Tetrahedron Letters, Vol. 33, No. 36, pp. 5165-5168, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

New Versatile Optically Active Bipyridines as Building Blocks for Helicating and Caging Ligands

Pascal Hayoz and Alex von Zelewsky*

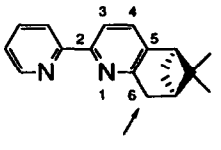
Institute of Inorganic Chemistry, University of Fribourg, Pérolles, CH-1700 Fribourg, Switzerland

Key Words: Optically active bipyridine, building block, cage compound, helicand.

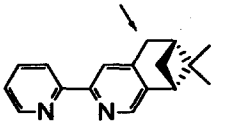
Abstract: Short and efficient syntheses of two new optically active bipyridines have been accomplished using α-pinene as source of chirality. The new bipyridines allow easy access to chiral helicating and caging ligands of sterically well defined shapes and properties.

In the last few years, many new and interesting ligands, such as helicands and caging ligands, have been described.[1,2] Metal complexes of these ligands [3,4] or interactions with guest molecules have been reported.[5] Most of the above mentioned ligands lead to chiral complexes or host-guest structures, but, due to the lack of optical activity of the ligands, only in the racemic forms.

We have now synthesised two new bipyridine derivatives, abbreviated as 6-CHIRABIPY **1** and 4-CHIRABIPY **2**, which contain rigid and chiral pinene type frameworks. Both molecules can be transformed easily to other chiral bipyridines. Deprotonation with LDA of **1** and **2** occurs 100% regiospecifically at the indicated positions. In a second step, the anions can be transformed stereospecifically in substitution or addition reactions in high yields. NOE experiments on the methylated **1** and **2** show, that the lithiated **1** and **2** substitute on the sterically less hindered side. The important feature is, that the substituents point out of the aromatic plane in a conformationally fixed way, which enables the synthesis of chiral ligands with well defined shapes and properties.

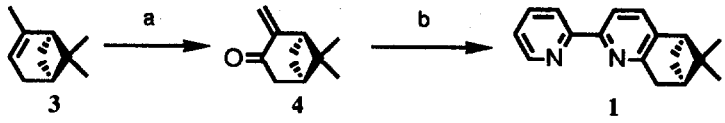


1

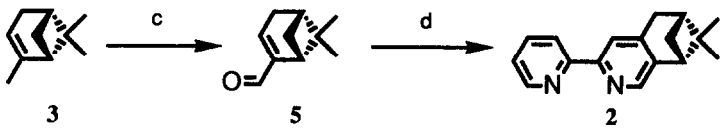


2

1[6] and **2**[7] were synthesised in two step reactions using α-Pinene **3** (commercially available in high optical purity in both enantiomeric forms) as source of chirality (scheme 1, 2):



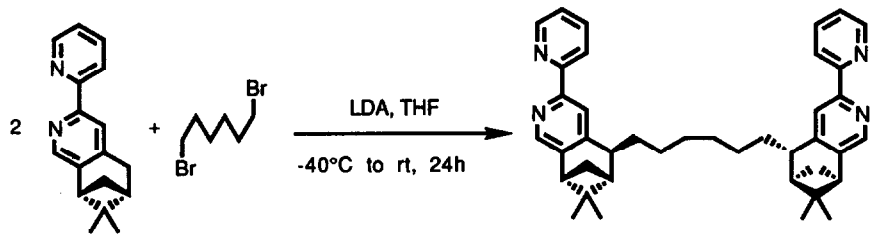
Scheme 1. a) $^1O_2$, Ac_2O, DMAP, CH_2Cl_2, 20°C, 2h Lit.[8]; b) 2-acetylpyridinepyridinium iodide,[9] NH_4OAc, formamide, 100°C, 12h, 55% yield.



Scheme 2. c) SeO_2, t-BuOOH, CH_2Cl_2, 35°C, 48h, Lit.[10]. d) 2-acetylpyridinepyridinium iodide,[9] NH_4OAc, formamide, 70°C, 6h, 75% yield. Alternatively natural (1R)-(-)-myrtenal **5** can be used directly in a one step reaction.

The enantiomeric excess of **1** and **2** has been determined by complexation with optically pure Δ-Ru(phenanthroline)$_2$(pyridine)$_2Cl_2$ as nmr-shift reagent.[11]
1 was synthesised from (1S)-(-)-α-Pinene (Fluka, $[\alpha]_D^{20}$ -42° (neat), purum). Determined ee of **1**: > 80 %.
2 was synthesised from (1R)-(-)-Myrtenal (Aldrich, $[\alpha]_D^{22}$ -15° (neat), purum). Determined ee of **2**: > 90 %.
The enantiomeric purity of the new bipyridines depends on the purity of the chiral precursors. α-pinene with high optical purity (up to 99% ee) can be obtained via the formation of diisopinocampheylboranes.[12]

In a typical synthesis of a chiral helicand, 10 mmol of **2** in 50 ml THF were deprotonated with 11 mmol of l ithiumdiisopropylamide (LDA) by stirring for 2 h at -40°C under nitrogen. At the same temperature, 5 mmol of 1,6-dibromohexane were then added. After 30 min the temperature was raised to about 20°C and and the solution was stirred for 24h. The THF was removed under reduced pressure and 40 ml of water was added to the residue. The slurry was extracted 3 times with 40 ml portions of dichloromethane. The organic phase was dried over $MgSO_4$ and concentrated. The residue was purified by silica gel column chromatography (hexane-ethyl acetate). The synthesis afforded **6**[13] in 78% yield (scheme 3).



2 6

Scheme 3. Alkylation of **2** with 1,6-dibromohexane and formation of a C_2-symmetrical helicand.

Interesting applications of ligand **6** are e.g. the syntheses of metal complexes such as $[Ru(\mathbf{6})(CO)_2]^{2+}$ (Figure 1), where the two chelating bpy units coordinate in a sterically predetermined helical fashion. **6** acts thereby as a "chiral basket".[14]

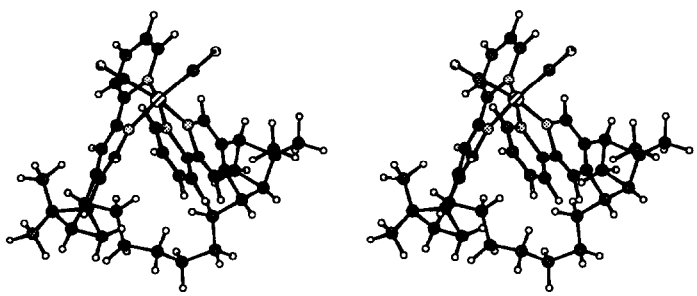


Figure 1. Stereo pair of the C_2-symmetrical complex Δ–$[Ru(\mathbf{6})(CO)_2]^{2+}$.

The complex was characterised by ^{1}H-NMR including NOE experiments, FAB-MS, UV/VIS and CD-spectroscopy. Such complexes are now used as enantiomerically pure building blocks for the synthesis of isomerically pure polynuclear species.[15]

1, 2 and their derivatives are also under investigation in chiral host - chiral guest recognition experiments and as auxiliary ligands in enantioselective catalysis.

Acknowledgement. The authors thank the Swiss National Science Foundation for financial support of this work.

References and Notes

1. Lehn, J.M.; Ziessel, R. *Helv. Chim. Acta*, **1988**, *71*, 1511-1516.
2. Constable, E.C.; Elder, S.M.; Healy, J.; Tocher, D.A. *J. Chem. Soc., Dalton Trans.*, **1990**, *5*, 1669-

1674.

3. Constable, E.C.; Ward, M.D.; Tocher, D.A. *J. Am. Chem. Soc.*, **1990**, *112(3)*, 1256-1258.
4. Youinou, M.; Ziessel, R.; Lehn, J.M. *Inorg. Chem.* **1991**, *30*, 2144-2148.
5. Vögtle, F.; Seel, C. *Angew. Chem.* **1992**, *104*, 542-563.
6. Physical data: **1**, colorless solid, $[\alpha]_D^{20}$ -22° (c 8 mM, CH_2Cl_2); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 0.65 (3H, s), 1.28 (1H, d, J=9.6 Hz), 1.39 (3H, s), 2.35-2.39 (1H, m), 2.66 (1H, dxt, J=9.6, 6.0 Hz), 2.78 (1H, t, J=5.7 Hz), 3.16 (2H, d, J=2.7 Hz), 7.22 (1H, dxd, J=4.9, 5.9 Hz), 7.30 (1H, d, J=7.9 Hz), 7.75 (1H, dxd, J=7.9, 6.0 Hz), 8.01 (1H, d, J=7.7 Hz), 8.32 (1H, d, J=8.0 Hz), 8.63 (1H, d, J=4.9 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 21.39, 26.10, 31.96, 36.75, 39.55, 40.26, 46.48, 117.91, 120.84, 123.05, 133.79, 136.78, 142.26, 149.16, 153.56, 156.51, 156.81; MS (EI, 70 eV) m/z (%): 250(M^+, 38), 207(100), 194(14), 78(12);
7. Physical data: **2**, colorless solid, $[\alpha]_D^{20}$ -21° (c 8 mM, CH_2Cl_2); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 0.61 (3H,s), 1.20 (1H, d, J=9.6 Hz), 1.37 (3H, s), 2.25-2.29 (1H, m), 2.66 (1H, dxt, J=9.6, 5.8), 2.83 (1H, t, J=5.5 Hz), 3.01 (1H, d, J=2.7 Hz), 7.23 (1H, dxd, J=7.5, 3.9 Hz), 7.75 (1H, dxd, J=7.6, 7.6 Hz), 8.15 (1H, s), 8.17 (1H, s), 8.31 (1H, d, J=8.0 Hz), 8.61 (1H, d, J=4.0 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 21.38, 26.06, 31.86, 32.94, 39.29, 40.14, 44.57, 120.47, 120.86, 123.23, 136.83, 143.00, 145.43, 145.56, 148.99, 154.50, 156.76; MS (EI, 70 eV) m/z (%): 250(M^+, 8.5), 207(100), 180(13);
8. Mihelich, E.D.; Eickhoff, D.J. *J. Org. Chem.* **1983**, *48*, 4135-4137.
9. Kröhnke, F. *Angew. Chem.* **1963**, *75*, 181-194.
10. de Richter, R.K.; Bonato, M.; Follet, M.; Kamenka, J.-M. *J. Org. Chem.* **1990**, *55*, 2855-2860.
11. Determination of the enantiomeric excess of **2**:
Complexation of enantiomerically pure Δ-$[Ru(phen)_2(py)_2]^{2+}$ [15] with **2** leads to the formation of two diastereomeric complexes. The ^{1}H-nmr spectrum (300 MHz, acetone) shows the singlets of the methyl protons of Δ-$[Ru(phen)_2((-)\text{-}\mathbf{2})](PF_6)_2$ at 0.77, 1.29 ppm and of Δ-$[Ru(phen)_2((+)\text{-}\mathbf{2})](PF_6)_2$ at 0.21, 1.17 ppm. The ratio of the signals of the two diastereomers is 31 : 1. This equals an ee-value of 93.8 %. For reference purpose, racemic $[Ru(phen)_2(py)_2]^{2+}$ was complexed with **2**. As expected, the ^{1}H-nmr spectrum of the resulting mixture of isomers showed the same chemical shifts for the methyl protons as above, but all signals occurringwith equal intensities. The ee of **1** was determined similarly.
12. Brown, H.C., Jadhav, P.K., Desai, M.C. *J. Org. Chem.* **1982**, *47*, 4583-4584.
13. Physical data: **6**, colorless solid, $[\alpha]_D^{20}$ +17° (c 4 mM, CH_2Cl_2); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.62 (2H, d), 8.32 (2H, d), 8.26 (2H, s), 8.16 (2H, s), 7.74 (2H, dxd), 7.22 (2H, dxd), 2.95 (2H, d), 2.82 (2H, dxd), 2.52 (2H,dxdxd), 2.25 (2H, dxd), 1.98 (2H, m), 1.54-1.30 (10H, m), 1.40 (6H, s), 1.24 (2H, d), 0.59 (6H, s); MS (EI, 70 eV) m/z (%): 582(42), 539(23), 263(71), 249(100), 233(45), 207(90);
14. Preliminary contribution at Euchem Conference on "Nitrogen Ligands in Organometallic Chemistry and Homogeneous Catalysis" in Alghero (Italy 10-15 May 1992).
15. Hua, X.; von Zelewsky, A. *Inorg. Chem.* **1991**, *30*, 3796-3798.

(Received in Germany 27 June 1992)