ARTICLE

OBC
www.rsc.org/obc

Synthetic routes for a new family of chiral tetradentate ligands containing pyridine rings†

Mathias Düggeli,[a] Catherine Goujon-Ginglinger,[a] Sarah Richard Ducotterd,[a] David Mauron,‡[a] Christophe Bonte,[a] Alexander von Zelewsky,*[a] Helen Stoeckli-Evans[b] and Antonia Neels[b]

[a] *Department of Chemistry, University of Fribourg, Pérolles, 1700 Fribourg, Switzerland. E-mail: alexander.vonzelewsky@unifr.ch; Fax: +41-26-300 97 38; Tel: +41-26-300 87 42*

[b] *Institute of Chemistry, University of Neuchâtel, Avenue de Bellevaux 51, 2007 Neuchâtel, Switzerland*

Received 30th October 2002, Accepted 10th April 2003
First published as an Advance Article on the web 28th April 2003

A series of new tetradentate ligands containing two bipyridine groups or two pyridine moieties carrying amine substituents has been synthesised either from 5′- and 6′-substituted chiral bipyridines, or from chiral pyridine derivatives. These precursors have been prepared from (−)-α-pinene or (−)-myrtenal, respectively. The structures of three tetradentate-, and of five chiral bipyridine ligands have been determined by X-ray diffraction.

Introduction

Since the introduction of an α-pinene moiety into bipyridine (bpy) ligands by Hayoz[1] in 1992, a large number of such pineno-annellated ligands[2] have been synthesised. These ligands are easily accessible in enantiomerically pure forms (generally *ca*. 98% ee) starting from commercially available (−)-α-pinene, or (−)-myrtenal, respectively (Fig. 1).§

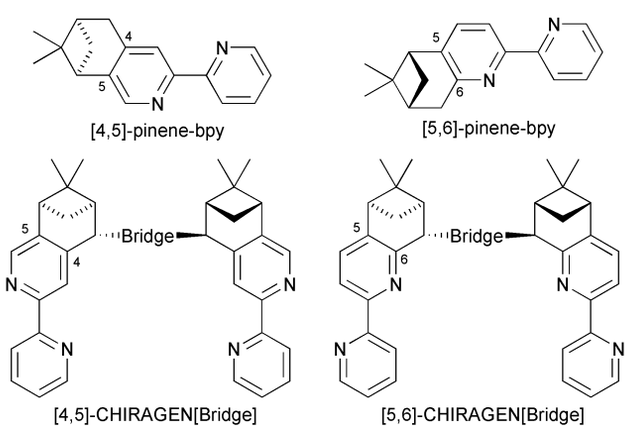


Fig. 1 [4,5]-Pinene-bpy and [5,6]-pinene-bpy and the corresponding tetradentate CHIRAGEN[bridge] derivatives.

Two [4,5]-pinene-bpy¶ moieties can be linked together to form tetradentate ligands with different bridges (Fig. 1). This type of tetradentate ligands has been called [4,5]-CHIRAGEN ligands (from CHIRAlity GENerators), due to their ability to induce predetermined configuration at the metal centers.[3] The analogous [5,6]-CHIRAGEN derivatives starting from [5,6]-pinene-bpy‖ can assemble spontaneously to supramolecular aggregates with Ag^{I} and Cu^{I} such as a sixfold circular helicate,[4] or a polymeric double helix,[5] or they form mononuclear metal complexes with several transition metals (Ag^{I}; Pd^{II}, Zn^{II}).[6] In all these cases the configuration at the metal centre is controlled by the ligand. Another derivative of [4,5]-pinene-bpy forms a helical square with Zn^{II}.[7] Other derivatives of pinene-bpy,[2i,8] and bis-pinene-bpy,[9,2l–2n] (each pyridine ring carries a pinene group) have been successfully used in enantioselective catalytic processes.

Herein we present the syntheses of new tetradentate ligands (**1a**–**c**, **2a**–**c** and **3**, Fig. 2). All of them are C_2-symmetric and contain two halfs of either chiral bipyridines (*cf*. **1a**–**c**, **2a**–**c**) or chiral pyridines with amine substituents (*cf*. **3**), which are linked *via* a *p*-xylene bridge (**1a**–**c**) or directly coupled together (**2a**–**c**, **3**). Starting from commercially available enantiopure (−)-α-pinene (98% ee), the chiral bipyridines and amino substituted pyridines can be obtained easily following the strategy of creating new pyridine rings.[1,10]

The first group of ligands (the {*R*}-[5,6]-CHIRAGEN[*p*-xyl] **1a**–**c**)) is expected to show a similar behaviour as the unsub-

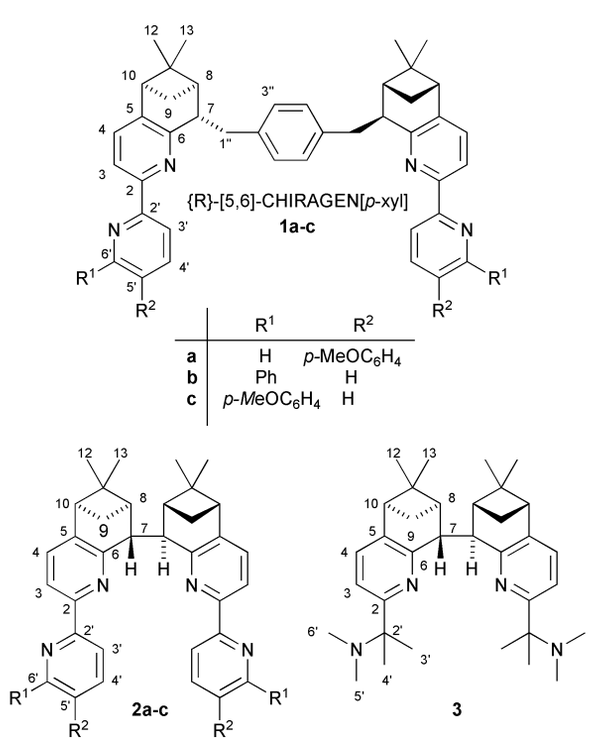


Fig. 2 Chiral tetradentate ligands.

† Electronic supplementary information (ESI) available: experimental details. See http://www.rsc.org/suppdata/ob/b2/b210625f/

‡ Deceased

§ In this publication always (*S*,*S*)-(−)-α-pinene (converted into (*R*,*R*)-(+)-pinocarvone) and (*R*,*R*)-(−)-myrtenal were used giving (*R*,*R*)-[5,6]-pinene-bpy and (*R*,*R*)-[4,5]-pinene-bpy derivatives (Fig. 1).

¶ [4,5]-pinene-bpy: IUPAC name: (6*R*,8*R*)-5,6,7,8-tetrahydro-7,7-dimethyl-3-(2′-pyridyl)-6,8-methanoisoquinoline.

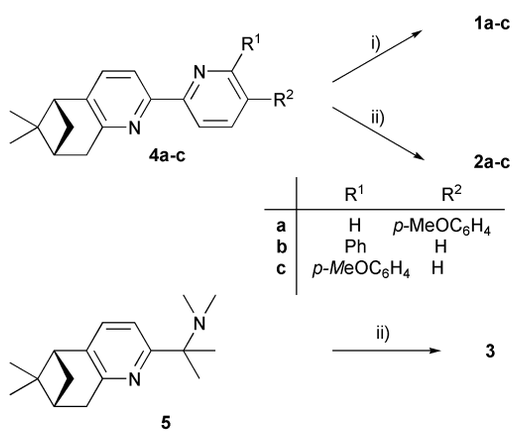
‖ [5,6]-pinene-bpy: IUPAC name: (5*R*,7*R*)-5,6,7,8-tetrahydro-6,6-dimethyl-2-(2′-pyridyl)-5,7-methanoquinoline.

DOI: 10.1039/b210625f

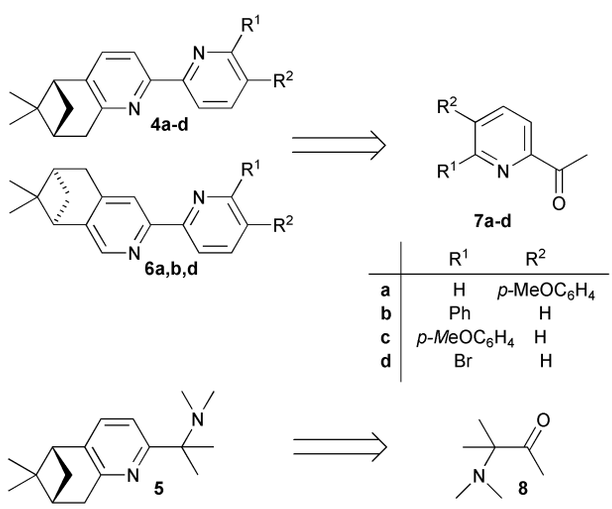
stituted [5,6]-CHIRAGEN[0].[4] The second family ({*R*}-CHIRAGEN[0](**2a**–**c** and **3**)) is designed for the synthesis of mononuclear complexes.[6]

Results and discussion

All these tetradentate ligands can be obtained by coupling reactions from the corresponding [5,6]-pinene-bpy compounds **4a**–**c** and **5** (Scheme 1). The extended 6′-substituted pinene-bpy ligand **4b**, **c** and **6b**, **c**, (Scheme 2) can be formed following two different synthetic routes: either *via* the acetyl-pyridine derivatives **7b** and **7c** or *via* the key intermediates **4d** and **6d**. Analogous reactions with β-pinene have been described previously.[11] 6′-Substituted pinene-bpy derivatives are accessible in one step from the bromo-compounds **4d** and **6d**. In this way **4c** has been obtained. Following the same methodology phenylene[12] and ferrocene[13] bridged bis-pinene-bpy ligands were synthesised in our research group. Other published 6′-pinene-bpy ligands could also be synthesised *via* the key intermediates **4d** and **6d**.[14]



Scheme 1 *Reagents and conditions*: i) LDA, THF, −40 °C, then α,α′-dibromo-*p*-xylene; ii) LDA, THF, −40 °C, then I_2.



Scheme 2 Retrosynthetic analysis for the synthesis of **4a**–**d**, **5** and **6a**–**d**.

For the corresponding 5′-substituted pinene-bpy ligands **4a** and **6a** as well as for ligand **5** only the first strategy *via* the acetyl-pyridine **7a** and **8**, respectively, is feasible, because the analogous bromo-substituted compounds are not available.

The published method[15] to synthesise 5-*p*-methoxyphenyl-2-acetylpyridine (**7a**) (4 steps) was replaced by a new three step synthesis (Scheme 3) starting from the commercially available 2-amino-5-iodopyridine (**9**).

The substitution of the amino function by bromine was carried out under acidic conditions (HBr 65%, Br_2) according to described procedures.[16] Compound **11** was obtained by a Suzuki cross coupling reaction using 2-bromo-5-iodopyridine (**10**) and *p*-methoxyphenylboronic acid in the presence of small amounts of $Pd(PPh_3)_4$ as catalyst (Scheme 3 and Table 1, entry 1).

Table 1 Suzuki cross-coupling reaction

Entry	Halides	Coupling product[a]	Yield	Conditions
1	**10**	**11**[b]	99	5 d, reflux
2	**7d**	**7b**[c]	91	2 h, rt
3	**7d**	**7c**[b]	64	15 h, reflux
4	**4c**	**1c**[b]	99	4 d, reflux

[a] Reaction of the halide with the boronic acid in a two phase system (toluene–K_2CO_3 in water), $Pd(PPh_3)_4$ as catalyst. [b] *p*-Methoxyphenylboronic acid was used. [c] Phenylboronic acid was used.

The acetyl function in **7a** and **7d** was introduced by reaction of **11** or **12**, respectively, with *n*-butyllithium followed by the addition of *N,N*-dimethylacetamide (Scheme 3).[9b,17] Analogous reaction conditions for the Suzuki cross-coupling were applied for the formation of the 6′-substituted acetylpyridines **7b**[9b] and **7c** (Table 1, entry 2,3).

The key molecule for the synthesis of pinene-py derivative (**5**) is the ketone **8**, which is synthesised in two steps starting from 2-methylbutan-3-one (**13**) (Scheme 3). After bromination and subsequent nucleophilic substitution, the desired ketone (**8**) is obtained. The analogous reaction sequence starting with 1,1-diphenylpropan-2-one (**15**) does not yield the corresponding diphenylacetyl derivative, but rather the known *N*,*N*-dimethyl-3,3-diphenylpropionamide (**17**)[18] (Scheme 4) in nearly quantitative yield. This is a new synthetic route for the formation of **17**, which can be explained by a Favorskii rearrangement.[19]

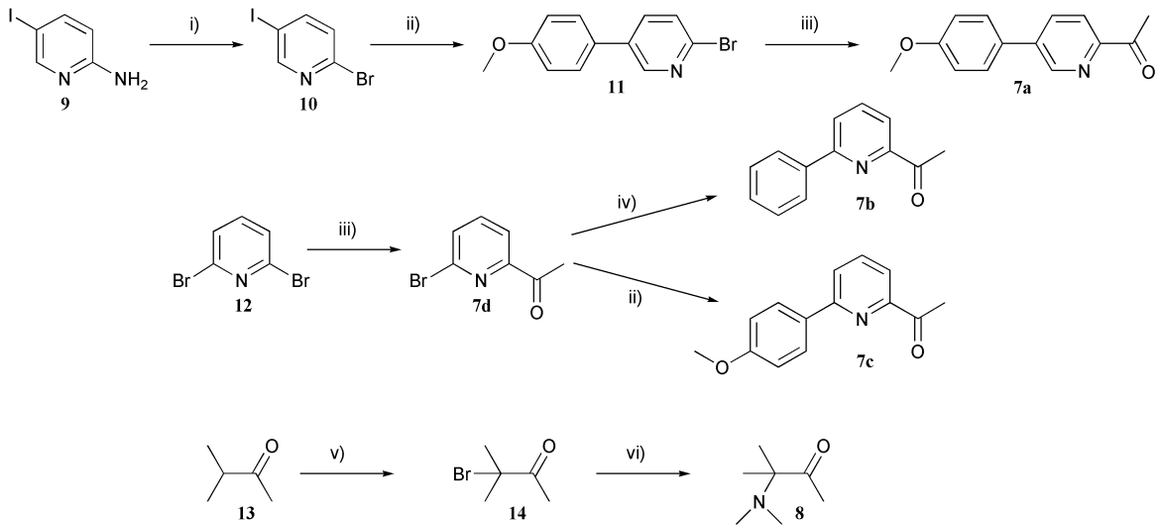
The Kröhnke salts **18a**, **b**,[9b] **d**[20] and **19** (Scheme 5, Scheme 6) are easily synthesised from the acetyl-pyridines **7a**, **b**, **d**, and **8**.

The reaction[1,10] of the Kröhnke salts **18a**, **b**, **d** and **19** with (+)-pinocarvone[21] and dry ammonium acetate in acetic acid leads to the [5,6]-pinene-bpy ligands **4a**, **b**,[9b] **d** or **5**, respectively (Scheme 5, 6). Analogous reactions with myrtenal in formamide lead to the [4,5]-pinene-bpy ligands **6a**, **b**, **d**. The reaction *via* the bromo-pinene-bpy ligands **4d** and **6d** represent a new versatile pathway for the synthesis of the pinene-bpy ligand[9b] since several 6′-substituted pinene-bpy ligands (*e.g.* ligand **4c**, Table 1, entry 4) are available in a one step reaction *via* the palladium-catalysed Suzuki cross-coupling.

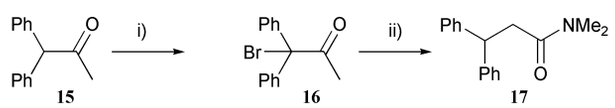
As described previously,[1] pinene annellated ligands can be deprotonated with lithium-diisopropylamide in a stereoselective manner. Addition of iodine to the deprotonated species results in a direct oxidative coupling.[22] Ligands **2a**–**c** and **3** are synthesised in this way. Addition of α,α′-dibromo-(*p*)-xylene[3] leads to xylene-bridged CHIRAGEN ligands **1a**–**c** (Scheme 1). Whereas the coupling reaction with the xylene derivative is completely stereoselective (the bridge is in *anti*-position (*S,S*) with regard to the two methyl-groups of the pinene), the coupling reaction with iodine leads to two different diastereomers *S,S* (*anti*) and *R,R* (*syn*) in a ratio of 9 to 1 (determined by NMR-spectroscopy). According to the postulated mechanism[6] the two products are formed *via* a radical lithium-templated intermediate.

Suitable crystals ** for X-ray analysis[23] were obtained from the CHIRAGEN ligands **1b**, **2c** and **3** and from the [5,6]-pinene-bpy ligands **4a**–**d** and **6d**. All three [5,6]-CHIRAGEN-ligands have a molecular C_2-axis. Whereas **2c** and **3** keep this C_2-axis in the crystal, as in the [5,6]-CHIRAGEN[0],[6] **1b** has no crystallographic C_2-axis, (one bpy conformation is coplanar, the other has a twist angle of about 23°). The plane angle between the

** CCDC reference numbers 196850,196851, 179702–179707. See http://www.rsc.org/suppdata/ob/b2/b210625f/ for crystallographic data in .cif or other electronic format.



Scheme 3 *Reagents and conditions*: i) HBr (65%), Br_2, then $NaNO_2$; ii) **7d/10** and *p*-methoxyphenylboronic acid in toluene, K_2CO_3 in H_2O, reflux; iii) *n*-BuLi, *N,N*-dimethylacetamide, THF, −60 °C; iv) **7d** and phenylboronic acid in toluene, K_2CO_3 in H_2O, reflux; v) Br_2, CCl_4, reflux; vi) dimethylamine, EtOH, 0 °C to rt.



Scheme 4 *Reagents and conditions*: i) Br_2, CCl_4; ii) dimethylamine, EtOH, 0 °C to rt.

two pyridine rings bearing the pinene moieties varies slightly, for [5,6]-CHIRAGEN[0][6] a plane angle of 79° is found, for **1b** 81°, **2c** 85° and for **3** 81°.

Conclusion

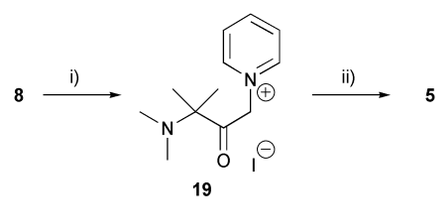
The family of chiral tetradentate ligands containing pyridine is significantly enlarged through the synthetic routes described in the present publication. Therewith various applications, such as the generation of stereochemically new supramolecular architectures and the fabrication of more intricate molecular structures can be envisaged.

Experimental

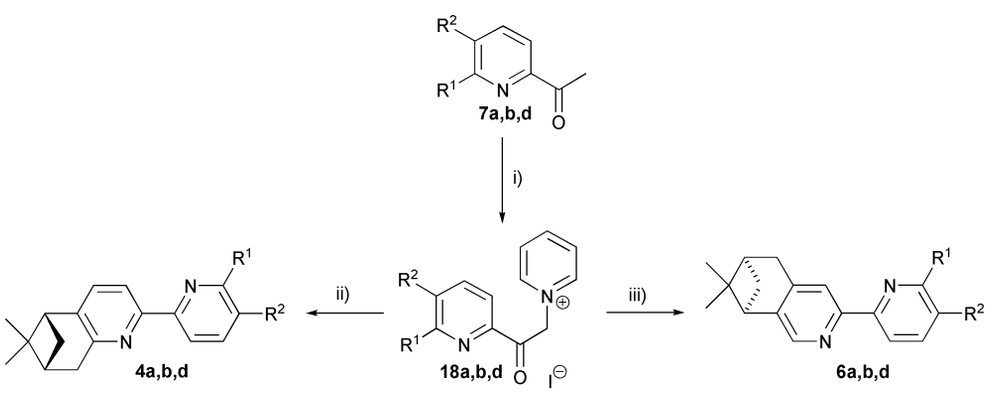
General

Solvents and reagents were purchased from Fluka or Aldrich. Pyridine was dried over KOH and freshly distilled. Ammonium acetate was dried for several days under vacuum. Diethyl ether and THF were distilled from sodium–benzophenone prior to use.

NMR spectra were recorded on a 'Varian Gemini 300' (300.075 MHz) or on a 'Bruker Avance DRX400' (400.13 MHz) spectrometer, chemical shifts are given in ppm using the solvent itself as internal standard, coupling constants *J* are given in Hertz. Attribution of the ^{1}H- and ^{13}C signals was performed by ^{1}H,^{1}H-COSY, DEPT, ^{13}C–^{1}H-HECTOR, ^{1}H–^{13}C-HMQC and ^{1}H–^{13}C-HMBC techniques. The numeration of the ligands is given in Fig. 2. The diastereotopic protons at carbon 9 of the pinene-moieties are labelled as H_a for the *endo*-oriented protons and H_b for the *exo*-oriented protons. The *exo* methyl groups are assigned as 12 and 12′, the *endo* oriented ones as 13 and 13′, respectively. The diastereotopic



Scheme 6 *Reagents and conditions*: i) I_2, pyridine; ii) (+)-pinocarvone, NH_4OAc, acetic acid.



entry	7	R^1	R^2	salt, yield	ratio (salt : HpyI)	4, yield	6, yield
1	**7a**	H	*p*-$MeOC_6H_4$	**18a**, 85 %	1.1 : 1.0	**4a**, 30	**6a**, 24
2	**7b**	Ph	H	**18b**, 99 %	2.0 : 1.0	**4b**, 55	**6b**, 52
3	**7d**	Br	H	**18d**, 92 %	1.1 : 1.0	**4d**, 50	**6d**, 29

Scheme 5 *Reagents and conditions*: i) I_2, pyridine; ii) (+)-pinocarvone, NH_4OAc, acetic acid; iii) (−)-myrtenal, NH_4OAc, formamide.

protons at carbon 1″ are labelled as H_a and H_b. For the methoxy-phenyl derivatives, the proton 8′, 9′, 11′ and 12′ form a spin-coupling system AA′XX′, they are just labelled as doublets with the coupling constant $^3J_{A,X}$. Mass spectral data were acquired a) on 'VG Instrument 7070E' equipped with a FAB inlet system, b) on Hewlett Packard 5988A quadrupol mass spectrometer with an electron ionisation (EI) source and c) on a Bruker FTMS 4.7 T BioApex II using a standard electrospray ion source (ESI). Elemental analysis was obtained from EIF (Ecole d'ingénieurs de Fribourg, Switzerland).

S,S-{5′-*p*-Methoxyphenyl}-[5,6]-CHIRAGEN[*p*-xyl] (1a)

To dry THF (40 ml) at −40 °C diisopropylamine (0.2 ml, 1.4 mmol) was added, followed by *n*-butyllithium (0.85 ml, 1.35 mmol, 1.6 M in hexane). The temperature was allowed to increase to 0 °C for 30 minutes and then lowered to −40 °C. *S,S*-{5′-*p*-Methoxyphenyl}-[5,6]-pinene-bpy (**4a**) (400 mg, 1.12 mmol) dissolved in dry THF (10 ml) was added dropwise over 1 hour. After stirring the solution at −40 °C for 2 hours, α,α′-dibromo-*p*-xylene (148 mg, 0.56 mmol) dissolved in THF (10 ml) was injected slowly (1 hour). The solution was warmed gradually to room temperature, and quenched by water (50 ml). The aqueous solution was extracted three times with diethyl ether. The combined organic layers were dried over magnesium sulfate, and the solvent was evaporated. The residual solid was further purified by column chromatography or recrystallisation (hexane–ethyl acetate–triethylamine: 1 : 1 : 0.5), yielding a slightly yellow powder (303 mg, 64%). Analytical data are given in the ESI†.

The ligands *S,S*-{6′-phenyl}-[5,6]-CHIRAGEN[*p*-xyl] (**1b**), *S,S*-{6′-*p*-methoxyphenyl}-[5,6]-CHIRAGEN[*p*-xyl] (**1c**), *S,S*-{5′-*p*-methoxyphenyl}-[5,6]-CHIRAGEN[0] (**2a**), *S,S*-{6′-phenyl}-[5,6]-CHIRAGEN[0] (**2b**), *S,S*-{6′-*p*-methoxyphenyl}-[5,6]-CHIRAGEN[0] (**2c**) and *S,S*-{2-*N,N*-dimethylamino-isopropyl}-[5,6]-CHIRAGEN[0] (**3**) were prepared analogously to the procedure for **1a** described above. More details are given in the ESI†.

S,S-{5′-*p*-Methoxyphenyl}-[5,6]-pinene-bpy (4a)

A mixture of 1-[2-acetyl-5-(*p*-methoxyphenyl)pyridyl]pyridinium iodide (**18a**) (3.8 g, 8.79 mmol), ammonium acetate (6.93 g, dried under vacuum) and *R,R*-(+)-pinocarvone (1.35 g, 9.0 mmol) was suspended in acetic acid (5 ml) and slowly heated over 42 hours from 50 °C up to 115 °C. After addition of water, the pH was adjusted to 9 by addition of sodium carbonate. This aqueous solution was extracted ten times with hexane and the combined organic layers were washed with water and dried over magnesium sulfate with activated charcoal. The solvent was evaporated under reduced pressure. The residual solid was further purified by column chromatography (hexane–ethyl acetate–triethylamine: 8 : 1 : 0.1) yielding a slightly yellow product **4a** (936 mg, 30%). Analytical data are given in the ESI†.

S,S-{6′-Phenyl}-[5,6]-pinene-bpy (**4b**), *S,S*-{6′-bromo}-[5,6]-pinene-bpy (**4d**) and *S,S*-{2-*N,N*-dimethylaminoisopropyl}-[5,6]-pinene-py (**5**) were prepared analogous to the procedure for **4a** described above. More details are given in the ESI†.

S,S-{6′-*p*-Methoxyphenyl}-[5,6]-pinene-bpy (4c)

A mixture of {6′-bromo}-[5,6]-pinene-bpy (**4d**) (3.3 g, 10 mmol), *p*-methoxyphenylboronic acid (1.65 g, 10 mmol) and $Pd(PPh_3)_4$ (0.2% eq.) as catalyst, was heated at 120 °C for 4 days in a mixture of toluene (100 ml) and an aqueous solution of K_2CO_3 (50 ml, 8.5 M). After cooling to room temperature the two layers were separated and the aqueous layer extracted three times with dichloromethane. The combined organic layers were washed until pH = 7 with water, dried over magnesium sulfate and the solvent was evaporated. Without further purification pure **4c** (3.59 g, 99%) was obtained. Analytical data are given in the ESI†.

S,S-{5′-*p*-Methoxyphenyl}-[4,5]-pinene-bpy (6a)

A mixture of 1-[2-acetyl-5-(*p*-methoxyphenyl)pyridyl]pyridinium iodide (**18a**) (223 mg, 0.52 mmol), ammonium acetate (560 mg, dried under vacuum) and *R,R*-(−)-myrtenal (90 mg, 0.6 mmol) was suspended in formamide (20 ml) and stirred at room temperature for 5 days, then it was slowly heated over 24 hours from 50 °C up to 100 °C. To the reaction mixture 50 ml of water was added and extracted five times with hexane and the combined organic layers were washed with water and dried over magnesium sulfate with activated charcoal. The solvent was evaporated under reduced pressure. The residual solid was further purified by column chromatography (hexane–ethyl acetate–triethylamine: 4 : 1 : 0.25), yielding the desired product (85 mg, 24%). Analytical data are given in the ESI†.

S,S-{6′-Phenyl}-[4,5]-pinene-bpy (**6b**) and *S,S*-{6′-bromo}-[4,5]-pinene-bpy (**6d**) were prepared analogous to the procedure for **6a** described above. More details are given in the ESI†.

2-Acetyl-5-(*p*-methoxyphenyl)pyridine (7a)

The introduction of the acetyl function starting from 2-bromo-5-(*p*-methoxyphenyl)pyridine (**11**) was carried out in similar manner as described for compound **7d**.[9b] 2-Bromo-5-(*p*-methoxyphenyl)pyridine (**11**) (2 g, 7.6 mmol) was dissolved in dry diethyl ether (250 ml) under argon and cooled to −60 °C, *n*-butyllithium (5 ml, 1.6 M in hexane) was added dropwise over 45 minutes. After stirring for 1¼ hours, *N,N*-dimethylacetamide (0.75 ml, 8 mmol) in diethyl ether (10 ml) was added over an hour. Overnight, the solution was allowed to warm to room temperature, quenched with saturated ammonium chloride solution and extracted five times with diethyl ether. Further purification was carried out by column chromatography (hexane– ethyl acetate–triethylamine: 8 : 1 : 0.5) yielding a white solid (1.04 g, 60%). The spectral data was in accordance with the literature.[15] Analytical data are given in the ESI†.

2-Acetyl-6-phenyl pyridine (**7b**) was prepared analogous to the procedure for **7a** described above. More details are given in the ESI†.

2-Acetyl-6-(*p*-methoxyphenyl)pyridine (7c)

A mixture of 2-acetyl-6-bromopyridine (**7d**) (2.00 g, 10 mmol), *p*-methoxyphenylboronic acid (347 mg, 10 mmol), and $Pd(PPh_3)_4$ (0.2% eq., 0.02 mmol) as catalyst, was heated at 120 °C for 15 hours in a solvent mixture of toluene (100 ml) and an aqueous solution of K_2CO_3 (50 ml, 8.5 M). After cooling to room temperature the two layers were separated and the aqueous layer extracted three times with dichloromethane. The combined organic layers were washed with water until pH = 7, dried over magnesium sulfate and the solvent was evaporated. Further purifications by recrystallisation (ethyl acetate–hexane: 1 : 4) yielded compound **7c** (1.45 g, 64%). Analytical data are given in the ESI†.

2-*N,N*-Dimethylamino-2-methylbutan-3-one (8)

The synthesis was carried out according to the published procedure by Gaset.[24] To a 0 °C cooled solution of 2-bromo-2-methylbutan-3-one (**14**) (10 g, 0.06 mmol), dimethylamine (22 ml, 0.12 mmol, 5.6 M in ethanol) was added over a period of 5 minutes. The reaction solution was stirred overnight at 0 °C, then warmed to 40 °C for 70 minutes. After cooling to room temperature the reaction mixture was filtered and the residual solid was washed with cold ethanol. To the filtrate hydrochloric acid (66 ml, 4 M) was added. Ethanol was removed under reduced pressure. To the acidic solution, sodium hydroxide (2 M) was added, until the pH > 7. The alkaline solution was extracted three times with diethyl ether. The

combined organic extracts were dried over magnesium sulfate and the solvent was removed under reduced pressure. The desired product was obtained (5.87 g, 76%). The spectral properties correspond to those reported.[24] Analytical data are given in the ESI †.

2-Bromo-5-(*p*-methoxyphenyl)pyridine (11)

A mixture of 2-bromo-5-iodopyridine (**10**) (5.67 g, 20 mmol), *p*-methoxyphenylboronic acid (3.34 g, 20 mmol) and $Pd(PPh_3)_4$ (0.02 mmol) as catalyst, was heated at 120 °C for 4 days in a mixture of toluene (80 ml) and an aqueous solution of K_2CO_3 (80 ml, 80 g, 8.5 M). After cooling to room temperature, the two layers were separated and the aqueous layer extracted three times with dichloromethane. The combined organic layers were washed until pH = 7 with water, dried over magnesium sulfate and the solvent was evaporated. Further purification was carried out by column chromatography (hexane–ethyl acetate–triethylamine: 5 : 1 : 0.1), yielding the desired product (5.3 g, 99%). Analytical data are given in the ESI †.

2-Bromo-2-methylbutan-3-one (14)

To a solution of 2-methylbutan-3-one (**13**) (25.85 g, 0.3 mol) in carbon tetrachloride (120 ml), bromine (48.0 g, 0.3 mol) in carbon tetrachloride (30 ml) was added dropwise under reflux over a period of 2 hours. After the addition the reaction mixture was kept under reflux for another 2 hours, then cooled to room temperature. Unreacted bromine was destroyed with sodium thiosulfate solution (10%). The organic layer was separated, dried with magnesium sulfate, the solvent was removed under reduced pressure. The crude product was further purified by vacuum distillation (100 mbar, 60 °C), yielding a colourless liquid (30.1 g, 60%). The spectral properties correspond to those reported.[25] Analytical data are given in the ESI †.

1-Bromo-1,1-diphenylpropan-2-one (**16**) was prepared analogously to the procedure for **14** described above. More details are given in the ESI †.

N,N-Dimethyl-3,3-diphenylpropionamide (17)

To a 0 °C cooled solution of 1-bromo-1,1-diphenylpropan-2-one (**16**) (2.0 g, 6.9 mmol), dimethylamine (2.5 ml, 13.8 mmol, 5.6 M in ethanol) was added over a period of 5 minutes. The reaction solution was stirred overnight at 0 °C, then warmed to 40 °C for 70 minutes. After cooling to room temperature, hydrochloric acid (50 ml, 4 M) was added to the reaction mixture. Ethanol was removed under reduced pressure. To the acidic solution, sodium hydroxide (2 M) was added, until the pH > 7. The alkaline solution was extracted three times with diethyl ether. The combined organic layers were dried over magnesium sulfate and the solvent was removed under reduced pressure, yielding product **17** (1.66 g, 95%). The spectral properties correspond to those reported.[18] Analytical data are given in the ESI †.

1-[2-Acetyl-5-(*p*-methoxyphenyl)pyridyl]pyridinium iodide (18a)

A mixture of pyridine (10 ml), iodine (280 mg, 1.1 mmol) and 2-acetyl-5-(*p*-methoxyphenyl)pyridine (**7a**) (210 mg, 0.925 mmol) was kept at 100 °C for 2 hours and at 0 °C for 20 min. After addition of dry diethyl ether, the desired product and pyridinium iodide precipitated and was filtered. The crude product (305 mg) was used without further purification. The ratio between **18a** (1.3 eq., 223 mg, 59%) and the pyridinium iodide (1 eq., 82 mg) was determined by ^{1}H-NMR-spectroscopy. Analytical data are given in the ESI †.

1-(2-Acetyl-6-phenylpyridyl)pyridinium iodide (**18b**), 1-(2-acetyl-6-bromopyridyl)pyridinium iodide (**18d**) and 1-(3-*N,N*-dimethylamino-3-methyl-2-oxobutyl)pyridinium iodide (**19**) were prepared analogously to the procedure for **18a** described above. More details are given in the ESI †.

References

1 (*a*) P. Hayoz and A. Von Zelewsky, *Tetrahedron Lett.*, 1992, **33**, 5165; (*b*) P. Hayoz, A. Von Zelewsky and H. Stoeckli-Evans, *J. Am. Chem. Soc.*, 1993, **115**, 5111.

2 (*a*) U. Knof and A. Von Zelewsky, *Angew. Chem., Int. Ed.*, 1999, **38**, 303; (*b*) A. Von Zelewsky, *Coord. Chem. Rev.*, 1999, **190–192**, 811; (*c*) A. Von Zelewsky and O. Mamula, *J. Chem. Soc., Dalton Trans.*, 2000, 219; (*d*) B. Kolp, D. Abeln, H. Stoeckli-Evans and A. Von Zelewsky, *Eur. J. Inorg. Chem.*, 2001, 1207; (*e*) L. Ghizdavu, B. Kolp, A. Von Zelewsky and H. Stoeckli-Evans, *Eur. J. Inorg. Chem.*, 1999, 1271; (*f*) L. Ghizdavu, A. Von Zelewsky and H. Stoeckli-Evans, *Eur. J. Inorg. Chem.*, 2001, 993; (*g*) G. Chelucci, G. A. Pinna and A. Saba, *Tetrahedron: Asymmetry*, 1997, **8**, 2571; (*h*) G. Chelucci and R. P. Thummel, *Chem. Rev.*, 2002, **102**, 3129; (*i*) G. Chelucci, G. A. Pinna and A. Saba, *Tetrahedron: Asymmetry*, 1998, **9**, 531; (*j*) G. Chelucci, S. Craba, A. Saba, F. Soccolini and G. Sotgiu, *J. Mol. Catal. A: Chem.*, 2000, **164**, 173; (*k*) G. Chelucci, A. Saba, D. Vignola and C. Solinas, *Tetrahedron*, 2001, **57**, 1099; (*l*) G. Chelucci and A. Saba, *Synth. Commun.*, 2001, **31**, 107; (*m*) A. V. Malkov, I. R. Baxendale, M. Bella, V. Langer, J. Fawcett, D. R. Russel, D. J. Mansfield, M. Valko and P. Kocovsky, *Organometallics*, 2001, **20**, 673; (*n*) A. V. Malkov, M. Bella, V. Langer and P. Kocovsky, *Org. Lett.*, 2000, **2**, 3047.

3 (*a*) H. Muerner, P. Belser and A. Von Zelewsky, *J. Am. Chem. Soc.*, 1996, **118**, 7989; (*b*) H. Muerner, A. von Zelewsky and G. Hopfgartner, *Inorg. Chim. Acta*, 1998, **271**, 36; (*c*) H. Muerner, A. von Zelewsky and H. Stoeckli-Evans, *Inorg. Chem.*, 1996, **35**, 3931.

4 (*a*) O. Mamula, A. Von Zelewsky and G. Bernardinelli, *Angew. Chem., Int. Ed.*, 1998, **37**, 290; (*b*) O. Mamula, F. J. Monlien, A. Porquet, G. Hopfgartner, A. E. Merbach and A. Von Zelewsky, *Chem. Eur. J.*, 2001, **7**, 533.

5 O. Mamula, A. Von Zelewsky, T. Bark and G. Bernardinelli, *Angew. Chem., Int. Ed.*, 1999, **38**, 2945.

6 O. Mamula, A. von Zelewsky, T. Bark, H. Stoeckli-Evans, A. Neels and G. Bernardinelli, *Chem. Eur. J.*, 2000, **6**, 3575.

7 (*a*) T. Bark, M. Dueggeli, H. Stoeckli-Evans and A. Von Zelewsky, *Angew. Chem., Int. Ed.*, 2001, **40**, 2848; (*b*) T. Bark and A. Von Zelewsky, *J. Chem. Soc., Perkin Trans. 1*, 2002, 1881.

8 (*a*) P. Collomb and A. von Zelewsky, *Tetrahedron: Asymmetry*, 1998, **9**, 3911; (*b*) P. Collomb and A. von Zelewsky, *Tetrahedron: Asymmetry*, 1995, **6**, 2903.

9 (*a*) D. Lötscher, S. Rupprecht, P. Collomb, P. Belser, H. Viebrock, A. von Zelewsky and P. Burger, *Inorg. Chem.*, 2001, **40**, 5675; (*b*) D. Lötscher, S. Rupprecht, H. Stoeckli-Evans and A. von Zelewsky, *Tetrahedron: Asymmetry*, 2000, **11**, 4341.

10 (*a*) W. Zecher and F. Kroehnke, *Chem. Ber.*, 1961, **94**, 690; (*b*) W. Zecher and F. Kroehnke, *Chem. Ber.*, 1961, **94**, 698; (*c*) W. Zecher and F. Kroehnke, *Chem. Ber.*, 1961, **94**, 707; (*d*) F. Kroehnke, *Synthesis*, 1976, 1.

11 F. Pezet, I. Sasaki, J.-C. Daran, J. Hydrio, H. Aït-Haddou and G. Balavoine, *Eur. J. Inorg. Chem.*, 2001, 2669.

12 L. E. Perret Aeby and A. Von Zelewsky, *Synlett*, 2002, **5**, 773.

13 B. Quinodoz, and A. Von Zelewsky, submitted.

14 (*a*) G. Baum, E. C. Constable, D. Fenske, C. E. Housecroft and T. Kulke, *Chem. Eur. J.*, 1999, **5**, 1862; (*b*) E. C. Constable, T. Kulke, G. Baum and D. Fenske, *Inorg. Chem. Commun.*, 1998, **1**, 80; (*c*) G. Baum, E. C. Constable, D. Fenske and T. Kulke, *Chem. Commun.*, 1997, 2043; (*d*) G. Baum, E. C. Constable, D. Fenske, C. E. Housecroft and T. Kulke, *Chem. Commun.*, 1999, 195 and ref. 2*m*, 2*n*.

15 J.-P. Sauvage and M. Ward, *Inorg. Chem.*, 1991, **30**, 3869.

16 (*a*) F. H. Case, *J. Am. Chem. Soc.*, 1946, **68**, 2574; (*b*) H.-P. Hsieh and L. W. McLaughlin, *J. Org. Chem.*, 1995, **60**, 5356; (*c*) F. Vögtle, R. Hochberg, F. Kochendörfer, P.-M. Windscheif, M. Volkmann and M. Jansen, *Chem. Ber.*, 1990, **123**, 2181; (*d*) P. M. Windscheif and F. Voegtle, *Synthesis*, 1994, 87.

17 (*a*) J. E. Parks, B. E. Wagner and R. H. Holm, *J. Organomet. Chem.*, 1973, **56**, 53; (*b*) M. A. Peterson and J. R. Mitchell, *J. Org. Chem.*, 1997, **62**, 8237.

18 (*a*) Gilbert, *J. Am. Chem. Soc.*, 1955, **77**, 4413; (*b*) T. Yamashita, K. Shiomori, M. Yasuda and S. Kensuke, *Bull. Chem. Soc. Jpn.*, 1991, **64**, 366; (*c*) T. Yamashita, M. Watanabe, R. Kojima, T. Shiragami, K. Shima and M. Yasuda, *J. Photochem. Photobiol. A*, 1998, **118**, 165.

19 (*a*) A. Favorskii, *J. Prakt. Chem.*, 1895, **51**, 533; (*b*) A. S. Kende, *Org. React.*, 1960, **11**, 261.

20 G. R. Newkome, D. C. Hager and G. E. Kiefer, *J. Org. Chem.*, 1986, **51**, 850.

21 (−)-α-Pinene is transformed into (+)-pinocarvone according to published procedure: E. D. Mihelich and D. J. Eickhoff, *J. Org. Chem.,*, 1983, **48**, 4135.
22 N. C. Fletcher, F. R. Keene, M. Ziegler, H. Stoeckli Evans, H. Viebrock and A. Von Zelewsky, *Helv. Chim. Acta*, 1996, **79**, 1192.
23 (*a*) G. M. Sheldrick, *Acta Crystallogr., Sect. A*, 1990, **46**, 467; (*b*) G. M. Sheldrick, SHELXL-97 Program for Crystal Structure Refinement, 1999, Universität Göttingen, Göttingen, Germany; (*c*) A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, M. C. Burla, G. Polidori, M. Camalli and R. Spagna, 1997 SIR97 – A package for crystal structure solution by direct methods and refinement, c/o Istituto di Ricerca per lo Sviluppo di Metodologie Cristallografiche, CNR, & Dipartimento Geomineralogico, Campus Universitario, Via Orabona 4, 70125 Bari.
24 A. Gaset, A. Verdier and A. Lattes, *Spectrochim. Acta. Part A*, 1975, **31**, 727.
25 F. Ros, J. de la Rosa and J. Enfedaque, *J. Org. Chem.*, 1995, **60**, 541.