Asymmetric Catalysis; 140:1 Tris(2-pyridyl)methane Derivatives with a Chiral Bridging Atom

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Received 19 July 2001; revised 7 September 2001

Abstract: Two different series of C₁-symmetric tris(2-pyridyl)methane tripod ligands were synthesized with pyridin-2-yl, 6-phenylpyridin-2-yl and 6-methoxy- or 6-menthoxypyridin-2-yl substituents. The menthox derivativs were resolved with respect to the bridging carbon atom by chromatography. In reactions with CuCl₂ and RhCl₃ complexes were obtained which could be analyzed by X-ray crystallography. In the formation of the Rh complex an ortho-metallation of the 6-phenyl substituent occurred giving rise to a Δ/Α-element of chirality. Whereas the chiral tripod ligand conferred a stable configuration to the Rh atom, a fast equilibration of the Δ- and Α-isomers was observed.

Key words: chiral tripod ligands, tris(2-pyridyl)methane derivatives, Cu-complex, Rh-complex, ortho-metallation, absolute configuration

Introduction

There are two different types of tridentate ligands. Either the ligand is flat and coordinates in a mer-fashion at an octahedron or the ligand is tripodal and coordinates in a fac-fashion at an octahedron. Chiral examples are the pybox ligand introduced by Nishiyama et al.⁵ (mer-type) and the trisphosphane ligands of Burk et al.⁴ and Huttner et al.⁵ (fac-type). Tris(pyrazolyl)borates are well known trisni-

trogen ligands which coordinate facially to transition metals. Their analogues are tris(2-pyridyl) compounds, in which the bridging atom can be carbon, nitrogen, phosphorus or arsenic.⁶ There are major differences between tris(pyrazolyl)borate and tris(2-pyridyl)methane tripods. The tris(pyrazolyl)borates are monoanionic, whereas the tris(2-pyridyl)methane ligands are neutral. Furthermore, pyridine is more basic than pyrazole, thus it should be a better σ-donor and it is reported to be a better π-acceptor than pyrazole.⁷ Chiral C₃-symmetric tris(pyrazolyl)borates⁸ and tris(2-pyridyl)methane derivatives⁹ are known, but only few C₁-symmetric tripods are mentioned in the literature¹⁰ and no C₁-symmetric tris(2-pyridyl) derivaties have been reported. Therefore, we synthesized tris(2-pyridyl) derivatives, in which a carbon atom bridges three different pyridine substituents, an unsubstituted 2-pyridine, a 6-methoxy- or 6-menthoxystituted 2-pyridine and a 6-phenyl-substituted 2-pyridine.¹¹ Some of the compounds were resolved with respect to the configuration of the bridging carbon atom.¹¹ As in a facial coordin-

ation, a tripod ligand with a chiral bridging atom confers chirality to the metal centre, this stereochemical aspect was investigated in Cu and Rh complexes.¹¹ According to a concept recently presented in this journal,¹² chiral C₁-symmetric tris(2-pyridyl) ligands should provide enanti-
oselective catalysts, in which the configuration at the metal atom is held constant throughout the catalysis.

Racemic Tris(2-pyridyl)methane Derivatives

For the preparation of tris(2-pyridyl)methane derivatives with a chiral branching atom the commercially available 2-phenylpyridine was converted into 2-bromo-6-phenylpyridine via 2-amino-6-phenylpyridine. The ketone 3 was accessible by addition of the lithiopyridine derivative obtained from 2-bromo-6-phenylpyridine to pyridine-2-carbonitrile. After a lithium-bromine exchange in 2-bromo-6-methoxypyridine the resulting organometallic compound was added to the ketone 3 to give the racemic tris(2-pyridyl)methanol derivative (Scheme 1).

For the resolution of rac-5 the formation of diastereomeric salts with the chiral acids (1S)-(+) -camphorsulfonic acid, (2R,3R)-(−)-dibenzoyltartaric acid, (R)-(−)-mandelic acid and (R)-(−)-4(2-chlorophenyl)-2-hydroxy-5,5-dimethyl-1,3,2-dioxophosphorane-2-oxide was attempted without success. Therefore, the chiral auxiliaries were covalently bound to 5 by esterification with (1R,2S,5R)-menthoxo- and (1S,2R,4S)-borneoxyacetic acid, respectively. These acids were prepared and transformed to the acid chlorides according to literature methods and reacted with deprotonated 5 (n-butyllithium) to give 81% and 54% of the diastereomeric esters 6 and 7, respectively (Figure 1).

The esters 6 and 7 were obtained as 1:1 mixtures of diastereomers differing in the configuration of the branching carbon atom of the tris(2-pyridyl)methane moiety. They are crystalline substances, which could be recrystallized from petroleum ether and diisopropyl ether. However, repeated recrystallizations did not result in an enrichment of one diastereomer. Therefore, the alcohol functionality was separated from the bridgehead atom by a methylene group. The alcohol 5 was transformed to the bromide 8 by deprotonation with n-BuLi and reaction with thionyl bromide. Lithium-bromine exchange and reaction with paraformaldehyde gave the 2,2,2-tris(2-pyridyl)ethanol derivative 9 with 79% yield (Scheme 2).

The ethanol derivative 9 could be transformed to the tosylate 10. Surprisingly, the reaction of 10 with sodium methoxide in methanol did not liberate the alcohol 9 but afforded the methane derivative 11 in 84% yield (Scheme 3). Carboxylates including (1R,2S,5R)-menthoxoacetate and (1S,2R,4S)-borneoxyacetate gave the same product, as did alkoxides (e.g. sodium menthoxide) and sodium hydride in toluene at 70°C. In the literature such a loss of formaldehyde has been reported for 2,2,2-trisphenylethanol but not for the analogous trispyridinethanol. The conversion of the ethyl alcohol 9 to the corresponding ethyl bromide derivative could be performed by refluxing in a solution of thionyl bromide in chloroform.

![Figure 1](image_url)

Scheme 2 (a) n-BuLi, THF, r.t., 2. SOBr₂, –70 °C → r.t.; (b) n-BuLi, Et₂O, –90 °C, 2. paraformaldehyde, –90 °C → r.t., 3. H₂O.

Scheme 3 (a) TsCl, py, r.t., 60 h; (b) CH₃ONa, CH₃OH, reflux, 14 h.
Diastereomeric Tris(2-pyridyl)methane Derivatives

Another possibility for the formation of diastereomeric tris(2-pyridyl)methane derivatives is to introduce one pyridyl group, which is substituted with a chiral substituent. The (1R,2S,5R)-menthyl group was chosen for this purpose. (1R,2S,5R)-Menthol was deprotonated with sodium hydride and reacted with 2,6-dibromopyridine to afford the menthoxy substituted bromopyridine in 83% yield. After lithium-bromine exchange in to give , reaction with the ketone gave the tris(2-pyridyl)methanol derivative (Scheme 1). The diastereomers of are formed as a 1:1 mixture. By repeated chromatography on silica gel it was possible to enrich the faster moving isomer to a ratio of 98:2.

The alcohol is the key intermediate for the subsequent syntheses. Deprotonation of with sodium hydride followed by addition of methyl iodide gave the methyl ether in 77% yield. In this reaction no epimerization took place since the diastereomeric excess of was retained in . The conversion of the alcohol to the bromomethane was performed with thionyl bromide. As the diastereomeric excess of the alcohol was almost completely lost in the reaction to the bromide a retention mechanism must be excluded. White and Faller proposed either a SN2 or a SN1 mechanism for the halogenation of tris(2-pyridyl)methanol with SOX2 (X = Br, Cl). The reaction of with n-BuLi led to an organometallic intermediate which could either be hydrolyzed with water to give the methane derivative (73%) or treated with oxetane in the presence of an equimolar amount of BF3·OEt2 to provide the 4,4,4-tris(2-pyridyl)butan-1-ol derivative with 56% yield (Scheme 4).

For both alcohols and the diastereomers could be enriched by chromatography, but only the butanol derivative was used subsequently, because it was configurationally stable at the branching carbon atom. Repeated chromatography of on silica gel gave a 95:5 enrichment of the faster moving diastereomer. An X-ray analysis of a rhodium complex of (see below) allowed the assignment of (S)-configuration at the bridging atom of the faster moving isomer. The propyl substituent with its terminal OH group at the end in has two major advantages. First, can be modified to adjust the solubility without changing the complexation properties of the tris(2-pyridyl) moiety, and second, the ligand can be heterogenized by covalent binding to a solid phase.

Metal Complexes

From the racemic methane derivative the CuCl2 complex was prepared in methanol in 72% yield. Exclusion of air is important, because the literature reports an example in which a methane derivative was air-oxidized to the corresponding methanol derivative. Diffusion of ether into a methanolic solution of and CuCl2 gave green crystals of suitable for X-ray analysis. In addition to the two chloride ligands the copper(II) centre is chelated by ligand in a bidentate way (Figure 2). Copper(II) complexes in which a tris(2-pyridyl)methane derivative coordinates as a tripod ligand are also known. The uncoordinated methoxy-substituted pyridine ring is rotated by 28° relative to the Cu1-C12-C13 plane. The structure can be described as distorted square planar. In the unit cell there are two pairs of enantiomers.

Scheme 4 (a) 1. NaH, DMF, r.t. 2 h, 2. CH3I, r.t.; (b) 1. n-BuLi, Et2O, –78 °C; 2. SOBr2, –78 °C à r.t., 3. NaHCO3; (c) 1. n-BuLi, Et2O, –90 °C à r.t., 2. H2O; (d) 1. n-BuLi, Et2O, –90 °C à r.t., 2. oxetane, BF3·OEt2, –90 °C à r.t., 3. H2O, HCl 4. K2CO3.
The rhodium complex 20 was synthesized from rhodium(III) chloride trihydrate and the butanol derivative 18 in ethanol. If a 65:35 mixture of the two diastereomers of 18 (the faster moving diastereomer in excess) is used, the ¹H NMR spectrum of the complex 20 exhibits four signals with the chemical shifts in DMSO-­d₆ of 9.25, 9.32, 9.55 and 9.62 ppm (integration 62:32:2:4) for the downfield proton py-H₆. This means that in solution four diastereomers are present. The X-ray analysis of 20 (see below) shows that in its formation an ortho-­metallation has taken place. In addition to the two asymmetric centres (bridgehead atom of the ligand and metal atom) the ortho-­metallation establishes a new element of chirality. The ortho-­metallation can occur at two different coordination sites, which define a right-handed helix (/c₆₈) and a left-handed helix (/c₇₆), respectively. In Figure 3 the four possible diastereomers are drawn schematically together with their configurational symbols starting with the asymmetric centre in the ligand. Provided that the specification of the metal chirality is based on the nitrogen atoms of the pyridine ligands in their respective priority, the metal has the opposite configuration compared to the bridgehead carbon atom.

For the separation of the main diastereomer, the 62:32:2:4 mixture of 20 was dissolved in DMSO (gentle warming). Then the solvent was distilled off in vacuo without warming above 50 °C, because at higher temperatures the complex reacts with the solvent,¹¹ until first crystals appeared. After standing for a few days at r.t. the crystals were filtered off. ¹H NMR experiments in DMF-d₇ showed at r.t. a ratio of 96.8:3.2 (only two isomers present). On dissolving the crystals at –25 °C in DMF-d₇, the ¹H NMR spectrum indicated a 98.4:1.6 distribution. The ratio shifted to 97.8:2.2 at 0 °C and to 96.8:3.2 at 21 °C. Recooling to –25 °C brought the ratio back to 98.4:1.6. Heating the solution to 50 °C gave an increase of the less abundant diastereomer to 3.6%. Further heating to about 80 °C caused a reversible broadening of the signals. However, at this temperature the ¹H NMR spectrum started to show irreversible changes. This temperature-sensitive equilibration is assigned to the interconversion of the /A-/­helicity.

Single crystals suitable for X-ray analysis were obtained from a concentrated solution of 20 in DMSO on standing in an open vessel (anhydrous DMSO is hygroscopic). An ORTEP representation of the complex 20, which has the configuration (Sₐ,Rₗ,Rₗₗ₇₆), is shown in Figure 4. Three crystals were measured and gave the same result. As a ¹H NMR study of the single crystals at r.t. gave an isomer ratio of 97:3, we assign the (Sₐ,Rₗ,Rₗ₇₆)-configuration to the 97% isomer (chemical shift in DMSO-d₆ 9.25 ppm) in the 97:3 mixture (identical with the 62% isomer in the 62:32:2:4 mixture) and we assume its rapid equilibration in solution with the (Rₗ,Sₐ,Rₗ₇₆)-isomer (9.55 ppm). Then the 32% isomer (9.32 ppm) in the 62:32:2:4 mixture should be the (Rₗ,Sₐ,Sₐ₇₆)-isomer and the 4% isomer (9.62 ppm) should have (Rₗ,Sₐ,Rₗ₇₆)-configuration.

20 has a distorted octahedral structure, in which the Rh-­Cl and Rh-­C bond lengths are in agreement with comparable rhodium complexes.²² However, the Rh-­N bonds differ considerably (1.98, 2.08 and 2.19 Å), whereas in the tris(2-pyridyl)methanol-­RhCl₃ complex the lengths vary only between 2.03 and 2.05 Å. This means that the ortho-­metallation has a significant influence on the Rh-­N distances. The bond Rh1-­N2 is shortened because of the

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**Figure 2** ORTEP representation (50% probability) of 19. Selected distances [Å] and angles [°]: Cu1-­Cl1 2.24, Cu1-­Cl2 2.27, Cu1-­N1 2.03, Cu1-­N3 2.03, Cl1-­Cu1-­Cl2 94, Cl1-­Cu1-­N1 93, Cl1-­Cu1-­N3 161, Cl2-­Cu1-­N1 155, Cl2-­Cu1-­N3 95, N1-­Cu1-­N3 87.

**Figure 3** Schematic representation of all possible diastereomers of 20.
five-membered chelate ring. In contrast, the bond Rh1-N3 is elongated as a result of the strong trans-effect of the phenyl substituent. These distortions also affect the Rh1-N1 bond. Surprisingly the bond Rh1-N2 is shorter than Rh1-C1.22b In the unit cell there are 6 molecules of the complex. The space group is P 6 1 and the crystal system hexagonal. At the edges of the unit cells along the c axis channels are formed, in which solvent molecules reside in a disordered manner. In Figure 5 six molecules of (S,C,Rh,Rh,Rh)-20 are shown in their arrangement around the channel along the c axis. On the left, the left-handed sense of the helix is obvious from the numbers 1–6. On the right, the side view is represented.

The preparation of air-sensitive compounds was carried out under purified N 2 using standard Schlenk techniques. Solvents were dried and degassed according to standard procedures and stored under N 2 . Commercial starting materials were used without further purification. For the chromatographies Merck Geduran® 60 silica gel (63–200 μm) was used. Reaction mixtures and chromatography fractions were analyzed with precoated silica gel 60 F 254 TLC plates (Merck). Melting points: SMP-20 (Büchi), not corrected. MS: MAT 311A (EI), MAT 95 (DCI) (both Finnigan) and TSQ 7000 (ESI) (ThermoQuest). Optical rotations: Perkin-Elmer 241 polarimeter (1 dm cells). IR spectra: Acculab 3 (Beckman). 1H NMR: AC250 (250 MHz) and ARX400 (400 MHz) (both Bruker), internal standard TMS. 13C NMR: ARX400 (1H decoupled, 101 MHz, Bruker).

The following compounds were synthesized according to the literature: 2-Amino-6-phenylpyridine,13 2-bromo-6-phenylpyridine,13 2-bromo-6-methoxypyridine (2),14 [(1R,2S,5R)-2-isopropyl-5-methylcyclohexyloxy]acetate acid,15 [(15,2R,4S)-1,7,7-trimethyl-bicyclo[2.2.1]hept-2-ylxoxy]acetic acid.16 n-Butyllithium was used as a

Figure 4 ORTEP representation (50% probability) of (S,C,Rh,Rh,Rh)-20. Selected distances [Å] and angles[°]: Rh1-Cl1 2.35, Rh1-Cl2 2.36, Rh1-C1 2.00, Rh1-N1 2.08, Rh1-N2 1.98, Rh1-N3 2.19, C11-Rh1-C12 89, C11-Rh1-N2 92, C11-Rh1-N3 88, C12-Rh1-N1 171, C11-Rh1-C1 84, C12-Rh1-N2 177, C12-Rh1-N3 91, C12-Rh1-C1 97, N1-Rh1-C1 103, N2-Rh1-N3 92, N2-Rh1-N1 84, N2-Rh1-C1 81, N3-Rh1-N1 85, N3-Rh1-C1 168.

Figure 5 Complex 20: a top view (along the c axis), b side view (along the b axis)
1.6 M solution in hexane (Merck). The acronym PE for petroleum ether (bp 40–60 °C) will be used. In the 1H NMR data the abbreviation py designates the unsubstituted pyridine ring, py' the methoxy- or menthoxyl-substituted ring and py" the phenyl-substituted ring.

(6-Phenylpyridin-2-yl)(pyridin-2-yl)methanone (3) To a suspension of 2-bromo-6-phenylpyridine (25.2 g, 107 mmol) in anhyd Et₂O (500 mL) was added n-BuLi (72 mL, 115 mmol, 1.6 M in hexane) within 1 h at −78 °C. The mixture was allowed to warm to r.t. (clear orange solution). The solution was cooled to −78 °C and a solution of 2-cyanopyridine (11.7 g, 120 mmol) in anhyd Et₂O (150 mL) was added after a period of 45 min. The mixture was allowed to warm to r.t. and poured into ice water (500 mL). HCl (2 M, 150 mL) was added and the solution stirred vigorously. After separation of the phases the organic phase was extracted with HCl (2 M, 3 × 100 mL). The combined organic phases were refluxed for 2 h and carefully neutralized at r.t. with solid KO₂CO₃. The resulting solution was extracted with CH₂Cl₂ (5 × 50 mL). The combined organic extracts were dried (Na₂SO₄) and evaporated. The residue was chromatographed through silica gel (6 cm × 6 cm Z) with CH₂Cl₂–EtO (1:1) and recrystallized from PE–acetone (10:1) to give 3 (11.3 g, 41%) as pale pink needles; mp 90–92 °C.

1H NMR (250 MHz, CDCl₃): δ = 8.80 (ddd, 1 H, J = 4.8 Hz, J₁ = 1.8 Hz, J₂ = 0.9 Hz, py-'; H₃), 8.17 (ddd, 1 H, J = 7.8 Hz, J₁ = 1.2 Hz, J₂ = 1.0 Hz, py-H₂), 8.10–7.91 (m, 5 H), 7.89 (ddd, 1 H, J = 1.8 Hz, J₁ = 7.8 Hz, J₂ = 7.6 Hz, J₃ = 1.8 Hz, py-H'), 7.50 (ddd, 1 H, J = 7.6 Hz, J₁ = 4.8 Hz, J₂ = 1.2 Hz, py-H'), 7.48–7.37 (m, 3 H, Ph).

IR (KBr): 1660s (C=O) cm⁻¹.

MS (PI-EL, 70 eV): m/z (%) = 260 (M, 100), 232 (M–CO–H, 85), 154 (M–pyCO–CN, 37), 128 (M–pyCO–CN), 34, 78 (C₆H₄N, 51) (C₆H₄, 12).


(6-Methoxypyridin-2-yl)(6-phenylpyridin-2-yl)pyridin-2-ylmethanone (5) A solution of 2 (8.22 g, 43.0 mmol) in anhyd THF (50 mL) was cooled to −75 °C and n-BuLi (29 mL, 46 mmol, 1.6 M in hexane) was added within 30 min. The resulting solution of 4 was cooled to −85 °C and a solution of the acid chloride (see above) in THF (25 mL) was added over a period of 45 min. The mixture was allowed to warm to r.t. and acidified with HCl (2 M, 200 mL). The organic mixture was collected after a period of 15 min. After stirring for 15 min a solution of the acid chloride (see above in THF) (25 mL) was added within 20 min. The mixture was warmed to 40 °C and stirred for 24 h. The cooled solution was quenched with H₂O (25 mL) and washed with sat. Na₂CO₃ (3 × 20 mL), dried (Na₂SO₄) and evaporated. The residue was recrystallized from disopropyl ether to give 5 (9.62 g, 81%) as colorless crystals; mp 65–68 °C. All attempts at enriching one diastereomer by recrystallization failed.

Analytical data for a 1:1 mixture of the two diastereomers: [α]D₉ (c = 0.5, n-hexane, r.t.): −40.1 (589 nm), −41.9 (578 nm), −47.7 (546 nm), −80.0 (436 nm), −125 (365 nm).

1H NMR (250 MHz, CDCl₃): The signals were not assigned to the different diastereomers. δ = 8.53 (ddd, 1 H, J = 4.8 Hz, J₁ = 1.8 Hz, J₂ = 0.9 Hz, py-H'), 8.53 (ddd, 1 H, J = 4.8 Hz, J₁ = 1.8 Hz, J₂ = 0.9 Hz, py-H'), 7.88–7.77 (m, 8 H), 7.72 (ddd, 1 H, J = 1.8 Hz, J₁ = 7.8 Hz, J₂ = 7.7 Hz, py-H'), 7.72 (ddd, 1 H, J = 7.8 Hz, J₁ = 7.7 Hz, py-H'), 7.64 (ddd, 1 H, J = 8.1 Hz, J₁ = 7.4 Hz, J₂ = 1.8 Hz, py-H'), 7.64 (ddd, 1 H, J = 8.1 Hz, J₁ = 7.4 Hz, J₂ = 1.8 Hz, py-H'), 7.60 (ddd, 1 H, J = 7.6 Hz, J₁ = 1.2 Hz, py-H'), 7.55 (ddd, 2 H, J = 8.1 Hz, J₁ = 7.5 Hz, py-H'), 7.43–7.30 (m, 8 H), 7.15 (ddd, 2 H, J = 7.4 Hz, J₁ = 4.8 Hz, J₂ = 1.2 Hz, py-H'), 6.60 (ddd, 2 H, J = 8.1 Hz, J₁ = 0.8 Hz, py-H'), 4.51 (AB, 1 H, J = 16.2 Hz, OCH₂Ph₂), 4.45 (AB, 1 H, J = 16.2 Hz, OCH₂Ph₂), 4.45 (AB, 1 H, J = 16.2 Hz, OCH₂Ph₂), 3.71 (s, 6 H, OCH₃), 3.18 (dt, 1 H, J = 10.5 Hz, J₁ = 2.1 Hz, OCH₂), 3.17 (dt, 1 H, J = 10.5 Hz, J₁ = 2.2 Hz, OCH₂), 2.37–2.24 (m, 2 H), 2.15–2.04 (m, 2 H), 1.67–1.55 (m, 4 H), 1.34–1.15 (m, 4 H), 0.73–0.63 (m, 7 H), 0.87 (d, 3 H, J = 6.5 Hz, CH₃), 0.86 (d, 3 H, J = 6.5 Hz, CH₃), 0.85 (d, 6 H, J = 7.1 Hz, CH₂), 0.70 (d, 3 H, J = 6.9 Hz, CH₃), 0.69 (d, 3 H, J = 6.9 Hz, CH₃).

IR (KBr): 1775s (C=O) cm⁻¹.

MS (PI-EL, 70 eV): m/z (%): 565 (M, 0.6), 368 (M–menOCH₂COO–C₅H₃NOCH₃+H, 11), 352 (M–menOCH₂COO, 100), 337 (M–menOCH₂COO–CH₃, 6), 245 (M–menOCH₂COO–C₅H₃NOCH₃+H, 7).

Anal calec for C₃₂H₃₄N₂O₃ (565.7): C, 74.31; H, 6.95; N, 7.43. Found: C, 74.03; H, 6.96; N, 7.36.

(6-Methoxypyridin-2-yl)(6-phenylpyridin-2-yl)pyridin-2-yl-1,7,7-trimethylbicyclo[2.2.1]hept-2-ylxacyclete (7) This compound was prepared by a method analogous to that used for 6. Thus, (1S,2R,4S)-1,7,7-trimethylbicyclo[2.2.1]hept-2-ylxacyclic acid (1.33 g, 6.25 mmol) and 5 (1.26 g, 3.4 mmol) gave the product 7. Recrystallization from pentane yielded colorless crystals of 7 (1.03 g, 54%) mp 104–106 °C. No enrichment of a diastereomer could be achieved by recrystallization.

Analytical data for a 1:1 mixture of the two diastereomers: [α]D₉ (c = 0.54, CH₂Cl₂, r.t.): −27.0 (589 nm), −27.0 (578 nm), −32.0 (546 nm), −58.1 (436 nm), −101 (365 nm).

1H NMR (250 MHz, CDCl₃): The signals were not assigned to the different diastereomers. δ = 8.53 (ddd, 1 H, J = 4.8 Hz, J₁ = 1.9 Hz, J₂ = 0.9 Hz, py-H'), 8.53 (ddd, 1 H, J = 4.8 Hz, J₁ = 1.9 Hz, J₂ = 0.9 Hz, py-H'), 7.72 (ddd, 1 H, J = 7.6 Hz, J₁ = 1.2 Hz, py-H'), 7.48–7.37 (m, 3 H, Ph).

Synthesis 2001, No. 16, 2484–2494 ISSN 0039-7881 © Thieme Stuttgart · New York
2- (6- Methoxy pyridinyl - 2) - yl 2 - (6- phenyl pyridinyl - 2) - yl pyridin - 2 - yl ethyl p - toluenesulfonate (10)

To a solution of 9 (2.20 g, 5.80 mmol) in anhyd pyridine (40 mL) was added p - TSCl (2.36 g, 12.0 mmol). After stirring the solution at r.t. for 60 h the mixture was quenched with ice water (50 mL). An aq solution of NaHCO3 (1 M, 10 mL) was added and the resulting emulsion extracted with CH2Cl2 (4 × 15 mL). The organic layer was washed with NaHCO3 (1 M, 5 × 10 mL), water (2 × 10 mL), dried (Na2SO4) and evaporated to dryness. The crude product was suspended in Et2O, stirred and filtered to give 10 as a slightly brownish powder (2.15 g, 69%); mp 127–129 °C.

1H NMR (250 MHz, CDCl3): δ = 8.41 (ddd, 1 H, J = 4.8 Hz, J = 1.9 Hz, J = 0.9 Hz, py-H3), 7.88–7.59 (m, 2 H, Ph); 7.66–7.55 (m, 2 H), 7.56 (ddd, 1 H, J = 1.9 Hz, J = 8.1 Hz, J = 1.9 Hz, py-H4); 7.49 (dd, 1 H, J = 8.1 Hz, J = 0.7 Hz, py-H5); 7.37–7.33 (m, 8 H), 7.14–7.05 (m, 2 H), 4.43 (AB, 2 H, J = 16.4 Hz, OCH2Ph); 4.41 (AB, 2 H, J = 16.4 Hz, OCH2Ph); 3.77–3.68 (m, 2 H), 3.71 (s, 3 H, OCH3); 3.71 (s, 3 H, OCH3); 2.17–2.00 (m, 4 H); 1.74–1.58 (m, 4 H), 1.29–1.06 (m, 6 H), 0.88 (s, 3 H, CH3); 0.88 (s, 3 H, CH3); 0.82 (s, 3 H, CH3); 0.76 (s, 3 H, CH3); 0.74 (s, 3 H, CH3).

IR (KBr): 1780s (C=O) cm−1.

MS (PI-EL, 70 eV) m/z (%): 563 (M, 0.7), 368 (M−bornOCH2COO−C5H3NOCH3 + H, 7).
which unreacted menthol was distilled off (95 °C/0.2 mbar). The residue was subjected to a fractional distillation to give 12 as a colorless liquid (36.4 g, 83%); bp 86–93 °C/10–3 mbar.

\[ \text{[c, c = 2.2, CHCl}_3\text{, r.t.]}: -85.0 \text{ (589 nm), } -89.4 \text{ (578 nm), } -103 \text{ (546 nm), } -195 \text{ (436 nm), } -372 \text{ (365 nm).} \]

1H NMR (250 MHz, CDCl\(_3\)): \( \delta = 8.57 \) (1.1H, \( J = 4.9 \text{ Hz, py-}H\)), 7.86–7.39 (1H, Ph), 7.27 (1H, Ph), 7.16 (1H, Ph), 6.89 (1H, Ph), 6.15 (1H, Ph), 4.97 (1H, Ph), 4.69 (1H, Ph), 3.81 (2H, CH(OH)), 2.63 (1H, CH(OH)), 2.25 (1H, CH(OH)), 1.89 (1H, CH(OH)), 1.86 (1H, CH(OH)), 1.81 (1H, CH(OH)), 1.31 (1H, CH(OH)), 1.26 (1H, CH(OH)), 0.94 (3H, CH(3)), 0.89 (3H, CH(3)), 0.83 (3H, CH(3)), 0.82 (3H, CH(3)), 0.80 (3H, CH(3)), 0.78 (3H, CH(3)), 0.76 (3H, CH(3)), 0.75 (3H, CH(3)), 0.74 (3H, CH(3)), 0.73 (3H, CH(3)), 0.72 (3H, CH(3)), 0.71 (3H, CH(3)), 0.70 (3H, CH(3)), 0.69 (3H, CH(3)), 0.68 (3H, CH(3)), 0.67 (3H, CH(3)), 0.66 (3H, CH(3)).

**Bromo[6-[(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl oxy]pyridin-2-yl](6-phenylpyridin-2-yl)pyridin-2-ylmethane (16)**

To a solution of 14 (1.48 g, 3.00 mmol) and NaH (suspension 80% in toluene) (105 mg, 3.50 mmol) was added DMF (10 mL). After stirring at r.t. for 2 h a solution resulted. A solution of methyl iodide (0.47 g, 3.3 mmol) in DMF (1 mL) was added and the mixture was stirred for 2 h. After addition of aq NaOH (2 M, 25 mL) and vigorous stirring the mixture was acidified with HCl (2 M). The combined and concentrated and heated in the Kugelrohr apparatus to 120 °C at a pressure of 10 mbar to remove the volatile residues. The residue was subjected to a fractional distillation to give a diastereomeric excess of the product was equal to the starting material.

Analytical data for a 1:1 mixture of the diastereomers:

**[c, c = 1.1, CHCl\(_3\), r.t.]: -57.7 (589 nm), -60.0 (578 nm), -68.1 (546 nm), -116 (436 nm), -180 (365 nm).**

1H NMR (250 MHz, CDCl\(_3\)): \( \delta = 8.62 \) (1.1H, \( J = 4.8 \text{ Hz, py-}H\)), 7.87–7.39 (1H, Ph), 7.27 (1H, Ph), 6.92–6.41 (1H, py-CH\(_3\)), 4.97 (1H, py-CH\(_3\)), 4.37 (1H, py-CH\(_3\)), 3.76 (2H, CH(OH)), 2.57 (1H, CH(OH)), 1.97 (1H, CH(OH)), 1.87 (1H, CH(OH)), 1.81 (1H, CH(OH)), 1.31 (1H, CH(OH)), 1.28 (1H, CH(OH)), 0.93 (3H, CH(3)), 0.88 (3H, CH(3)), 0.83 (3H, CH(3)), 0.81 (3H, CH(3)).

**Bromo[6-[(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl oxy]pyridin-2-yl](6-phenylpyridin-2-yl)pyridin-2-ylmethane (16)**

To a solution of 14 (1.48 g, 3.00 mmol) and NaH (suspension 80% in toluene) (105 mg, 3.50 mmol) was added DMF (10 mL). After stirring at r.t. for 2 h a solution resulted. A solution of methyl iodide (0.47 g, 3.3 mmol) in DMF (1 mL) was added and the mixture was stirred for 2 h. After addition of aq NaOH (2 M, 25 mL) and vigorous stirring the mixture was acidified with HCl (2 M). The combined and concentrated and heated in the Kugelrohr apparatus to 120 °C at a pressure of 10 mbar to remove the volatile residues. The residue was subjected to a fractional distillation to give a diastereomeric excess of the product was equal to the starting material.

Analytical data for a 1:1 mixture of the diastereomers:

**[c, c = 1.1, CHCl\(_3\), r.t.]: -57.7 (589 nm), -60.0 (578 nm), -68.1 (546 nm), -116 (436 nm), -180 (365 nm).**
r.t. and stirred for 12 h. The reaction was quenched by addition of sat. aq NaHCO₃ (50 mL). After addition of CH₂Cl₂ (50 mL) the organic layer was separated, washed with sat. aq NaHCO₃ (3 × 30 mL), half sat. aq NaCl (3 × 30 mL) and dried (Na₂SO₄). The evaporation of the solvent yielded the crude product, which was purified by chromatography through silica gel (8 cm × 5 cm) with Et₂O (Rₑ ≈ 0.85) to give 16 (8.79 g, 89%) as a yellow, glassy substance.

Analytical data for a 1:1 mixture of the diastereomers:

\[ \text{[1]} \delta (c = 1.2, \text{CHCl}_3, \text{r.t.}) = -69.6 (589 \text{ nm}), -72.8 (578 \text{ nm}), -83.4 (546 \text{ nm}). \]

1H NMR (250 MHz, CDCl₃): The signals were not assigned to the different diastereomers. δ = 8.66 (1 d, J = 4.8 Hz, J = 1.8 Hz, J = 1.0 Hz, py-HP), 8.65 (1 d, J = 4.8 Hz, J = 1.9 Hz, J = 1.0 Hz, py-HP), 7.89–7.82 (m, 4 Hz, Ph), 7.73–7.61 (m, 4 Hz), 7.60 (dd, 2 H, J = 1.8 Hz, J = 7.5 Hz, J = 1.9 Hz, py-HP), 7.56 (dd, 1 H, J = 8.2 Hz, J = 7.5 Hz, py-HP), 7.55 (dd, 1 H, J = 8.2 Hz, J = 7.5 Hz, py-HP), 7.46 (dd, 1 H, J = 7.5 Hz, J = 1.2 Hz, py-HP), 7.45 (dd, 1 H, J = 7.5 Hz, J = 1.3 Hz, py-HP), 7.40–7.23 (m, 10 H), 7.19 (dd, 1 H, J = 7.5 Hz, J = 4.8 Hz, J = 1.1 Hz, py-HP), 7.18 (dd, 1 H, J = 7.5 Hz, J = 1.8 Hz, J = 4.9 Hz, py-HP), 6.55 (dd, 2 H, J = 8.2 Hz, J = 0.7 Hz, py-HP), 4.54 (dt, 1 H, J = 10.8 Hz, J = 4.3 Hz, OCH₃), 4.51 (dt, 1 H, J = 10.8 Hz, J = 4.3 Hz, OCH₃), 2.05–1.66 (m, 4 H), 1.60–1.47 (m, 4 Hz), 1.22–0.66 (m, 6 H), 0.80 (d, 3 H, J = 7.0 Hz, CH₃), 0.79 (d, 3 H, J = 7.0 Hz, CH₃), 0.73 (d, 3 H, J = 6.5 Hz, CH₃), 0.69 (d, 3 H, J = 6.5 Hz, CH₃), 0.51 (d, 3 H, J = 7.0 Hz, CH₃), 0.51 (d, 3 H, J = 7.0 Hz, CH₃).

MS (PI-DNIC) m/z (%): 558/556 (MH, 57/54), 478 (MH+Br⁻, 100).

[6-[(1RS,5SR)-2-Isopropyl-5-methylcyclohexyloxy]pyridin-2-yl](6-phenylpyridin-2-yl)pyridin-2-ylmethylene (17)

To a solution of 16 (1.11 g, 2.00 mmol) in Et₂O (40 mL) was added n-BuLi (1.50 mL, 2.40 mmol, 1 M in hexane) over a period of 30 min at −90 °C. The solution was allowed to warm slowly to r.t. and quenched with water (10 mL). After the addition of HCl (2 M, 10 mL) the phases were separated. The aq layer was extracted with CH₂Cl₂ (3 × 5 mL). The combined organic phases were washed with sat. aq K₂CO₃ (3 × 10 mL), dried over Na₂SO₄ and evaporated. The crude product was chromatographed through silica gel, (20 cm × 1.5 cm) with CH₂Cl₂–Et₂O, 1.1:1 (Rₑ = 0.40) to provide 17 (0.78 g, 73%) as a colorless, highly viscous oil.

Analytical data for a 1:1 mixture of the two diastereomers:

\[ \text{[1]} \delta (c = 0.4, \text{CHCl}_3, \text{r.t.}) = -60.6 (589 \text{ nm}), -69.6 (578 \text{ nm}), -79.5 (546 \text{ nm}), -143 (436 \text{ nm}), -251 (365 \text{ nm}). \]

1H NMR (400 MHz, CDCl₃): δ = 8.56 (dd, 1 H, J = 4.9 Hz, J = 1.9 Hz, J = 0.9 Hz, py-HP), 8.55 (dd, 1 H, J = 4.9 Hz, J = 1.9 Hz, J = 0.9 Hz, py-HP), 7.96–7.92 (m, 4 Hz, Ph), 7.65–7.51 (m, 6 Hz), 7.47 (dd, 2 H, J = 8.2 Hz, J = 7.5 Hz, py-HP), 7.45–7.31 (m, 8 Hz), 7.23 (dd, 1 H, J = 6.8 Hz, J = 2.0 Hz, py-HP), 7.21 (dd, 1 H, J = 7.0 Hz, J = 1.8 Hz, py-HP), 7.11 (dd, 1 H, J = 7.3 Hz, J = 4.9 Hz, J = 1.1 Hz, py-HP), 7.11 (dd, 1 H, J = 7.3 Hz, J = 4.9 Hz, J = 1.2 Hz, py-HP), 6.89 (dd, 1 H, J = 7.5 Hz, J = 0.7 Hz, py-HP), 6.89 (dd, 1 H, J = 7.5 Hz, J = 0.7 Hz, py-HP), 6.49 (dd, 2 H, J = 8.2 Hz, J = 0.6 Hz, py-HP), 4.70 (dt, 1 H, J = 10.8 Hz, J = 4.3 Hz, OCH₃), 4.70 (dt, 1 H, J = 10.7 Hz, J = 4.1 Hz, OCH₃), 3.63 (t, 4 H, J = 6.1 Hz, CH₂OH), 3.15–2.94 (m, 4 H), 2.10–1.94 (m, 2 H), 1.90–1.80 (m, 2 H), 1.68–0.74 (m, 18 Hz), 0.84 (dd, 6 H, J = 7.0 Hz, CH₃), 0.80 (d, 6 H, J = 6.5 Hz, CH₃), 0.60 (d, 6 H, J = 7.0 Hz, CH₃), OH protons at about 3 ppm very broad.

MS (PI-DNIC) m/z (%): 536 (MH, 100).

Anal. calc. for C₂H₁₈NO₂ (535.7): C, 78.47; H, 7.71; N, 7.84.
Found: C, 77.68; H, 7.95; N, 7.30.

Analytical data for (S)-18 in a 95:5 mixture of (S)-18:(R)-18:

\[ \text{[1]} \delta (c = 1.2, \text{CHCl}_3, \text{r.t.}) = -46.3 (589 \text{ nm}), -48.0 (578 \text{ nm}), -54.4 (546 \text{ nm}), -90.6 (436 \text{ nm}), -129 (365 \text{ nm}). \]

1H NMR (400 MHz, CDCl₃): δ = 8.55 (dd, 1 H, J = 4.9 Hz, J = 1.9 Hz, J = 0.9 Hz, py-HP), 7.96–7.92 (m, 2 H, Ph), 7.63–7.56 (m, 2 H), 7.54 (dd, 1 H, J = 8.1 Hz, J = 7.4 Hz, J = 1.9 Hz, py-HP), 7.47 (dd, 1 H, J = 8.2 Hz, J = 7.5 Hz, py-HP), 7.44–7.33 (m, 4 H), 7.21 (dd, 1 H, J = 7.6 Hz, J = 1.2 Hz, py-HP), 7.12 (dd, 1 H, J = 7.4 Hz, J = 4.9 Hz, J = 1.1 Hz, py-HP), 6.88 (dd, 1 H, J = 7.5 Hz, J = 0.7 Hz, py-HP), 6.48 (dd, 1 H, J = 8.2 Hz, J = 0.7 Hz, py-HP), 4.67 (dt, 1 H, J = 10.8 Hz, J = 4.2 Hz, OCH₃), 3.62 (t, 2 H, J = 6.1 Hz, CH₂OH), 3.10–2.97 (m, 2 H), 2.04–1.93
solution of quality yellow prisms were obtained by leaving a concentrated so-

\[ \text{Dichloro[6-methoxyipyridin-2-yl](6-phenylpyridin-2-yl-N)} \]

the crystals were suitable for X-ray analysis.

\[ \text{J}_{2} \] \(= 1.3 \text{ Hz}, \text{ J}_{3} \) \(= 6.6 \text{ Hz}, \text{ H}_{2} \), \(0.60 \) (d, \( 3 \text{ H, J}_{2} \) \(= 6.9 \text{ Hz}, \text{ CH}_{2} \)), \(0.26 \) (d, \( 3 \text{ H, J}_{1} \) \(= 7.0 \text{ Hz}, \text{ CH}_{3} \)).

Diiodo(6-methoxyipyridin-2-yl)(6-phenylpyridin-2-yl-N) (pyridin-2-yl-N) methanecopper(ii) (19)

Anhyd CuCl_{2} (28.0 mg, 0.21 mmol) was dissolved in a solution of racemic 11 (73.0 mg, 0.21 mmol) in MeOH (2 mL). After diffusion of Et_{2}O into the methanolic solution 19 (72.0 mg, 72%) was obtained as green, air-stable crystals; mp 185 °C (decomp). Some of the crystals were suitable for X-ray analysis.

MS (EI-ESI) m/z (%): 451 (M + Cl, 43), 415 (M + Cl-HCl, 100), 354 (M - CuCl_{2}, 25).

Anal. calcld for C_{3}H_{6}OCl CuN_{6}O (478.9): C, 56.62; H, 3.93; N, 8.61. Found: C, 56.28; H, 4.09; N, 8.37.

\((R_{Bia}A_{0a})-\text{Dichloro[S-(4-[(1R,2S,5R)-2-isopropyl-5-methylcycl}evenyl]pyridin-2-yl-N)-] (4-[(2-phenylpyridin-2-yl-N)pyridin-2-yl-N]Nbutan-1-ol}(rhodium)(III) (20)

To a solution of 18 (S : R = 65:35, 1.50 g, 2.80 mmol) in EtOH (150 mL) was added rhodium(III) chloride trihydrate (645 mg, 2.45 mmol) at ambient temperature. This solution was stirred for 12 h and the resulting yellow solid was filtered off, washed with Et_{2}O (4 × 5 mL), Et_{2}O (4 × 5 mL), and dried. After addition of Et_{2}O (30 mL) and PE (20 mL) to the mother liquid the solution was stirred for 12 h to give a second fraction of 20. Concentration of the mother liquid to a volume of 25 mL gave a third fraction. The yield of the fine crystalline air-stable powder was altogether 1.35 g (78%); mp > 250 °C.

For separation of the major diastereomer, a 62:32:2:4 mixture of 20 (300 mg) was dissolved in DMSO (25 mL) at 45 °C. The solution was submitted to a Kugelrohr distillation at 45 °C/10⁻³ mbar to remove the solvent until first crystals appeared. This sat. solution was allowed to stand for several days. Then the product was filtered off to give 20 (90 mg) as fine yellow needles, with a de of 94%. X-ray quality yellow prisms were obtained by leaving a concentrated solution of 20 in DMSO undisturbed in an open vessel for about two weeks.

Analytical data for \((S_{C_{6}H_{5}Cl_{2}N_{6}})\text{Cl}(20)\) in a 97.3 mixture of \((S_{C_{6}H_{5}Cl_{2}N_{6}})\text{Cl}(20)-20(S_{C_{6}H_{5}Cl_{2}N_{6}})\text{Cl}(20-)

[\alpha]_{D}^{25} (c = 0.26, DMSO, r.t.): -58.0 (589 nm), -50.2 (578 nm), -17.0 (546 nm).

\[ ^{1}H \text{NMR (400 MHz, DMF-d}_{6}) \]: \( \delta = 9.50 \) (ddd, 1 H, \( J_{2} = 5.4 \text{ Hz}, J_{1} = 1.8 \text{ Hz}, J_{3} = 0.6 \text{ Hz, py-H}^{'})\), 8.96 (ddd, 1 H, \( J_{2} = 7.7 \text{ Hz}, J_{1} = 1.3 \text{ Hz}, J_{3} = 0.4 \text{ Hz, Ph-H}^{'})\), 8.20 (ddd, 1 H, \( J_{2} = 8.2 \text{ Hz}, J_{1} = 1.3 \text{ Hz}, J_{3} = 0.8 \text{ py-H}^{'})\), 8.15 (ddd, 1 H, \( J_{2} = 8.1 \text{ Hz}, J_{1} = 1.3 \text{ Hz}, J_{3} = 1.8 \text{ Hz, py-H}^{'})\), 8.03–7.95 (m, 3 H, py)), 7.89 (dd, 1 H, \( J_{2} = 8.4 \text{ Hz}, J_{1} = 7.9 \text{ Hz, py-H}^{'})\), 7.79 (ddd, 1 H, \( J_{2} = 7.7 \text{ Hz}, J_{1} = 1.3 \text{ Hz}, J_{3} = 0.3 \text{ Hz, Ph-H}^{'})\), 7.64 (dd, 1 H, \( J_{2} = 7.9 \text{ Hz}, J_{1} = 1.0 \text{ Hz, py-H}^{'})\), 7.47 (ddd, 1 H, \( J_{2} = 7.4 \text{ Hz}, J_{1} = 1.4 \text{ Hz, py-H}^{'})\), 7.28 (ddd, 1 H, \( J_{2} = 7.7 \text{ Hz}, J_{1} = 1.5 \text{ Hz, Ph-H}^{'})\), 7.25 (dd, 1 H, \( J_{2} = 8.5 \text{ Hz}, J_{1} = 1.0 \text{ Hz, py-H}^{'})\), 7.03 (ddd, 1 H, \( J_{2} = 7.6 \text{ Hz}, J_{1} = 7.3 \text{ Hz}, J_{3} = 1.2 \text{ Hz, Ph-H}^{'})\), 5.05 (s, 1 H, OH), 4.44 (dt, 1 H, \( J_{1} = 10.5 \text{ Hz}, J_{3} = 4.7 \text{ Hz, OH})$, 3.92 (m, 2 H, CH_{2}OH), 3.74–3.64 (m, 1 H, pyppy'CC'H'H), 3.47–3.37 (m, 1 H, pyppy'CC'H'H), 2.13–1.97 (m, 3 H, mole-

\[ ^{13}C(1H) \text{NMR (101 MHz, CDCl}_{3}) \]: \( \delta = 164.6 \text{ (C)}, 164.2 \text{ (C)}, 162.4 \text{ (C)}, 162.1 \text{ (C)}, 155.0 \text{ (C)}, 147.6 \text{ (CH)}, 139.4 \text{ (C)}, 138.6 \text{ (CH)}, 136.0 \text{ (CH)}, 135.1 \text{ (CH)}, 128.6 \text{ (CH}, 128.5 (2 CH), 126.2 (2 CH), 126.0 (12 CH), 121.0 (CH), 117.2 (CH), 115.3 (CH), 108.6 (CH), 74.1 (CH), 63.1 (C), 62.9 (CH), 47.0 (CH), 40.5 (CH), 34.4 (CH), 33.6 (CH), 31.2 (CH), 28.7 (CH), 26.2 (CH), 23.7 (CH), 22.1 (CH), 20.5 (CH), 16.4 (CH).

\( ^{13}C[1H] \text{NMR (101 MHz, DMF-d}_{6}) \]: \( \delta = 171.6 \) (d, \( 25.7 \text{ Hz), C-} \)

Rh), 169.4 (C), 168.8 (C), 159.3 (C), 156.7 (C, 1 H, py'-py-

\( ^{13}C[1H] \text{NMR (101 MHz, DMSO-d}_{6}) \]: \( \delta = 2098.2(3) \text{ Å}^{3}; \text{ wR} = 2.82 \text{<} 25.90 \text{°; 69461 reflections collected, 6627 independent, 5942}

\( ^{13}C[1H] \text{NMR (101 MHz, DMSO-d}_{6}) \]: \( \delta = 2098.2(3) \text{ Å}^{3}; \text{ wR} = 2.82 \text{<} 25.90 \text{°; 69461 reflections collected, 6627 independent, 5942}

The value was located at (0, 0, 0), it had a size of 533 Å and contained 29 electrons.

X-Ray Structure Analysis, General Remarks

The structures were solved by direct methods (SIR-97) and refined by full-matrix anisotropic least squares (SHELXL97) on \( F^{2} \). The H atoms were calculated geometrically and a riding model was applied during the refinement process. Absorption corrections were not used. For the measurement a diffractometer of the type STOE- IPDS with Mo-K\( \alpha \) radiation and graphite monochromator was used. Further details of the crystal structure investigation may be obtained, free of charge, from the Cambridge Crystallographic Data Centre, where the structures have been deposited.

Synthesis 2001, No. 16, 2484–2494 ISSN 0039-7881 © Thieme Stuttgart · New York
References

(1) X-ray structure analyses.


