

Communications

Synthesis of Cylindrically Chiral Ferrocenedicarboxylic Acids

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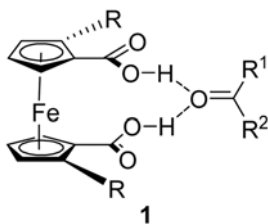
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Received January 5, 2007

Key Words : Cylindrically chiral dicarboxylic acid, Bidentate Brønsted acid, Rhodium carboxylate, Asymmetric cyclopropanation

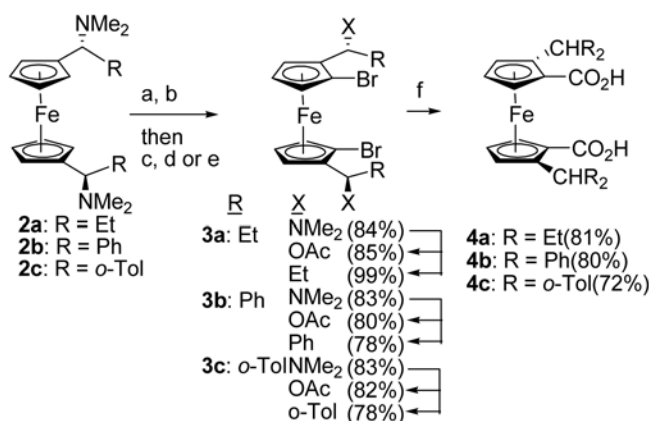
Enantiomerically pure dicarboxylic acids with well defined chirality may be useful as a bidentate Brønsted acid catalyst in double activation of functional groups,¹ and as a chirality-bearing anionic part of metallic carboxylate, which may be used as an asymmetric catalyst such as the rhodium dimers of chiral carboxylic acid.² The latter has been particularly useful in catalytic asymmetric cyclopropanation by transfer of the carbene fragments from diazoalkanes to alkenes.³

In designing such systems, the two carboxy groups must be situated in such a way that the mutual distance between them is appropriate enough for double coordination onto a functional group such as **1** (a carbonyl group in the present case). Herein are reported new cylindrically chiral⁴ dicarboxylic acids with ferrocene backbone and a brief survey of the compounds as the catalysts for the catalytic asymmetric cyclopropanation.



The modular preparation of the ferrocene dicarboxylic acid derivatives is summarized in Schemes 1. The diastereomerically pure diamines **2**⁵ were treated with *n*-BuLi in THF (two-fold introduction of planar chirality) and the resulting doubly *ortho*-lithiated species were quenched with dibromotetrachloroethane to give *ca.* 80% yields of diastereomerically pure bromides **3**. Subsequently, the diamine moieties were converted to the corresponding hydrocarbon by the reaction with Ac₂O, followed by reductive alkylation of the acetates with AlEt₃ or PhZnBr-BF₃·OEt₂.

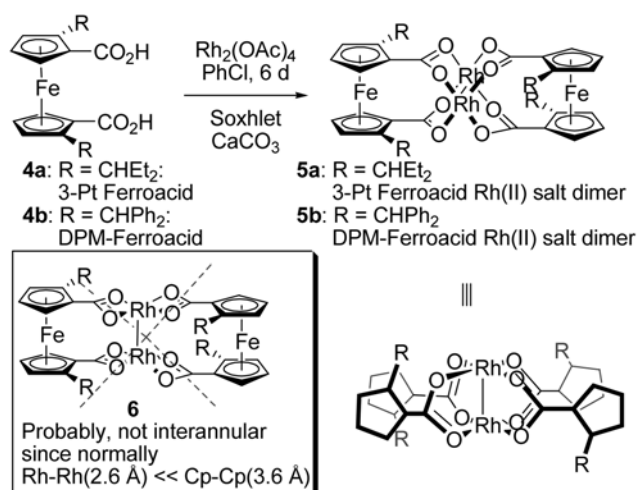
The subsequent preparation of ferrocenedicarboxylic acid derivatives **4** (hereafter abbreviated as Ferroacid) was accomplished by double lithium-bromine exchange with *n*-BuLi in THF at -78 °C followed by bubbling of CO₂ gas into the flask containing the di-lithiated species via cannula, which furnished the dicarboxylic acids in acceptable yields after acidic work-up and recrystallization (81% (**4a**: ethyl



Scheme 1. Reagents and conditions: a) (i) *n*-BuLi, Et₂O, rt, 12 h, (ii) (CCl₂Br)₂, THF, -78 °C to rt; b) Ac₂O, Et₃N, DMAP (cat), 70 °C, 10 h; c) Me₃Al, CH₂Cl₂, -78 °C to rt, 1 h; d) PhMgBr, ZnBr₂, BF₃·OEt₂, THF, 0 °C to rt, 1 h; e) *o*-ToIMgBr, ZnBr₂, BF₃·OEt₂, THF, 0 °C to rt, 1 h; f) (i) *n*-BuLi, THF, -78 °C, 2 h, (ii) CO₂.

acetate) and 80% (**4b**: CH₂Cl₂ and *n*-hexane)) or chromatography (**4c**).⁶ (Scheme 1)

With the new chiral dicarboxylic acids in hands, preparation of the rhodium dimers for catalytic asymmetric cyclopropanation was carried out to quickly test the chiral environment of the dicarboxylic acids. The preparation of the rhodium(II) salt dimers of Ferroacid **4** was accomplished by the ligand exchange reaction^{2a}: A mixture of the dicarboxylic acid **4** (3.0 equiv) and dirhodium tetraacetate was refluxed in chlorobenzene under an argon atmosphere for 6 days through a Soxhlet extractor filled with CaCO₃. During the reaction, the liberated acetic acid was trapped by CaCO₃, which would accelerate the ligand exchange process. Even with this well-established procedure, the preparations were not universally successful; Increase in steric size of the CHR₂ group in **4** resulted in formation of polymers. In line with the assertion, the pure rhodium(II) dimer of 3-pentylferrocene, **5a**, could be obtained after recrystallization with THF and *n*-hexane in *ca.* 50% yields, while the preparation of the corresponding diphenylmethyl derivative, **5b**, was erratic, giving polymeric materials in some cases.⁷ On the other hand, the corresponding dimer from the sterically more demanding DTM-Ferroacid, **8c**, could not be obtained clean-

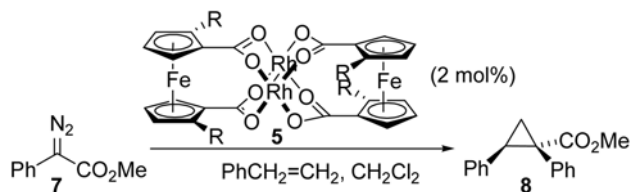


Scheme 2. Preparation of Rh(II) salts of Ferroacids.

ly under the numerous conditions.

Unfortunately, we have been so far unable to obtain crystals of **5a** appropriate for X-ray crystal structure determination. But among the two possible structures, **5** and **6**, with the same correct mass, the structure of the D₂-symmetric bridging dimer **5** seems to be more reasonable than the interannular structure **6** because the usual distance between the two Cp rings of ferrocenes, 3.6 Å, is far longer than the usual bond length of Rh-Rh in the usual rhodium dimers, 2.6 Å⁸ (Scheme 2).

The D₂ symmetry of the rhodium(II) catalyst may be useful in providing high ee's in catalytic asymmetric cyclopropanation, which was proven even by conformationally rigid D₂-symmetric catalysts.² Consequently, with the new chiral catalyst in hands, asymmetric cyclopropanation of styrene was carried out. Even though the cyclopropanation reaction of ethyl diazoacetate did not provide meaningful asymmetric induction, ethyl phenyldiazoacetate did indeed give high diastereoselectivity with moderate enantioselection.⁹ For example, the reaction of ethyl phenyldiazoacetate with 5 equiv. of styrene in the presence of 2 mol% of the rhodium (II) dimer derived from 3-Pt-Ferroacid **5a** in CH₂Cl₂ (0.12 M) at 20 °C under N₂ atmosphere gave the cyclopropane product **8** of 21% ee in 76% yield. The reaction with a crude rhodium(II) dimer derived from DPM-Ferroacid **5b** (meaning that the compound contained varying amounts of the polymer salts) gave the cyclopropane product **8** of much improved 48% ee in 79% yield, even though the reactions were not highly reproducible.



In conclusion, we have succeeded in the synthesis of new cylindrically chiral ferrocenyldicarboxylic acid. Although the ee value of catalytic asymmetric cyclopropanation was

only moderate, it was the first catalytic asymmetric cyclopropanation using the cylindrical chirality. A thorough study of the catalyst dimers is guaranteed in other reactions.

Acknowledgments. The present work was supported by the Korea Research Foundation Grant funded by the Korean Government through the program of "Advanced Basic Research Laboratory" and Sogang University.

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- Selected spectroscopic data. 3-Pt Ferroacid {(p₅,p₅S)-1,1'-di(3-pentyl)-2,2'-ferrocenedicarboxylic acid} **4a**: [α]_D²⁵ +152 (c 0.5, DMSO); MS (TOF) m/z (relative intensity): 413.4441 (100, M-H), 414.4666 (25.8), 415.4713 (5.2); ¹H NMR (DMSO, 500 MHz): δ 12.101 (bs, 2H), 4.474-4.471 (m, 2H), 4.253-4.247 (m, 4H), 3.006-2.992 (m, 2H), 1.955-1.908 (m, 2H), 1.516-1.419 (m, 4H), 1.369-1.315 (m, 2H), 1.008-0.978 (t, J_{HH} = 7.5 Hz, 6H), 0.480-0.451 (t, J_{HH} = 7.5 Hz, 6H); ¹³C NMR (DMSO, 125.7 MHz): δ 171.687, 97.557, 73.058, 71.615, 70.561, 70.309, 36.328, 25.749, 23.972, 12.470, 8.385. DPM-Ferroacid {(p₅,p₅S)-1,1'-bis(diphenylmethyl)-2,2'-ferrocene dicarboxylic acid} **4b**: [α]_D²⁵ +394 (c 0.5, CH₂Cl₂); MS (TOF) m/z (relative intensity): 629.1393 (100, M+Na), 630.1290 (45.8), 631.1313 (9.7), 632.1815 (3.2); ¹H NMR (CDCl₃, 500 MHz): δ 7.342-6.883 (m, 20H), 5.925 (s, 2H), 5.021 (s, 2H), 3.929 (s, 2H), 3.651 (s, 2H); ¹³C NMR (CDCl₃, 125.7 MHz): δ 176.408, 144.967, 143.811, 129.891, 128.365, 128.195, 128.118, 126.792, 126.165, 96.536, 75.111, 72.872, 72.532, 71.857, 49.305. DTM-Ferroacid {(p₅,p₅S)-1,1'-bis(di-*o*-tolylmethyl)-2,2'-ferrocene dicarboxylic acid} **4c**: ¹H NMR (CDCl₃, 300 MHz): δ 7.316-6.680 (m, 16H), 6.256 (s, 2H), 5.057 (s, 2H), 4.070 (s, 2H), 3.809 (s, 2H), 2.828 (s, 6H), 2.195 (s, 6H).
- Selected spectroscopic data for 3-Pt-Ferroacid rhodium(II) dimer **5a**: anal. calcd. for C₄₄H₅₆Fe₂O₈Rh₂: C, 51.29; H, 5.48. Found: C, 51.227; H, 5.549; Mass for C₄₄H₅₆Fe₂O₈Rh₂: 1030.0784 (m/z). Found (FAB, high resolution): 1030.0786; IR (KBr) 2961.18, 2935.05, 2874.27, 1661.13, 1564.63, 1462.40, 1375.56 cm⁻¹; DPM-Ferroacid rhodium(II) dimer **5b**: Mass for C₇₆H₅₆Fe₂O₈Rh₂: 1414.0784. Found (FAB, low resolution): 1414; IR (KBr) 3059.19, 3026.87, 2956.41, 1623.50, 1599.73, 1563.79, 1492.88, 1461.41, 1372.38, 1244.80 cm⁻¹.
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