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Simultaneous Construction of Planar and Central Chiralities as well as Unprecedented Axial Chirality on and around A Ferrocene Backbone

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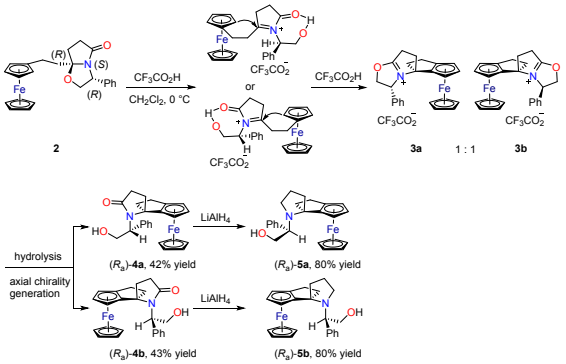
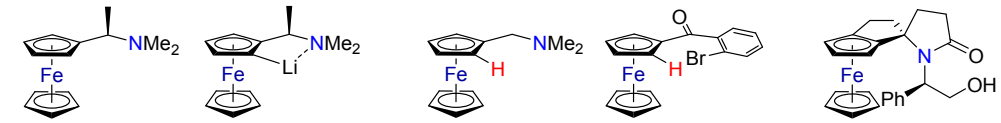


ABSTRACT: Simultaneous generation of planar, central and axial chiralities on and around a ferrocene backbone via a *D*-phenylglycinol-induced intramolecular iminium cyclization was disclosed, which is rare and differs from known methods. A series of chiral spiro[cyclopentadienyl 1,2,3,3a-tetrahydropentalenyl iron (II)-1,2′-pyrrolidine] derivatives were prepared in the new method, and their structures characterized unambiguously. The axial chirality caused by the ferrocene backbone and the rigid spiral structure was verified by NOESY and variable temperature NMR experiments, and single-crystal XRD analyses. Mechanism for the stereoselective iminium cyclization reaction was suggested, which was influenced by steric hindrance and hydrogen bonding.

INTRODUCITON

The synthesis of ferrocene was a milestone in the development of organometallic chemistry. It was the first organometallic sandwich compound reported.[1] Since the discovery of ferrocene, various ferrocene compounds have been reported, and they have been used for a broad range of chemical applications.[2] Ferrocene-derived diphosphines[3–7] are used as chiral ligands for asymmetric reactions, taking advantage of the planar chiral structure brought by ferrocene. Xyliphos[3] is used for the iridium-catalysed asymmetric hydrogenation of an imine to produce (*S*)-metolachlor in a large-scale asymmetric process. Dimethylamino pyridine (DMAP) derivatives bearing a planar chiral ferrocene backbone were developed by Fu and used in asymmetric reactions.[8]

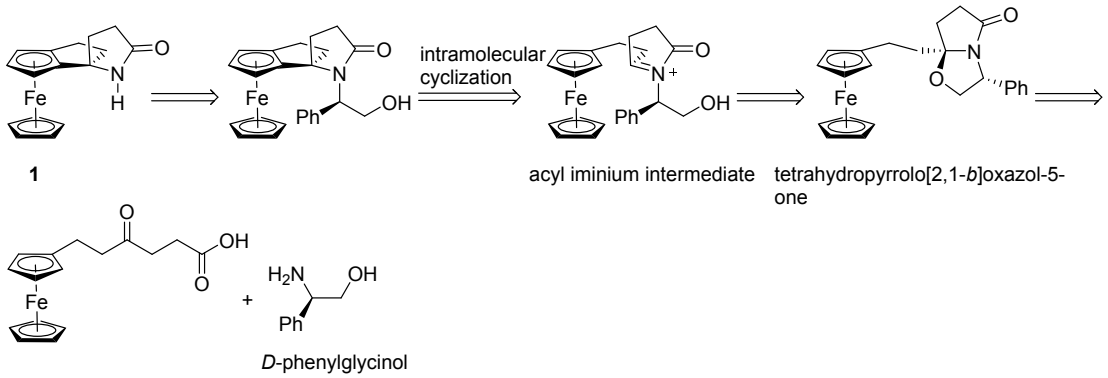
Great efforts have been devoted to the synthesis of chiral compounds from ferrocene to fully exploit the planar chirality that could be built on the ferrocene backbone. Ugi's amine (Figure 1a), has been used to prepare planar chiral ferrocene derivatives via dimethylamino-directed *ortho*-lithiation (Figure 1b) followed by electrophilic substitution.[9] Hayashi and Kumada pioneered the preparation of ferrocenylphosphines with planar chirality.[10] Catalytic asymmetric C–H bond functionalizations reported by You[11] and Gu[12] (Figure 1c) emerged as efficient methods to introduce planar chirality to ferrocene. Here, we report an unprecedented simultaneous installation of both planar chirality and a carbon stereocenter controlled by a remote stereogenic center in *D*-phenylglycinol (Figure 1d).



(a) Ugi's amine (b) Directed *ortho*-lithiation (c) Catalytic asymmetric C-H functionalization (d) Our method: asymmetric one-pot cyclization

Figure 1. Known methods and our method for introducing planar chirality to ferrocene.

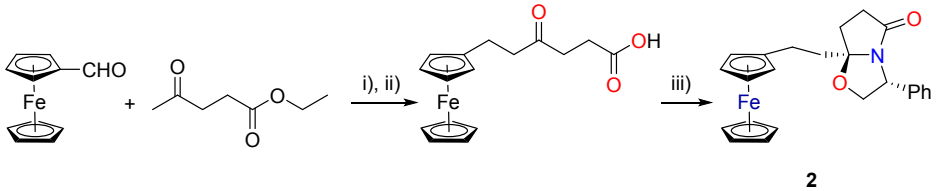
We aimed to prepare spiro[cyclopentadienyl 1,2,3,3a-tetrahydropentalenyl iron (II)-1,2′-pyrrolidin]-5′-one (**1**) and explore the use of its derivatives as chiral ligands in the future (Scheme 1). We expected to prepare **1** via an intramolecular cyclization initiated by an acyl iminium intermediate, which was generated from a tetrahydropyrrolo[2,1-*b*]oxazol-5-one precursor. Meyers'[13] and Vernon's[14] methods could be used to construct the bicyclic unit. *D*-Phenylglycinol was used as a chiral inductor as well as to form diastereomers that could be separated in a facile manner.



Scheme 1. Retrosynthesis of spiro[cyclopentadienyl 1,2,3,3a-tetrahydropentalenyl iron (II)-1,2′-pyrrolidin]-5′-one (**1**).

RESULTS AND DISCUSSION

We commenced our synthesis with ferrocenecarboxaldehyde and ethyl levulinate (Scheme 2). A piperidine and acetic acid-mediated aldol condensation followed by hydrogenation and hydrolysis produced 6-ferrocenyl-4-oxo-hexanoic acid in 87% yield, which was verified by single-crystal XRD analysis (Figure 2). Condensation of 6-ferrocenyl-4-oxo-hexanoic acid with *D*-phenylglycinol gave compound **2** in 85% yield. The crystal structure clearly showed the newly generated carbon stereocenter was in the (*R*)-configuration and the nitrogen stereocenter was in the (*S*)-configuration (Figure 2). The relative *syn*-configuration of the two substituents at the 3- and 7a- positions of the bicyclic ring was previously reported for several compounds.[13]



Scheme 2. Preparation of (3*R*,4*S*,7a*R*)-7a-(2-ferrocenylethyl)-3-phenyltetrahydropyrrolo[2,1-*b*]oxazol-5-one (**2**): i) piperidine, acetic acid, benzene, reflux, 88% yield; ii) Pd/C, 1 atm H_2, rt; aq. NaOH. 99% yield; iii) *D*-phenylglycinol, toluene, reflux, 85% yield.

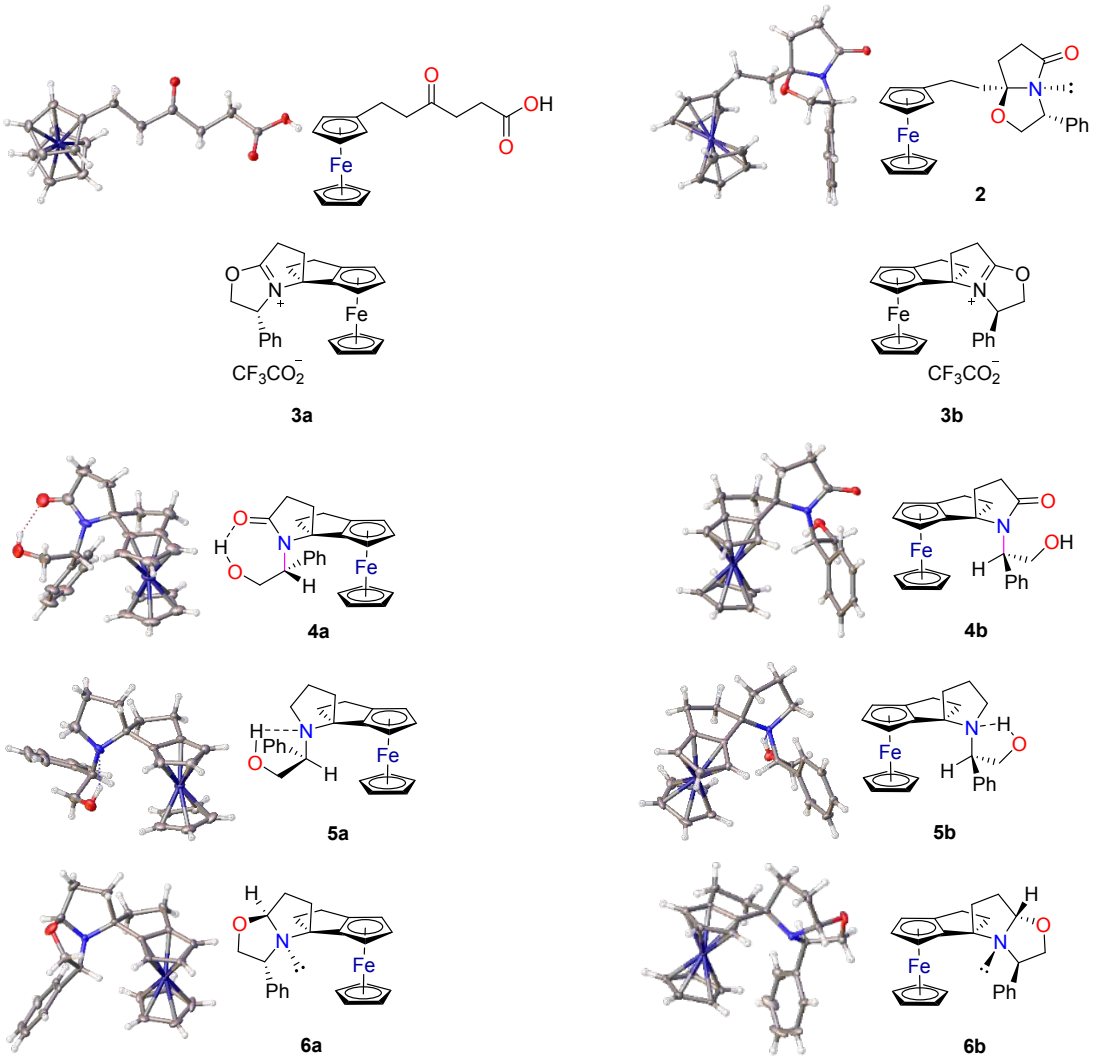
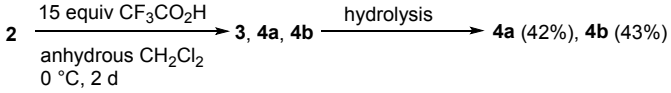


Figure 2. Crystal structures of 6-ferrocenyl-4-oxo-hexanoic acid, (3*R*,4*S*,7a*R*)-**2**, (R_a)-**4a**, (R_a)-**4b**, (R_a)-**5a**, (R_a)-**5b**, (R_p,1*R*,3′*R*,4′*R*,7′a*S*)-**6a** and (S_p,1*S*,3′*R*,4′*R*,7′a*S*)-**6b**.

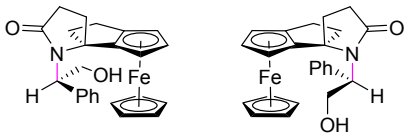
With **2** in hand, we attempted the intramolecular cyclization reaction. We first tested $AlCl_3$ as a Lewis acid. Despite laborious attempts, disappointing results were obtained. A complicated mixture that could not be separated by chromatography was obtained with approximately 10% of the starting material recovered. Trifluoroacetic acid was used as a Brønsted acid to promote the intramolecular cyclization reaction (Scheme 3). After optimizations of the reaction conditions, we identified three compounds **3**, **4a**, and **4b** (Figure 2) in the reaction mixture by thin layer chromatography (TLC). Compound **3** was the major species in the crude product. After aqueous workup and column chromatography on silica gel, we isolated and characterized **3**, **4a** and **4b** by ^1H and ^{13}C NMR. Repeated silica gel chromatographies of the crude product showed that **3** was unstable under chromatographic conditions and tended to convert into **4a** and **4b** though NMR indicated **3** thus obtained was a pure compound. The conversion of **3** to **4b** was faster than **4a**.

Then, a crude mixture containing predominantly **3** and small amounts of **4a** and **4b** was treated with wet tetrahydrofuran (THF) at rt (Scheme 3). A 1:1 mixture of **4a** and **4b** was observed with the complete disappearance of **3**. Single crystals of **4a** and **4b** were obtained. Crystal structures showed **4a** had an (R_p,1*R*,*R*) configuration and **4b** had an (S_p,1*S*,*R*) configuration (Figure 2). Careful

examination of the crystal structures of **4a** and **4b** prompted us to hypothesize the possibility of axial chirality, which could be caused by restricted rotation about the C–N bond highlighted in pink (Figure 2, 3). As far as we know, the axial chirality due to restricted rotation about a N–C_{sp3} bond as in **4a** or **4b**, has not been reported. Tentatively, we assigned the new chirality as (R_a).[15] Thus, three consecutive stereogenic elements that give the molecule planar, central and axial chirality were generated due to induction by *D*-phenylglycinol.



Scheme 3. Intramolecular cyclization of **2** promoted by CF_3CO_2H and subsequent hydrolysis of **3**, **4a**, **4b**.

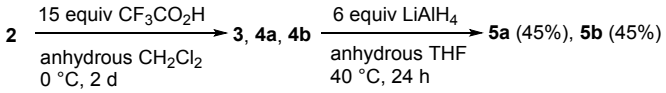


atropisomer of **4a** atropisomer of **4b**

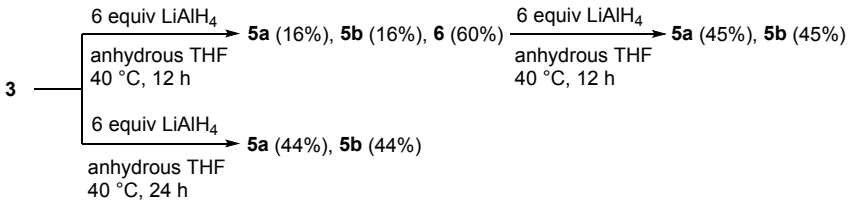
Figure 3. Supposed atropisomers of **4a** and **4b**.

To clarify the structure of **3**, we treated **2** with CF_3CO_2H under strictly anhydrous conditions. Upon complete consumption of **2**, the reaction mixture was concentrated under vacuum with no aqueous workup. The resulting crude product was promptly chromatographed on silica gel to give **3** in high purity. Both the ^1H and ^{13}C NMR spectra of **3**[16] indicated it was a mixture of two diastereomers, which were inseparable by TLC. HRMS indicated the [M+H] for **3** was 512.1130. According to these data, we suggested that two oxazolinium salts of CF_3CO_2H (**3a**, **3b**), formed from CF_3CO_2H and **4a** or **4b** by dehydrative cyclization, were present in **3** (Figure 2). Oxazolinium salts of BF_4^-,[17] I^-,[18] Br^-,[19] TfO^-,[20] TsO^-,[21] ClO_4^-,[22] and $CF_3CO_2^-$ [17c] have been reported previously. These reported oxazolinium salts were only moderately stable and could decompose upon chromatography, which was consistent with the observed properties of **3**. The initially isolated **3** (Scheme 3) was actually **3a**, which was a result due to the hydrolysis of **3b** to **4b** during workup.

When a mixture of **3**, **4a** and **4b** was subjected to $LiAlH_4$ reduction in THF (Scheme 4), two products, **5a** and **5b**, were obtained in 90% yield and were easily separated by chromatography. The structures of **5a** and **5b**, having (R_a)[15] axial chirality, were verified by XRD analyses (Figure 2). When **3**, prepared with no aqueous workup, was reduced with $LiAlH_4$ in THF for 12 h, **6** was produced in 60% yield in addition to **5a** (16% yield) and **5b** (16% yield) (Scheme 5). ^1H and ^{13}C NMR indicated **6** was a mixture of two diastereomers,[16] though the two components were inseparable by TLC. Single crystals of **6a** were obtained from the mixture of reaction products. Pure **6b** was prepared in a different method, the structure of which was verified by XRD analysis (Figure 2), ^1H and ^{13}C NMR. The crystal structures of **6a** and **6b** (Figure 2) clearly showed that five stereogenic elements were present in the molecules, and four of them, including one nitrogen chiral center, were formed by induction. When a mixture of **5a**, **5b** and **6** (Scheme 5) was further reduced with $LiAlH_4$ in THF, **5a** and **5b** were obtained and **6** disappeared. In another experiment, when **3** was reduced with $LiAlH_4$ in THF for 24 h (Scheme 5), **5a** and **5b** were obtained in 88% yield without **6**.



Scheme 4. Intramolecular cyclization of **2** promoted by CF_3CO_2H and subsequent reduction of **3**, **4a**, **4b**.



Scheme 5. Reductions of **3** by $LiAlH_4$.

To confirm **4a**, **4b**, **5a** or **5b** was an atropisomer instead of a conformer, we did NOESY experiments at rt in $CDCl_3$ on **4b**, **5b** and the *p*-bromobenzoates **7** and **8**, which were prepared from **4a** and **5a**, respectively. **7** or **8** was used in order to exclude possible influences to the C–N_{sp3} bond rotation caused by intramolecular hydrogen bond. The crystal structures of **7** and **8** were shown in Figure 4. The observed NOE[16] in **4b**, **5b**, **7** or **8** indicated the hydrogen in the chiral center of *D*-phenylglycinol and the hydrogen in the unsubstituted Cp ring were in proximity, which quite possibly meant the C–N_{sp3} bond rotation was restricted and a single atropisomer resembling the structure in the crystal (Figure 2, Figure 4) was present in each compound.

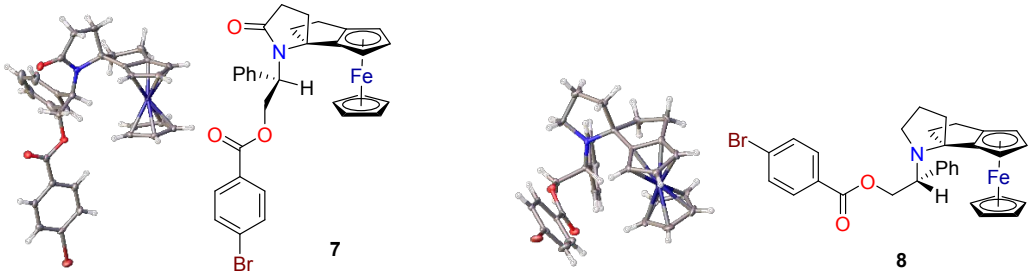
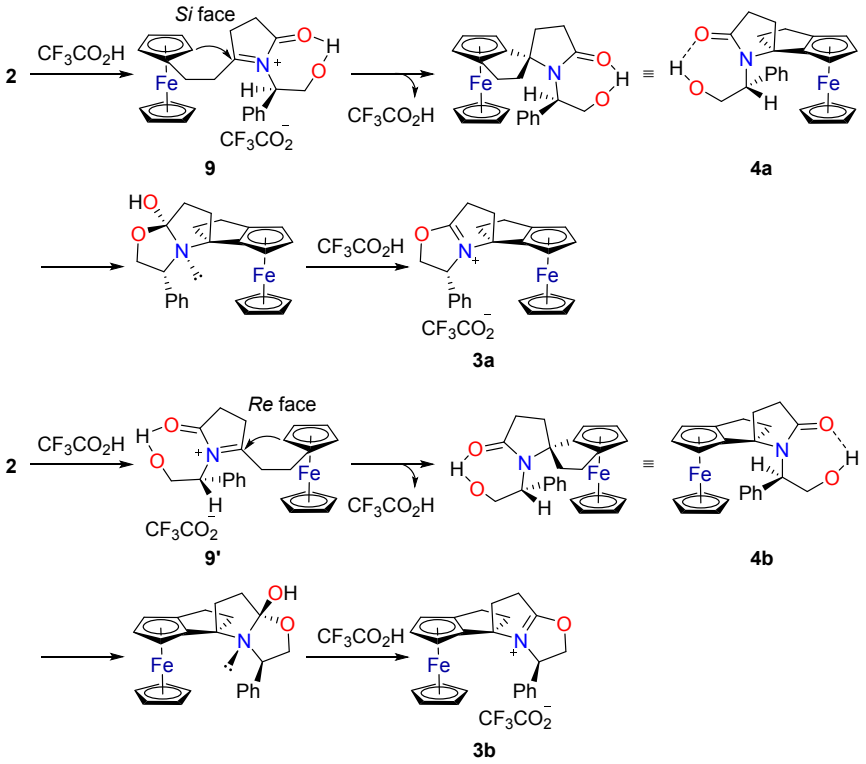


Figure 4. Crystal structures of (R_a)-**7** and (R_a)-**8**.

Possible formation pathways of **3a**, **3b**, **4a**, and **4b** from **2** are shown in Scheme 6. The acyl iminium salt, formed from **2** and CF_3CO_2H, adopted two reactive conformations denoted **9** and **9′**, and rapidly underwent intramolecular cyclization giving (R_p,1*R*)-**4a** or (S_p,1*S*)-**4b** having exclusively (R_a) axial chirality. Due to its distance from the reacting Cp ring, the stereocenter in the *D*-phenylglycinol did not influence the conformations **9** and **9′**, which were equally possible, leading to a 1:1 ratio of the two components in **3**. The inaccessible conformations to produce the unobserved (S_p,1*R*) or (R_p,1*S*) diastereomers are shown in Figure 5a, which might cause severe repulsion between the substituted Cp ring and the phenylglycinol substructure (pink colored). Concerning the formation of the (R_a) chirality, hydrogen bonding contributed to the exclusive selectivity. In both cases (shown in Scheme 6), hydrogen bonding between the carbonyl and the hydroxy groups should stabilize the conformations **9** and **9′**, which resulted in the (R_a) axial chirality in the corresponding product. The reaction conformations, which might lead to the atropisomers as shown in Figure 3, were unfavourable due to the absence of the hydrogen bonding (Figure 5b). Once **4a** or **4b** was formed, excess CF_3CO_2H would immediately convert it to the corresponding oxazolinium salt, respectively, which accounted for **3** being the major species in the reaction mixture.



Scheme 6. Possible pathways for the formation of **3a**, **3b**, **4a** and **4b** from **2**.

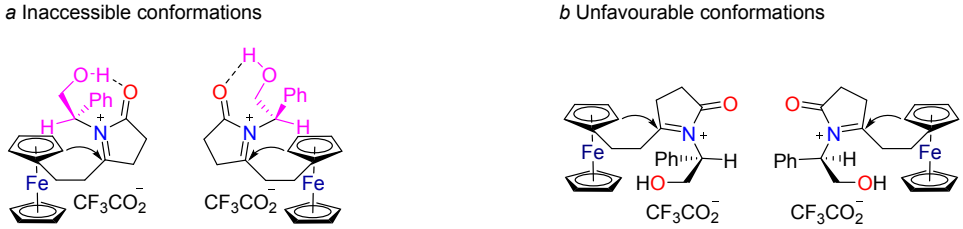
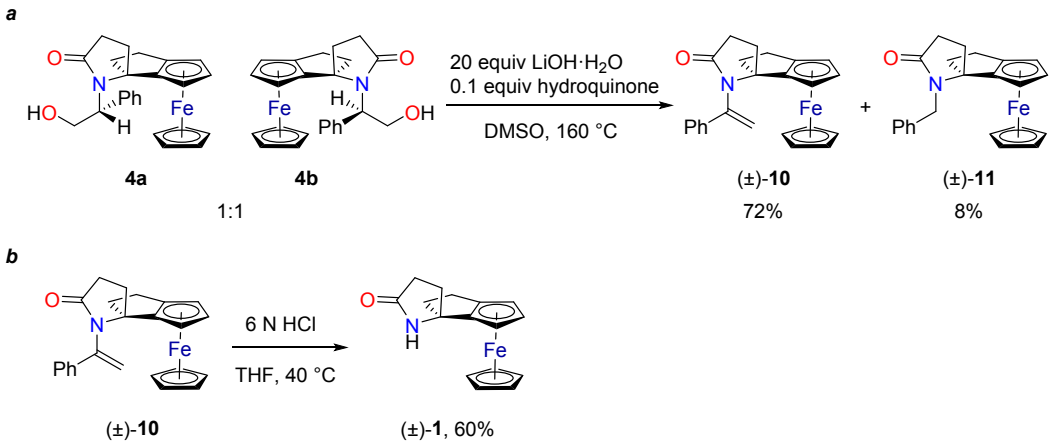


Figure 5. Inaccessible and unfavourable conformations of the acyl iminium salt from **2**.

We attributed the generation of the axial chirality in **4a** or **4b** to the rigidity of both the ferrocene backbone and the neighbouring spiral structure. The phenyl ring and the hydroxymethyl group originating from the *D*-phenylglycinol moiety were too bulky to allow the C–N bond to rotate freely in the crowded space adjacent to the ferrocene backbone. Once the hydroxymethyl group was converted to a smaller one, the C–N bond would rotate freely. We tried to simultaneously eliminate the axial chirality as well as the central chirality from the *D*-phenylglycinol by derivatization. An equimolar mixture of **4a** and **4b** was treated with $LiOH·H_2O$ in dimethyl sulfoxide (DMSO) at 160 °C (Scheme 7a). Racemic dehydration product **10** bearing a styrene substructure was obtained in 72% yield. In addition, the racemate of **11** was isolated in 8% yield as a side product, and its structure was clearly identified by XRD analysis (Figure 6). The formation of **10** and **11** as racemates clearly indicated the disappearance of the axial and central chirality in **4a** and **4b**. Hydrolysis of (±)-**10** gave (±)-**1** in 60% yield (Scheme 7b), the structure of which was determined by XRD analysis (Figure 6).



Scheme 7. *a* Simultaneous elimination of the axial and central chiralities from **4a** and **4b**. *b* Hydrolysis of (±)-**10**.

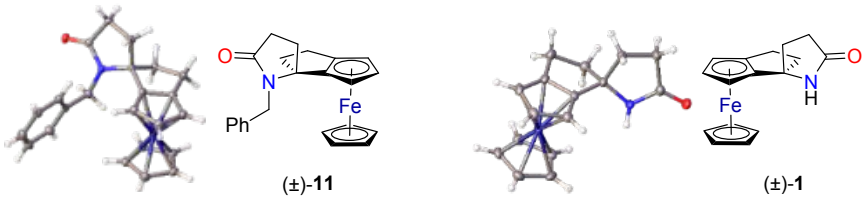
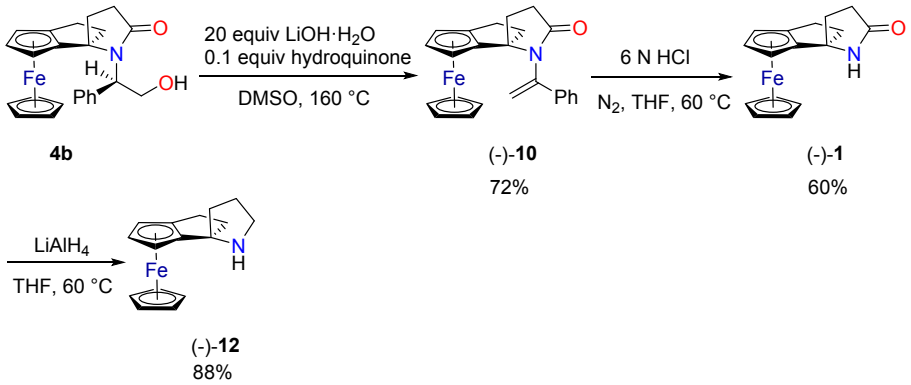


Figure 6. Crystal structures of (±)-**11** and (±)-**1**.

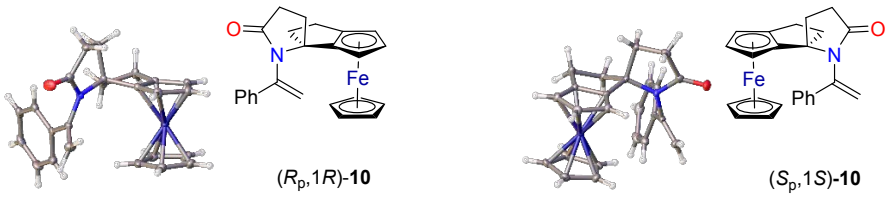


Scheme 8. Preparations of (−)-**1**, (−)-**10**, and (−)-**12**.

The absence of axial chirality in enantiomerically pure **10** at rt and the presence of axial chirality in (S_p,1*S*,R_a,*R*)-**4b** at rt were verified by the following variable temperature ^{1}H NMR experiments. We prepared (R_p,1*R*)-**10** and (S_p,1*S*)-**10** from **4a** and **4b** (Scheme 8), respectively, and further converted them to **12** via **1**. The crystal structures of (R_p,1*R*)-**10** and (S_p,1*S*)-**10** are shown in Figure 7a. Enantiomerically pure (R_p,1*R*)-**10** was subjected to ^{1}H NMR analyses in the temperature range from 25 °C to −60 °C (Figure 7d). The "singlet" peaks (δ = 6.29 and 5.48 at 25 °C), corresponding to the two ethylenic protons of CH_2=C, each began to separate into two peaks at −20 °C and became two completely isolated peaks at temperatures of −40 °C and lower. The integration of each set of newly formed peaks indicated a ratio of 3:2. A peak (δ = 7.60 at 25 °C) corresponding to two phenyl ring protons showed similar changes as the temperature decreased. At temperatures below −10 °C, two isolated singlets corresponding to two distinct unsubstituted Cp rings (δ = 4.09 and 3.78 at −40 °C) appeared. We believed the 3:2 ratio was for an atropisomeric mixture of (R_p,1*R*,S_a)-**10** (Figure 7b)

and (R_p,1R,R_a)-**10** (Figure 7c), among which (R_p,1R,S_a)-**10**, existing in the crystal, was the major species. These results showed the C–N single bond rotated freely at rt, and the rotation was restricted to produce axial chirality at −40 °C and below. For comparison, enantiomerically pure **4b** was also subjected to variable temperature ^{1}H NMR experiments (Figure 7e). None of the "singlet" peaks became two peaks as the temperature decreased from 25 °C to −60 °C. The peak corresponding to the CH_2O proton shifted from $\delta = 4.71$ to $\delta = 5.50$, and the peak corresponding to the proton of NCH shifted from $\delta = 6.12$ to $\delta = 6.29$. The above NMR results clearly supported that the axial chirality in **4a**, **4b**, **5a**, **5b**, **7** or **8** was indeed present and stable at rt, while (R_p,1R)-**10** did not show axial chirality at rt. Further, the ^{1}H NMR spectra of **4b**, which had been heated at 150 °C for 24 h, was compared with that of **4b** in DMSO-d_6.[16] No obvious changes were observed for all the peaks. Variable temperature (20–140 °C) ^{1}H NMR spectra of **4b** in DMSO-d_6 also indicated no obvious changes of the peaks.[16] These results clearly support the axial chirality in **4b** is stable in a temperature range up to 150 °C.

a



(R_p,1R)-**10** (S_p,1S)-**10**

b ***c***

(R_p,1R,S_a)-**10** (R_p,1R,R_a)-**10**

d

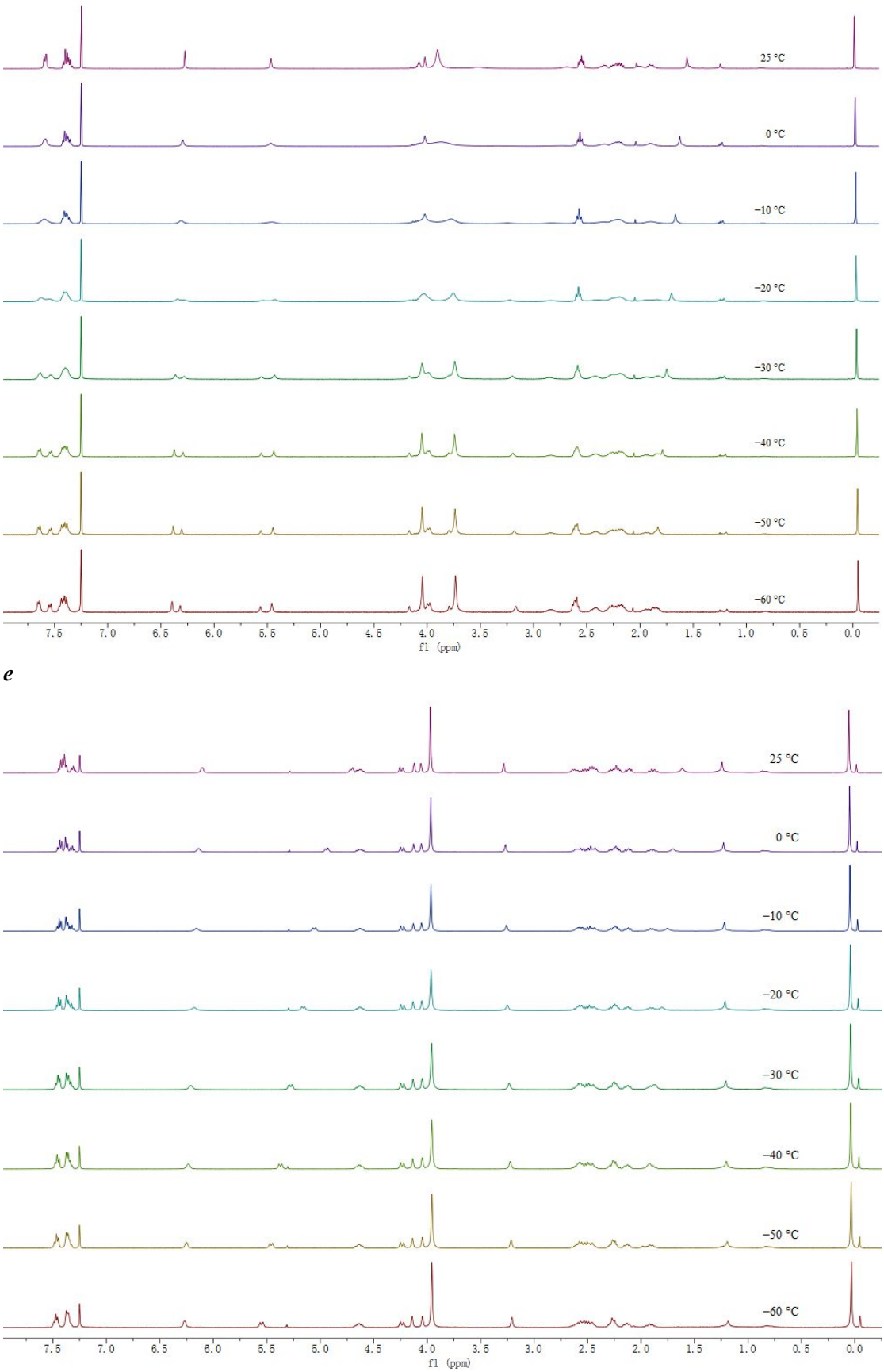


Figure 7. *a* Crystal structures of (R_p,1*R*)-**10** and (S_p,1*S*)-**10**. *b* Putative structure of (R_p,1*R*,S_a)-**10**. *c* Putative structure of (R_p,1*R*,R_a)-**10**. *d* Variable temperature ^{1}H NMR spectra of (R_p,1*R*)-**10** in $CDCl_3$.

e Variable temperature ^{1}H NMR spectra of (S_p,1*S*,R_a,*R*)-**4b** in $CDCl_3$.

CONCLUSION

In summary, we reported the synthesis of a new class of chiral compounds bearing a ferrocene backbone and a chiral center *α* to the Cp ring. The unique chiral structure was built in a single step with simultaneous generation of planar, central and axial chiralities. To the best of our knowledge, such a simultaneous generation of multiple chiralities on and surrounding a ferrocene backbone has not been reported previously. The axial chirality caused by restricted N–C_{sp3} bond rotation, which differs from chiralities caused by restricted C–C bond rotation and those present in 2-substituted or 2,6-disubstituted aniline derivatives, is unprecedented, and was verified by NOESY and variable temperature ^{1}H NMR experiments. Studies on the preparation and use of chiral compounds bearing a spiro[cyclopentadienyl 1,2,3,3a-tetrahydropentalenyl iron (II)-1,2′-pyrrolidine] structure are ongoing in our laboratory.

EXPERIMENTAL SECTION

All glassware for reactions using anhydrous solvents were dried under high vacuum (< 0.1 torr) using a heat gun. General Schlenk techniques were applied for addition and transfer operations.

Commercial reagents and solvents were purchased from Acros, Alfa Aesar, J&K Scientific Ltd., Sinopharm Chemical Reagent Co. or Beijing Chemical Works, and used as received unless otherwise noted. THF was distilled over sodium benzophenone ketyl under N_2. CH_2Cl_2 was distilled over CaH_2 under N_2. Silica gel products were purchased from Qingdao Haiyang Chemical Co.. Thin-layer chromatography was performed on precoated silica gel (0.2–0.25 mm thick) plates with fluorescent indicator 254 nm. The plate was visualized with 254 nm UV lamp, PMA or $KMnO_4$ stain. Column chromatography was performed on 200–300 mesh silica gel.

^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL ECZ 600R spectrometer at 600 MHz and 150 MHz respectively. Chemical shifts of ^{1}H NMR and ^{13}C NMR were referred to TMS (δ = 0) or chloroform (δ = 7.26 for ^{1}H NMR, 77.0 for ^{13}C NMR) respectively. The following abbreviations were used to denote the multiplicity of each peak: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), m (multiplet). IR spectra were recorded on a Nicolet AVATAR 360 FT-IR spectrometer. The sample was prepared as a thin-film on a NaCl disc. MS spectra were obtained on a Waters Quattro Micro triple quadrupole mass spectrometer. Specific rotation was measured on a Perkin-Elmer 343 Polarimeter using the 589 nm D-line of sodium lamp and a quartz cell with 10 cm path length. X-ray diffraction experiment was conducted on a Rigaku Oxford Diffraction SuperNova Dual Atlas S2 diffractometer using Mo or Cu Kα radiation.

Ferrocenecarboxaldehyde

To a dry flask, *N*-methylformanilide (10.6 mL, 80.0 mmol) and $POCl_3$ (4.7 mL, 50.0 mmol) were added. After stirring for 5 min, ferrocene (5.58 g, 30.0 mmol) was added in portions over 20 min. The mixture was stirred at room temperature for 1 h and then at 40 °C for 5 h. The mixture was cooled to 0 °C, and NaOAc solution (25 g in 200 mL H_2O) was added. After stirring at 0 °C overnight, the reaction mixture was extracted with CH_2Cl_2. The organic layers were combined, washed with 1 N HCl, saturated $NaHCO_3$ and H_2O (all saturated with NaCl). The CH_2Cl_2 solution was concentrated to about 20 mL. Saturated $NaHSO_3$ (100 mL) was added while stirring. The mixture was cooled to 0 °C. The precipitate was collected by filtration, washed with ice-cold saturated $NaHSO_3$ and CH_2Cl_2 to get a yellow solid. To a round-bottom flask, the yellow solid and

1 N NaOH (100 mL) were added. The mixture was stirred at room temperature for 1 h. Then, it was extracted with CH_2Cl_2. The organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The remaining solvent was removed under high vacuum to afford ferrocenecarboxaldehyde as a dark-red solid (4.87 g, 76% yield).

(*E*)-Ethyl 6-ferrocenyl-4-oxo-5-hexenoate

To a three-necked flask with a Dean-Stark apparatus, ethyl levulinate (4.7 mL, 33 mmol), piperidine (0.65 mL, 6.5 mmol), acetic acid (1.96 mL, 34.0 mmol) and benzene (22 mL) were added. The mixture was heated to gentle reflux. Ferrocenecarboxaldehyde (3.52 g, 16.5 mmol) in benzene (22 mL) was added dropwise. Then the mixture was stirred at 90 °C (oil bath) for 16 h. Water was removed via Dean-Stark apparatus. The solvent was removed by rotary evaporation. The residue was dissolved in CH_2Cl_2, washed with 2 N HCl, saturated $NaHCO_3$ and brine, and dried over anhydrous Na_2SO_4. CH_2Cl_2 was evaporated, and excess ethyl levulinate was distilled out under high vacuum and recovered. The crude product was purified by column chromatography (4:1 hexanes/AcOEt) to afford (*E*)-ethyl 6-ferrocenyl-4-oxo-5-hexenoate as a purple solid (4.93 g, 88% yield). TLC (hexanes/ethyl acetate, 4:1 v/v): $R_f = 0.32$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J = 16.0 Hz, 1H), 6.37 (d, J = 16.0 Hz, 1H), 4.51 (t, J = 2.0 Hz, 2H), 4.44 (t, J = 1.6 Hz, 2H), 4.20–4.13 (m, 7H), 2.92 (t, J = 6.8 Hz, 2H), 2.67 (t, J = 6.8 Hz, 2H), 1.27 (t, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 197.3, 173.0, 144.5, 123.3, 78.6, 71.2, 69.7, 68.8, 60.5, 34.8, 28.3, 14.2; IR (film) ν_{max} 3096, 2980, 2907, 1732, 1657, 1616, 1601, 1364, 1157, 1105, 1028, 822, 496, 482 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{20}FeNaO_3$ 363.0660; Found 363.0654.

Ethyl 6-ferrocenyl-4-oxo-hexanoate

To a round-bottom flask, (*E*)-ethyl 6-ferrocenyl-4-oxo-5-hexenoate (4.93 g, 14.5 mmol), 10% Pd/C (0.2 g), and EtOH (40 mL) were added. The mixture was well stirred under hydrogen atmosphere overnight. Pd/C was filtered and washed with EtOH. The filtrate was concentrated and the residue dried in vacuo to give ethyl 6-ferrocenyl-4-oxo-hexanoate as a yellow liquid, which was directly used without further purification. TLC (hexanes/ethyl acetate, 2:1 v/v): $R_f = 0.78$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.16–4.05 (m, 11H), 2.73–2.57 (m, 8H), 1.26 (t, J = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 208.3, 172.8, 87.7, 68.5, 68.0, 67.3, 60.6, 44.2, 37.2, 28.0, 23.6, 14.2; IR (film) ν_{max} 3092, 2980, 2926, 2851, 1732, 1717, 1410, 1371, 1350, 1308, 1182, 1105, 1024, 1001, 924, 820, 598, 484, 436 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{22}FeNaO_3$ 365.0816; Found 365.0810.

6-Ferrocenyl-4-oxo-hexanoic acid

To a round-bottom flask, ethyl 6-ferrocenyl-4-oxo-hexanoate and EtOH/H_2O (25 mL/25 mL) were added. To this solution, NaOH (1.16 g, 29.0 mmol) in 25 mL H_2O was added dropwise. After stirring for 1 h at room temperature, 1 N HCl was added dropwise till pH was approximately 7. EtOH was evaporated. 1 N HCl was added dropwise with stirring till pH was about 1. The precipitate was filtered and washed with hexanes. The product was dried in vacuo to obtain a yellow solid (4.52 g, 99% yield). TLC (hexanes/ethyl acetate, 2:1 v/v): $R_f = 0.39$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.10 (s, 5H), 4.04 (s, 4H), 2.70–2.62 (m, 8H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 208.1, 178.7, 87.6, 68.5, 67.9, 67.3, 44.1, 36.9, 27.7, 23.6; IR (film) ν_{max} 3092, 2924, 2861, 1709, 1410, 1369, 1287, 1254, 1227, 1175, 1105, 1001, 924, 820, 484 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{18}FeNaO_3$ 337.0503; Found 337.0497; m.p. 117.7–118.9 °C.

(3*R*,4*S*,7a*R*)-7a-(2-Ferrocenylethyl)-3-phenyltetrahydropyrrolo[2,1-*b*]oxazol-5-one (2)

To a three-necked flask, 6-ferrocenyl-4-oxo-hexanoic acid (11.57 g, 36.8 mmol), *D*-phenylglycinol

(5.05 g, 36.8 mmol) and 80 mL toluene were added. The reaction mixture was heated at 130 °C (oil bath) to reflux. Water was removed by a Dean-Stark apparatus. After stirring for 36 h, the solvent was removed by rotary evaporation. The residue was purified by column chromatography (4:1 hexanes/AcOEt) to afford **2** as a yellow solid (13.01 g, 85% yield). TLC (hexanes/ethyl acetate, 2:1 v/v): R_f = 0.44; $[\alpha]_D^{20}$ −77.0 (*c* 1.03, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.25 (m, 5H), 5.23 (t, *J* = 7.4 Hz, 1H), 4.65 (t, *J* = 8.4 Hz, 1H), 4.14 (dd, *J* = 8.8, 6.8 Hz, 1H), 4.01–3.93 (m, 9H), 2.90–2.80 (m, 1H), 2.61 (ddd, *J* = 17.6, 10.2, 2.8 Hz, 1H), 2.40–2.33 (m, 3H), 2.24–2.15 (m, 1H), 1.98–1.90 (m, 1H), 1.84–1.76 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 179.3, 140.0, 128.7, 127.5, 125.4, 102.2, 87.7, 72.3, 68.3, 67.7, 67.4, 67.1, 57.4, 37.5, 33.1, 30.8, 23.7; IR (film) ν_{max} 3090, 2951, 2928, 2880, 1713, 1497, 1450, 1364, 1292, 1236, 1028, 820, 716, 484 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{26}FeNO_2$ 416.1313; Found 416.1307; m.p. 101.6–103.5 °C.

Intramolecular cyclization of 2 promoted by CF_3CO_2H and subsequent hydrolysis

A Schlenk tube was charged with anhydrous CH_2Cl_2 (13 mL) and anhydrous CF_3CO_2H (5.02 mL, 75.0 mmol) under N_2 atmosphere. The solution was cooled to 0 °C. Compound **2** (2.08 g, 5.0 mmol) was added in one portion. The mixture was stirred at 0 °C for 48 h. Saturated $NaHCO_3$ was added to quench the reaction. The mixture was extracted with CH_2Cl_2 for several times. The organic layers were combined and washed with brine. The solvent was removed by rotary evaporation to give a mixture of **3**, **4a**, and **4b**. Silica gel chromatography would give pure **3a**, **4a** and **4b**. The mixture could be used directly for hydrolysis without further purification.

A mixture of **3**, **4a**, and **4b** was dissolved in a solution of THF/H_2O (10 mL/25 mL), and then stirred overnight. When **3** was completely converted, the volatiles were removed by rotary evaporation. The residue was extracted with CH_2Cl_2 for several times. The CH_2Cl_2 solution was dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography (2:1 hexanes/AcOEt) to afford **4a** as a yellow solid (0.87 g, 42% yield) and **4b** as a yellow solid (0.89 g, 43% yield).

(*R*$_p$,1*R*,3′*R*)-3′-Phenyl-spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,5′-tetrahydro pyrrolo[2,1-*b*]oxazolium trifluoroacetate] (3a)

TLC (hexanes/ethyl acetate, 1:1 v/v): R_f = 0.65; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.46–7.33 (m, 5H), 6.22 (dd, *J* = 9.6, 7.2 Hz, 1H), 5.58 (dd, *J* = 10.8, 9.0 Hz, 1H), 5.00 (dd, *J* = 10.8, 6.6 Hz, 1H), 4.27 (t, *J* = 2.1 Hz, 1H), 4.16 (m, 1H), 4.12 (s, 5H), 3.85 (d, *J* = 2.4 Hz, 1H), 2.52–2.45 (m, 2H), 2.42–2.32 (m, 2H), 2.22–2.17 (m, 1H), 2.10–2.07 (m, 1H), 1.95 (dd, *J* = 12.0, 6.6 Hz, 1H), 1.80–1.75 (m, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 178.1, 156.9 (q, *J* = 43 Hz, $CF_3\mathbf{C}O_2$), 137.2, 128.9, 128.0, 127.0, 114.9 (q, *J* = 287 Hz, CF_3), 97.3, 91.0, 71.0, 69.7, 69.5, 68.4, 61.9, 57.4, 54.9, 39.5, 34.0, 29.6, 22.9; IR (film) ν_{max} 3086, 2939, 1786, 1690, 1439, 1408, 1354, 1223, 1153, 1107, 825, 698 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{25}F_3FeNO_3$ 512.1136; Found 512.1130.

***N*-((*R*)-2-Hydroxy-1-phenethyl)-(*R*$_p$,1*R*,*R*$_a$)-spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,2′-pyrrolidin]-5′-one (4a)**

TLC (hexanes/ethyl acetate, 1:1 v/v): R_f = 0.25; $[\alpha]_D^{20}$ +211 (*c* 1.02, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42–7.35 (m, 4H), 7.30 (t, *J* = 7.2 Hz, 1H), 6.07 (d, *J* = 4.8 Hz, 1H), 4.88 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.52–4.47 (m, 1H), 4.27–4.24 (m, 2H), 4.16 (s, 6H), 3.80 (d, *J* = 3.0 Hz, 1H), 2.58–2.43 (m, 3H), 2.35 (dd, *J* = 14.7, 8.1 Hz, 1H), 2.24–2.18 (m, 1H), 2.16–2.12 (m, 1H), 1.94 (dd, *J* = 11.1, 6.3 Hz, 1H), 1.83–1.78 (m, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 177.9, 138.0, 128.7, 127.1, 126.7, 97.9, 90.9, 70.7, 70.1, 69.5, 66.1, 61.9, 58.6, 57.3, 39.4, 34.3, 29.5, 23.0; IR (film) ν_{max} 3366, 3329, 2937, 2855, 1665, 1495, 1449, 1420, 1356, 1294, 1179, 1107, 1080, 1055, 1032, 1001,

824, 808, 729, 698, 679, 511, 459 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{26}FeNO_2$ 416.1313; Found 416.1307; m.p. 117.6–118.4 °C.

_N_-((_R_)-2-Hydroxy-1-phenethyl)-(S_p,1_S_,R_a)-spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,2′-pyrrolidin]-5′-one (4b)

TLC (hexanes/ethyl acetate, 1:1 v/v): R_f = 0.11; $[\alpha]_D^{20}$ −77.9 (_c_ 1.01, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.45–7.40 (m, 4H), 7.32 (t, _J_ = 7.2 Hz, 1H), 6.13 (d, _J_ = 4.8 Hz, 1H), 4.72–4.70 (m, 1H), 4.67–4.62 (m, 1H), 4.26 (m, 1H), 4.13 (d, _J_ = 1.2 Hz, 1H), 4.07 (t, _J_ = 2.4 Hz, 1H), 3.97 (s, 5H), 3.29 (d, _J_ = 1.8 Hz, 1H), 2.66 (dd, _J_ = 18.3, 9.9 Hz, 1H), 2.58–2.44 (m, 3H), 2.30–2.22 (m, 2H), 2.14–2.10 (m, 1H), 1.92–1.86 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 177.8, 136.7, 128.5, 126.9, 126.4, 97.6, 91.3, 70.5, 69.8, 69.7, 65.7, 61.6, 58.4, 57.7, 38.3, 33.6, 29.6, 23.0; IR (film) ν_{max} 3366, 3090, 2932, 2853, 1670, 1449, 1420, 1356, 1296, 1177, 1051, 910, 822, 806 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{26}FeNO_2$ 416.1313; Found 416.1307; m.p. 216.8–217.2 °C.

Preparation of 3 with no aqueous workup

A Schlenk tube was charged with anhydrous CH_2Cl_2 (4 mL) and anhydrous CF_3CO_2H (1.0 mL, 15.0 mmol) under N_2 atmosphere. The solution was cooled to 0 °C. Compound **2** (416 mg, 1.0 mmol) was added in one portion. The mixture was stirred at 0 °C for 48 h. The volatiles were removed under vacuum and the crude product promptly chromatographed on silica gel to give **3** as a brown oil (362 mg, 71%). ^1H NMR indicated a molar ratio of **3a**:**3b** = 0.87:1. The NMR data of **3b** was identified from that for a mixture of **3a** and **3b**.

Mixture of 3a and 3b

IR (film) ν_{max} 2936, 2855, 1792, 1786, 1695, 1686, 1560, 1541, 1364, 1356, 1223, 1153, 826, 808, 731, 698 cm^{-1}.

(S_p,1_S_,3′_R_)-3′-Phenyl-spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,5′-tetrahydro pyrrolo[2,1-_b_]oxazolium trifluoroacetate] (3b)

TLC (hexanes/ethyl acetate, 1:1 v/v): R_f = 0.65; ^1H NMR (600 MHz, $CDCl_3$): δ 7.46–7.33 (m, 5H), 6.15 (dd, _J_ = 10.2, 5.2 Hz, 1H), 5.58 (dd, _J_ = 10.8, 9.0 Hz, 1H), 5.04 (dd, _J_ = 10.8, 6.0 Hz, 1H), 4.13 (m, 1H), 4.07 (m, 1H), 3.97 (s, 5H), 3.22 (m, 1H), 2.65 (dd, _J_ = 18.6, 10.8 Hz, 1H), 2.56 (m, 1H), 2.48 (m, 2H), 2.26 (m, 1H), 2.19 (m, 1H), 2.11 (m, 1H), 1.83 (m, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 177.9, 157.2 (q, _J_ = 43 Hz, CF_3CO_2), 135.2, 128.7, 128.0, 126.4, 114.5 (q, _J_ = 287 Hz, CF_3), 96.8, 91.0, 70.6, 70.3, 69.5, 68.0, 61.7, 58.3, 54.1, 37.8, 33.4, 29.5, 23.0.

Reductions of 3 and 4a, 4b by $LiAlH_4$

A mixture of **3**, **4a**, and **4b** was prepared from **2** (2.08 g, 5.0 mmol) according to the above procedure. A Schlenk tube was charged with the mixture of **3**, **4a**, and **4b**, and anhydrous THF (50 mL). The solution was cooled to 0 °C. $LiAlH_4$ (1.14 g, 30.0 mmol) was added in portions at 0 °C. After that, the mixture was stirred at 40 °C for 24 h. The mixture was cooled to 0 °C. 1 N NaOH (30 mL) was added dropwise at 0 °C to quench the reaction. AcOEt was added and the mixture well stirred for 40 min. The mixture was filtered through Celite, and the filter cake washed with AcOEt. The filtrate was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (20:1 hexanes/AcOEt) to afford **5a** as a yellow liquid (0.91 g, 45% yield) and **5b** as an orange solid (0.91 g, 45% yield).

_N_-((_R_)-2-Hydroxy-1-phenethyl)-(R_p,1_R_,R_a)-spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,2′-pyrrolidine] (5a)

TLC (hexanes/ethyl acetate, 6:1 v/v): R_f = 0.15; $[\alpha]_D^{20}$ +15.0 (_c_ 1.03, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.42–7.36 (m, 4H), 7.29 (t, _J_ = 7.2 Hz, 1H), 5.28 (dd, _J_ = 10.8, 6.0 Hz, 1H), 4.21–4.05

(m, 7H), 3.91 (dd, *J* = 10.2, 5.4 Hz, 1H), 3.83 (t, *J* = 10.2 Hz, 1H), 3.79 (d, *J* = 1.8 Hz, 1H), 3.17–3.14 (m, 3H), 2.67–2.62 (m, 1H), 2.36 (dd, *J* = 14.4, 7.2 Hz, 1H), 2.15–2.10 (m, 1H), 1.89 (dd, *J* = 10.8, 6.0 Hz, 1H), 1.78–1.71 (m, 3H), 1.55 (m, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 140.5, 128.3, 128.2, 127.0, 101.9, 90.6, 69.4, 69.2, 62.6, 61.1, 59.0, 57.8, 45.4, 40.2, 39.8, 23.8, 22.5; IR (film): 3422, 3084, 2953, 2936, 2851, 1447, 1312, 1288, 1175, 1105, 1030, 1001, 818, 704 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{28}FeNO$ 402.1520; Found 402.1514; m.p. 134.6–136.0 °C.

***N*-((*R*)-2-Hydroxy-1-phenethyl)-(S_p,1*S*,R_a)-spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,2′-pyrrolidine] (5b)**

TLC (hexanes/ethyl acetate, 6:1 v/v): R_f = 0.13; $[\alpha]_D^{20}$ −214 (*c* 1.01, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.8 Hz, 2H), 7.39 (t, *J* = 7.2 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 1H), 5.54 (dd, *J* = 9.3, 5.7 Hz, 1H), 4.10–4.06 (m, 8H), 3.80 (t, *J* = 9.9 Hz, 1H), 3.63 (d, *J* = 1.8 Hz, 1H), 3.12–3.08 (m, 1H), 2.97 (td, *J* = 8.7, 4.2 Hz, 1H), 2.94 (s, 1H), 2.59 (dd, *J* = 14.4, 7.8 Hz, 1H), 2.40 (dd, *J* = 14.4, 7.8 Hz, 1H), 2.17–2.06 (m, 2H), 1.87–1.71 (m, 3H), 1.55 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 140.5, 128.3, 128.0, 126.8, 98.9, 91.9, 70.6, 69.6, 69.5, 62.7, 61.1, 59.6, 59.3, 45.3, 43.3, 38.8, 23.6, 22.9; IR (film) ν_{max} 3422, 3088, 2953, 2940, 2851, 1491, 1447, 1375, 1306, 1288, 1229, 1207, 1180, 1142, 1105, 1030, 883, 818, 746, 702, 459 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{28}FeNO$ 402.1520; Found 402.1514; m.p. 105.0–106.1 °C.

Reduction of 3 by $LiAlH_4$

A Schlenk tube was charged with **3** (1.02 g, 2 mmol) and anhydrous THF (20 mL). The mixture was cooled to 0 °C. $LiAlH_4$ (456 mg, 12.0 mmol) was added in portions at 0 °C. After that, the mixture was stirred at 40 °C for 12 h. The mixture was cooled to 0 °C. 1 N NaOH (12 mL) was added dropwise at 0 °C to quench the reaction. AcOEt was added and the mixture well stirred for 40 min. The mixture was filtered through Celite, and the filter cake washed with AcOEt. The filtrate was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (20:1 hexanes/AcOEt) to afford **6** as orange solids (480 mg, 60% yield), **5a** as a yellow liquid (128 mg, 16% yield) and **5b** as an orange solid (132 mg, 16% yield).

Orange single crystals of **6a** were obtained from a solution of **6a** and **6b**, which were inseparable by silica gel chromatography.

(R_p,1*R*,3′*R*,4′*R*,7′a*S*)-3′-Phenyl-spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,5′-hexahydropyrrolo[2,1-*b*]oxazole] (6a)

TLC (hexanes/ethyl acetate, 6:1 v/v): R_f = 0.60; $[\alpha]_D^{20}$ +105 (*c* 1.03, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.54 (d, *J* = 7.8 Hz, 2H), 7.36 (t, *J* = 8.1 Hz, 2H), 7.23 (t, *J* = 7.5 Hz, 1H), 6.07 (t, *J* = 6.3 Hz, 1H), 4.98 (d, *J* = 4.2 Hz, 1H), 4.41 (t, *J* = 7.8 Hz, 1H), 4.18 (t, *J* = 1.8 Hz, 1H), 4.06 (d, *J* = 1.8 Hz, 1H), 3.98 (s, 5H), 3.83 (d, *J* = 1.8 Hz, 1H), 3.72 (dd, *J* = 8.4, 6.0 Hz, 1H), 2.63–2.58 (m, 1H), 2.35–2.31 (m, 1H), 2.17–2.05 (m, 3H), 1.95–1.87 (m, 2H), 1.70–1.65 (m, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 144.9, 128.5, 126.5,125.7, 98.6, 97.1, 92.8, 74.3, 71.4, 70.3, 69.4, 62.6, 61.3, 60.1, 44.3, 37.5, 29.0, 23.5; IR (film) ν_{max} 3084, 3023, 2937, 2853, 1719, 1601, 1493, 1449, 1373, 1308, 1287, 1163, 1132, 1105, 1074, 1043, 1024, 1001, 820, 806, 735, 702, 662, 505, 478, 461 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{26}FeNO$ 400.1364; Found 400.1358; m.p. 117.8–119.5 °C.

(S_p,1*S*,3′*R*,4′*R*,7′a*S*)-3′-Phenyl-spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,5′-hexahydropyrrolo[2,1-*b*]oxazole] (6b)

TLC (hexanes/ethyl acetate, 6:1 v/v): R_f = 0.60; $[\alpha]_D^{20}$ −180 (*c* 1.00, $CHCl_3$); ^1H NMR (400 MHz,

$CDCl_3$) δ: 7.55 (m, 2H), 7.37 (m, 2H), 7.23 (m, 1H), 5.11 (d, *J* = 5.1 Hz, 1H), 4.85 (t, *J* = 6.9 Hz, 1H), 4.35 (t, *J* = 7.9 Hz, 1H), 4.02 (m, 1H), 3.94 (m, 1H), 3.81 (m, 1H), 3.78 (s, 5H), 3.67 (dd, *J* = 8.0, 6.7 Hz, 1H), 2.69 (m, 1H), 2.39 (m, 1H), 2.18–2.04 (m, 3H), 1.95–1.86 (m, 2H), 1.71–1.57 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ: 143.6, 128.4, 126.9, 126.5, 103.0, 98.9, 90.3, 74.3, 70.6, 68.8, 68.7, 62.2, 60.5, 58.2, 37.1, 36.8, 29.1, 24.4; IR (film) ν_{max} 3084, 2958, 2935, 2855, 1448, 1369, 1298, 1107, 1074, 999, 815, 700 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{26}FeNO$ 400.1364; Found 400.1358; m.p. 147.5–148.2 °C.

_N_-((_R_)-2-(4-Bromobenzoyloxy)-1-phenethyl)-(R_p,1_R_,R_a)-spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,2′-pyrrolidine]-5′-one (7)

To a Schlenk tube were added **4a** (415 mg, 1.0 mmol), DMAP (122 mg, 1.0 mmol), Et_3N (0.3 mL, 2.0 mmol) and CH_2Cl_2 (10 mL). The mixture was cooled in an ice bath. *p*-Bromobenzoyl chloride (439 mg, 2.0 mmol) in CH_2Cl_2 (10 mL) was added dropwise. Then the mixture was stirred at rt for 3 h before it washed with 1 N HCl, saturated aq. $NaHCO_3$ and brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified by column chromatography (4:1 hexanes/AcOEt) to give (R_a)-**7** as a yellow solid (572 mg, 96% yield). R_f = 0.38 (hexanes/AcOEt, 1:1 v/v); $[\alpha]_D^{20}$ +261 (*c* 1.00, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.97 (d, *J* = 8.5 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 7.6 Hz, 2H), 7.41(t, *J* = 7.4 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 1H), 6.11 (t, *J* = 7.3 Hz, 1H), 5.32 (d, *J* = 7.4 Hz, 2H), 4.12 (s, 7H), 3.60 (s, 1H), 2.51 (m, 2H), 2.42 (m, 1H), 2.35 (m, 1H), 2.20 (m, 1H), 2.08 (m, 1H), 2.01 (m, 1H), 1.75 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ: 176.2, 165.1, 138.0, 131.6, 130.8, 128.8, 128.3, 127.9, 127.2, 126.9, 97.1, 90.4, 70.4, 69.3, 69.2, 65.5, 61.5, 57.1, 55.4, 38.9, 33.8, 29.4, 22.6.; IR (film) ν_{max}: 3090, 3030, 2938, 2855, 2245, 1714, 1589, 1410, 1269, 1105, 1069, 756, 731, 698 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{31}H_{29}BrFeNO_3$ 598.0680; Found 598.0675; m.p. 151.8–152.3 °C.

_N_-((_R_)-2-(4-Bromobenzoyloxy)-1-phenethyl)-(R_p,1_R_,R_a)-spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,2′-pyrrolidine] (8)

A dry Schlenk tube was charged with **5a** (147 mg, 0.35 mmol), DMAP (43 mg, 0.5 equiv), Et_3N (0.7 mL, 2.0 equiv) and CH_2Cl_2 (5 mL). The mixture was cooled to 0 °C. 4-Bromobenzoyl chloride (154 mg, 2.0 equiv) in CH_2Cl_2 (5 mL) was added dropwise. The mixture was stirred at 0 °C for 24 h. After that, the mixture was washed with 1 N HCl, saturated $NaHCO_3$, and brine. The mixture was dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography (10:1 hexanes/AcOEt) to afford (R_a)-**8** as a pale brown crystalline solid (103 mg, 50% yield).

TLC (hexanes/ethyl acetate, 6:1 v/v): R_f = 0.75; $[\alpha]_D^{20}$ +67.5 (*c* 1.01, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.53 (t, *J* = 7.8 Hz, 4H), 7.38 (t, *J* = 7.2 Hz, 2H), 7.28–7.27 (m, 1H), 5.80 (t, *J* = 7.2 Hz, 1H), 4.99 (dd, *J* = 12.0, 7.8 Hz, 1H), 4.72 (dd, *J* = 11.4, 7.2 Hz, 1H), 4.12–4.05 (m, 7H), 3.70 (d, *J* = 1.8 Hz, 1H), 3.19–3.08 (m, 2H), 2.55–2.50 (m, 1H), 2.33 (dd, *J* = 14.4, 7.2 Hz, 1H), 2.13–2.08 (m, 1H), 1.90–1.83 (m, 2H), 1.78–1.72 (m, 2H), 1.52–1.47 (m, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 165.9, 141.9, 131.8, 131.1, 128.3, 127.6, 126.7, 100.2, 91.4, 69.6, 69.4, 69.2, 66.9, 61.1, 58.5, 55.6, 46.8, 41.3, 39.7, 23.4, 22.9; IR (film) ν_{max} 2959, 2934, 1719, 1589, 1267, 1173, 1115, 1103, 1070, 1013, 818, 806, 756 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{31}H_{31}BrFeNO_2$ 584.0888; Found 584.0880; m.p. 175.1–176.0 °C.

Dehydration of 4a and 4b

A dry Schlenk tube was charged with a mixture of **4a** and **4b** (415 mg, 1.0 mmol), DMSO (20 mL), hydroquinone (11 mg, 0.1 mmol) and $LiOH{\cdot}H_2O$ (0.84 g, 20.0 mmol). The mixture was stirred at

160 °C for 18 h. DMSO was removed by vacuum distillation. To the residue was added CH_2Cl_2, and the solution was stirred for 12 h. The mixture was filtered through Celite, and the filter cake washed with CH_2Cl_2. The filtrate was dried over anhydrous Na_2SO_4 and then concentrated. The residue was purified by column chromatography (3:1 hexanes/AcOEt) to afford (±)-**10** as a yellow solid (285 mg, 72% yield) and (±)-**11** as an orange solid (31 mg, 8% yield).

(±)-*N*-(1-Phenylethenyl)-spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,2′-pyrrolidin]-5′-one (10)

TLC (hexanes/ethyl acetate, 1:2 v/v): R_f = 0.37; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.58 (d, J = 7.2 Hz, 2H), 7.41–7.34 (m, 3H), 6.27 (s, 1H), 5.45 (s, 1H), 4.13–3.59 (m, 8H), 2.62–2.52 (m, 3H), 2.25–2.21 (m, 3H), 2.09–1.95 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.7, 141.4, 135.8, 128.7, 128.4, 125.3, 117.2, 98.2, 90.0, 70.8, 70.1, 69.6, 61.1, 58.7, 39.6, 34.7, 29.7, 23.2; IR (film) ν_{max} 3084, 2965, 2936, 2853, 1701, 1626, 1493, 1447, 1360, 1296, 1175, 912, 810, 777, 714 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{24}H_{24}FeNO$ 398.1207; Found 398.1201.

(R_p,*R*)-*N*-(1-Phenylethenyl)-spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,2′-pyrrolidin]-5′-one (10)

$[\alpha]_D^{20}$ +225 (*c* 1.01, $CHCl_3$); m.p. 173.8–175.8 °C.

(±)-*N*-Benzyl-spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,2′-pyrrolidin]-5′-one (11)

TLC (hexanes/ethyl acetate, 1:1 v/v): R_f = 0.39; ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36 (t, J = 8.4 Hz, 2H), 7.29–7.25 (m, 3H), 5.10 (d, J = 15.6 Hz, 1H), 5.01 (d, J = 15.6 Hz, 1H), 4.19–4.11 (m, 7H), 3.72 (s, 1H), 2.62 (d, J = 8.4 Hz, 1H), 2.51–2.42 (m, 2H), 2.34 (s, 1H), 2.27–2.22 (m, 1H), 2.15–2.10 (m, 1H), 1.98–1.96 (m, 1H), 1.85–1.80 (m, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 176.1, 138.3, 128.5, 126.7, 126.0, 98.0, 91.2, 70.5, 69.8, 68.5, 61.8, 57.8, 42.8, 39.7, 34.3, 29.2, 23.2; IR (film) ν_{max} 2940, 1690, 1676, 1398, 1387, 1358, 1180, 1107, 1001, 820, 806, 731, 706, 459 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{23}H_{24}FeNO$ 386.1207; Found 386.1201.

(R_p,*R*)-*N*-Benzyl-spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,2′-pyrrolidin]-5′-one (11)

$[\alpha]_D^{20}$ +242 (*c* 0.990, $CHCl_3$).

(±)-Spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,2′-pyrrolidin]-5′-one (1)

A dry Schlenk tube was charged with (±)-**10** (153 mg, 0.38 mmol), THF (3 mL) and H_2O (3 mL). The solution was degassed in three freeze-vacuum-thaw cycles. Concentrated HCl (3.0 mL) was added dropwise under N_2 atmosphere. Then the mixture was stirred at 40 °C under N_2 for 24 h. After that, saturated $NaHCO_3$ was added dropwise at 0 °C to quench the reaction. The mixture was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography (3:1 hexanes/AcOEt) to afford (±)-**1** as a yellow solid (68 mg, 60% yield). TLC (hexanes/ethyl acetate, 1:2 v/v): R_f = 0.26; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.71 (s, 1H), 4.13-4.11 (m, 7H), 3.95 (d, J = 2.4 Hz, 1H), 2.66–2.28 (m, 6H), 2.17–2.11 (m, 1H), 2.02–1.94 (m, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 176.9, 98.1, 93.1, 70.3, 69.0, 64.2, 61.9, 57.8, 43.7, 34.4, 31.0, 23.5; IR (film) ν_{max} 3196, 3094, 3075, 2980, 2965, 2934, 2847, 1688, 1474, 1449, 1429, 1406, 1381, 1358, 1296, 1215, 1175, 1103, 1015, 995, 980, 824, 810, 754, 696, 665, 538, 521, 480 cm^{-1}; HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{16}H_{18}FeNO$ 296.0738; Found 296.0732; m.p. 200 °C decompose.

(R_p,*R*)-Spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,2′-pyrrolidin]-5′-one (1)

$[\alpha]_D^{20}$ +336 (*c* 1.02, $CHCl_3$); m.p. 200 °C decompose.

(S_p,*S*)-Spiro[cyclopentadienyl tetrahydropentalenyl iron (II)-1,2′-pyrrolidine (12)

A dry Schlenk tube was charged with (S_p,*S*)-**1** (48 mg, 0.16 mmol) and anhydrous THF (5 mL). The solution was cooled to 0 °C. $LiAlH_4$ (37 mg, 0.96 mmol) was added at 0 °C. After that, the mixture was stirred at 60 °C overnight. The mixture was cooled to 0 °C. 1 N NaOH (1 mL) was added dropwise at 0 °C to quench the reaction. AcOEt was added and the mixture well stirred for 40 min. The mixture was filtered through Celite, and the filter cake washed with AcOEt. The filtrate was dried over Na_2SO_4 and concentrated. (S_p,*S*)-**12** was obtained as a brown oil (40 mg, 88% yield). TLC (ethyl acetate): R_f = 0.05; $[\alpha]_D^{20}$ −84.9 (*c* 0.990, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.67 (br s, 1H), 4.22 (s, 5H), 4.08 (s, 1H), 4.04 (s, 1H), 4.03 (s, 1H), 3.28 (br s, 2H), 2.85–2.77 (m, 1H), 2.49–2.44 (m, 1H), 2.33–2.22 (m, 2H), 2.06–1.85 (m, 3H), 1.72–1.66 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 99.1, 93.1, 69.9, 69.2, 68.4, 61.3, 58.3, 45.7, 43.5, 37.5, 24.8, 24.1; IR (film) ν_{max} 3383, 3086, 2928, 2855, 1562, 1543, 1400, 1377, 1308, 1103, 1042, 810 cm^{-1}; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{20}FeN$ 282.0945; Found 282.0937.

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Supporting Information

NOESY and ROESY spectra, variable temperature ^{1}H NMR spectra of **4b** in DMSO-d_6, ^{1}H and ^{13}C NMR spectra, and crystal data.

Accession Codes

The X-ray crystallographic data for all the reported crystals have been deposited at the Cambridge Crystallographic Data Centre (CCDC). 6-Ferrocenyl-4-oxo-hexanoic acid: CCDC 1855403; (±)-**1**: CCDC 1855412; **2**: CCDC 1855404; **4a**: CCDC 1855405; **4b**: CCDC 1855406; **5a**: CCDC 1857202; **5b**: CCDC 1855409; **6a**: CCDC 1855407; **6b**: CCDC 1867995; **7**: CCDC 1886077; **8**: CCDC 1855408; (R_p,1*R*)-**10**: CCDC 1855410; (S_p,1*S*)-**10**: CCDC 1857203; (±)-**11**: CCDC 1855411.

Notes

The authors declare no competing financial interests.

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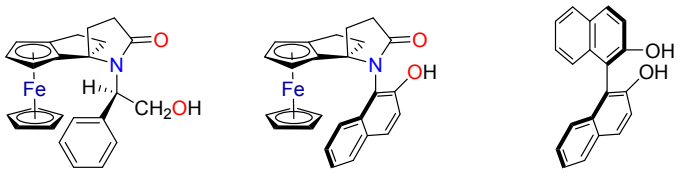
(15) We suggest the following rule to define the sense of the new type of axial chirality. Since the hydrogen atom of phenylglycinol should be uniformly positioned close to the iron (II) nucleus no matter what the chiral sense of phenylglycinol is (see the text), the phenyl group, the hydroxymethyl group and the carbon stereocenter of phenylglycinol are imagined to resemble 2-hydroxynaphthyl as shown below. Comparison of the chiral sense of (*R*)-BINOL with that of an imagined model compound from **4b** is shown below. Accordingly, **4b** is suggested to have (R_a) chirality.



4b model compound similar to (R_a)-**4b** (*R*)-BINOL

(16) See Supporting Information for details.

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