Synthesis of a Chiral Bis(bipyridine) Ligand of the *Chiragen* Family for the Self-Assembly of Enantiomerically Pure Helicates

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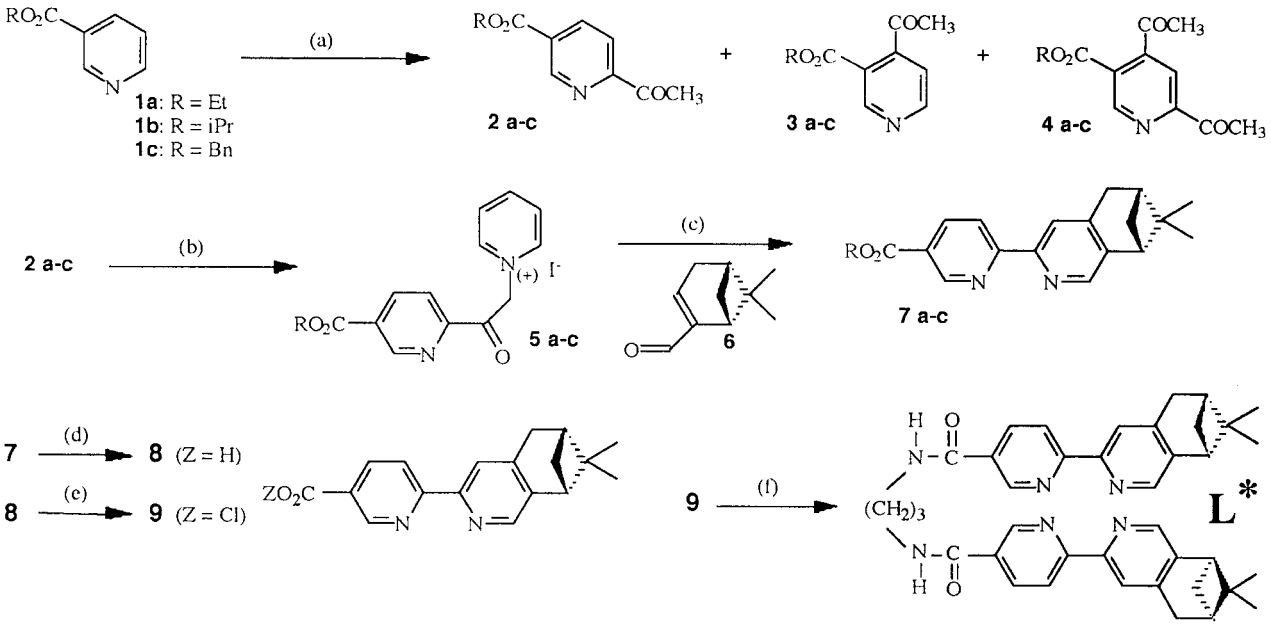
Abstract: The chiral bis(bipyridine) ligand **L***, belonging to the "chiragen" family, has been synthesized. The synthetic pathway involves an original preparation of acylnicotinates which is of synthetic value. The synthetic strategy described here may allow the access to various bisbidentate ligands, well-suited to the self-assembly of enantiomerically pure helicates.

Key words: free radical acylation, acylnicotinates, Kröhnke reaction, chiral bis(bipyridine) ligand

Metal-directed self-assembling processes, to give double or triple helical supramolecular complexes, have attracted considerable attention over the past ten years.[1, 2] Triple-stranded helicates resulting from the self-assembly in a **[L_3M_2]** manner of ligands **L**, consisting of two bidentate moieties linked by a spacer, and octahedral metallic **M** ions, are chiral supramolecular assemblies. The triple helical assembling implies homochirality of the two metallic centers.[3] In the unusual and so called achiral "*meso* helicate" (Δ–Λ isomers), the intercrossing of the threads is not observed.[4] The resulting chirality of triple helical complexes is due both to the Δ/Λ chirality of the metal centers and to the *P/M* sense of the twisting of the strands (the latter being induced by the former). Usually, the helicates described in the literature are racemic mixtures.[2] A spontaneous resolution has been observed by Lehn and co-workers[5] and resolution has been achieved by Williams and co-workers.[6] Nevertheless, the preparation of enantiopure triple helicates has been achieved in few cases by incorporation of a chiral element in the ligand **L**.[7-10] The preparation of enantiopure well-suited ligands is therefore required. Various strategies have been envisaged which introduce the chirality: (i) in the spacer between the two bidentate units,[7, 11] (ii) at the ends of the ligands.[9, 10, 12]

We describe herein a ligand system in which the two identical bidentate moieties at its ends are chiral. This ligand **L*** may be considered as a chiral version of the ligand **L** (two bidentate bipyridine moieties linked by a spacer) previously described by us, which had led to a racemic $L_3Fe^{II}_2$ homochiral triple helical complex.[3] The enantiopure **L*** (Scheme) bears two pairs of *R* stereogenic centers derived from (–)-myrtenal. **L*** is highly inspired by the chiragen ligand family designed and described by von Zelewsky and co-workers.[13–18]

The chiral ligand **L*** is based on two pineno-[4′,5′]-fused-2,2′-bipyridine-5-carboxamido groups, linked through an aliphatic C_3-chain. The chiral building block comes from commercial (–)-myrtenal **6** (Scheme). Coupling of the bipyridine carboxylic acid **8** to propane-1,3-diamine was readily achieved via the corresponding acid chloride **9**. The key intermediate ester **7** was prepared in a simple two-step procedure starting with 2-acetyl-5-alkoxycarbonylpyridine, by transformation into the pyridinium salt **5** followed by a Kröhnke-type reaction[19, 20, 21] with (–)-myrtenal.



(a) H_2SO_4 (1 equiv), $FeSO_4$•7 H_2O (2.5 equiv), MeCHO, tBuOOH, <15 °C. (b) I_2 (1 equiv), pyridine, reflux, 0.5 h then r.t. overnight. (c) **6**, NH_4OAc (2 equiv), formamide, 75 °C, 6 h. (d) **7a**, **7b**: 1. KOH, EtOH; 2. H_3O^+; **7c**: H_2, Pd/C, EtOH. (e) $SOCl_2$. (f) H_2N-$(CH_2)_3NH_2$, Et_3N, CH_2Cl_2.

Scheme

A multistep preparation of 2-acetyl-5-ethoxycarbonylpyridine (**2a**), involving as starting material diethyl pyridine-2,5-dicarboxylate, has been described.[22–24] We prepared the precursors **2** by a one-step procedure, through free-radical acylation.[25, 26] in acidic conditions of commercial alkyl nicotinate **1**. The acetyl radicals were generated from acetaldehyde with *tert*-butyl hydroperoxide and iron(II) sulfate. This direct acylation of a protonated pyridine ester is, as far as we know, unprecedented and seemed to us of synthetic interest because of the simplicity of the experimental conditions. The reaction of nucleophilic free radicals $CH_3CO^{\bullet}$ led to a mixture of 2-acetyl- (**2**), 4-acetyl- (**3**), and 2,4-diacetyl- (**4**) nicotinates. As previously observed,[25–27] the first acetyl group activates the pyridine ring towards further acylation, even with low conversion of the starting material. A brief study was undertaken in order to improve the yield of 2-monoacetylated derivative. First, the ratio substrate/reagent was varied from 1:1 to 1:10 and we observed (^{1}H NMR titration on the crude mixture) that the maximum yield of **2** was obtained for a ratio 1:2.5. It is worthy to note that total conversion of substrate **1** is reached for a ratio 1:5; under these conditions, the diacetyl derivative **4** becomes the major product of the reaction. Second, the ester group was varied (**a** = Et; **b** = *i*-Pr; **c** = Bn): more hindered benzyl ester **2c** gave a better yield of 2-acetyl derivative than ethyl or isopropyl esters **2a** and **2b** respectively. Moreover, later cleavage of the benzyl protecting group by hydrogenolysis led to a much more convenient procedure for the isolation of carboxylic acid **8**. Interestingly, the separation by column chromatography is very easy and compound **2** is eluted first, allowing a very fast procedure. The yields are satisfactory and the reaction can be performed on rather large quantities. So, this way of preparation of acylnicotinates seems to us of preparative value in spite of the formation of a mixture.

Table 1. Acetylation of **1a–c**

Substrate (R_f)[a]	Conversion (%)	Product Distribution (%) (R_f)[a]			Isolated Yield (%)[b] of **2**
		2	**3**	**4**	
1a (0.40)	55	35 (0.70)	32 (0.22)	33 (0.64)	19[c]
1b (0.43)	70	43 (0.75)	30 (0.25)	27 (0.66)	30[d]
1c (0.50)	70	56 (0.80)	22 (0.27)	22 (0.70)	39[d]

[a] TLC (silica gel, hexane/EtOAc 2:1):
[b] Column (Si 60 Geduran Merck, 0.040-0.063 mm, hexane/EtOAc 0 to 20%).
[c] Oil.
[d] Colorless solid, mp < 50°C.

Preliminary complexation studies evidenced the formation of enantiopure triple helicate complexes with iron(II) salts. The structural and chiroptical properties of these complexes will be described in a separate paper.[28]

The synthetic strategy used here may be generalized, allowing the preparation of unknown diversely 5′-substituted "pineno"-[4,5]-fused 2,2′-bipyridine derivatives. These derivatives are precursors for various bis-bidentate ligands (different spacers can be used) which constitute an extension of the "chiragen" family. These ligands may be well-suited to the self-assembly of enantiomerically pure helicates. Investigations on the enantioselectivity of metal helicate complexes self-assembly are currently in progress.

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC 200, WM 250 or Varian U$^+$ 500 NMR spectrometer, using DEPT techniques and QUATD sequence for the assignment of the multiplicity of carbon atoms; unless otherwise stated, the spectra were taken in $CDCl_3$/TMS.
FT-IR spectra were recorded as films on NaCl plates or as KBr pellets (1%) on a Nicolet Impact 400 spectrometer. MS [EI (70 eV), or CI (NH_3, iBuH)] were recorded on a Nermag mass spectrometer. Optical rotations were measured on a Perkin Elmer polarimeter 341.
Reagents were of commercial grade and were not further purified; (–)-(1*R*)-myrtenal, $[\alpha]_D$ –15 (22°C, neat), was purchased from Aldrich. Solvents were purified by standard methods. Mps: Büchi 530 (uncorrected). Chiral HPLC was performed on a Chiracel OD-H column with a UV-vis spectrometer (254 nm) as detector.

2-Acetyl-5-benzyloxycarbonylpyridine (2c); Typical Procedure:
To a solution of commercial benzyl nicotinate (**1c**) (24.86 g, 0.116 mol), H_2SO_4 (11.43 g, 0.292 mol), and MeCHO (12.76 g, 0.290 mol) in degassed water (50 mL), cooled at 5–10°C under argon, were simultaneously added dropwise a solution of $FeSO_4 \bullet 7H_2O$ (80.6 g, 0.29 mol) in degassed water (200 mL) and 70% *t*-BuOOH in water (40 mL). The mixture was stirred for 15 min and then extracted with $CHCl_3$ (3 × 150 mL); the solution was washed with brine (100 mL). After drying, the solvent was removed under vacuum. The product distribution (Table 1) was determined by ^{1}H NMR analysis of the crude mixture. The starting material and the products of the reaction are well-separated in TLC (silica gel 60 $F_{254,}$ aluminum sheets, hexane/EtOAc 2:1), see Table 1. The mixture was chromatographed on a silica gel column using 0 to 20% EtOAc/hexane, giving **2c** (11.53 g, 39%).
2a (19%); **2b** (30%). For spectroscopic data, see Table 2.

1-[2-(5-Benzyloxycarbonyl-2-pyridy1)-2-oxoethyl]pyridinium Iodide (5c); Typical Procedure:
To a solution of **2c** (6.21 g, 24 mmol) in pyridine (50 mL) was added iodine (6.22 g, 24 mmol). The mixture was refluxed under argon for 0.5 h and then stirred at r.t. overnight. The solvent was eliminated (evaporation and azeotrope with toluene) and the black residue was treated with water. After drying of the solid under vacuum, the product was purified by recrystallization (95% EtOH). **5c**: 10.95 g (98%). The same procedure led to **5a** (53%) and **5b** (87%). For spectroscopic data, see Table 3.

3-(5-Benzyloxycarbonyl-2-pyridyl)-7,7-dimethyl-5,6,7,8-tetrahydro-6,8-methanoisoquinolines (7c); Typical Procedure:
A solution of iodo derivative **5c** (7.27 g, 160 mol), (–)-myrtenal (**6**) (2.53 g, 160 mol) and NH_4OAc (2.6 g, 330 mol) in formamide (100 mL) was heated at 75 °C for 6 h. The resulting black mixture was concentrated and treated with water. The product was extracted with hexane/Et_2O (6 × 100 mL) and the organic phase washed with brine (200 mL). After drying, the solvents were evaporated. The resulting oil was purified by column chromatography (silica gel, 0 to 10% EtOAc/hexane). **7c:** 4.3 g (70%).
7a (38%); **7b** (43%). For spectroscopic data, see Table 4.
Enantiomeric purity of ester **7c** was determined by chiral HPLC (elution: iPrOH/hexane, 15:85, 0.5 mL · min^{-1}). The observed value of 98% reflects the enantiomeric purity of commercial (–)-(1*R*)-myrtenal.

3-(5-Carboxy-2-pyridyl)-7,7-dimethyl-5,6,7,8-tetrahydro-6,8-methanoisoquinoline (8):
From **7a** *or* **7b***:*
A mixture of ester **7** (4 mmol : **a** = 1.29 g; **b** = 1.34 g), KOH (500 mg) in EtOH (30 mL) was refluxed for 12 h. The solvent was evaporated

Table 2. Spectroscopic data for Compounds **2a–c, 3c, 4c**

Product[a]	R	^{1}H NMR ($CDCl_3$/TMS) δ, J (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ	MS (m/z)	IR ν (cm^{-1})
2a	Et	1.44 (t, 3H, J = 7.1), 2.76 (s, 3H), 4.45 (q, 2H, J = 7.1), 8.10 (d, 1H, J = 8.1), 8.42 (dd, 1H, J = 1.7/8.1), 9.26 (d, 1H, J = 1.7)	14.2 (CH_3), 25.9 (CH_3), 61.8 (CH_2), 120.9 (CH), 128.7 (Cq), 137.8 (CH), 150.1 (CH), 155.7 (Cq), 164.5 (Cq), 199.3 (Cq)	(EI): 194 (M+H), 165 (MH-Et), 151 (MH-Ac)	1731.0, 1702.2
2b	iPr	1.41 (d, 6H, J = 6.2), 2.76 (s, 3H), 5.29 (m, 1H, J = 6.2), 8.09 (dd, 1H, J = 8. l/0.5), 8.40 (dd, 1H, J = 2.0/8.1), 9.26 (dd, 1H, J = 1.7/0.5)	21.8 (CH_3), 26.0 (CH_3), 69.6 (CH), 121.0 (CH), 129.1 (Cq), 137.9 (CH), 150.2 (CH), 155.7 (Cq), 164.0 (Cq), 199.4 (Cq)	(CI): 208 (M+H)	1731.4, 1708.1
2c	Bn	2.74 (s, 3H), 5.42 (s, 2H), 7.27-7.49 (m, 5H), 8.08 (d, 1H, J = 7.9), 8.42 (dd, 1H, J = 2.4/7.9), 9.30 (d, 1H, J = 2.1)	25.9 (CH_3), 67.4 (CH_2), 121.0 (CH), 128.3 (CH), 128.5 (CH), 128.55 (Cq), 128.6 (CH), 128.7 (CH), 135.1 (Cq), 138.0 (CH), 150.3 (CH), 155.8 (Cq), 164.3 (Cq), 199.3 (Cq)	(EI): 255 (M), 227 (M-EtH), 213 (MH-Ac), 148 (M-OBn)	1728.6, 1701.5
3**c**	Bn	2.47 (s, 3H), 5.36 (s, 2H), 7.23 (dd, 1H, J = 5.0/0.5), 7.35-7.42 (m, 5H), 8.81 (d, 1H, J = 5.0), 9.18 (d, 1H, J = 0.5)	30.1 (CH_3), 67.6 (CH_2), 119.4 (CH), 122.1 (Cq), 128.4 (CH), 128.5 (CH), 128.7 (CH), 134.5 (Cq), 150.5 (Cq), 150.9 (CH), 153.3 (CH), 164.4 (Cq), 201.5 (Cq)		
4c	Bn	2.49 (s, 3H), 2.73 (s, 3H), 5.37 (s, 2H), 7.34–7.43 (m, 5H), 7.95 (s, 1H), 9.18 (s, 1H)	25.7 (CH_3), 29.7 (CH_3), 68.0 (CH_2), 117.5 (CH), 128,4 (CH), 128.5 (CH), 128.6 (CH), 134.4 (Cq), 150.5 (CH), 150.9 (Cq), 155.7 (Cq), 164.1 (Cq), 198.4 (Cq), 201.5 (Cq)		

[a] Elemental analysis of **2a–c**: C ± 0.20; H ± 0.27; N + 0.42.

Table 3. Spectroscopic data for Compounds **5a–c**

Product	R	^{1}H NMR δ, J (Hz)	^{13}C NMR δ, J (Hz)
5a	Et	(C_6D_6 + DMSO-d_6): 1.10 (t, 3H, J = 7.2), 4.15 (q, 2H, J = 7.2), 6.81 (s, 2H), 7.81 (m, 2H), 8.03 (d, 1H, J = 8.2), 8.1 (m, 1H), 8.28 (dd, 1H, J = 1.7/8.2). 9.22 (m, 2H), 9.27 (d, 1H, J = 1.7)	(C_6D_6 + DMSO-d_6): 14.2 (CH_3), 61.9 (CH_2), 67.4 (CH_2), 122.4 (CH), 129.9 (CH), 138.7 (CH), 146,1 (CH), 146.7 (Cq), 146.8 (CH), 150.3 (CH), 153.7 (Cq), 164.2 (Cq), 191.2 (Cq)
5b	iPr	($CDCl_3$ + DMSO-d_6): 1.43 (d, 6H, J = 6.8), 5.31 (m, 1H), 6.82 (s, 2H), 8.14–8.25 (m, 3H), 8.52 (dd, 1H, J = 1.7/7.8), 8.71 (m, 1H), 9.27–9.30 (m, 3H)	($CDCl_3$ + DMSO-d_6): 21.1 (CH_3), 66.3 (CH_2), 69.3 (CH), 121.3 (CH), 127.2 (CH), 129.7 (Cq), 137.7 (CH), 145.5 (CH), 145.8 (CH), 149.6 (CH), 151.9 (Cq), 162.7 (Cq), 189.4 (Cq)
5c	Bn	($CDCl_3$): 5.44 (s, 2H), 6.8 (s, 2H), 7.37–7.50 (m, 5H), 8.14–8.22 (m, 3H), 8.53 (dd, 1H, J = 1.7, 7.6), 8.68 (m, 1H), 9.23 (m, 2H), 9.43 (d, 1H, J = 1.7)	($CDCl_3$): 66.5 (CH_2), 67.0 (CH_2), 121.6 (CH), 127.4 (CH), 127.8 (2 CH), 128.1 (CH), 129.3 (Cq), 134.3 (Cq), 138.1 (CH), 145.7 (CH), 147.9 (CH), 149.9 (CH), 152.2 (Cq), 163.2 (Cq), 189.4 (Cq)

under vacuum and the residue was treated with water and acidified to pH 1–2 with aq HCl. The solution was extracted with $CHCl_3$. Drying and elimination of the solvent gave pure acid.
7a as starting material gave **8** (0.69 g; 59%); **7b** gave **8** (1.01 g; 86%).

From **7c***:*
A mixture of benzyl ester **7c** (1.6g, 4.1 mmol), 10% Pd/C (0.4 g) in EtOH (100 mL) and CH_2Cl_2 (30 mL) was treated with H_2 at r.t. The reaction was monitored by TLC (silica gel, hexane/EtOAc 3:1). The solvent was evaporated and the residue was treated with Et_2O giving pure **8** as a beige powder: 1.08 g (88%).
For spectroscopic data, see Table 5.

Preparation of Ligand L*:
Acid Chloride **9***:*
Acid **8** (955 mg, 3.25 mmol) in $SOCl_2$ (20 mL) was stirred under argon at r.t. for 1 h. $SOCl_2$ was removed under vacuum and the residue was treated with pentane. The crude product (as dihydrochloride, 1.25 g, quant.) was pure enough for the following reaction. For spectroscopic data, see Table 5.

Coupling with Propane-1,3-diamine:
To a suspension of acid chloride **9** (dihydrochloride, 1.25 g, 3.25 mmol) in CH_2Cl_2 (40 mL) was added dropwise, at r.t., a solution of propane-1,3-diamine (118 mg, 1.6 mmol), Et_3N (969 mg, 9.6 mmol) in CH_2Cl_2 (20 mL). The mixture was stirred for 12 h under argon, then treated with aq KOH. Extraction with $CHCl_3$, drying and evaporation of the solvent gave the crude product as a beige powder. The diamide **L*** was purified by column chromatography (alumina, 1–2% MeOH/CH_2Cl_2) giving a colorless powder (858 mg, 85%); mp 152 °C.
^{1}H NMR (500 MHz, CD_3CN): δ = 0.63 (s, 6H), 1.19 (d, 2H, J = 9.6 Hz), 1.41 (s, 6H), 1.87 (5^t, 2H, J = 6.3 Hz), 2.33–2.30 (m, 2H), 2.72 (dt, 2H, J = 9.6/5.6 Hz), 2.88 (t, 2H, J = 5.6 Hz), 3.08 (d, 4H, J = 2.6 Hz), 3.52 (4^t, 4H, J = 6.3/6.3 Hz), 7.58 (t, 2H, J = 6.3 Hz, NH), 8.19 (s, 2H), 8.22 (dd, 2H, J = 2.3/8.3 Hz), 8.24 (s, 2H), 8.42 (dd, 2H, J = 8.3/0.6 Hz), 9.03 (dd, 2H, J = 0.6/2.3 Hz).

Table 4. Spectroscopic and Physical Data for Compounds **7a–c**

Product[a]	R	Yield (%)	^{1}H NMR ($CDCl_3$/TMS) δ, J (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ	MS (m/z)	IR ν (cm^{-1})	Physical Data
7a	Et	38	0.66 (s, 3H), 1.25 (d, 1H, J = 9.5), 1.43 (m, 6H), 2.31–2.37 (m, 1H), 2.70 (dt, 1H, J = 9.5/5.8), 2.89 (t, 1H, J = 5.5), 3.07 (d, 2H, J = 2.6), 4.44 (q, 2H, J = 7.2), 8.24 (s, 1H), 8.27 (s, 1H), 8.38 (dd, 1H, J = 2.0/8.2), 8.45 (d, 1H, J = 8.2), 9.25 (dd, 1H, J = 0.7/2.0)	14.28 (CH_3), 21.32 (CH_3), 25.93 (CH_3), 31.69 (CH_2), 32.86 (CH_2), 39.18 (Cq), 39.96 (CH), 44.50 (CH), 61.28 (CH_2), 120.13 (CH), 121.18 (CH), 125.39 (Cq), 137.77 (CH), 143.88 (Cq), 145.54 (Cq), 145.70 CH), 150.3 (CH), 153.30 (Cq), 159.87 (Cq), 165.34 (Cq)	EI: 322 (M), 293 (M-Et), 279, 251	1718.8	mp 96 °C
7b	*i*-Pr	43	0.67 (s, 3H), 1.25 (d, 1H, J = 9.5), 1.41 (d, 6H, J = 6.2), 1.44 (s, 3H), 2.30–2.38 (m, 1H), 2.73 (dt, 1H, J = 9.5/5.8), 2.89 (t, 1H, J = 5.5), 3.07 (d, 2H, J = 2.6), 5.30 (m, 1H, J = 6.2), 8.24 (s, 1H), 8.27 (s, 1H), 8.37 (dd, 1H, J = 2.0/8.7), 8.47 (dd, 1H, J = 8.7/0.8), 9.24 (dd, 1H, J = 0.8/2.0)	21.32 (CH_3), 21.88 (CH_3), 25.93 (CH_3), 31.69 (CH_2), 32.86 (CH_2), 39.18 (Cq), 39.95 (CH), 44.45 (CH), 68.85 (CH), 120.03 (CH), 121.14 (CH), 125.74 (C*q*), 137.72 (CH), 143.82 (Cq), 145.53 (Cq), 145.70 (CH), 150.30 (CH), 153.30 (Cq), 159,73 (Cq), 164.83 (Cq)	EI: 336 (M), 293 (M-iPr), 279, 25l	1719.7	mp 115 °C **[**α**]**$_D^{20}$ –73.0 (c = 2.09, CH_2Cl_2)
7c	Bn	70	0.66 (s, 3H), 1.24 (d, 1H, J = 9.6), 1.43 (s, 3H), 2.30–2.37 (m, 1H), 2.72 (dt, 1H, J = 9.6/5.8), 2.89 (t, 1H, J = 5.5), 3.08 (d, 2H, J = 2.7), 5.42 (s, 2H), 7.35–7.50 (m, 5H), 8.23 (s, 1H), 8.26 (s, 1H), 8.39 (dd, 1H, J = 2.0/8.3), 8.46 (dd, 1H, J = 8.3/1.0), 9.29 (dd, 1H, J = 1.0/2.0)	21.33 (CH_3), 25.93 (CH_3), 31.69 (CH_2), 32.87 (CH_2), 39.18 (Cq), 39.95 (CH), 44.50 (CH), 66.95 (CH_2), 120.14 (CH), 121.21 (CH), 125.07 (Cq), 128.24 (CH), 128.34 (CH), 128.60 (CH), 135.55 (Cq), 137.91 (CH), 143.98 (Cq), 145.54 (Cq), 145.73 (CH), 150.45 (CH), 153.23 (Cq), 160.07 (Cq), 165.18 (Cq)	(CI): 385 (M+H) 341	1725.6	mp 97 °C [α]$_D^{20}$ –64.4 (c = 2.04, CH_2Cl_2)

[a] Element Analysis of **7b** and **7c** · 0.25 H_2O; C ± 0.25; H ± 0.07; N ± 0.15.

Table 5. Spectroscopic and Physical Data for Compounds **8** and **9**

Product	^{1}H NMR ($CDCl_3$/TMS) δ, J (H_2)	^{13}C NMR ($CDCl_3$/TMS) δ	Data
8[a]	0.68 (s, 3H), 1.27 (d, 1H, J = 9.6), 1.44 (s, 3H), 2.32-2.38 (m, 1H), 2.75 (dt, 1H, J = 9.6/5.5), 2.94 (t, 1 H, J = 5.5), 3.10 (d, 2 H, J = 2.6), 8.28 (s, 1H), 8.36 (s, 1H), 8.44–8.54 (m, 2H), 8.69 (brd s, 1H, OH), 9.38 (brd s, 1H)	21.33 (CH_3), 25.79 (CH_3), 31.50 (CH_2), 33.02 (CH_2), 39.12 (Cq), 39.79 (CH), 44.46 (CH), 121.02 (CH), 122.20 (CH), 126.30 (Cq), 138.72 (CH), 144.48 (CH), 144.49 (C*q*), 147.43 (Cq), 150.82 (CH), 152.52 (Cq), 158.46 (Cq), 168.16 (Cq)	mp 226°C [α]$_D^{20}$ –76.1 (c = 0.44, CH_2Cl_2) MS (EI): m/z = 294 (M) 279 (M-CH_3), 265, 251 IR: ν (cm^{-1}) = 1710
9	0.71 (s, 3H), 1.31 (d, 1H, J = 10.2), 1.51 (s, 3H), 2.49 (brd s, 1 H), 2.85–2.96 (m, 1H), 3.16 (m, 1H), 3.34 (d, 2H, J = 2.6), 8.58 (s, 1H), 8.67 (s, 1H), 8.68–8.73 (m, 1H), 9.33 (brd d, 1H), 9.39 (d, 1H, J = 1.7)	21.27 (CH_3), 25.11 (CH_3), 30.64 (CH_2), 34.16 (CH_2), 38.69 (Cq), 38.78 (CH), 44.38 (CH), 123.14 (CH), 125.08 (CH), 130.28 (Cq), 136.97 (CH), 140.77 (CH), 144.81 (Cq), 148.25 (Cq), 151.28 (CH), 151.36 (Cq), 158.40 (Cq), 165.89 (Cq)	

[a] Elemental Analysis **8**: calcd. for $C_{18}H_{18}N_2O_2$ (Found): C 73.45 (73.22), H 6.16 (6.33), N 9.52 (9.41).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.32 (CH_3), 25.87 (CH_3), 29.53 (CH_2), 31.64 (CH_2), 32.86 (CH_2), 36.35 (CH_2), 39.12 (Cq), 39.90 (CH), 44.39 (CH), 120.30 (CH), 121.02 (CH), 128.90 (Cq), 135.66 (CH), 143.70 (Cq), 145.53 (CH), 145.54 (Cq), 147.92 (CH), 153.35 (Cq), 158.84 (Cq), 166.27 (Cq).
MS (CI, NH_3, isobutane): m/z = 627 (M), 377 (MH-$C_{17}H_{17}N_2$).
IR (KBr): ν = 3451, 3318, 3078, 1649, 1603, 1545 cm^{-1}.
[α]$_D^{21.5}$–77.4 *(χ = 2.0, CH_2Cl_2).*
Anal. Calcd for $C_{39}H_{42}N_6O_2$•0.75 H_2O (Found): C 73.16 (73.19), H 6.85 (6.88), N 13.12 (13.24).

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