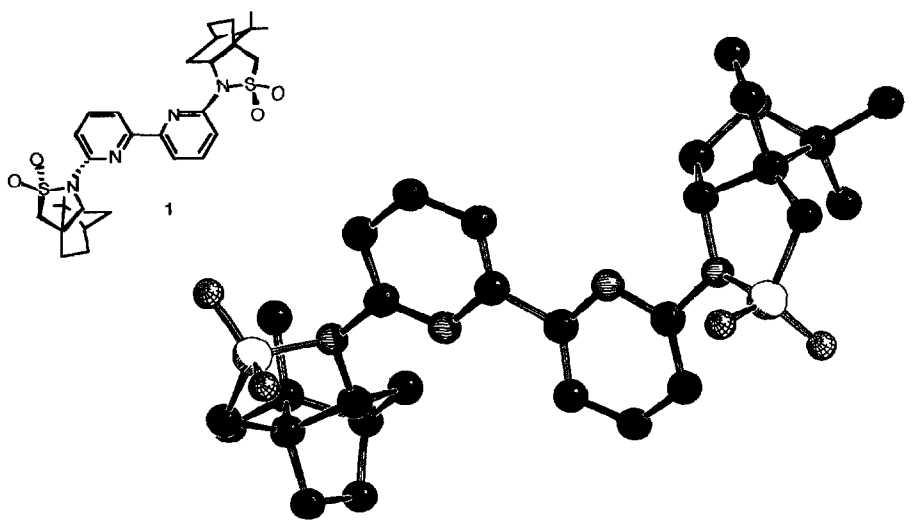
We introduce a short, efficient, and versatile way to the bipyridines and phenanthrolines **1** - **5** bearing camphor

sultam as direct substituent or in remote position[9]. The direct substitution yielding the symmetrical bipyridine **1** is achieved in refluxing collidine under copper oxide catalysis[10], starting with 6,6′-bis-bromo-2,2′-bipyridine **6**, which is prepared by a one step literature method[11]. The monosubstituted bipyridine **2** is prepared using 6-bromo-2,2′-bipyridine **7** as precursor[11]. In the case of the phenanthroline series, only the bis-chloro derivative **9** is described in the literature[12]. Due to the lower reactivity of chloro derivatives or because of steric hindrance only the monosubstituted phenanthroline **3** could be isolated in moderate yield.

Scheme 1

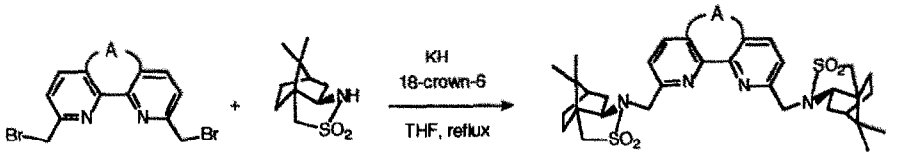


The x-ray analysis of **1** shows the expected *anti*-conformation of 6,6′-disubstituted bipyridines[13]:



To vary the steric requirements, it should be useful to bind the camphor sultam in a more remote position. Using the bis-bromomethyl substituted precursors **10**[14] and **11**[15], the corresponding ligands **4** and **5** are obtained in good yields[16].

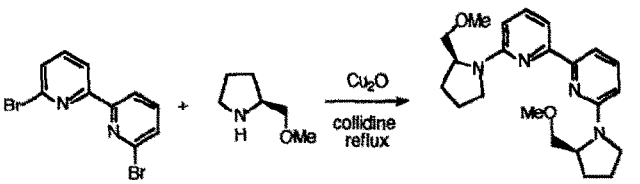
Scheme 2



10 A = -H H- **8** **4** A = -H H- 68 %
11 A = -CH=CH- **5** A = -CH=CH- 60 %

The copper catalyzed functionalisation of bromopyridines is also a versatile method to introduce other chiral N-nucleophiles. For example, with prolinol methyl ether **6**[17] a new potential C_2-symmetrical ligand **13** is formed in moderate yield. Employing this method, many amino acid derived auxiliaries may be used to design chiral N-chelating ligands.

Scheme 3



6 **12** **13** 20-30 %

Now we are introducing these new ligands in catalytic metal mediated oxidations and are checking their potential in known metal catalyzed reactions.

Acknowledgements: Financial support by the Bundesministerium für Wirtschaft through the Arbeitsgemeinschaft industrieller Forschungsvereinigungen (AIF-Nr. 8463), the Fonds der Chemischen Industrie, and BASF Aktiengesellschaft is gratefully acknowledged. C.K. is thankful for a fellowship by the Studienstiftung des Deutschen Volkes.

References and Notes

1. Botteghi, C.; Schionato, A.; Chelucci, G.; Brunner, H.; Kürzinger, A.; Obermann, U. *J. Organomet. Chem.* **1989**,*379*, 17.
2. Bolm,C.; Ewald, M.; Felder, M.; Schlingloff, G. *Chem. Ber.* **1992**, *125*, 1169.
3. Ito, K.; Tabuchi, S.; Katsuki, T. *Synlett* **1992**, 575.
4. Chelucci, G.; Falorni, M.; Giacomelli, G. *Tetrahedron* **1992**, *48*, 3653.
5. Bolm, C.; Ewald, M.; Zehnder, M.; Neuburger, M. *Chem. Ber.* **1992**, *125*, 453.
6. *Ger.Offen.* DE 3015113 A1; *Chem. Abstr.* **1982**, *96*, 104222x.
7. for a review see: Oppolzer, W. *Pure Appl. Chem.* **1990**, *62*, 1241.
   Kim, B.; Lee, J. *Tetrahedron: Asymmetry* **1991**, 2, 1354.
8. Oppolzer, W.; Chapuis, C.; Bernardinelli, G. *Helv.Chim.Acta* **1984**, *67*, 1397.
9. All new compounds are fully characterized by ^1H and ^{13}C spectroscopy. They give satisfactory elemental analyses as well as correct high resolution mass spectra. Optical rotation and ^1H chemical shifts (200 MHz; $CDCl_3$) are as follows.
   1: $[\alpha]_D^{20}$ = - 252 (0.41; $CHCl_3$); δ 8.08 (2H, dd, J=7.8, 0.8), 7.78 (2H, dd, J=8.1; 7.8), 7.48 (2H,

dd, J=7.8; 0.8), 4.24 (2H, dd, J=7; 5.2), 3.50 (2H, d, J=18.2), 3.44 (2H, d, J=18.2), 2.05-2.30 (4H, m), 2.04-1.85 (6H, m), 1.67-1.40 (4H, m), 1.23 (6H, s), 0.99 (6H, s).
2: $[\alpha]_D^{21}$ = - 108 (0.97; $CHCl_3$), δ 8.65 (1H, dm, J=6), 8.35 (1H, ddd, J=7.9; 7;1), 8.16 (1H, dd, J=7; 0.8), 7.81 (1H, ddd, J=7.9; 7; 2), 7.77 (1H, dd, J=8.1; 7), 7.47 (1H, dd, J=8.1; 0.8) 7.28 (1H, ddd, J=7; 6; 1.1), 4.24 (1H, dd, J=6.5; 5.3), 3.50 (1H, d, J=17), 3.42 (1H, d, J=17), 2.16 (2H, m), 2.04-1.85 (3H, m). 1.68-1.43 (4H, m), 1.23 (3H, s), 1.01 (3H, s).
3: $[\alpha]_D^{22}$ = - 109 (0.41; $CHCl_3$), δ 10.19 (1H, s), 8.14 (1H, d, J=8.6), 7.87 (1H, d, J=8.6), 7.83 (1H, d, J=9.5), 7.53 (1H, d, J=10.8), 7.49 (1H, d, J=10.8), 6.83 (1H, dd, J=9.5; 2.2), 4.39 (1H, dd, J=7.8; 3), 3.56 (1H, d, J=19), 3.50 (1H, d, J=19), 2.40-1.60 (7H, m), 1.24 (3H, s), 1.03 (3H, s).
4: $[\alpha]_D^{16}$ = - 44,7 (0.90; $CHCl_3$), δ 8.35 (2H, dd, J=7.8; 1.3), 7.79 (2H, dd, J=7.8; 7.8), 7.51 (2H, dd, J=7.8; 1.3), 4.59 (2H, d, J=14.8), 4.05 (d, J=14.8), 3.22 (2H, dd, J=8.1; 5.2), 3.18 (4H, s), 2,15-1.60 (8H, m), 1.55-1.37 (4H, m)1.35-1.15 (3H, m), 1.09 (6H, s), 0.89 (6H, s).
5: $[\alpha]_D^{21}$ = - 133 (1.00; $CHCl_3$), δ 8.23 (2H, d, J=8.6), 7.91 (2H, d, J=8.6), 7.77 (2H, s), 4.93 (2H, d, J=15.1), 4.40 (2H, d, J=15.1), 3.32 (2H, dd, J=7.8; 2.6), 3.22 (4H, s), 2.00-1.15 (16H, m), 1.13 (6H, s), 0.90 (6H, s).
13: $[\alpha]_D^{18}$ = - 182.7 (0.33; $CHCl_3$), δ 7.69 (2H, dd, J=7.6, 0.7), 7.53 (2H, dd, J=8.3; 7.6), 6.40 (2H, dd, J=8.3; 0.7), 4.39 (2H, m), 3.74 (2H, dd, J=9.1; 3.6), 3.56 (2H, dm, J=7.4), 3.41 (6H, s), 3.37 (2H, m), 3.35 (2H, dd, J=9.1; 7.4), 2.20-1.70 (8H, m).

10. Typical procedure: **8** (935 mg / 4,4 mmol) and **6** (661 mg / 2,1 mmol) are dissolved by ultrasonication in 45 ml degassed collidine. Cu_2O (343 mg / 2,4 mmol) is added and the mixture is refluxed under oxygen free atmosphere for 1 d. After cooling, 80 ml dichloromethane are added and the mixture is poured into 500 ml sulfuric acid (5%) followed by filtration. The filtrate is extracted several times with dichloromethane. The organic phase is washed with sulfuric acid (5%), dried over sodium sulfate and the solvent evaporated. The crude product is extracted with ethanol. As residue pure **1** (803 mg /1,38 mmol) remains. see also: Sato M.; Ebine S. *Synthesis* **1981**, 472.
11. Parks, J.; Wagner, B.; Holm, R. *J. Organomet. Chem.* **1973**, *56*, 253.
12. Lewis, J.; Donoghue, T. *J. Chem. Soc. Dalton Trans.* 1980, 736.
Ogawa, S.; Yamaguchi, T.; Gatoh, N. *J. Chem. Soc. Perkin Trans.1* **1974**, 976.
13. X-ray determination of **1**: Crystal dimensions 0.60 x 0.30 x 0.30 mm^3, measured on a Siemens P4 diffractometer with Mo-K_α-radiation at 293 K. Data collection of 5527 reflexes, 1152 (F>4s) observed. Cell dimensions: a = 972.9(3), b = 1529.2(6), c = 2029.8(6) pm, V = 3.019(2) nm^3, ρ_{cal} = 1.28 g/cm^3 (Z = 4), R = 0.044, orthorombic, space group $P2_12_12_1$. Further details of the crystal structure investigation are available on request from the Fachinformationszentrum Karlsruhe GmbH, D-7514 Eggenstein-Leopoldshafen 2 on quoting the depository number CSD-320565.
14. Newkome, G.R.; Pantaleo, D.C.; Puckett, W.E.; Ziefle, P.L.; Deutsch, W.A. *J. Inorg. Nucl. Chem.* **1981**, *43*, 1529; Rodriguez-Ubis, R.; Alpha, B.; Plancherel, D.; Lehn, J.-M. *Helv. Chim. Acta* **1984**, *67*, 2264.
15. Chandler, C.; Deady, L.; Reiss, J. *J. Heterocycl. Chem.* **1981**, *18*, 599.
16. Typical procedure: **8** (430 mg / 2 mmol) is treated with KH (84 mg / 2,1 mmol) under Argon at 0 °C. for 5 min. Then 18-crown-6 (10 mg) and **11** (366 mg / 1 mmol) are added. This suspension is stirred 90 min at room temperature and then refluxed for 2 d. After usual work up with chloroform the crude product is chromatographied on silca gel (dichloromethane/methanol 30:1) to give pure **5** (380 mg / 0,59 mmol). see also: Nordlander, J.; Stansfield, R. *Tetrahedron Lett.* **1978**, *50*, 4987.
17. Seebach, D.; Kalinowski, H.-O.; Bastani, B.; Cross, G.; Daum, H.; Dörr, H.; DuPreez, N.P.; Ehrig, V.; Langer, W.; Nüssler, C.; Oei, H.-A.; Schmidt, M. *Helv. Chim. Acta* **1977**, *60*, 301.