Preparation of Optically Active α-Amino[3]ferrocenophanes − Building Blocks for Chelate Ligands in Asymmetric Catalysis

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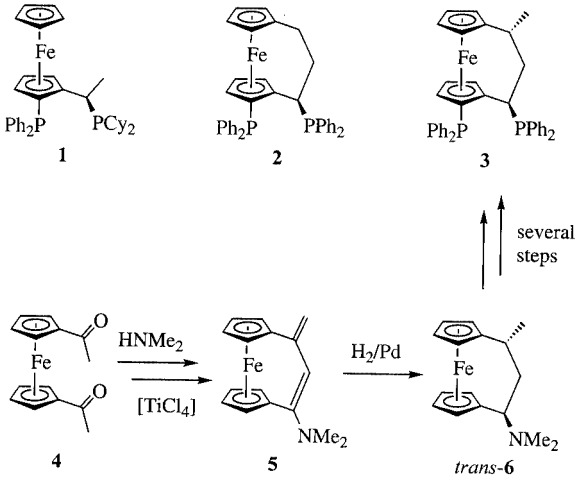
Treatment of 1,1′-diacetylferrocene (**4**) with dimethylamine and $TiCl_4$ yielded the unsaturated dimethylamino-substituted [3]ferrocenophane product **5**. Its catalytic hydrogenation gave the corresponding saturated [3]ferrocenophane system **6** (*trans*/*cis* ≈ 7:1). The *rac*-[3]ferrocenophane amine **6** was partially resolved (to ca. 80% *ee*) by means of L- or D-*O*,*O*′-dibenzoyltartrate salt formation. Treatment of **4** with the pure (*R*)- or (*S*)-methyl(1-phenylethyl)amine (**8**)/$TiCl_4$ gave the corresponding optically active unsaturated [3]ferrocenophane amines (*R*)-(+)-**9** and (*S*)-(−)-**9**, respectively. Their catalytic hydrogenation again proceeded *trans*-selectively, giving the corresponding saturated diastereomeric [3]ferrocenophane amines (1*R*,3*R*,5*R*)-**10a** and (1*S*,3*S*,5*R*)-**10b** [starting from (*R*)-**9**], their enantiomers *ent*-**10a** and *ent*-**10b** were obtained from (*S*)-**9**, but with a poor asymmetric induction (**10a**/**10b** < 2:1). Quaternization of **6** (CH_3I) followed by amine exchange using (*R*)- or (*S*)-methyl(1-phenylethyl)-amine (**8**), respectively, proceeded with overall retention. Subsequent chromatographic separation gave the pure diastereoisomers (1*R*,3*R*,5*R*)-**10a** and (1*S*,3*S*,5*R*)-**10b** [from (*R*)-**8**, *ent*-**10a** and *ent*-**10b** from (*S*)-**8**] in > 60% yield. Subsequently, the benzylic (1-phenylethyl) auxiliary was removed from the nitrogen atom by catalytic hydrogenolysis to yield the enantiomerically pure (> 98%) ([3]ferrocenophanyl)-methylamines (1*R*,3*R*)-**11** and (1*S*,3*S*)-**11**, respectively, which were converted into the corresponding dimethylamino-substituted [3]ferrocenophanes (1*R*,3*R*)-**6** and (1*S*,3*S*)-**6**. Each enantiomer from the following enantiomeric pairs was isolated in its pure form and characterized by X-ray diffraction: (*R*)-**9**/(*S*)-**9**; (1*R*,3*R*,5*R*)-**10a**/(1*S*,3*S*,5*S*)-**10a**; (1*R*,3*R*,5*S*)-**10b**/(1*S*,3*S*,5*R*)-**10b**; (1*R*,3*R*)-**11**/(1*S*,3*S*)-**11**.

Introduction

Ferrocene-derived chelate ligands have found significant use in asymmetric catalysis.[1] A prime example is the "*Josiphos*" ligand (**1**) which has served as a very useful ligand especially in asymmetric hydrogenation.[2] Many variations of this ligand type have become known. Among them the [3]ferrocenophane systems may eventually find some specific use because of their very rigid framework. Based on early work by the Dijon group,[3] Weissensteiner et al. have developed synthetic pathways to optically active chelate bis(phosphanyl)[3]ferrocenophanes, such as **2**.[4,5] We had recently found an interesting complementary synthetic entry into such functionalized [3]ferrocenophane ligand systems that was based on the very readily available 1,1′-diacetylferrocene[6] (**4**) starting material. Treatment of **4** with e.g. dimethylamine in the presence of titanium tetrachloride probably gave the corresponding enamine[7] that was, however, not stable under the applied reaction conditions. It underwent an intramolecular Mannich-type condensation reaction to yield the unsaturated [3]ferrocenophane system **5**[8,9] (see Scheme 1). Subsequent (heterogeneous) catalytic hydrogenation in the presence of Pd/C gave a ca. 7:1 mixture of *trans*-**6**/*cis*-**6**. The major product of this surprisingly high *trans*-selective reduction (*trans*-**5**) was obtained in its pure



Scheme 1

[‡] X-ray crystal structure analyses.
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form after recrystallization.[10] The product *rac-trans*-**6** was then converted into a series of chelate ligands, especially to the bis(phosphanyl)[3]ferrocenophane *rac*-**3**, which was used to generate a very active Pd-based catalyst for the alternating CO/ethene copolymerization.[11,12]

So far our chemistry leading to **3** and a number of related compounds was carried out at the stage of the racemic compounds which were also used in the first catalytic test reactions.[11] We have now developed a viable synthetic entry to the amino-substituted [3]ferrocenophane enantiomers (1*R*,3*R*)-**6** and (1*S*,3*S*)-**6** and related systems that will eventually allow us to prepare both enantiomers of the chelate ligand **3** and other related [3]ferrocenophane-derived chelate systems. Several possible pathways were tested that will briefly be described in this account before the rather simple route was successfully established that led to the practically optically pure α-amino[3]ferrocenophanes. The essential products along this pathway had their structural assignments secured by X-ray diffraction.

Results and Discussion

Attempted Asymmetric Enamine Hydrogenation

The observation that the catalytic hydrogenation of the doubly unsaturated enamine **5** in the presence of palladium on charcoal proceeded predominantly with an overall *trans* stereochemistry[10] indicated a stepwise hydrogenation pathway with an active involvement of the amino group at the surface of the catalyst. Therefore, it needed to be tested whether the attachment of a chiral amino auxiliary would lead to a considerable asymmetric induction. For this reason we selected the secondary amine methyl(1-phenylethyl)-amine [(*R*)-**8**, (*S*)-**8**] as the amine component in the enamine formation/Mannich condensation sequence. The respective enantiomers of **8** were prepared starting from the optically active (1-phenylethyl)amine by $LiAlH_4$ reduction of their methyl carbamates (**7**).[13]

Right from the beginning the chosen reaction sequence proceeded unsatisfactorily. The Mannich coupling required a ca. 16 fold excess of the expensive amino component [(*R*)-**8** or (*S*)-**8**] to produce the corresponding [3]ferrocenophane derivatives [(*R*)-**9**, (*S*)-**9**], but even under these forced conditions the optically active aminoferrocenophane derivatives were only isolated in less than 20% yield. The enantiomers are characterized by an optical rotation of $[\alpha]_D^{20} = +44$ [(*R*)-**9**]. Figure 1 shows the CD spectrum of (*R*)-**9**, featuring a negative Cotton effect at the short wavelength edge of the spectrum [$\Delta\varepsilon$ (λ_{max}) = −0.37 (348), +0.11 (444)].

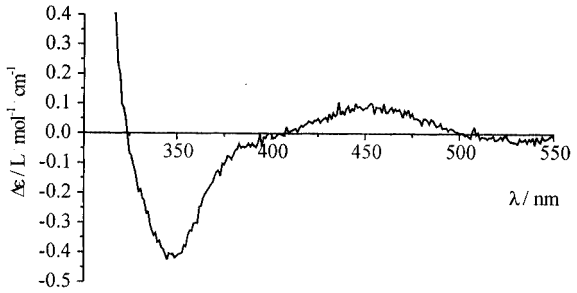


Figure 1. CD spectrum of the [3]ferrocenophane derivative (*R*)-**9** (8×10^{-4} g mL^{-1}) in CH_3CN

Single crystals that were suitable for characterization by X-ray diffraction were obtained for both enantiomers (*R*)-**9** and (*S*)-**9**. Figure 2 provides a view of the structures of the pair of enantiomers in the crystal. Since the solved structures are enantiomeric, only some of the data from enantiomer (*R*)-**9** will be given. The ferrocene framework of

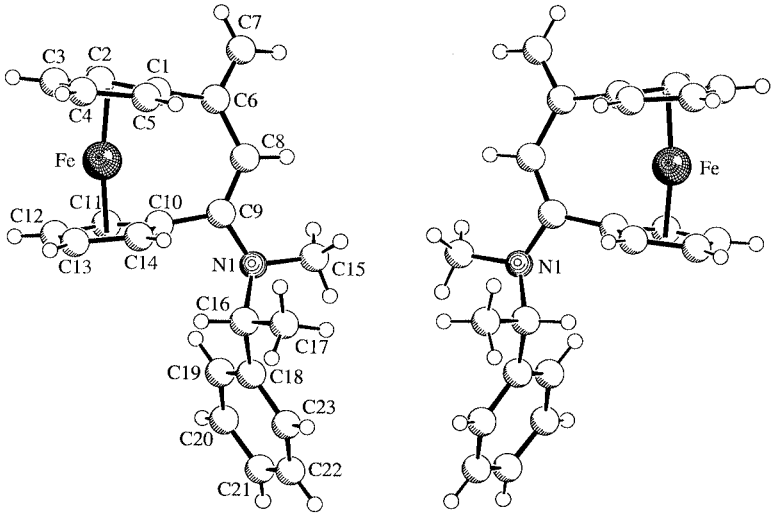


Figure 2. A view of the molecular geometries of the pair of the enantiomers (*R*)-(+)-**9** (left) and (*S*)-(−)-**9** (right) (with unsystematical atom numbering scheme), originating from different enantiomorphic crystals; selected bond lengths [Å] and angles [°] [values are from (*R*)-(+)-**9**]: C1−C6 1.491(5), C6−C7 1.333(5), C6−C8 1.471(5), C8−C9 1.362(4), C9−C10 1.477(5), C9−N1 1.408(4), N1−C15 1.455(4), N1−C16 1.481(4), C16−C17 1.526(5), C16−C18 1.525(5); C1−C6−C7 117.2(3), C1−C6−C8 122.3(3), C7−C6−C8 120.5(3), C6−C8−C9 129.0(3), C8−C9−C10 124.1(3), C8−C9−N1 121.4(3), C10−C9−N1 114.2(3), C9−N1−C15 117.9(3), C9−N1−C16 119.6(3), C15−N1−C16 114.1(3), N1−C16−C17 111.1(3), N1−C16−C18 109.3(3), C17−C16−C18 115.2(3)

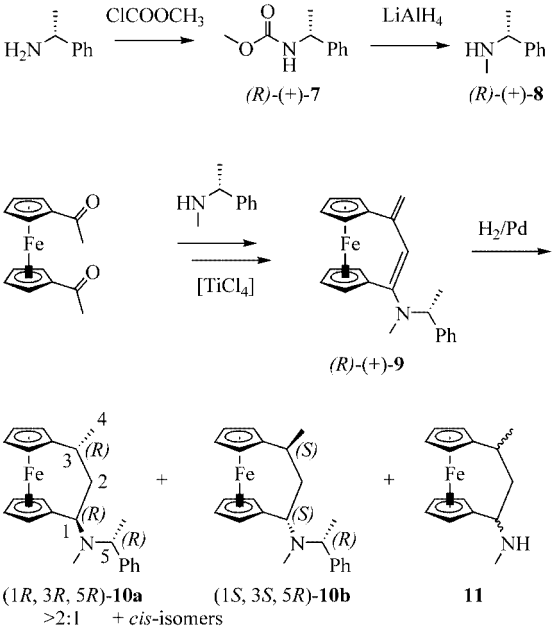
(*R*)-**9** is almost undistorted. The Cp(centroid)−Fe−Cp(centroid) angle amounts to 171.9°. Both Fe−C1/C10 [*ipso*-C(Cp)] linkages [2.001(4), 1.995(3) Å] are slightly shorter than the adjacent proximal Fe−CH(Cp) distances [ranging between 2.017(3) and 2.037(3) Å], which are in turn slightly shorter than the distal Fe−C(Cp) bonds [range: 2.045(3) Å for Fe−C4 to 2.062(4) Å for Fe−C12]. The substituted 1-aminobutadienediyl unit that bridges between the pair of Cp ligands in (*R*)-**9** is planar and features the expected bond alternation sequence[14] [C1−C6 1.491(5) Å, C6−C7 1.333(5) Å, C6−C8 1.471(5) Å, C8−C9 1.362(4) Å, C9−C10 1.477(5) Å, see Figure 2]. The bond angles inside the [3]ferrocenophane bridge amount to 122.3(3)° (C1−C6−C8), 129.0(3)° (C6−C8−C9), and 124.1(3)° (C8−C9−C10), which indicates a rather unstrained situation. The connecting C9−N bond is found at 1.408(4) Å, and the sum of the bonding angles at the nitrogen atom is 351.6°.[15]

The ^{1}H NMR spectrum of compound **9** shows the expected split signals of the butadienediyl $=CH_2$ terminus (δ = 4.99, 4.62 ppm; $^2J_{H,H}$ = 2.5 Hz) and a singlet of the corresponding central =CH− butadienediyl methine-H (δ = 5.52 ppm). The attached chiral amino substituents make the C_5H_4 methine CH groups pairwise diastereotopic. This is clearly resolved for the 2-H/5-H (δ = 4.30/4.29 ppm) and 2′-H/5′-H (δ = 4.35/4.32 ppm) pairs but not for their adjacent "distal" CH moieties.

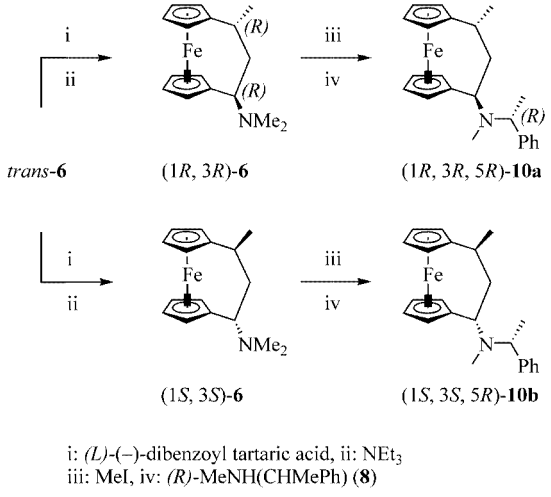
The catalytic hydrogenation of (*R*)-(+)-**9** was carried out in THF at room temperature and an atmospheric pressure of hydrogen in the presence of a heterogeneous Pd/C catalyst (Scheme 2). Workup after a typical reaction time of 2 h gave a complicated mixture of products. Since we had prepared the expected hydrogenation products separately as pure isomers (see below) it was possible to positively identify the major components of the mixture as the two saturated [3]ferrocenophane derivatives (1*R*,3*R*,5*R*)-**10a** and (1*S*,3*S*,5*R*)-**10b** (both of the *trans* series) and the product *trans*-**11**, which was derived from the *trans*-**10** compounds by hydrogenolytic removal of the benzylic-type "protective" group at the nitrogen atom.[16] In addition, there were several other [3]ferrocenophane products, probably the corresponding *cis* isomers or compounds derived from them. Most significantly, the ratio of the major products (1*R*,3*R*,5*R*)-**10a**/(1*S*,3*S*,5*R*)-**10b** was found as < 2:1. This meant that a significant enrichment had not been achieved in either of the expected diastereomers. Therefore, we decided to pursue other ways of preparing the diastereomerically and enantiomerically pure [3]ferrocenophanylamines.

Resolution of the trans-6 Enantiomers by Dibenzoyltartrate Salt Formation

The separation of the enantiomers of chiral (aminoalkyl)ferrocenes had previously been achieved by resolution via L- or D-*O*,*O*′-dibenzoyltartrate salt formation.[17] We therefore treated the racemate of the dimethylamino-substituted [3]ferrocenophane *trans*-**6** with L(−)-*O*,*O*′-dibenzoyltartaric acid. Salt formation in refluxing methanol followed by crystallization gave two fractions, a solid enriched in the dibenzoyltartrate of (1*R*,3*R*)-**6**, and a mother liquor that contained an excess of the respective salt of (1*S*,3*S*)-**6** (see Scheme 3). The resolution procedure was repeated once. The combined fractions of the respective enriched diastereomeric salts were then treated with excess triethylamine to liberate the free bases of **6**. The enantiomerically enriched compounds were obtained in almost equal amounts (total yield: 46%) and they are equally enriched as judged from their optical rotations {found: enriched (1*R*,3*R*)-**6**: $[\alpha]_D^{20}$ = +71; enriched (1*S*,3*S*)-**6**: $[\alpha]_D^{20}$ = −72}. The enantiomeric excess that was actually achieved by the dibenzoyltartrate resolution procedure was determined by converting samples of the enriched (1*R*,3*R*)-**6** material to their diastereomeric amine derivatives (1*R*,3*R*,5*R*)-**10** and (1*S*,3*S*,5*R*)-**10**, respectively, by an amine exchange reaction with (*R*)-methyl(1-phenylethyl)amine, subsequent to quat-



Scheme 2



Scheme 3

ernization with methyl iodide.[18] The ^{1}H NMR spectroscopic analysis showed the presence of a ca. 9:1 ratio of the (1*R*,3*R*,5*R*)-**10**/(1*S*,3*S*,5*R*)-**10** diastereoisomers in the resulting reaction mixture. The isolated product featured an optical rotation of $[\alpha]_D^{20} = +108$. We will see later that the pure (1*R*,3*R*,5*R*)-**10a** isomer has an optical rotation of $[\alpha]_D^{20} = +129$. Thus, from these measurements we must conclude that the resolution of *trans*-**6** via L(−)-*O*,*O*′-dibenzoyltartrate salt formation has resulted in a ca. 80% *ee* of (1*R*,3*R*)-**6** and (1*S*,3*S*)-**6**, respectively.

To achieve an independent absolute stereochemical assignment the partially resolved isolated complex (1*R*,3*R*)-**6** was treated with L-tartaric acid to form the respective salt **12** [i.e. L-tartrate·(1*R*,3*R*)-**6**], and the corresponding ca. 80% enantiomerically enriched (1*S*,3*S*)-**6** sample was treated with D-tartaric acid to give the salt *ent*-**12** [i.e. D-tartrate·(1*S*,3*S*)-**6**]. Single crystals of each of these independently prepared salts were obtained from methanol into which diethyl ether vapor was allowed to diffuse. The X-ray crystal structure analyses of the two sets of crystals confirmed the structural assignments to be correct (see Figure 3).

Inside the [L-tartrate·(1*R*,3*R*)-**6**] salt (**12**), the substituted symmetry-equivalent [3]ferrocenophane units attain a very typical conformation. The C8 methylene group is characteristically placed outside the C1−C6/C9−C13 plane, so that the substituents at the saturated C3 bridge [C1−C6 1.515(3), C6−C8 1.546(4), C8−C9 1.537(3), C9−C10 1.502(3) Å; C1−C6−C8 112.6(2), C6−C8−C9 112.5(2), C8−C9−C10 113.9(2)°] have become oriented pseudo-axially (CH_3 at C6) or pseudo-equatorially (NMe_2 at C9).[10] The corresponding dihedral angles of the [3]ferrocenophane framework amount to 63.8(3)° (C1−C6−C8−C9) and −79.0(2)° (C6−C8−C9−C10). The respective substituent positions at this framework are characterized by dihedral angles of −63.6(3)° (C7−C6−C8−C9) and 153.1(2)° (C6−C8−C9−N1). The C9−N1 bond length is 1.515(3) Å. The sum of C−N−C bonding angles at N1 is only 336.0°, which indicates that the amino nitrogen atom is protonated and connected to the tartrate oxygen O20 in the crystal by means of a hydrogen bond (N1−O20 distance 2.707Å). The tartrate dianion is bridging between a pair of protonated enantiomeric (dimethylamino)[3]ferrocenophane units. The tartrate conformation is as expected with the $-CO_2-$ groups arranged *antiperiplanar* (C18−C21−C21*−C18* −157.8(3)°] and the −OH substituents *gauche* (θ O22−C21−C21*−O22* −53.2(3)°].

Resolution of the Amino[3]ferrocenophanes by Separation of Covalent Diastereomeric Derivatives

It is well established that amine exchange by a suitable nucleophile at the α-carbon position at the ferrocene proceeds in a sequential two-step pathway with a neighboring group participation of the Fe metal center to result in overall stereochemical retention.[18,19] Early work by the Dijon group[3] supported by recent work e.g. by Weissensteiner et al.[4] has shown that this double inversion pathway also governs the stereochemical outcome of the respective substitution reactions at the [3]ferrocenophane framework.[11] We have therefore quaternized the (dimethylamino)[3]ferrocenophane system **6** by treating it with methyl iodide and then with a slight excess of the secondary amine (*R*)-methyl(1-phenylethyl)amine [(*R*)-**8**].[13] The amine exchange reaction was complete after 40 h of refluxing in acetonitrile in the presence of potassium carbonate. The mixture of the diastereomeric products (1*R*,3*R*,5*R*)-**10a** and (1*S*,3*S*,5*R*)-**10b**

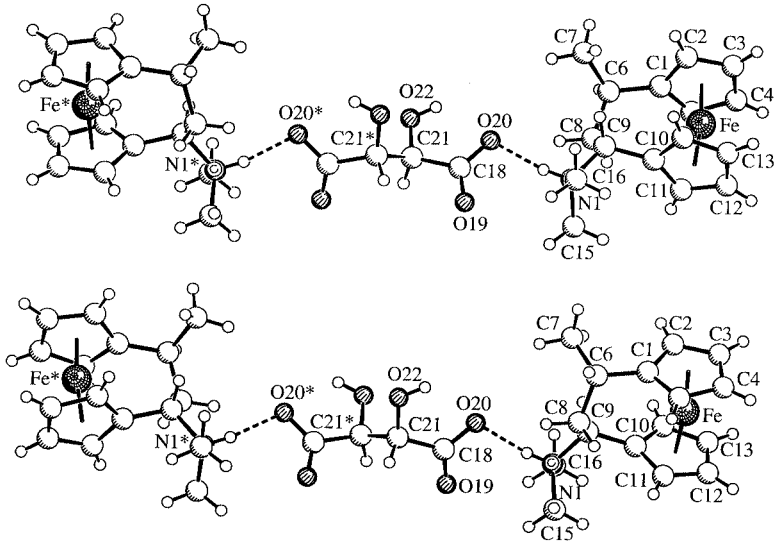


Figure 3. Views of the molecular structures of the independently prepared enantiomeric L-tartrate salt of (1*R*,3*R*)-**6** (**12**, top) and the D-tartrate salt of (1*S*,3*S*)-**6** (*ent*-**12**, bottom); selected bond lengths [Å] and angles [°] of the L-tartrate-derived enantiomer **12**: C1−C6 1.515(3), C6−C7 1.526(4), C6−C8 1.546(4), C8−C9 1.537(3), C9−C10 1.503(3), C9−N1 1.515(3), N1−C15 1.486(3), N1−C16 1.490(3), C18−O19 1.242(4), C18−O20 1.264(3), C18−C21 1.528(3), C21−C21* 1.524(5), C21−O22 1.412(3); C1−C6−C7 112.3(3), C1−C6−C8 112.6(2), C7−C6−C8 111.5(2), C6−C8−C9 112.5(2), C8−C9−C10 113.9(2), C8−C9−N1 110.6(2), C10−C9−N1 112.5(2), C9−N1−C15 114.8(2), C9−N1−C16 111.1(2), C15−N1−C16 110.1(2), O19−C18−O20 126.3(3), O19−C18−C21 117.6(3), O20−C18−C21 116.0(2), C18−C21−C21* 111.7(3), C18−C21−O22 113.0(2), O22−C21−C21* 111.7(2)

was obtained in a near to quantitative yield. Chromatographic separation of the diastereoisomers was achieved by column chromatography on silica gel using a mixture of cyclohexane, THF, and ethyl acetate in a ratio of 34:5:1 as an eluent. The two *trans* isomers [R_f = 0.83 for (1*S*,3*S*,5*R*)-**10a**;R_f = 0.74 for (1*R*,3*R*,5*R*)-**10b**] were clearly separated from each other and from residual reagent [(*R*)-**8**: R_f = 0.30]. The respective minor *cis* isomers were apparently lost during the separation and workup procedure; they could not be recovered. Subsequent recrystallization from diethyl ether gave the pure (1*R*,3*R*,5*R*)-**10a** and (1*S*,3*S*,5*R*)-**10b** isomers each in almost equal quantities (ca. 2 g, 66% yield). Their respective enantiomers were prepared analogously by amine exchange from **6** and the enantiomeric amine reagent (*S*)-**8** and the diastereoisomers *ent*-**10a** (1*S*,3*S*,5*S*) and *ent*-**10b** (1*R*,3*R*,5*S*) were separated accordingly. The (1*R*,3*R*,5*R*)-**10a** diastereomer is characterized by an optical rotation of $[\alpha]_D^{20}$ = +129 ($c = 4 \times 10^{-3}$ g mL^{-1}, CH_3CN), the (1*S*,3*S*,5*R*)-**10b** diastereomer by $[\alpha]_D^{20}$ = −49 ($c = 4 \times 10^{-3}$ g mL^{-1}, CH_3CN). Figure 4 shows the CD curves of the enantiomeric pair of the complexes **10b** (1*S*,3*S*,5*R*) and *ent*-**10b** (1*R*,3*R*,5*S*).

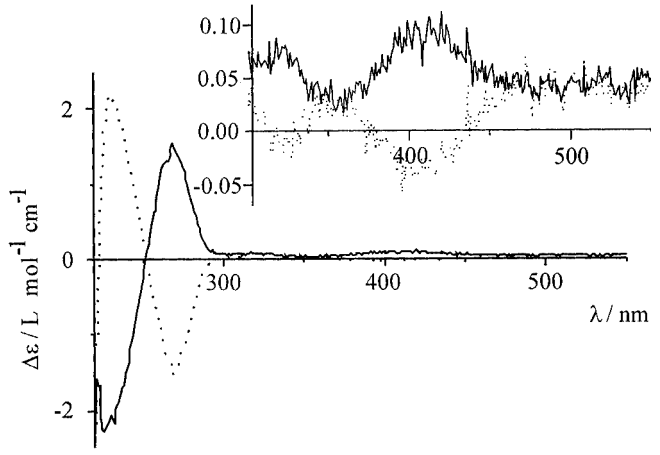


Figure 4. CD spectra of the enantiomeric pair of the complexes **10b** (solid line, 8×10^{-5} g mL^{-1}) and *ent*-**10b** (dotted line, 8×10^{-5} g mL^{-1}) in CH_3CN

The overall pattern of the NMR spectra of **10a** and **10b** are similar although distinctly different in detail. The ^{1}H NMR spectroscopic features of the 3-CH_3 group occur at δ = 0.91 (**10a**) and 1.16 (**10b**) ppm, respectively [corresponding ^{13}C NMR signals at δ = 16.8 (**10a**) and 17.3 (**10b**) ppm]. The 1-H, 2-H/H′ and 3-H signals of **10a** were found at δ = 3.39 (^{13}C: δ = 52.8 ppm), 2.55, 1.92 (^{13}C: δ = 47.9 ppm), and 2.65 ppm, whereas the corresponding **10b** NMR resonances were observed at δ = 3.57 (^{13}C: δ = 52.4 ppm), 2.42, 2.11 (^{13}C: δ = 45.6 ppm), and 2.76 ppm. Also, the NCH_3 (**10a**: δ = 2.25/33.8 ppm; **10b**: δ = 2.14/34.5 ppm) and the 5-CH_3 resonances inside the amino substituent (**10a**: δ = 1.24 ppm; **10b**: δ = 1.30 ppm) are sufficiently different to allow for an easy determination of the diastereomeric purity of the obtained samples. Within the limits of the 600 MHz ^{1}H NMR spectroscopic detection the isolated **10a** and **10b** diastereoisomers were > 99% isomerically pure. A close to complete isomeric separation was thus achieved (see Figure 5 for an illustration).

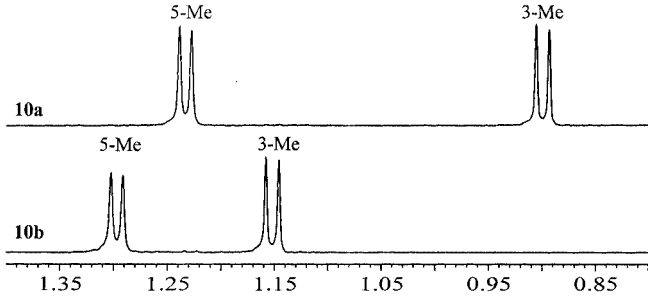


Figure 5. A comparison of the 3-CH_3 and 5-CH_3 ^{1}H NMR region of the (1*R*,3*R*,5*R*)-**10a** and (1*S*,3*S*,5*R*)-**10b** diastereoisomers isolated after chromatographic separation and recrystallization from diethyl ether

The absolute stereochemical assignment was again secured by X-ray diffraction. Single crystals were obtained from all stereoisomers (i.e. **10a**, *ent*-**10a**, **10b**, and *ent*-**10b**). Figure 6 shows the molecular structures of the enantiomeric pairs of both diastereoisomers.

The structural features of the two diastereomers are very similar. This may be illustrated by a comparison of some typical structural parameters of the [3]ferrocenophane frameworks of the complexes **10a** and *ent*-**10b** (values in parentheses), that both contain an (*R*)-configurated methyl(1-phenylethyl)amino substituent. The complexes feature almost identical bond lengths and angles of the central core, e.g. C1−C6 1.511(2) [1.508(2) Å], C6−C8 1.543(2) [1.549(2) Å], C8−C9 1.538(3) [1.545(2) Å], C9−N1 1.486(2) [1.487(2) Å], C9−C10 1.523(2) Å [1.511(2) Å]; C1−C6−C8 112.6(2) [112.8(1)°], C1−C6−C7 112.4(2) [112.2(1)°], C7−C6−C8 111.9(2) [112.1(1)°], C6−C8−C9 115.1(2) [114.3(1)°], N1−C9−C10 115.7(1) [115.8(1)°], N1−C9−C8 109.2(1)° [109.5(1)°]. However, there are a few conformational differences between the diastereomers with regard to the orientation of the methyl(1-phenylethyl)amino substituent. In **10a**, the phenyl group is rotated away from the central [3]ferrocenophane framework, whereas in *ent*-**10b** it is the adjacent methyl substituent that is rotated away. Typically this can be expressed by the characteristic differences in the C15−N1−C16−C17 dihedral angles of **10a** [−43.9(2)°] and *ent*-**10b** [179.6(2)°]. The remaining dihedral angles around the substituted nitrogen atom are again quite similar in both complexes, e.g. C10−C9−N1−C16 74.4(2) (**10a**), −65.7(2) (*ent*-**10b**); C9−N1−C16−C18: 67.7(2) (**10a**), −173.4(1) (*ent*-**10b**); C10−C9−N1−C15: −55.1(2) (**10a**), 59.3(2)° (*ent*-**10b**).

Conversion of the Enantiomerically Pure [3]Ferrocenophanes 10: Removal of the Chiral Auxiliary

We anticipated that the optically active systems **10** could be directly employed in the synthesis of chiral chelate ligands such as **3** in the enantiomerically pure form.[2a,11,20] However, it turned out that the specific systems **10** proved to be rather unreactive. Directed *ortho*-metalation[2,18] of

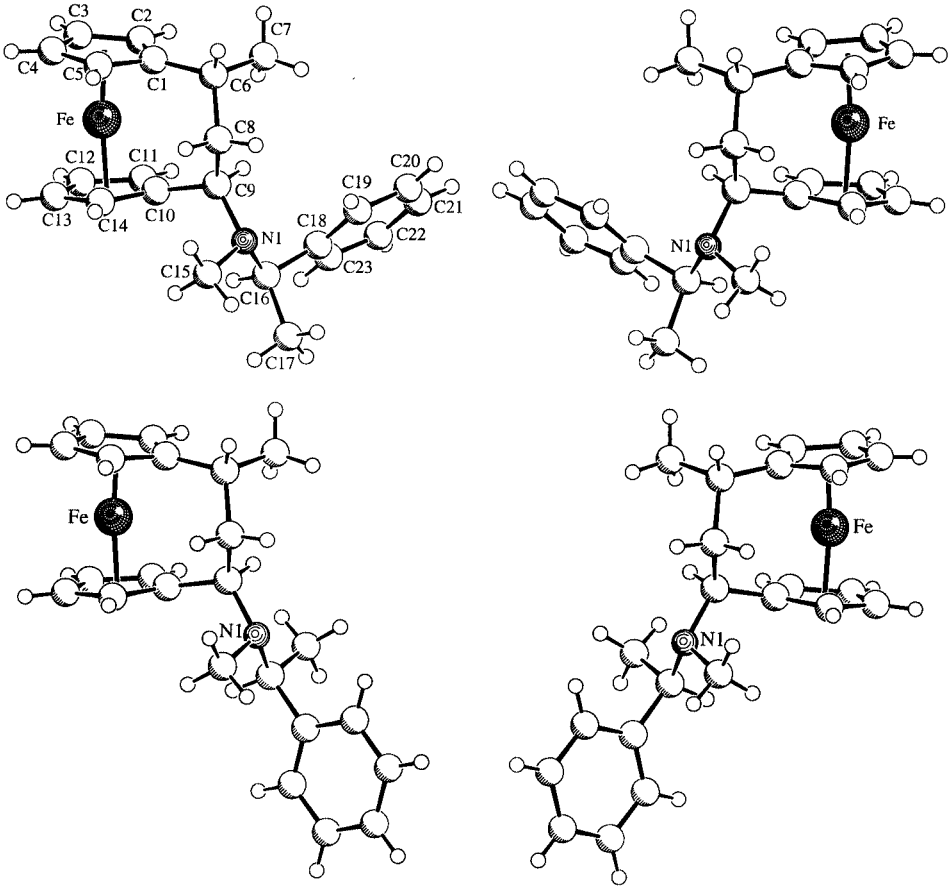


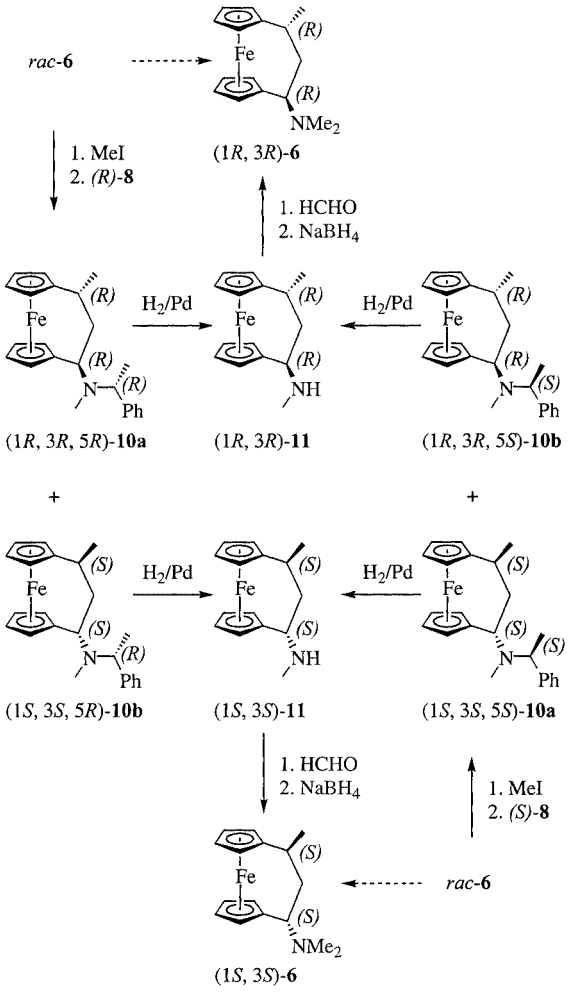
Figure 6. A comparison of the molecular geometries of the enantiomeric pairs (**10**/*ent*-**10**) of the diastereomers **10a** and **10b** [top left: **10a** (1*R*,3*R*,5*R*); top right: *ent*-**10a** (1*S*,3*S*,5*S*); bottom left: **10b** (1*R*,3*R*,5*S*); bottom right: *ent*-**10b** (1*S*,3*S*,5*R*)] (with unsystematical atom numbering scheme)

the adjacent Cp ring was unsuccessful. Moreover, the compounds **10** turned out to be unsuited for amine versus external nucleophile exchange, at least under the various conditions that we tried.

We therefore had to take a short detour to convert the complexes **10** into established building blocks for the synthesis of chiral [3]ferrocenophane-based chelate ligand systems. This was achieved by catalytic hydrogenolysis (see Scheme 4). The methyl(1-phenylethyl)amino substituent in this respect behaved as a typical benzylic amine.[16] Catalytic hydrogenolysis at ambient conditions in methanol (90 min) selectively removed the −CHMePh substituent from the nitrogen atom to yield the product **11** (isolated in ca. 90% yield). It shows the typical ^{1}H NMR spectroscopic features of the *trans*-1,3-disubstituted [3]ferrocenophane system with the framework hydrogen resonances appearing at δ = 3.28 (1-H), 2.00 (2-H$_{exo}$), 2.20 (2-H$_{endo}$) and 2.50 (3-H) ppm. The observed set of coupling constants [^3J(1-H,2-H$_{exo}$) = 3.0, ^3J(1-H,2-H$_{endo}$) = 8.0, ^3J(2H$_{exo}$,3-H) = 7.5, ^3J(2-H$_{endo}$,3-H) = 3.1, ^2J(2-H$_{exo}$,2-H$_{endo}$) = 13.6 Hz] shows that the 3-CH$_3$ group [δ = 1.21 ppm; $^3J_{H,H}$ = 7.3 Hz] attains a pseudo-axial orientation, whereas the NHCH$_3$ substituent is placed pseudo-equatorially at the non-planar saturated [3]ferrocenophane framework.

This was confirmed by X-ray diffraction. Single crystals of each of the enantiomers (1*R*,3*R*)-**11** and (1*S*,3*S*)-**11** were obtained from diethyl ether. Figure 7 shows a view of both structures. They feature the typical arrangement of the non-planar three-carbon containing bridge with the 3-CH$_3$ and 1-NH(CH$_3$) substituents in a *trans* position to one another. In the crystal the NHCH$_3$ group adopts a conformation that leads to maximum extension of the C6−C7−C8−N9−C16 chain (see Figure 7). The carbon−nitrogen bond lengths were found at 1.475(3) (C9−N1) and 1.462(3) Å (N1−C15); the C15−N1−C9 angle amounts to 113.3(2)°.

Each of the enantiomers of **11** was then subsequently *N*-methylated by treatment with formaldehyde/NaBH$_4$ (see Scheme 4) to yield the enantiomers (1*R*,3*R*)-**6** {$[\alpha]_D^{20}$ = +86 (c = 2 × 10^{-3} g mL^{-1}, CH$_3$CN)} and (1*S*,3*S*)-**6** {$[\alpha]_D^{20}$ = −85 (c = 2 × 10^{-3} g mL^{-1}, CH$_3$CN)} almost quantitatively. Their CD spectra are shown in Figure 8. The enantiomers (1*R*,3*R*)-*trans*-**6** and (1*S*,3*S*)-*trans*-**6** were thus prepared in a 5-step synthesis (plus one chromatographic separation), starting from 1,1′-diacetylferrocene and obtained in an overall yield of ca. 23% (out of a possible 50%). We will now use these compounds as building blocks for the preparation of optically active [3]ferrocenophane-derived



Scheme 4

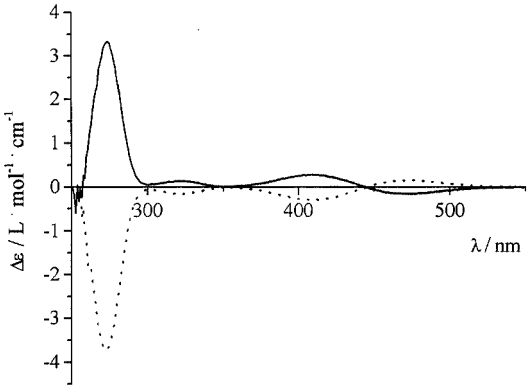


Figure 8. CD spectra of (1*R*,3*R*)-**6** (solid line, 4×10^{-4} g mL^{-1}) and (1*S*,3*S*)-**6** (dotted line, 4×10^{-4} g mL^{-1}) in CH_3CN

chelate ligands to study their potential for asymmetric catalysis.[11,21]

Experimental Section

General Methods: All reactions were carried out under dry argon in Schlenk-type glassware or in a glove-box. Solvents were dried and distilled prior to use. NMR spectra were recorded with a Varian UNITY*plus* 600 (^{1}H: 599.9 MHz; ^{13}C: 150.8 MHz) spectrometer. The atom numbering scheme used for the description of the NMR spectra in the Exp. Sect. deviates from the IUPAC nomenclature used in the text − it is equivalent as depicted in Figures 2, 3, 6, and 7. Most assignments were confirmed by 2D NMR spectra,[22] for details see the Supporting Information. The following instruments were used for additional physical characterization: IR spectroscopy: Nicolet 5DXC FT-IR spectrometer; melting points: DSC 2010 (TA instruments); elemental analyses: Foss Heraeus CHN-O-Rapid; optical rotation: Perkin−Elmer polarimeter 351; circular dichroism: Jobin Yvon-Spex CD-6 dichro-

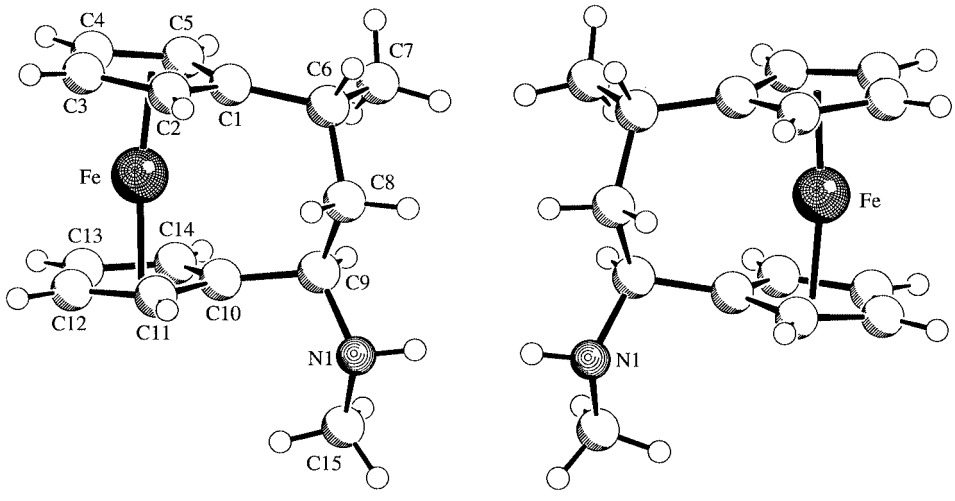


Figure 7. Molecular geometries of the isolated enantiomers (1*R*,3*R*)-**11** (left) and (1*S*,3*S*)-**11** (right) (with unsystematical atom numbering scheme); selected bond lengths [Å] and angles [°] [from the solution of the (1*R*,3*R*)-**11** structure]: C1−C6 1.523(3), C6−C7 1.527(4), C6−C8 1.537(3), C8−C9 1.530(3), C9−C10 1.514(2), C9−N1 1.475(3), N1−C15 1.462(3); C1−C6−C7 112.1(2), C1−C6−C8 112.1(2), C7−C6−C8 112.1(2), C6−C8−C9 116.4(2), C8−C9−C10 113.4(2), C8−C9−N1 108.4(2), C10−C9−N1 110.3(2), C9−N1−C15 113.3(2)

graph. The following starting materials were prepared according to literature procedures: 1,1′-diacetylferrocene (**4**),[6] ferrocenophane **6**,[9] carbamate **7**,[13] methyl(1-phenylethyl)amine (**8**).[13]

X-ray Diffraction: Data sets were collected with a Nonius KappaCCD diffractometer, equipped with a rotating anode generator Nonius FR591. Programs used: data collection COLLECT (Nonius B.V., **1998**), data reduction Denzo-SMN,[23] absorption correction SORTAV[24], structure solution SHELXS-97,[25] structure refinement SHELXL-97,[26] graphics SCHAKAL.[27] CCDC-205072 to -205081 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Preparation of 6 (from 11): A solution of (1*S*,3*S*)-**11** (100 mg, 0.37 mmol) in MeOH (4 mL) was cooled to 4 °C and treated with formaldehyde solution (4 mL, 37% in MeOH). After stirring at this temperature for 10 min, $NaBH_4$ (233 mg, 6.2 mmol) was added in small portions. The reaction mixture was stirred at room temperature for 1 h and then heated to 75 °C for 18 h. After removal of the solvent under reduced pressure, the residue was extracted with water/CH_2Cl_2. The organic phases were washed with water and brine and dried with $MgSO_4$. Evaporation of the solvent yielded (1*S*,3*S*)-**6** as a yellow solid (104 mg, 97%). $[\alpha]_D^{20} = -85$ ($c = 2 \times 10^{-3}$ g mL^{-1}, CH_3CN). CD: $\Delta\varepsilon$ (λ_{max}) = −3.70 (274), −0.15 (326), −0.28 (412), +0.15 (476) ($c = 4 \times 10^{-4}$ g mL^{-1}, CH_3CN). $C_{16}H_{21}FeN$ (283.20): calcd. C 67.86, H 7.47, N 4.95; found C 67.78, H 7.32, N 4.84. (1*R*,3*R*)-**6** was prepared analogously starting from (1*R*,3*R*)-**11** (443 mg, 1.65 mmol), yield: 453 mg (97%). $[\alpha]_D^{20} = +86$ ($c = 2 \times 10^{-3}$ g mL^{-1}, CH_3CN). CD: $\Delta\varepsilon$ (λ_{max}) = +3.33 (274), +0.14 (326), +0.28 (412), −0.15 (476) ($c = 4 \times 10^{-4}$ g mL^{-1}, CH_3CN). $C_{16}H_{21}FeN$ (283.20): calcd. C 67.86, H 7.47, N 4.95; found C 67.62, H 7.25, N 4.93.

Synthesis of 9: A suspension of 1,1′-diacetylferrocene (**4**) (4.0 g, 14.8 mmol) and either (*S*)- or (*R*)-**8** (35 mL, 240 mmol) in pentane (200 mL) was cooled to 4 °C. Over a period of 20 min a solution of $TiCl_4$ (2.0 mL, 18.2 mmol) in pentane (90 mL) was added dropwise. Afterwards, the reaction mixture was stirred at room temperature overnight. The resulting deep red suspension was filtered through Celite and the solvent removed in vacuo. Unchanged amine **8** could be regained by vacuum condensation of the product at 72 °C. The enantiomers (*S*)-**9** and (*R*)-**9** were each obtained as red to brown solids [(*S*)-**9**: 1.08 g, 20%; (*R*)-**9**: 1.03 g, 19%], m.p. 75 °C (DSC). IR (KBr): $\tilde{\nu}$ = 3855 (m), 3757 (m), 3085 (m), 2980 (s), 2868 (w), 2796 (w), 2380 (w), 1598 (vs), 1479 (vs), 1275 (vs), 1098 (vs), 1019 (vs), 907 (s), 802 (vs), 696 (vs) cm^{-1}. Crystals suitable for X-ray structure analysis were grown by slow diffusion of pentane into an Et_2O solution. ^{1}H NMR (599.9 MHz, CD_2Cl_2, 25 °C): δ = 1.35 [d, $^3J_{H,H}$ = 6.9 Hz, 3 H, C(17)−H], 2.47 [s, 3 H, C(15)−H], 4.13 [m, 2 H, C(2−4)−H], 4.21 [m, 2 H, C(11−14)−H], 4.28 [m, 1 H, C(2−4)−H], 4.29 [m, 1 H, C(2−4)−H], 4.31 [m, 1 H, C(11−14)−H], 4.34 [m, 1 H, C(11−14)−H], 4.64 [d, $^2J_{H,H}$ = 2.5 Hz, 1 H, C(7)−H$_{exo}$], 4.82 [q, $^3J_{H,H}$ = 6.9 Hz, 1 H, C(16)−H], 4.98 [d, $^2J_{H,H}$ = 2.5 Hz, 1 H, C(7)−H$_{endo}$], 5.50 [s, 1 H, C(8)−H], 7.21 (m, 1 H, Ph$_{para}$), 7.23 (m, 2 H, Ph$_{ortho}$), 7.30 (m, 2 H, Ph$_{meta}$) ppm. ^{13}C{^{1}H} NMR (150.8 MHz, CD_2Cl_2, 25 °C): δ = 15.6 [C(17)], 32.1 [C(15)], 56.4 [C(16)], 70.0 [C(2−4)], 70.1 [C(2−4)], 70.3 [C(11−14)], 70.4 [C(2−4)], 70.6 [C(2−4)], 71.8 [C(11−14)], 71.9 [C(11−14)], 84.2 [C(10)], 90.5 [C(1)], 109.0 [C(7)], 109.2 [C(8)], 127.0 (Ph$_{para}$), 127.3 (Ph$_{ortho}$), 128.4 (Ph$_{meta}$), 142.8 [C(6/9)], 142.9 (Ph$_{ipso}$), 146.2 [C(6/9)] ppm. (*S*)-**9**: $[\alpha]_D^{20} = -43$ ($c = 2 \times 10^{-3}$ g mL^{-1}, $CHCl_3$); (*R*)-**9**: $[\alpha]_D^{20} = +44$ ($c = 2 \times 10^{-3}$ g mL^{-1}, $CHCl_3$). CD: (*S*)-**9**: $\Delta\varepsilon$ (λ_{max}) = −4.56 (284), +0.30 (348), −0.09 (444) ($c = 8 \times 10^{-5}$ g mL^{-1}, CH_3CN); (*R*)-**9**: $\Delta\varepsilon$ (λ_{max}) = +6.37 (284), −0.37 (348), +0.11 (444) ($c = 8 \times 10^{-5}$ g mL^{-1}, CH_3CN). $C_{23}H_{23}FeN$ (369.29): calcd. C 74.81, H 6.28, N 3.79; (*S*)-**9**: found C 74.32, H 6.50, N 3.79; (*R*)-**9**: found C 74.41, H 6.26, N 3.71.

X-ray Crystal Structure Analysis of (*R*)-(+)-9: Empirical formula $C_{23}H_{23}FeN$, M = 369.29, red crystal, 0.50 × 0.20 × 0.10 mm, a = 6.216(1), b = 12.121(1), c = 23.536(1) Å, V = 1773.3(3) Å^3, $\rho_{calcd.}$ = 1.383 g cm^{-3}, μ = 8.55 cm^{-1}, empirical absorption correction (0.675 ≤ T ≤ 0.919), Z = 4, orthorhombic, space group $P2_12_12_1$ (no. 19), λ = 0.71073 Å, T = 198 K, ω and φ scans, 8928 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.68 Å^{-1}, 4355 independent (R_{int} = 0.055) and 3156 observed reflections [$I \geq 2\sigma(I)$], 228 refined parameters, R = 0.049, wR^2 = 0.092, Flack parameter 0.01(2), max. residual electron density 0.44 (−0.43) e·Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

X-ray Crystal Structure Analysis of (*S*)-(−)-9: Empirical formula $C_{23}H_{23}FeN$, M = 369.29, yellow crystal, 0.30 × 0.07 × 0.03 mm, a = 6.201(1), b = 12.119(1), c = 23.604(1) Å, V = 1773.8(3) Å^3, $\rho_{calcd.}$ = 1.383 g cm^{-3}, μ = 8.54 cm^{-1}, empirical absorption correction (0.784 ≤ T ≤ 0.975), Z = 4, orthorhombic, space group $P2_12_12_1$ (no. 19), λ = 0.71073 Å, T = 198 K, ω and φ scans, 12989 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.66 Å^{-1}, 4168 independent (R_{int} = 0.063) and 3222 observed reflections [$I \geq 2\sigma(I)$], 228 refined parameters, R = 0.051, wR^2 = 0.080, Flack parameter 0.02(2), max. residual electron density 0.51 (−0.26) e·Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

Preparation of 10. a) By Hydrogenation: The Pd/C catalyst (10 mg, 10% Pd) was added to a solution of (*R*)-**9** (200.0 mg, 0.54 mmol) in THF (40 mL). Hydrogenation was carried out at ambient pressure under vigorous stirring for 2 h. The reaction mixture was filtered through Celite and the solvent removed in vacuo. An orange oil (179.0 mg) was obtained which was identified to be a complex mixture of all possible isomers of **10** and **11**. **b) By Amine Exchange:** A solution of *rac-trans*-**6** (6.00 g, 21.2 mmol) in CH_3CN (120 mL) was treated with CH_3I (84 mL) and stirred at room temperature for 1 h. Excess CH_3I was then removed in vacuo. K_2CO_3 (6.44 g, 46 mmol), (*R*)-**8** (3.8 mL, 26 mmol) and CH_3CN (300 mL) were added to the obtained trimethylammonium salt. The mixture was heated to reflux for 40 h. After removal of the solvent in vacuo, the residue was suspended in pentane (100 mL). Filtration through Celite and concentration of the filtrate yielded the crude product as a mixture of diastereomers (6.90 g, 87%). Purification was achieved by column chromatography (SiO_2; cyclohexane/THF/ethyl acetate, 34:5:1). (1*R*,3*R*,5*R*)-**10a**: R_f = 0.74; (1*S*,3*S*,5*R*)-**10b**: R_f = 0.83. Furthermore, the products were recrystallized from Et_2O.

(1*R*,3*R*,5*R*)-10a: orange solid, 2.01 g (34%) isolated from 6.0 g of crude product; m.p. 87 °C (DSC). IR (KBr): $\tilde{\nu}$ = 3855 (m), 3750 (m), 3085 (m), 3019 (w), 2973 (s), 2927 (s), 2881 (s), 2855 (s), 2796 (s), 2361 (w), 1664 (m), 1558 (m), 1460 (vs), 1032 (vs), 815 (vs), 769 (vs), 696 (vs) cm^{-1}. Crystals suitable for X-ray structure analysis were grown from an Et_2O solution at −18 °C. ^{1}H NMR (599.9 MHz, CD_2Cl_2, 25 °C): δ = 0.91 [d, $^3J_{H,H}$ = 7.3 Hz, 3 H, C(7)−H], 1.24 [d, $^3J_{H,H}$ = 6.7 Hz, 3 H, C(17)−H], 1.92 [ddd, $^3J_{H,H}$ = 3.7, $^3J_{H,H}$ = 2.0, $^2J_{H,H}$ = 12.9 Hz, 1 H, C(8)−H$_{exo}$], 2.25 [s, 3 H, C(15)−H], 2.55 [ddd, $^3J_{H,H}$ = 11.4, $^3J_{H,H}$ = 4.0, $^2J_{H,H}$ = 12.9 Hz, 1 H, C(8)−H$_{endo}$], 2.65 [m, 1 H, C(6)−H], 3.39 [dd, $^3J_{H,H}$ = 11.4, $^3J_{H,H}$ = 1.8 Hz, 1 H, C(9)−H], 3.48 [q, $^3J_{H,H}$ = 6.7 Hz, 1 H, C(16)−H], 3.80 [m, 1 H, C(11−14)−H], 3.86 [m, 1 H,

C(2−5)−H], 3.97 [m, 1 H, C(2−5)−H], 4.00 [m, 1 H, C(11−14)−H], 4.02 [m, 1 H, C(2−5)−H], 4.09 [m, 1 H, C(2−5)−H], 4.11 [m, 1 H, C(11−14)−H], 4.25 [m, 1 H, C(11−14)−H], 7.25 (m, 1 H, Ph_{para}), 7.35 (m, 2 H, Ph_{meta}), 7.37 (m, 2 H, Ph_{ortho}) ppm. $^{13}C\{^1H\}$ NMR (150.8 MHz, CD_2Cl_2, 25 °C): δ = 16.8 [C(7)], 21.9 [C(17)], 28.2 [C(6)], 33.8 [C(15)], 47.9 [C(8)], 52.8 [C(9)], 62.5 [C(16)], 66.9 [C(2−5)], 68.2 [C(11−14)], 68.3 [C(11−14)], 68.4 [C(2−5)], 68.5 [C(2−5)], 69.1 [C(2−5)], 69.4 [C(11−14)], 72.1 [C(11−14)], 79.1 [C(10)], 93.3 [C(1)], 126.9 (Ph_{para}), 127.8 (Ph_{ortho}), 128.5 (Ph_{meta}), 146.8 (Ph_{ipso}) ppm. $[\alpha]_D^{20}$ = +129 ($c = 4 \times 10^{-3}$ g mL^{-1}, CH_3CN). CD: Δε (λ_{max}) = +1.19 (273), +0.12 (320), +0.21 (456) ($c = 8 \times 10^{-5}$ g mL^{-1}, CH_3CN). $C_{23}H_{27}FeN$ (373.32): calcd. C 74.00, H 7.29, N 3.75; found C 74.01, H 7.24, N 3.83.

(1*S*,3*S*,5*S*)-10a (= *ent*-10a): In an analogous procedure, starting from *rac-trans*-**6** (5.9 g, 20.8 mmol) in CH_3CN (120 mL), CH_3I (75 mL) followed by (*S*)-**8** (3.8 mL, 25 mmol) and K_2CO_3 (6.44 g, 46 mmol) in CH_3CN (200 mL), 1.28 g (16%) of an orange solid were isolated.

X-ray Crystal Structure Analysis of 10a: Empirical formula $C_{23}H_{27}FeN$, M = 373.32, yellow-orange crystal, 0.40 × 0.40 × 0.05 mm, a = 10.826(1), b = 8.042(1), c = 10.934(1) Å, β = 98.09(1)°, V = 942.5(2) Å^3, $\rho_{calcd.}$ = 1.315 g cm^{-3}, μ = 8.04 cm^{-1}, empirical absorption correction ($0.739 \le T \le 0.924$), Z = 2, monoclinic, space group $P2_1$ (no. 4), λ = 0.71073 Å, T = 198 K, ω and φ scans, 5778 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.66 Å^{-1}, 3776 independent (R_{int} = 0.030) and 3629 observed reflections [$I \ge 2\sigma(I)$], 229 refined parameters, R = 0.026, wR^2 = 0.065, Flack parameter −0.02(1), max. residual electron density 0.23 (−0.27) e·Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

X-ray Crystal Structure Analysis of *ent*-10a: Empirical formula $C_{23}H_{27}FeN$, M = 373.32, yellow crystal, 0.30 × 0.20 × 0.05 mm, a = 10.827(1), b = 8.029(1), c = 10.938(1) Å, β = 98.07(1)°, V = 941.4(2) Å^3, $\rho_{calcd.}$ = 1.317 g cm^{-3}, μ = 8.05 cm^{-1}, empirical absorption correction ($0.794 \le T \le 0.961$), Z = 2, monoclinic, space group $P2_1$ (no. 4), λ = 0.71073 Å, T = 198 K, ω and φ scans, 8282 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.67 Å^{-1}, 4038 independent (R_{int} = 0.029) and 3544 observed reflections [$I \ge 2\sigma(I)$], 229 refined parameters, R = 0.039, wR^2 = 0.075, Flack parameter −0.04(2), max. residual electron density 0.26 (−0.26) e·Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

(1*S*,3*S*,5*R*)-10b: Orange solid, 1.97 g (33%) isolated from 6.0 g of crude product; m.p. 88 °C (DSC). IR (KBr): ṽ = 3432 (w), 3086 (m), 2979 (vs), 2955 (s), 2842 (s), 2796 (s), 1975 (w), 1886 (w), 1820 (w), 1657 (w), 1599 (s), 1473 (vs), 1374 (s), 1242 (s), 1150 (s), 1080 (vs), 1032 (vs), 947 (s), 815 (vs), 703 (vs) cm^{-1}. Crystals suitable for X-ray structure analysis were grown from an Et_2O solution at −18 °C. ^1H NMR (599.9 MHz, CD_2Cl_2, 25 °C): δ = 1.16 [d, $^3J_{H,H}$ = 7.3 Hz, 3 H, C(7)−H], 1.30 [d, $^3J_{H,H}$ = 6.6 Hz, 3 H, C(17)−H], 2.11 [ddd, $^3J_{H,H}$ = 3.9, $^3J_{H,H}$ = 2.0, $^2J_{H,H}$ = 13.1 Hz, 1 H, C(8)−H_{exo}], 2.14 [s, 3 H, C(15)−H], 2.42 [ddd, $^3J_{H,H}$ = 11.3, $^3J_{H,H}$ = 3.8, $^2J_{H,H}$ = 13.1 Hz, 1 H, C(8)−H_{endo}], 2.76 [m, 1 H, C(6)−H], 3.57 [dd, $^3J_{H,H}$ = 11.3, $^3J_{H,H}$ = 2.0 Hz, 1 H, C(9)−H], 3.68 [q, $^3J_{H,H}$ = 6.6 Hz, 1 H, C(16)−H], 3.94 [m, 1 H, C(2−5)−H], 4.01 [m, 1 H, C(11−14)−H], 4.03 [m, 1 H, C(11−14)−H), 4.05 [m, 1 H, C(2−5)−H], 4.11 [m, 1 H, C(11−14)−H], 4.13 [m, 1 H, C(2−5)−H], 4.14 [m, 1 H, C(2−5)−H], 4.32 [m, 1 H, C(11−14)−H], 7.22 (m, 1 H, Ph_{para}), 7.31 (m, 2 H, Ph_{meta}), 7.36 (m, 2 H, Ph_{ortho}) ppm. $^{13}C\{^1H\}$ NMR (150.8 MHz, CD_2Cl_2, 25 °C): δ = 17.3 [C(7)], 18.0 [C(17)], 28.2 [C(6)], 34.5 [C(15)], 45.6 [C(8)], 52.4 [C(9)], 61.2 [C(16)], 67.2 [C(2−5)], 67.8 [C(11−14)], 68.2 [C(11−14)], 68.6 [C(2−5)], 68.6 [C(2−5)], 69.2 [C(2−5)], 69.4 [C(11−14)], 71.3 [C(11−14)], 82.7 [C(10)], 93.0 [C(1)], 126.8 (Ph_{para}), 127.8 (Ph_{ortho}), 128.4 (Ph_{meta}), 146.6 (Ph_{ipso}) ppm. $[\alpha]_D^{20}$ = −49 ($c = 4 \times 10^{-3}$ g mL^{-1}, CH_3CN). CD: Δε (λ_{max}) = +2.16 (228), −1.52 (269), −0.03 (320), −0.05 (408) ($c = 8 \times 10^{-5}$ g mL^{-1}, CH_3CN). $C_{23}H_{27}FeN$ (373.32): calcd. C 74.00, H 7.29, N 3.75; found C 73.97, H 7.37, N 3.78.

(1*R*,3*R*,5*S*)-10b (= *ent*-10b): In an analogous procedure, starting from *rac-trans*-**6** (5.9 g, 20.8 mmol) in CH_3CN (120 mL), CH_3I (75 mL) followed by (*S*)-**8** (3.8 mL, 25 mmol) and K_2CO_3 (6.44 g, 46 mmol) in CH_3CN (200 mL), 2.78 g (34%) of an orange solid were isolated.

X-ray Crystal Structure Analysis of 10b: Empirical formula $C_{23}H_{27}FeN$, M = 373.32, yellow crystal, 0.30 × 0.25 × 0.20 mm, a = 9.739(1), b = 8.135(1), c = 12.652(1) Å, β = 109.59(1)°, V = 944.4(2) Å^3, $\rho_{calcd.}$ = 1.313 g cm^{-3}, μ = 8.03 cm^{-1}, empirical absorption correction ($0.795 \le T \le 0.856$), Z = 2, monoclinic, space group $P2_1$ (no. 4), λ = 0.71073 Å, T = 198 K, ω and φ scans, 5835 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.68 Å^{-1}, 4060 independent (R_{int} = 0.042) and 3663 observed reflections [$I \ge 2\sigma(I)$], 229 refined parameters, R = 0.036, wR^2 = 0.083, Flack parameter 0.04(2), max. residual electron density 0.24 (−0.34) e·Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

X-ray Crystal Structure Analysis of *ent*-10b: Empirical formula $C_{23}H_{27}FeN$, M = 373.32, yellow crystal, 0.35 × 0.25 × 0.20 mm, a = 9.737(1), b = 8.135(1), c = 12.634(1) Å, β = 109.59(1)°, V = 942.8(2) Å^3, $\rho_{calcd.}$ = 1.315 g cm^{-3}, μ = 8.04 cm^{-1}, empirical absorption correction ($0.766 \le T \le 0.856$), Z = 2, monoclinic, space group $P2_1$ (no. 4), λ = 0.71073 Å, T = 198 K, ω and φ scans, 8847 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.67 Å^{-1}, 4119 independent (R_{int} = 0.030) and 3969 observed reflections [$I \ge 2\sigma(I)$], 229 refined parameters, R = 0.023, wR^2 = 0.057, Flack parameter −0.02(1), max. residual electron density 0.18 (−0.41) e·Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

Synthesis of 11: A suspension of (1*R*,3*R*,5*R*)-**10a** (245 mg, 0.65 mmol) and Pd/C catalyst (25 mg, 10% Pd) in MeOH (12.5 mL) was hydrogenated at 0.75 bar under vigorous stirring for 90 min. The reaction mixture was filtered through Celite and the solvent removed in vacuo to yield (1*R*,3*R*)-**11** as a yellow solid (161 mg, 91%), m.p. 99 °C (DSC). IR (KBr): ṽ = 3552 (sh), 3493 (sh), 3420 (s), 3236 (sh), 2972 (m), 1657 (m), 1617 (m), 1137 (m), 801 (m) cm^{-1}. Crystals suitable for the X-ray structure analysis were grown by slow evaporation of an Et_2O solution. ^1H NMR (599.9 MHz, $CDCl_3$, 25 °C): δ = 1.21 [d, $^3J_{H,H}$ = 7.3 Hz, 3 H, C(7)−H], 2.00 [ddd, $^3J_{H,H}$ = 3.0, $^3J_{H,H}$ = 7.5, $^2J_{H,H}$ = 13.6 Hz, 1 H, C(8)−H_{exo}], 2.20 [ddd, $^3J_{H,H}$ = 3.1, $^3J_{H,H}$ = 8.0, $^2J_{H,H}$ = 13.6 Hz, 1 H, C(8)−H_{endo}], 2.39 [s, 3 H, C(15)−H], 2.50 [ddd, $^3J_{H,H}$ = 3.1, $^3J_{H,H}$ = 7.3, $^3J_{H,H}$ = 7.5 Hz, 1 H, C(6)−H], 3.28 [dd, $^3J_{H,H}$ = 3.0, $^3J_{H,H}$ = 8.0 Hz, 1 H, C(9)−H], 3.99 [m, 2 H, C(2−5)−H, C(11−14)−H], 4.00 [m, 1 H, C(2−5)−H], 4.03 [m, 2 H, C(11−14)−H], 4.06 [m, 1 H, C(2−5)−H], 4.07 [m, 1 H, C(2−5)−H], 4.20 [m, 1 H, C(11−14)−H] ppm. $^{13}C\{^1H\}$ NMR (150.8 MHz, $CDCl_3$, 25 °C): δ = 19.4 [C(7)], 25.5 [C(6)], 35.0 [C(15)], 49.9 [C(8)], 53.0 [C(9)], 66.5 [C(11−14)], 66.9 [C(2−5)], 67.8 [C(2−5)/C(11−14)], 68.1 [C(11−14)], 68.2 [C(11−14)], 68.3 [C(2−5)], 69.0 [C(2−5)/C(11−14)], 69.2 [C(2−5)], 87.9 [C(10)], 91.5 [C(1)] ppm. (1*R*,3*R*)-**11**: $[\alpha]_D^{20}$ = +105 ($c = 2 \times 10^{-3}$ g mL^{-1}, CH_3CN). CD: Δε (λ_{max}) = +0.87 (275), −0.07 (334), +0.39 (416), −0.09 (483) ($c = 4 \times 10^{-4}$ g mL^{-1}, CH_3CN). $C_{15}H_{19}FeN$ (269.17): calcd. C 66.93, H 7.11, N 5.20; found C 66.75, H 6.97, N 5.13. The complex (1*S*,3*S*)-**11** was prepared analogously starting from

(793 mg, 1.12 mmol) of (1*S*,3*S*,5*R*)-**10b**, 720 mg (90%) isolated. $[\alpha]_D^{20} = -104$ ($c = 2 \times 10^{-3}$ g mL^{-1}, CH_3CN). CD: $\Delta\varepsilon$ (λ_{max}) = −0.86 (275), +0.09 (334), −0.38 (416), +0.09 (483) ($c = 4 \times 10^{-4}$ g mL^{-1}, CH_3CN). $C_{15}H_{19}FeN$ (269.17): calcd. C 66.93, H 7.11, N 5.20; found C 66.74, H 6.90, N 5.13.

X-ray Crystal Structure Analysis of (1*R*,3*R*)-11: Empirical formula $C_{15}H_{19}FeN$, $M = 269.17$, yellow crystal, 0.25 × 0.15 × 0.10 mm, $a = 7.420(1)$, $b = 10.017(1)$, $c = 8.255(1)$ Å, $\beta = 99.29(1)°$, $V = 605.5(1)$ Å^3, $\rho_{calcd.} = 1.476$ g cm^{-3}, $\mu = 12.20$ cm^{-1}, empirical absorption correction ($0.750 \le T \le 0.888$), $Z = 2$, monoclinic, space group $P2_1$ (no. 4), $\lambda = 0.71073$ Å, $T = 198$ K, ω and φ scans, 4068 reflections collected ($\pm h$, $\pm k$, $\pm l$), [(sinθ)/λ] = 0.66 Å^{-1}, 2503 independent ($R_{int} = 0.028$) and 2385 observed reflections [$I \ge 2\sigma(I)$], 159 refined parameters, $R = 0.026$, $wR^2 = 0.065$, Flack parameter 0.02(2), max. residual electron density 0.33 (−0.33) e·Å^{-3}, hydrogen atom at N1 from difference map, others calculated and all refined as riding atoms.

X-ray Crystal Structure Analysis of (1*S*,3*S*)-11: Empirical formula $C_{15}H_{19}NFe$, $M = 269.17$, yellow crystal, 0.30 × 0.30 × 0.20 mm, $a = 7.415(1)$, $b = 10.009(1)$, $c = 8.250(1)$ Å, $\beta = 99.26(1)°$, $V = 604.3(1)$ Å^3, $\rho_{calcd.} = 1.479$ g cm^{-3}, $\mu = 12.23$ cm^{-1}, empirical absorption correction ($0.711 \le T \le 0.792$), $Z = 2$, monoclinic, space group $P2_1$ (no. 4), $\lambda = 0.71073$ Å, $T = 198$ K, ω and φ scans, 3352 reflections collected ($\pm h$, $\pm k$, $\pm l$), [(sinθ)/λ] = 0.68 Å^{-1}, 2467 independent ($R_{int} = 0.030$) and 2349 observed reflections [$I \ge 2\sigma(I)$], 159 refined parameters, $R = 0.033$, $wR^2 = 0.088$, Flack parameter 0.00(2), max. residual electron density 0.50 (−0.62) e·Å^{-3}, hydrogen atom at N1 from difference map, others calculated and all refined as riding atoms.

(1*R*,3*R*)-11: The complex (1*R*,3*R*)-**11** was prepared analogously starting from (1*R*,3*R*,5*S*)-**10b** (1.00 g, 2.68 mmol), 0.65 g (91%) were isolated.

(1*S*,3*S*)-11: The complex (1*S*,3*S*)-**11** was prepared analogously starting from (1*S*,3*S*,5*S*)-**10a** (250 mg, 0.67 mmol), 175 mg (97%) were isolated.

Synthesis of 12: A solution of L-(−)-*O*,*O*′-dibenzoyltartaric acid (3.94 g, 11.0 mmol) in MeOH (21 mL) was heated to 60 °C and added to a solution of *rac*-*trans*-**6** (3.12 g, 11.0 mmol) in MeOH (11 mL) at this temperature. The mixture was heated to reflux for 1 h. Next, it was allowed to gradually cool to room temperature over the course of 4 h. After storage at 4 °C overnight, a yellow precipitate was collected and washed with cold MeOH. The mother liquor and the filtrates were combined and freed from solvent in vacuo. The precipitate and the residue were individually converted into the free bases by treatment with NEt_3 (1.6 mL, 11.5 mmol) and extraction with water/Et_2O. The organic phases were washed with water and brine and dried with $MgSO_4$. After removal of the solvent, the yield was 0.98 g (3.46 mmol) from the former precipitate and 1.01 g (3.57 mmol) from the former mother liquor. In a second resolution step, the free base from the former precipitate was again treated with L-(−)-*O*,*O*′-dibenzoyltartaric acid (1.24 g, 3.46 mmol) in MeOH (10.4 mL) under reflux (1 h) and processed as described above. Optically enriched (1*R*,3*R*)-**6** was obtained as a yellow solid (0.720 g, 2.55 mmol, 23%). $[\alpha]_D^{20} = +71$ ($c = 4 \times 10^{-3}$ g mL^{-1}, CH_3CN). Crystals of the L-tartrate salt (**12**) suitable for X-ray structure analysis were grown by reaction of a solution of optically enriched (1*R*,3*R*)-**6** (50 mg, 0.18 mmol) in MeOH (1 mL) with a solution of L-tartaric acid (26 mg, 0.18 mmol) in MeOH (1 mL). The reaction mixture was heated to 70 °C and slowly cooled to room temperature. The precipitate was collected, redissolved in MeOH (0.5 mL) and Et_2O was allowed to slowly diffuse into this solution. The free base from the former mother liquor was treated with D-(+)-*O*,*O*′-dibenzoyltartaric acid (1.28 g, 3.57 mmol) in MeOH (10.7 mL) under reflux (1 h) and processed as described above. Optically enriched (1*S*,3*S*)-**6** was obtained as a yellow solid (0.72 g, 2.55 mmol, 23%). $[\alpha]_D^{20} = +72$ ($c = 4 \times 10^{-3}$ g mL^{-1}, CH_3CN). Crystals of the D-tartrate salt (*ent*-**12**) suitable for X-ray structure analysis were grown by reaction of a solution of optically enriched (1*S*,3*S*)-**6** (50 mg, 0.18 mmol) in MeOH (1 mL) with a solution of D-tartaric acid (26 mg, 0.18 mmol) in MeOH (1 mL). The reaction mixture was heated to 70 °C and slowly cooled to room temperature. The precipitate was collected, redissolved in MeOH (0.5 mL) and Et_2O was allowed to slowly diffuse into this solution. Amine exchange with (*R*)-**8** (see **10**) followed by integration of suitable signals in the ^{1}H NMR spectrum showed an enantiomeric excess of 78% after the tartrate resolution.

X-ray Crystal Structure Analysis of (1*R*,3*R*)-12: Empirical formula $C_{16}H_{22}FeN{\cdot}0.5\ C_4H_4O_6$, $M = 358.23$, yellow crystal, 0.30 × 0.15 × 0.07 mm, $a = 16.234(1)$, $b = 8.513(1)$, $c = 12.723(1)$ Å, $\beta = 109.84(1)°$, $V = 1654.0(3)$ Å^3, $\rho_{calcd.} = 1.439$ g cm^{-3}, $\mu = 9.26$ cm^{-1}, empirical absorption correction ($0.769 \le T \le 0.938$), $Z = 4$, monoclinic, space group $C2$ (no. 5), $\lambda = 0.71073$ Å, $T = 293$ K, ω and φ scans, 5331 reflections collected ($\pm h$, $\pm k$, $\pm l$), [(sinθ)/λ] = 0.66 Å^{-1}, 3401 independent ($R_{int} = 0.027$) and 3154 observed reflections [$I \ge 2\sigma(I)$], 215 refined parameters, $R = 0.031$, $wR^2 = 0.068$, Flack parameter −0.01(2), max. residual electron density 0.32 (−0.42) e·Å^{-3}, hydrogen atom at N1 from difference map, others calculated and all refined as riding atoms.

X-ray Crystal Structure Analysis of (1*S*,3*S*)-12: Empirical formula $C_{16}H_{22}FeN{\cdot}0.5\ C_4H_4O_6$, $M = 358.23$, yellow crystal, 0.35 × 0.20 × 0.05 mm, $a = 16.168(1)$, $b = 8.457(1)$, $c = 12.715(1)$ Å, $\beta = 110.15(1)°$, $V = 1632.1(3)$ Å^3, $\rho_{calcd.} = 1.458$ g cm^{-3}, $\mu = 9.38$ cm^{-1}, empirical absorption correction ($0.735 \le T \le 0.955$), $Z = 4$, monoclinic, space group $C2$ (no. 5), $\lambda = 0.71073$ Å, $T = 198$ K, ω and φ scans, 5402 reflections collected ($\pm h$, $\pm k$, $\pm l$), [(sinθ)/λ] = 0.66 Å^{-1}, 3475 independent ($R_{int} = 0.029$) and 3324 observed reflections [$I \ge 2\sigma(I)$], 215 refined parameters, $R = 0.027$, $wR^2 = 0.061$, Flack parameter −0.01(1), max. residual electron density 0.29 (−0.28) e·Å^{-3}, hydrogen atom at N1 from difference map, others calculated and all refined as riding atoms.

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