

Asymmetric Cyclopropanation of Styrene Catalyzed by Chiral Macrocyclic Iron(II) Complexes

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Three chiral tetraaza macrocyclic ligands (**4a–c**) were synthesized by the cyclization reaction of diamines with dithioaldehydes. The iron(II) complexes of ligands **4a** and **4c**, as well as two chiral iron(II) porphyrin complexes, Fe^{II}(D₄-TpAP) and Fe(α₂β₂-BNP), are efficient catalysts for the cyclopropanation of styrene with diazoacetate reagents. The cyclopropyl esters were produced with high diastereoselectivities and good yields. However, the enantioselectivities were modest at best. The rationalization of the stereoselectivity in these cyclopropanation reactions is presented. The results of a single-crystal X-ray analysis of the ligand **4a** are also reported.

Introduction

Transition metal-catalyzed cyclopropanation has been an area of intensive study over the past several decades.¹ Since the first report² of chiral induction in cyclopropanation, a number of excellent catalyst systems have been developed that achieve highly selective asymmetric results.³ In this context, chiral ruthenium porphyrin catalysts have received much attention recently.⁴ However, despite the presence of a wide variety of chiral iron porphyrins and their remarkable efficiency and selectivity in catalytic epoxidation of olefins,⁵ few of these have been tested as cyclopropanation catalysts. In fact, chiral iron porphyrins were not used in cyclopropanation until 1999.⁶

Due to the structural resemblance to porphyrins, the related tetraaza macrocyclic ligands seemed to be a logical extension to metalloporphyrin chemistry. We

have examined the application of an iron complex of tetramethyldibenzotetraaza[14]annulene (tmtaa) in catalytic nonchiral cyclopropanation reactions.⁷ These ligands provide the possibility of introducing auxiliary stereogenic centers in close proximity to the active metal sites, making them promising candidates in asymmetric catalysis studies.

In this paper, we report the nontemplate synthesis of chiral macrocyclic ligands and the application of their iron(II) complexes in asymmetric cyclopropanation catalysis. In addition, we report the catalytic results of two chiral iron porphyrin complexes (Chart 1).

Experimental Section

General Procedures. All manipulations involving air- or moisture-sensitive iron(II) complexes were performed under a nitrogen atmosphere using a Vacuum Atmospheres glovebox equipped with a Model MO40-1 Dri-Train gas purifier. Solvents used in the catalytic reactions were dried and degassed. The starting materials, 4-phenyl-1,2-dithiolium iodide (**2a**), and 4-(*p*-nitrophenyl)-1,2-dithiolium iodide (**2b**) were prepared according to literature methods.⁸ The chiral diamine, (*R,R*)-(–)-1,2-diaminocyclohexane (dach), was resolved from a commercial mixture by a published procedure.⁹ A reported method was used to synthesize (1*R*,3*R*,4*S*)-(–)-menthyl diazoacetate.¹⁰ Fe(D₄-TpAP) was prepared by reaction of the free base porphyrin¹¹ and anhydrous iron(II) bromide in the presence of 2,6-lutidine according to the procedure of Collman.¹² Fe(α₂β₂-BNP) was prepared by reduction of Fe(α₂β₂-BNP)Cl¹³ with Zn/Hg amalgam in THF or toluene.¹⁴ The reactivity pattern and UV–vis spectral properties were similar with those of Fe(TTP). All other reagents were used as purchased.

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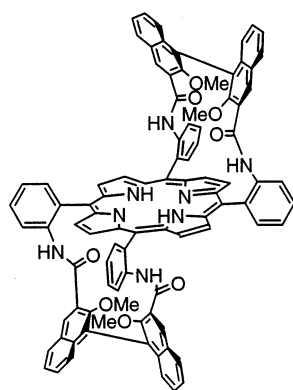
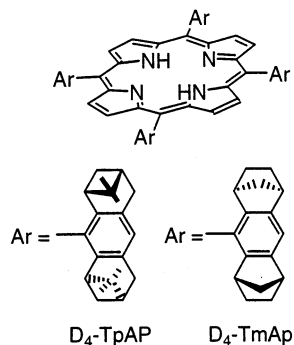
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Chart 1. Structures of Chiral Porphyrins Used in this Studybis-biaphthyl porphyrin
 α_2, β_2 -BNP

¹H and ¹³C NMR data were acquired on Varian VXR (300 MHz, 20 °C) or Bruker DRX (400 MHz, 25 °C) spectrometers. Chemical shifts were referenced to residual solvent peaks (δ 7.24, CHCl₃; 7.15, C₆D₅H). UV-vis data were recorded on a HP8452A diode array spectrophotometer and reported as λ_{max} in nm (log ϵ). Elemental analyses (C, H, N) were performed by Iowa State University Instrument Services. Optical rotation data were measured on a JASCO DIP-370 digital polarimeter at 589 nm. GC-MS studies were performed on a Varian gas chromatograph coupled to an ITS 40 ion trap mass spectrometer (capillary column DB-5MS). GC analyses were performed on a HP 5890 gas chromatograph equipped with a flame ionization detector and a DB-5 capillary column (30 m \times 0.32 mm i.d.). Chiral capillary GC analyses were performed on a HP 5890 gas chromatograph equipped with a flame ionization detector and a CP-Chirasil-Dex CB capillary column (25 m \times 0.25 mm i.d.).

Preparation of Dithioaldehyde 3a. In a typical preparation, 4-phenyl-1,2-dithiolium iodide, **2a** (8.24 g, 26.9 mmol), was suspended in dry benzene (200 mL), and (*R,R*)-dach (3.18 g, 27.8 mmol) in benzene (50 mL) was added slowly. After stirring for 1 h, the yellow precipitate was removed by filtration and the filtrate taken to dryness under reduced pressure to afford **3a**, which was used for the next step without further purification. Yield: 5.04 g (92%). ¹H NMR (CDCl₃, 300 MHz): δ 14.30 (s, 2H, NH), 10.15 (d, ³J_{H-H} = 3 Hz, 2H, CH(=S)), 7.47 (dd, ³J_{H-H} = 12.9 Hz, 3 Hz, 2H, C=CHNH), 7.09–7.29 (m, 10H, aromatic), 3.21 (m, 2H, CHN), 2.31 (m, 2H, C₆H₁₀), 1.91 (m, 2H, C₆H₁₀), 1.63 (m, 2H, C₆H₁₀), 1.48 (m, 2H, C₆H₁₀).

Preparation of Dithioaldehyde 3b. In a typical preparation, 4-(*p*-nitrophenyl)-1,2-dithiolium iodide, **2b** (350 mg, 0.997 mmol), was suspended in dry benzene (10 mL), and (*R,R*)-dach (113 mg, 0.990 mmol) in benzene (6 mL) was added slowly. After stirring for 1 h, the yellow precipitate was removed by filtration and the filtrate taken to dryness under reduced pressure to afford **3b**, which was used for the next step without further purification. Yield: 198 mg (80%). ¹H NMR (CDCl₃, 300 MHz): δ 14.32 (s, 2H, NH), 10.30 (d, ³J_{H-H} = 3 Hz, 2H, CH(=S)), 3.29 (m, 2H, CHN), 2.34 (m, 2H, C₆H₁₀), 1.98 (m, 2H, C₆H₁₀), 1.4–1.7 (m, 4H, C₆H₁₀). Imine and aromatic peaks between 7.2 and 8.2 ppm were obscured by impurities.

Synthesis of H₂[HPhH(dach)₂] (4a). To a hot solution of **3a** (2.52 g, 6.20 mmol) in benzene (250 mL) was added (*R,R*)-dach (1.29 g, 11.30 mmol) in benzene (70 mL) through a pressure-equalizing dropping funnel over 3 h. The mixture was kept briskly boiling for 12 h and reduced to dryness in vacuo. Addition of methanol induced the separation of a yellow solid. Further purification was achieved by layering a filtered chloroform solution of **4a** and precipitating with methanol (1:2 v/v). Filtering the solid and drying in air produced light yellow crystals. Yield: 0.772 g (28%). ¹H NMR (CDCl₃, 300 MHz): δ 11.62 (s, 2H, NH), 7.71 (s, 4H, C=CHN), 7.26 (m, 4H, *m*-C₆H₅), 7.20 (m, 4H, *o*-C₆H₅), 7.09 (m, 2H, *p*-C₆H₅), 3.19 (m, 4H, CHN), 2.18 (m, 4H, C₆H₁₀), 1.89 (m, 4H, C₆H₁₀), 1.47 (m, 4H, C₆H₁₀), 1.39 (m, 4H, C₆H₁₀). ¹³C NMR (CDCl₃, 300 MHz): δ 150.7 (C=CHN), 141.9, 128.5, 125.3, 124.2, 105.8, 64.6 (CHN on C₆H₁₀), 29.5, 24.9. IR (KBr): 3500, 2930, 2851, 1635, 1578, 1290, 1265 cm⁻¹. UV-vis (CHCl₃): 296 nm (4.82), 331 (4.72), 420 (3.46). MS (EI): 452 (M⁺). [α]_D²⁶ -739.5° (c 0.0064, CHCl₃). Anal. Calcd for C₃₀H₃₆N₄·0.5H₂O: C, 78.05; H, 8.08; N, 12.14. Found: C, 78.10; H, 7.79; N, 11.95.

Alternatively, **4a** could be prepared from dithioaldehyde **3c** and excess (*R,R*)-dach by an amine exchange reaction. To a hot solution of **3c** (70.0 mg, 0.191 mmol) in benzene (20 mL) was added (*R,R*)-dach (72.6 mg, 0.636 mmol) in benzene (5 mL) through a pressure-equalizing dropping funnel over 3 h. The mixture was kept briskly boiling for 12 h and reduced to dryness in vacuo. The workup procedure as described above yielded light yellow crystals. Yield: 24 mg (28%). The ¹H NMR spectrum was identical to the above data.

Synthesis of H₂[H(*p*-NO₂-Ph)H(dach)₂] (4b). To a hot solution of **3b** (669 mg, 1.35 mmol) in benzene (120 mL) was added (*R,R*)-dach (293 mg, 2.57 mmol) in benzene (20 mL) through a pressure-equalizing dropping funnel over 3 h. The mixture was kept briskly boiling for 12 h and reduced to dryness in vacuo. The workup procedure as described for **4a** was used to afford a red-orange product. Yield: 341 mg (47%). ¹H NMR (CDCl₃, 300 MHz): δ 12.25 (s, 2H, NH), 8.10 (d, ³J_{H-H} = 9 Hz, 4H, C₆H₄NO₂), 7.90 (s, 4H, C=CHN), 7.27 (d, ³J_{H-H} = 9 Hz, 4H, C₆H₄NO₂), 3.26 (m, 4H, CHN), 2.27 (m, 4H, C₆H₁₀), 1.98 (m, 4H, C₆H₁₀), 1.45 (m, 8H, C₆H₁₀). ¹³C NMR (CDCl₃, 300 MHz): 151.3 (C=CHN), 148.9, 124.6, 123.5, 103.7, 64.5 (CHN on C₆H₁₀), 29.5, 24.8. IR (KBr): 3500, 2930, 2857, 1635, 1578, 1334, 1284, 1280, 1110 cm⁻¹. UV-vis (THF): 437 (4.43). MS (EI): 542 (M⁺). MS (CI/NH₃): 543 (M + H⁺), 560 (M + NH₄⁺). [α]_D²⁶ -466.0 (c 0.0013, CHCl₃).

Synthesis of H₂[HPhH(dpen)₂] (4c). An amine exchange reaction was used to prepare **4c** from dithioaldehyde **3c** and (*R,R*)-1,2-diphenylethylenediamine (dpen). To a hot solution of **3c** (174 mg, 0.474 mmol) in benzene (50 mL) was added (*R,R*)-1,2-diphenylethylenediamine (203 mg, 0.956 mmol) in benzene (25 mL) through a pressure-equalizing dropping funnel over 3 h. The mixture was kept briskly boiling for 12 h and reduced to dryness in vacuo. The workup procedure as described for **4a** was used to produce light yellow crystals. Yield: 76 mg (25%). ¹H NMR (CDCl₃, 400 MHz): δ 12.42 (s, 2H, NH), 7.51 (d, ³J_{H-H} = 7.6 Hz, 8H, *o*-C₆H₅ on ethylene bridge), 7.44 (d, ³J_{H-H} = 6.4 Hz, 4H), 7.38 (t, ³J_{H-H} = 7.6 Hz, 8H, *m*-C₆H₅ on ethylene bridge), 7.29 (t, ³J_{H-H} = 7.6 Hz, 4H, *p*-C₆H₅ on ethylene bridge), 7.09 (t, ³J_{H-H} = 7.6 Hz, 4H,

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m-C₆H₅), 6.95 (m, 6H, *o,p*-C₆H₅), 4.80 (s, 4H, NCH). ¹³C NMR (CDCl₃, 300 MHz): 155.5, 144.0, 140.8, 128.7, 128.5, 127.5, 127.3, 125.1, 124.4, 73.3 (NCH). UV-vis (THF): 302 (3.92), 339 (3.94). MS (EI): 648 (M⁺). MS(CI/NH₃): 649 (M + H⁺). [α]_D²⁶ -28.9 (c 0.0020, CHCl₃).

Preparation of Lithium Salt Li₂[HPhH(dach)₂]. A solution of **4a** (133 mg, 0.294 mmol) and LiN(TMS)₂ (644 mg, 3.85 mmol) in dry THF (20 mL) was allowed to stir at ambient temperature under an inert atmosphere for 12 h and then reduced to dryness under vacuum. The residue was taken up with THF (4 mL) and layered with hexane (12 mL). After cooling overnight at -25 °C, an orange product was filtered, washed with hexane, and dried in vacuo. Yield: 102 mg (74%). ¹H NMR (C₆D₆, 300 MHz): δ 8.40 (s, 4H, C=CHN), 7.56 (d, ³J_{H-H} = 7.8 Hz, 4H, *o*-C₆H₅), 7.37 (t, ³J_{H-H} = 7.8 Hz, 4H, *m*-C₆H₅), 7.07 (t, ³J_{H-H} = 7.8 Hz, 2H, *p*-C₆H₅), 3.05 (m, 4H, CHN), 2.29 (m, 4H), 1.83 (m, 4H), 1.30 (m, 8H). Variable amounts of THF were included in crystals as observed by ¹H NMR.

Iron(II) Complexes. Compound Fe[HPhH(dach)₂] (**4a-Fe**) was prepared by reaction of the lithiated ligand and anhydrous FeBr₂ in THF and purified by column chromatography on alumina eluted with THF-toluene (1:10) as a purple solid. Due to the high sensitivity to air, no satisfactory analytical data could be obtained. However, a broad peak around 21 ppm was observed in ¹H NMR, and the mass analysis showed the molecular ion at *m/z* 504. The complexes were used in catalytic reactions immediately. Complexes **4b-Fe** and **4c-Fe** were prepared similarly.

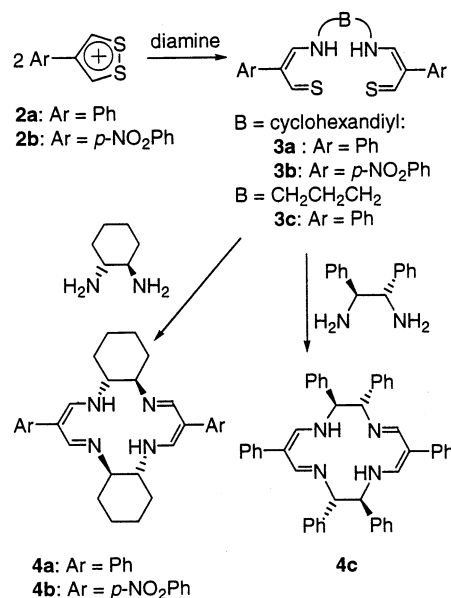
Catalytic Cyclopropanation Reactions by Iron Porphyrin Complexes. In a typical experiment, styrene (2 mmol), iron porphyrin (0.1–0.4 mol % relative to diazoacetates), and *n*-dodecane (30 μL, internal standard) were placed into a round-bottom flask and dissolved in 3 mL of solvent. A solution of ethyl diazoacetate (0.2 mmol) in 10 mL of solvent was added dropwise through a pressure-equalizing dropping funnel over 30 min to 6 h. After the addition was finished, an aliquot of the reaction mixture was taken and analyzed by GC.

Catalytic Cyclopropanation Reactions by Fe(II) Complexes of 4a, 4b, and 4c. In a typical experiment, styrene (2 mmol), iron complex (1–2 mol % relative to diazoacetates), and *n*-dodecane (30 μL, internal standard) were placed into a round-bottom flask and dissolved in 3 mL of solvent. A solution of ethyl diazoacetate (0.2 mmol) in 10 mL of solvent was added dropwise through a pressure-equalizing dropping funnel over 30 min to 6 h. After the addition was finished, an aliquot of the reaction mixture was taken and analyzed by GC.

Structural Determination of 4a. A yellow prismatic crystal with approximate dimensions 0.5 × 0.5 × 0.2 mm³ was mounted on a glass fiber. Data collections at 173 K were performed on a Bruker SMART 1000 CCD-based diffractometer with graphite-monochromated Mo Kα radiation (0.71073 Å), using the full-sphere ω/2θ scan routine. The datasets were corrected for Lorentz and polarization effects. The absorption correction was based on fitting a function to the empirical transmission surface as sampled by multiply equivalent measurements.¹⁵

The systematic absences in the diffraction data were consistent for the space groups *P2*₁ and *P2*/*m*. The *E*-statistics suggested strongly the non-centrosymmetric space group *P2*₁. This yielded chemically reasonable and computationally stable results of refinement. The structure has a pseudo inversion center. However, all attempts to convert the unit cell to higher symmetry failed. The positions of all non-hydrogen atoms were found by direct methods and refined in a full-matrix anisotropic approximation. All hydrogen atoms except those bonded to N atoms were placed at calculated positions and refined using a riding model. The hydrogen atoms bonded to N atoms

Scheme 1. Synthesis of Chiral Macrocylic Ligands



were found from a Fourier map and were treated with a riding model using fixed temperature factors and an occupancy of 0.5.

Results

Synthesis of the Chiral Ligands. New chiral tetraaza macrocycles were synthesized by a modification of a literature procedure that was used for nonchiral N₄-ligands.¹⁶ The iodide salt of 4-phenyl-1,2-dithiolium was treated with (*R,R*)-dach to afford the open chain dithioaldehyde **3a**, which was further cyclized by excess diamine under high dilution conditions to afford H₂-[HPhH(dach)₂] (**4a**) as light yellow crystals in 17–32% yield (Scheme 1). No attempt was made to optimize the yield. Analogously, macrocycle **4b** was prepared as a brick-red powder, starting from 4-(*p*-nitrophenyl)-1,2-dithiolium iodide. In an alternative route, **4a** could be prepared from the open chain dithioaldehyde **3c** and excess (*R,R*)-dach by amine exchange to afford similar yields. Ligand **4c** was obtained in this way from **3c** and (*R,R*)-diphenylethylenediamine.

The structure of macrocyclic ligand **4a** was further determined by a diffraction analysis. X-ray crystallographic data for **4a** are compiled in Table 1, and significant bond lengths and bond angles are collected in Table 2. The N–C distances within the 1,3-propanediiminato linkages are virtually identical, ranging over 1.298–1.310 Å. The C–C distances within the 1,3-propanediiminato linkages averaged between 1.46 and 1.471 Å. This is somewhat different from those found for a closely related tetraaza macrocyclic free ligand, H₂tmtaa, where the corresponding N–C distances are slightly longer and the C–C distances are slightly shorter.¹⁷ Due to the steric interaction of the methyl groups and the benzenoid rings, H₂tmaa adopts a nonplanar saddle shape with two N–H atoms directed

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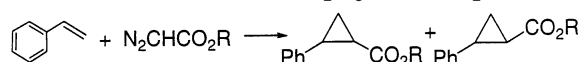
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Table 1. Crystal Data and Structure Refinement for Ligand 4a

empirical formula	C ₃₀ H ₃₆ N ₄
fw	452.63
temperature	173(2) K
wavelength	0.71073 Å
cryst syst	Monoclinic
space group	<i>P</i> 2 ₁
<i>a</i>	6.2799(5) Å
<i>b</i>	11.1105(9) Å
<i>c</i>	17.5679(14) Å
α	90°
β	96.6780(10)°
γ	90°
volume	1217.45(17) Å ³
<i>Z</i>	2
density(calcd)	1.235 mg/m ³
data/restraints/params	5566/1/323
goodness-of-fit on <i>F</i> ²	0.848
final <i>R</i> indices [<i>I</i> > 2 σ (<i>I</i>)]	<i>R</i> 1 = 0.0437, w <i>R</i> 2 = 0.0826
<i>R</i> indices (all data)	<i>R</i> 1 = 0.0759, w <i>R</i> 2 = 0.0902
abs struct param	0(2)
largest diff peak and hole	0.165 and -0.200 e·Å ⁻³

Table 2. Selected Bond Lengths (Å) and Bond Angles (deg) for 4a

C(1)–N(1)	1.460(2)	N(1)–C(1)–C(2)	114.46(16)
C(1)–C(2)	1.520(3)	N(1)–C(1)–C(6)	108.27(14)
C(1)–C(6)	1.534(2)	C(2)–C(1)–C(6)	110.32(15)
C(2)–C(3)	1.528(2)	C(1)–C(2)–C(3)	111.51(16)
C(3)–C(4)	1.522(2)	C(4)–C(3)–C(2)	110.57(16)
C(4)–C(5)	1.521(3)		
C(5)–C(6)	1.528(2)		
C(6)–N(2)	1.463(2)		
C(7)–N(2)	1.306(2)		
C(7)–C(8)	1.414(3)		
C(8)–C(15)	1.399(2)		
C(15)–N(3)	1.306(2)		

Table 3. Asymmetric Cyclopropanation of Styrene with Chiral Iron(II) Porphyrin Complexes^a

R	ligand	yield %	t/c	% ee ^b trans	% ee ^b cis	solv
Et	D ₄ -TpAP	99	21	45(<i>S,S</i>) ^c	21(1 <i>R</i> ,2 <i>S</i>)	PhMe
t-Bu	D ₄ -TpAP	99	7.5	20	30	PhMe
menthyl	D ₄ -TpAP	78	10	27	78	PhMe
Et	$\alpha_2\beta_2$ -BNP	94.8	5.8	27(<i>R,R</i>)	25(1 <i>R</i> ,2 <i>S</i>)	PhMe
t-Bu	$\alpha_2\beta_2$ -BNP	85.6	3.2	24	74	PhMe
menthyl	$\alpha_2\beta_2$ -BNP	64.3	3.3	55	40	PhMe

^a See Experimental Section for reaction conditions. ^b de for menthyl ester. ^c Absolute configurations were assigned according to refs 21c and 24.

out of the N₄-plane. The free ligand **4a** however has a planar geometry with in-plane N–H bonds.

Asymmetric Cyclopropanation Catalyzed by Fe^{II}(D₄-TpAP). Iron(II) porphyrins are effective catalysts in the cyclopropanation of olefins with ethyl diazoacetate (EDA).¹⁸ With suitable chiral auxiliaries incorporated into the periphery of iron porphyrin complexes, asymmetric cyclopropanation was anticipated. Two chiral iron(II) porphyrins (Chart 1) were examined as catalysts in the cyclopropanation of styrene, and the results are summarized in Table 3. Fe(D₄-TpAP) was found to be an efficient cyclopropanation catalyst for styrene and alkyl diazoacetate. Slow addition of a toluene solution of EDA to a toluene solution containing

styrene and Fe(D₄-TpAP) afforded cyclopropyl esters in excellent yield, 99% based on EDA, with a trans/cis ratio of 21. No EDA coupling products, fumarate or maleate, were detected. However, the asymmetric induction was poor to modest at 45% ee for the trans isomer and 21% ee for the cis isomer. This result is inferior to an analogous chiral ruthenium porphyrin catalyst, Ru(D₄-TmAP) (Chart 1). As observed in other iron porphyrin-catalyzed cyclopropanation reactions, the trans/cis ratio displayed a modest solvent dependence. When THF was used as the solvent, the trans/cis ratio increased to 44. This is among the highest trans selectivity obtained to date for these reagents. In CH₃CN, the ratio dropped to 12.

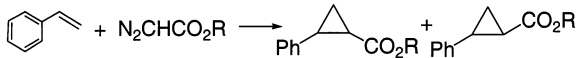
The effect of diazo reagents on the stereo- and enantioselectivity was examined by applying two bulkier diazo reagents, *tert*-butyl and (–)-menthyl diazoacetates as the carbene sources in catalytic cyclopropanation reactions. The cyclopropanation yields were good to excellent, 99% and 78%, respectively. However, the stereochemical outcome was not as good as hoped. Both stereo- and enantioselectivity decreased. For example, trans/cis ratios of 7.5 and 20% ee for the trans isomer were obtained with *tert*-butyl diazoacetate.

Asymmetric Cyclopropanation Catalyzed by Fe^{II}($\alpha_2\beta_2$ -BNP). Fe^{III}($\alpha_2\beta_2$ -BNP)Cl was shown to be an efficient catalyst for asymmetric epoxidation of terminal olefins, with up to 90% ee achieved for some simple olefins.¹³ However, when Fe^{II}($\alpha_2\beta_2$ -BNP) was employed as a catalyst in the cyclopropanation reaction of styrene, poor results were obtained. The trans/cis ratio of 3–6 was generally observed. Performing the reaction in donor solvents such as THF did not improve the selectivity significantly. The enantioselectivity was also inferior. Only 27% and 25% ee were observed for trans and cis cyclopropane isomers from the EDA reaction, respectively. The chiral induction for the trans isomer was opposite of that obtained in the Fe(D₄-TpAP)-catalyzed reaction, while the same chiral preference for the cis isomer was observed for both catalysts. Again, no significant improvement resulted when diazo reagents bearing bulky ester groups were used as carbene sources.

Asymmetric Cyclopropanation Catalyzed by Fe(II)[HPhH(dach)₂] and Fe(II)[H(*p*-NO₂-Ph)H(dach)₂]. Enantiomerically pure *trans*-1,2-diamino-cyclohexane derivatives have found great utility as chiral auxiliaries or ligands in asymmetric catalysis.¹⁹ We thus synthesized a tetraaza macrocyclic ligand, **4a**, incorporating two (*R,R*)-dach bridges. The iron(II) complex of this ligand was investigated in catalytic cyclopropanation of styrene. The results are contained in Table 4. A total yield of 87% was obtained with a trans/cis ratio of 7.4 when EDA was used. However, the enantioselective outcome was only modest, 42% ee for both cis and trans products. Changing the ester substituents from ethyl to *tert*-butyl resulted in a significant drop of both productivity (15%) and diastereoselectivity (trans/cis 4.5) of cyclopropanation products, while (–)-menthyl diazoacetate resulted in higher yield (95%) and higher selectivity (trans/cis 13.3).

(18) Wolf, J. R.; Hamaker, C. G.; Djukic, J.-P.; Kodadek, T.; Woo, L. K. *J. Am. Chem. Soc.* **1995**, *117*, 9194.

(19) Bennani, Y. L.; Hanessian, S. *Chem. Rev.* **1997**, *97*, 3161, and references therein.

Table 4. Asymmetric Cyclopropanation of Styrene by Iron(II) Chiral Macrocylic Complexes with 4a, 4b, and 4c^a


R	ligand	yield %	t/c	% ee ^b trans	% ee ^b cis	solv
Et	4a	87	7.4	42(<i>R,R</i>) ^c	42(<i>1S,2R</i>) ^c	PhMe
t-Bu	4a	15	4.5	19	32	PhMe
menthyl	4a	95	13.3	79	n.d. ^d	PhMe
Et	4b	16	3.1	38	48	PhMe
Et	4c	54	9.1	~0	~0	PhMe
t-Bu	4c	46	10.1	~0	~0	PhMe
menthyl	4c	71	14.9	55	45	PhMe

^a See Experimental Section for reaction conditions. ^b de for menthyl ester. ^c Absolute configurations were assigned according to refs 21c and 24. ^d Not determined.

Furthermore, Fe-**4a** was also found active in catalyzing cyclopropanation of styrene with aryl diazomethane. When mesityl diazomethane was used as the carbene source a 90% yield of cyclopropanation was obtained with a trans/cis ratio of 2.3. However, only trivial enantioselectivity was observed.

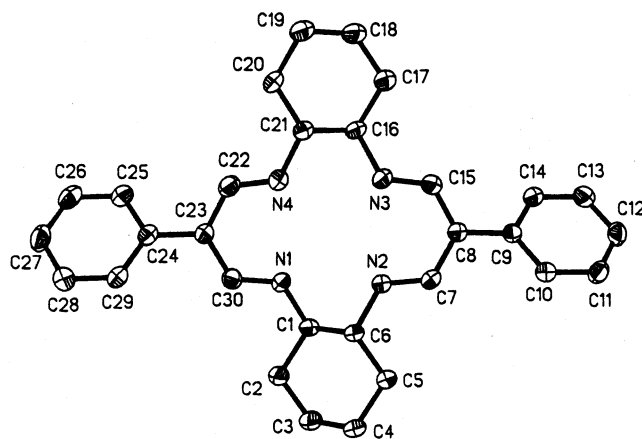
For metalloporphyrin catalysts, attachment of electron-withdrawing groups at *meso*- or β -pyrrole positions generally increases the reactivity of catalysts.²⁰ Thus **4b**, an analogue of **4a** bearing two *para* nitro groups, was examined as a ligand in the cyclopropanation reaction of styrene and EDA. Similar asymmetric induction was achieved. However, the chemical yield and diastereoselectivities were low; only a 16% yield of cyclopropane was obtained with a trans/cis ratio of 3.1.

Asymmetric Cyclopropanation Catalyzed by Fe(II)[HPhH(dpem)]₂. In an attempt at tuning the steric properties of the N₄-macrocylic ligands, (*R,R*)-diphenylethylenediamine bridges were introduced into the macrocylic ligand, in place of (*R,R*)-dach. The corresponding iron complexes gave reasonable chemical yields and good trans selectivity of cyclopropyl esters by treatment of styrene with ethyl, *tert*-butyl, or (-)-menthyl diazoacetates in the presence of the catalyst, but failed to produce any notable enantio differentiation in the former two diazoacetates. With (-)-menthyl diazoacetate, 55% de and 45% de were observed for the trans and cis isomers, respectively.

Discussion

Effect of Diazo Reagent and Ligand on Cyclopropanation. As with other iron porphyrins, Fe^{II}(D₄-TpAP) and Fe^{II}($\alpha_2\beta_2$ -BNP) both were efficient catalysts for the catalytic cyclopropanation of styrene with diazoacetates. Fe^{II}(D₄-TpAP) usually gave higher cyclopropanation yields and better diastereoselective control than Fe^{II}($\alpha_2\beta_2$ -BNP) did. When compared with the reaction of styrene and ethyl diazoacetate catalyzed by Ru(D₄-TmAP), a similar catalyst with less bulky *meso*-substituents, Fe^{II}(D₄-TpAP) gave comparable stereoselective control and the same sense of chiral induction for both trans and cis cyclopropyl esters. The difference was that Ru(D₄-TmAP) induced high enantiomeric excesses for the trans product (81–91% ee) and very low

(20) See for example: Lim, M. H.; Lee, Y. J.; Goh, Y. M.; Nam, W.; Kim, C. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 707.

**Figure 1.** Thermal ellipsoid representation of the molecular structure of ligand **4a**.

enantiomeric excesses for the cis product (2–9% ee).^{4a} Fe(D₄-TpAP) gave modest enantiomeric excesses for both diastereomers. It appears that the increase of steric bulk at the porphyrin periphery is not very beneficial for cyclopropanation of styrene in terms of enantioselectivity, although a higher trans/cis ratio was achieved.

In cyclopropanation reactions, bulkier diazo reagents are commonly used to improve the enantio- and stereoselectivity.²¹ In the catalytic systems investigated here, however, increasing the steric bulk from ethyl to menthyl diazoacetates, did not result in better trans/cis ratios or enantiomeric excesses. This is suggestive of a subtle interaction between the ligands and the diazo reagents.

Explanation of the Enantioselectivity in Iron Macrocycle-Catalyzed Cyclopropanation. The active intermediate in the iron porphyrin-catalyzed reactions is likely to be an iron carbene species formed by reaction of the iron porphyrin with diazo reagents. We have spectroscopically observed the formation of iron carbene complexes, (TTP)Fe=CHR (R = mesityl or trimethylsilyl).⁷ An iron carbene complex supported by a non-porphyrin macrocylic ligand, (tmtaa)Fe=CPh₂,²² was isolated and characterized by X-ray crystallography. In this complex, the carbene plane defined by C(C_{ipso})₂ is nearly parallel to a pair of trans Fe–N bonds. In contrast, the carbene plane usually bisects the adjacent M–N bonds in metalloporphyrin carbene complexes.^{4a,23}

The enantioselectivity occurring in these cyclopropanation reactions can be correlated to the orientation of the carbene ligand and the approach of the incoming olefin. In cyclopropanation by group 8 metalloporphyrin carbene complexes, the approach of the olefin with its C=C axis parallel to the M=C bond is strongly preferred.⁷ The likely orientation of the carbene intermediate in the Fe[HPhH(dach)]₂ reaction is shown in Figure 2, with the carbene plane parallel to either pair of trans

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(22) Klose, A.; Solari, E.; Floriani, C.; Re, N.; Chiesi-Villa A.; Rizzoli, C. *Chem. Commun.* **1997**, 2297.

(23) (a) Djukic, J.-P.; Smith, D. A.; Young, V. G., Jr.; Woo, L. K. *Organometallics* **1994**, *13*, 3020. (b) Mansuy, D.; Lange, M.; Chottard, J. C.; Bartoli, J. F.; Chevrier, B.; Weiss, R. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 781.

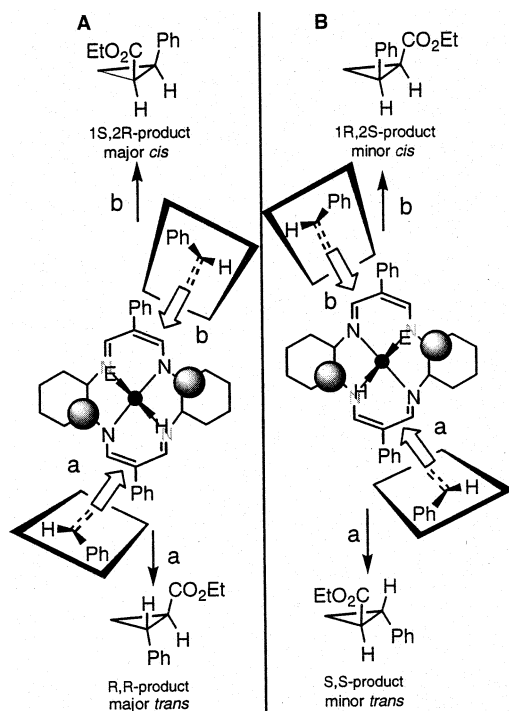


Figure 2. Illustration of enantiocontrol in **4a**-catalyzed cyclopropanation viewed from above the carbene complex. The carbene ligand (E = carboethoxy) is oriented out of the plane of the page, and the styrene double bond is perpendicular to the page.

Fe–N bonds. Minimizing steric interactions between the ester group and the axial proton of the chiral cyclohexyl ring should favor the orientation in Figure 2A. Approach of styrene along path “a” minimizes the steric interference of the axial proton of the cyclohexyl bridge with the olefin phenyl group. This produces the favored trans product with an (*R,R*)-configuration. The major cis enantiomer results from approach along path “b”. This is also in agreement with the observed data.

The Fe(D_4 -TpAP)-catalyzed cyclopropanation gave the same sense of chiral induction as did the analogous Ru(D_4 -TmAP) complex, indicating a similar preferred orientation in both catalytic reactions. The favored carbene orientation is shown in Figure 3A. Approach of styrene from the left side in Figure 3A results in a large steric interaction of the phenyl group with the isopropylidene fragment of the *meso*-substituent. Thus, styrene prefers to approach from the right side of the carbene plane. This leads to the major trans enantiomer with an (*S,S*)-configuration. Likewise, using the steric model proposed for Fe^{III}($\alpha_2\beta_2$ -BNP)Cl in the epoxidation of olefins,¹³ the stereochemical outcome of the Fe^{II}($\alpha_2\beta_2$ -BNP)-catalyzed cyclopropanation can be reasonably predicted. Figure 3B shows the carbene orientation with the minimum steric interaction between the carbene ester group and the binaphthyl bridge. This leads to the major trans enantiomer having an (*R,R*)-configuration. The trans/cis ratios of cyclopropyl esters produced in

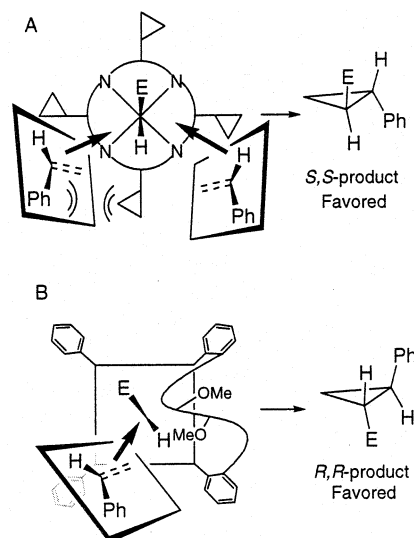


Figure 3. Chiral induction of iron porphyrin complexes. The carbene ligand is oriented out of the plane of the page with the styrene double bond perpendicular to the page. See text for discussion.

these reactions are merely 3–6:1, lower than the selectivity induced by simple porphyrins such as H₂TTP ligand.

It should be noted that the orientation of the ester substituents in the carbene intermediate alone does not determine the overall stereochemical outcome of the cyclopropanation reactions.²⁴ Nevertheless, this simplified analysis provides useful information about the reaction mechanism and for the future design of new ligands.

Conclusion

We have shown that a number of chiral iron(II) complexes, with macrocyclic ligands, serve as effective catalysts for the cyclopropanation of styrene by diazoacetates. On the basis of previous structural data on the orientation of carbene ligands in macrocyclic iron complexes and the approach of the incoming styrene, the stereochemical outcome can be reasonably understood. However, the chiral induction of these catalysts is modest, at best. Further rational modification of ligands is needed to achieve higher enantioselectivity.

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Supporting Information Available: Tables giving crystallographic data for **4a** including atomic coordinates, bond lengths and angles, and anisotropic displacement parameters. This information is available free of charge via the Internet at <http://pubs.acs.org>.

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