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Iron-Catalyzed Diastereoselective Intramolecular Olefin Aminobromination with Bromide Ion

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Abstract

A new iron-catalyzed diastereoselective aminobromination method is reported for both internal and terminal olefins (yield up to 90% and dr up to >20:1). In this transformation, a functionalized hydroxylamine and bromide ion were used as the nitrogen and bromine source, respectively. This method is compatible with a broad range of olefins and provides a convenient approach to synthetically valuable vicinal bromo primary amines. Our studies suggest that both the diastereoselectivity and enantioselectivity for the olefin aminobromination can be controlled by iron catalysts.

Keywords

iron; nitrogen; bromine; alkenes; diastereoselectivity

Stereoselective olefin difunctionalization through nitrogen and bromine atom-transfer is an important transformation because it can readily convert hydrocarbons to vicinal bromo primary amines, a class of chiral building blocks valuable for organic synthesis.[2] Although a range of excellent methods for asymmetric olefin bromo-oxygenation were reported,[3] catalytic enantioselective olefin aminobromination methods are less developed.[4] Additionally, most of the existing asymmetric olefin aminobromination reactions proceed through electrophilic bromonium ion intermediates. In contrast, enantioselective aminobromination of internal olefins using nucleophilic bromide ion has not been developed. In particular, stereoselective olefin aminobromination reactions via iron-nitrenoid intermediates have not been reported.[5] Herein, we describe an iron-catalyzed diastereoselective intramolecular aminobromination method for a broad range of olefins (Scheme 1, yield up to 90% and dr up to >20:1). In this reaction, a functionalized hydroxylamine and bromide ion were used as nitrogen and bromine sources, respectively. Most notably, both the diastereoselectivity and enantioselectivity of this new method can be conveniently controlled by nitrogen-based ligands.

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Supporting Information

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Prior to this research, Yoshimitsu and co-workers reported an $FeBr_2$-catalyzed racemic intramolecular olefin aminobromination reaction with an *N*-tosyloxycarbamate, tetrabutylammonium bromide (TBAB), and *t*-BuOH under ligand-free conditions.[6] In their studies, modest diastereoselectivity was observed with five substrates (1.5 to 3.8:1 dr). Our present method reported here has some unique features that complement the existing iron-catalyzed olefin aminobromination method. First, excellent *anti*-selectivity has been observed across a wide range of both acyclic and cyclic olefins (20:1 dr). Next, excellent asymmetric induction has been achieved with chiral iron-ligand complexes (up to 89% ee).

We selected an acyloxyl carbamate **1** as a model substrate for catalyst screening and observed that $FeBr_2$ catalyzed a nondiastereoselective reaction in the presence of tetraethylammonium bromide (TEAB) under the ligand free condition (Table 1, entry 1, 84% yield, 0.86:1 dr). Interestingly, the $FeBr_2$-phenanthroline **L1** complex catalyzed the *anti*-aminobromination with a significantly improved dr, but in a decreased yield (entry 2, 58% yield, 18:1 dr). However, the $Fe(OTf)_2$-**L1** complex revealed essentially the same diastereoselectivity, but gave an improved yield (entry 3, 78% yield, 18:1 dr). Notably, the $Fe(NTf_2)_2$-**L1** complex provided both excellent yield and dr (entry 4, 81% yield, >20:1 dr). We also observed that the $Fe(NTf_2)_2$-**L2** and $Fe(NTf_2)_2$-**L3** complexes are less effective for diastereocontrol with *trans*-olefinic substrate **1** (entries 5, 6).[7]

Since nonstereospecificity was observed in the iron-catalyzed olefin aminochlorination,[8] *cis*-olefin **1′** was subsequently evaluated for the aminobromination reaction (Scheme 2). To our surprise, the $Fe(NTf_2)_2$-**L1** complex catalyzed an essentially nondiastereoselective reaction (1.5:1 dr), while the $Fe(NTf_2)_2$-**L2** complex catalyzed an *anti*-selective addition with a significant diastereomeric ratio (5.8:1 dr). The different reaction profiles for isomeric olefins **1** and **1′** revealed that the aminobromination reaction is neither stereospecific nor fully stereoconvergent. These results also suggest that the aminobromination occurs in a stepwise fashion and the C–N bond formation step may be ratedetermining.

With the optimized conditions in hand, a variety of substrates were explored to evaluate the scope and limitations of this *anti*-aminobromination method (Scheme 3). First, disubstituted styrenyl olefins are found to be generally good substrates; both electron-donating and -withdrawing substituents can be tolerated by this method (Scheme 3, entries 1–4). Notably, this method is also compatible with *ortho*-substituents and pyridyl groups (entries 5, 6). Furthermore, isomeric naphthyl olefins are both excellent substrates for providing high diastereoselectivity (entries 7, 8). *Cis*- and *trans*-eneynes are also good substrates for the stereoconvergent and *anti*-selective method (entry 9). Additionally, both styrenyl and nonstyrenyl trisubstituted olefins underwent aminobromination smoothly with excellent diastereoselectivity (entries 10, 11). Furthermore, a cyclohexyl-substituted olefin could participate in the reaction with reasonable yield and diastereoselectivity (entry 12, 58% yield, 4:1 dr). Moreover, 1,1-disubstituted olefins and dienes are viable substrates with excellent regioselectivity (entries 13, 14). Finally, a cyclic olefin proved to be an excellent substrate for the *anti*-aminobromination reaction (entry 15, dr >20:1 dr).

Since the iron–ligand complexes can control diastereoselectivity and they are involved in the stereo-determining transition state, the asymmetric aminobromination was further explored

with chiral iron–ligand complexes. We discovered that the $Fe(NTf_2)_2$-chiral ligand **L4** complex catalyzed both diastereoselective and enantioselective aminobromination of *trans*-olefin **1** (Scheme 4, >20:1 dr, 89% ee for **2a**). Interestingly, the $Fe(NTf_2)_2$-**L4** complex also catalyzed a less-stereoselective reaction with *cis*-olefin **1′** (5.0:1 dr, 77% ee for both **2a** and **2b**), a phenomenon that is very different from iron-catalyzed intramolecular olefin aminochlorination reaction.[8] This result suggests that there may be mechanistic subtleties between the chlorine- and bromine-atom-transfer step.

In conclusion, we have described an iron-catalyzed diastereoselective aminobromination method for both internal and terminal olefins. In this reaction, a functionalized hydroxylamine and a bromide ion were used as the nitrogen and bromine source, respectively. This method is compatible with a broad range of olefins and provides a convenient approach to vicinal bromo primary amines, a class of valuable building blocks in synthetic chemistry. Our studies suggest that both the diastereoselectivity and enantioselectivity for this reaction can be controlled by the iron ligand complexes and our efforts were focused on the method of development for the stereoselective intermolecular olefin aminobromination.

All reactions were performed in flame-dried round-bottomed flasks and vials. Stainless steel syringes and cannula were used to transfer air- and moisture-sensitive liquids. Flash chromatography was performed using silica gel 60 (230–400 mesh) from Sigma-Aldrich. Et_4NBr (TEAB) and tetraoctylammonium bromide (TOAB) were purchased from Sigma-Aldrich. They were further purified by recrystallization from Et_2O–acetone mixture and stored in a glove box under N_2 atmosphere. Other reagents were purchased from Sigma-Aldrich, Fluka, EM Science, and Lancaster, and used directly as received. All solvents were used after being freshly distilled. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker UltraShield-400 (400 MHz). The mass spectroscopic data were obtained at the Georgia State University mass spectrometry facility using a Micromass Platform II single quadruple instrument. IR spectra were obtained using a PerkinElmer Spectrum 100 FT-IR spectrometer.

Racemic Diastereoselective Olefin Aminobromination; General Procedure

To a flame-dried sealable 2-dram vial (vial **A**) equipped with a magnetic stir bar were added $Fe(NTf_2)_2$ (12.3 mg, 0.02 mmol, 10 mol%) and 1,10-phenanthroline (7.2 mg, 0.04 mmol, 20 mol%). After the vial was evacuated and backfilled three times with N_2, anhydrous CH_2Cl_2 (1.0 mL) was added and the mixture was stirred at r.t. for 20 min. During this time, the olefinic substrate (0.2 mmol) and anhydrous TEAB (51 mg, 0.24 mmol) were dissolved in CH_2Cl_2 (4.0 mL) in a second flame-dried 3-dram vial (vial **B**) with a magnetic stir bar and freshly activated 4 Å molecular sieves under N_2 atmosphere. Both vials were degassed twice by brief evacuation and backfilling with N_2. The vial **B** was cooled down to 0 °C, and the solution in vial **A** was added to vial **B** dropwise via a syringe. The resulting solution was stirred at the same temperature until all the starting material was fully consumed monitored by TLC (eluent: hexanes–acetone, 10:1). The reaction was quenched by sat. aq $NaHCO_3$ (1 mL). After extraction with CH_2Cl_2 (3 × 1.5 mL), the combined organic phases were concentrated and the residue was purified through a gradient silica gel flash column

chromatography (hexanes–acetone, 15:1 to 4:1) to afford the product. The dr was determined by ^{1}H NMR analysis.

4-[Bromo(phenyl)methyl]oxazolidin-2-one (2a)

By following the General Procedure, **2a** was obtained as a white solid; yield: 41 mg (81%); dr >20:1; mp 113–115 °C.

IR (ATR, neat): 3232 (m), 3133 (w), 2957 (w), 2853 (w), 1730 (s), 1236 (s), 1094 (s), 1022 (s), 650 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.32 (m, 5 H), 5.22 (s, 1 H), 4.76 (d, *J* = 9.4 Hz, 1 H), 4.69–4.58 (m, 1 H), 4.52–4.36 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.0, 137.0, 129.7, 129.4, 128.0, 69.5, 58.0, 54.5.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{10}BrNO_2Na^+$ ($M + Na^+$): 277.9793; found: 277.9801.

4-[Bromo(phenyl)methyl]oxazolidin-2-one (2b)

By following the General Procedure under the conditions described in Table 1 entry 1, **2a** and **2b** were obtained as a mixture; yield: 38 mg (84%); dr 0.86:1; mp 111–118 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.31 (m, 5 H), 5.68 (s, 1 H), 4.87 (d, *J* = 9.6 Hz, 1 H), 4.50–4.43 (m, 1 H), 4.23 (t, *J* = 9.4 Hz, 1 H), 3.92 (dd, *J* = 9.5, 5.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.9, 136.4, 129.7, 129.4, 127.9, 67.3, 58.7, 56.7.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{10}BrNO_2Na^+$ ($M + Na^+$): 277.9793; found: 277.9799.

4-[Bromo(*p*-tolyl)methyl]oxazolidin-2-one (S1)

By following the General Procedure under the conditions described in Scheme 3, **S1** was obtained as a white solid; yield: 46 mg (86%); dr >20:1; mp 121–123 °C.

IR (ATR, neat): 3239 (m), 3099 (w), 2921 (w), 1748 (s), 1239 (m), 1028 (m), 650 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.17 (m, 4 H), 5.09 (s, 1 H), 4.77 (d, *J* = 9.1 Hz, 1 H), 4.72–4.61 (m, 1 H), 4.55–4.39 (m, 2 H), 2.38 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.1, 139.8, 134.0, 130.0, 127.9, 69.5, 57.9, 54.7, 21.2.

HRMS (ESI): *m*/*z* calcd for $C_{11}H_{13}BrNO_2^+$ ($M + H^+$): 270.0130; found: 270.0127.

Methyl 4-[Bromo(2-oxooxazolidin-4-yl)methyl]benzoate (S2)

By following the General Procedure under the conditions described in Scheme 3, **S2** was obtained as a white solid; yield: 56 mg (90%); dr >20:1; mp 101–103 °C.

IR (ATR, neat): 3323 (m), 2946 (w), 2834 (w), 1656 (m), 1449 (m), 1019 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 7.9 Hz, 2 H), 7.48 (d, *J* = 7.9 Hz, 2 H), 5.25 (s, 1 H), 4.79 (d, *J* = 9.2 Hz, 1 H), 4.71–4.63 (m, 1 H), 4.51–4.41 (m, 2 H), 3.93 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.1, 158.0, 141.7, 131.3, 130.6, 128.2, 69.4, 57.8, 53.4, 52.4.

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{13}BrNO_4^+$ ($M + H^+$): 314.0028; found: 314.0027.

4-[Bromo(3-chlorophenyl)methyl]oxazolidin-2-one (S3)

By following the General Procedure under the conditions described in Scheme 3, **S3** was obtained as a white solid; yield: 50 mg (86%); dr >20:1; mp 107–109 °C.

IR (ATR, neat): 3240 (w), 2985 (w), 2863 (w), 1737 (s), 1235(s), 1044 (s), 732 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.27 (m, 4 H), 5.64 (s, 1 H), 4.71 (d, *J* = 8.8 Hz, 1 H), 4.67–4.57 (m, 1 H), 4.46–4.36 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.4, 139.0, 135.2, 130.6, 129.82, 128.3, 126.3, 69.4, 57.9, 53.5.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{10}BrClNO_2^+$ ($M + H^+$): 289.9583; found: 289.9584.

4-[Bromo(2-chlorophenyl)methyl]oxazolidin-2-one (S4)

By following the General Procedure under the conditions described in Scheme 3, **S4** was obtained as a white solid; yield: 51 mg (87%); dr >20:1; mp 123–125 °C.

IR (ATR, neat): 3260 (m), 3102 (w), 2923 (w), 1752 (s), 1475 (m), 1233 (m), 1030 (m), 734 (m), 509 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (dd, *J* = 7.7, 1.3 Hz, 1 H), 7.43 (dd, *J* = 7.7, 1.2 Hz, 1 H), 7.39–7.29 (m, 2 H), 5.40 (s, 1 H), 5.39 (d, *J* = 8.8 Hz, 1 H), 4.66–4.54 (m, 2 H), 4.45 (dd, *J* = 8.8, 4.3 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.3, 134.5, 133.9, 130.6, 130.4, 129.1, 128.0, 69.1, 57.0, 49.5.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{10}BrClNO_2^+$ ($M + H^+$): 289.9583; found: 289.9580.

4-[Bromo(pyridin-3-yl)methyl]oxazolidin-2-one (S5)

By following the General Procedure under the conditions described in Scheme 3, **S5** was obtained as a white solid, yield: 33 mg (65%); dr >20:1; mp >200 °C.

IR (ATR, neat): 3300 (m), 2985 (w), 1737 (s), 1372 (m), 1234 (s), 1044 (s), 504 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.62 (s, 1 H), 8.56 (d, *J* = 4.0 Hz, 1 H), 7.77 (d, *J* = 8.0 Hz, 1 H), 7.35 (dd, *J* = 7.9, 4.8 Hz, 1 H), 5.60 (s, 1 H), 4.78 (d, *J* = 9.0 Hz, 1 H), 4.66 (t, *J* = 8.2 Hz, 1 H), 4.50–4.41 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.7, 150.1, 148.8, 136.1, 133.5, 124.1, 69.2, 58.0, 51.4.

HRMS (ESI): *m*/*z* calcd for $C_9H_{10}BrN_2O_2^+$ ($M + H^+$): 256.9926; found: 256.9935.

4-[Bromo(naphthalen-1-yl)methyl]oxazolidin-2-one (S6)

By following the General Procedure under the conditions described in Scheme 3, **S6** was obtained as a white solid; yield: 40 mg (66%); dr >20:1; mp 119–121 °C.

IR (ATR, neat): 3242 (m), 2913 (w), 1766 (s), 1702 (s), 1480 (m), 1410 (m), 1212 (s), 1028 (s), 763 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (s, 1 H), 7.92 (t, *J* = 7.7 Hz, 2 H), 7.66–7.62 (m, 2 H), 7.57 (t, *J* = 7.2 Hz, 1 H), 7.51 (t, *J* = 7.7 Hz, 1 H), 5.63 (s, 1 H), 5.09 (s, 1 H), 4.90–4.80 (m, 1 H), 4.76 (t, *J* = 9.2 Hz, 1 H), 4.61 (dd, *J* = 9.3, 5.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.0, 134.1, 130.7, 130.5, 129.3, 127.3, 126.6, 125.4, 122.5, 77.2, 69.9, 56.7.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{13}BrNO_2^+$ ($M + H^+$): 306.0105; found: 306.0110.

4-[Bromo(naphthalen-2-yl)methyl]oxazolidin-2-one (S7)

By following the General Procedure under the conditions described in Scheme 3, **S7** was obtained as a white solid; yield: 45 mg (73%); dr >20:1; mp 116–118 °C.

IR (ATR, neat): 3250 (m), 3134 (w), 2920 (w), 1756 (s), 1712 (s), 1434 (m), 1409 (m), 1248 (s), 1019 (s), 766 cm^{-1} (s).

^{1} H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 8.6 Hz, 1 H), 7.88–7.79 (m, 3 H), 7.59–7.52 (m, 2 H), 7.50 (d, *J* = 8.5 Hz, 1 H), 5.02 (s, 1 H), 4.92 (d, *J* = 9.6 Hz, 1 H), 4.66 (t, *J* = 8.4 Hz, 1 H), 4.60–4.51 (m, 1 H), 4.48 (dd, *J* = 8.7, 4.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.0, 134.1, 133.6, 132.9, 129.7, 128.1, 127.8, 127.8, 127.4, 127.2, 124.5, 69.6, 57.8, 55.1.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{13}BrNO_2^+$ ($M + H^+$): 306.0105; found: 306.0110.

4-(1-Bromo-3-phenylprop-2-yn-1-yl)oxazolidin-2-one (S8a)

By following the General Procedure under the conditions described in Scheme 3, **S8a** and its *syn*-diastereomer **S8b** were obtained as a white foam; yield: 47 mg (85%); dr 7.1:1.

S8a—^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.44 (m, 2 H), 7.37–7.32 (m, 3 H), 6.71 (s, 1 H), 4.73 (d, *J* = 5.7 Hz, 1H), 4.59–4.51 (m, 2 H), 4.29–4.19 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1, 132.0, 129.4, 128.4, 121.0, 89.3, 82.5, 67.6, 57.4, 39.0.

S8b—IR (ATR, neat): 3269 (m), 2987 (w), 2224 (m), 1754 (s), 1228 (w), 1037 (m), 933 (m), 758 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.44 (m, 2 H), 7.37–7.32 (m, 3 H), 6.61 (s, 1 H), 4.70 (d, *J* = 6.2 Hz, 1 H), 4.59–4.51 (m, 2 H), 4.40 (dd, *J* = 9.5, 4.1 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1, 132.1, 129.6, 128.5, 120.8, 88.9, 81.8, 67.1, 57.6, 39.2.

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{11}BrNO_2^+$ ($M + H^+$): 279.9973; found: 279.9976.

4-(1-Bromo-1-phenylethyl)oxazolidin-2-one (S9)

By following the General Procedure under the conditions described in Scheme 3, **S9** was obtained as a white solid; yield: 24 mg (45%); dr >20:1; mp 121–123 °C.

IR (ATR, neat): 3270 (m), 3101 (w), 2995 (w), 1751 (s), 1407 (w), 1239 (m), 1052 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 7.3 Hz, 2 H), 7.43–7.32 (m, 3 H), 5.57 (s, 1 H), 4.56–4.50 (m, 3 H), 2.15 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.7, 140.9, 128.9, 127.1, 67.6, 67.4, 62.3, 24.9.

HRMS (ESI): *m*/*z* calcd for $C_{11}H_{13}BrNO_2^+$ ($M + H^+$): 270.0130; found: 270.0138.

4-(2-Bromopropan-2-yl)oxazolidin-2-one (S10)

By following the General Procedure under the conditions described in Scheme 3, **S10** was obtained as a white solid; yield: 27 mg (64%); mp 65–68 °C.

IR (ATR, neat): 2920 (s), 2870 (s), 1767 (s), 1483 (w), 1342 (m), 1215 (s), 1040 (s), 859 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20 (s, 1 H), 4.48 (t, *J* = 9.2 Hz, 1 H), 4.37 (dd, *J* = 9.5, 4.7 Hz, 1 H), 4.01 (dd, *J* = 8.3, 4.7 Hz, 1 H), 1.73 (s, 3 H), 1.72 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 67.6, 65.4, 62.4, 29.7, 27.9.

HRMS (ESI): *m*/*z* calcd for $C_6H_{11}BrNO_2^+$ ($M + H^+$): 207.9922; found: 207.9926.

(±)-4-[Bromo(cyclohexyl)methyl]oxazolidin-2-one (S11a)

By following the General Procedure under the conditions described in Scheme 3, **S11a** and its diastereomer **S11b** were obtained as a white solid, which can be separated through a gradient silica gel flash column chromatography (hexanes–acetone, from 15:1 to 4:1); combined yield: 30 mg (58%); dr 4:1.

S11a—Mp 72–76 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.88 (s, 1 H), 4.54 (t, *J* = 8.7 Hz, 1 H), 4.30 (dd, *J* = 9.1, 5.7 Hz, 1 H), 4.20 (td, *J* = 8.6, 5.6 Hz, 1 H), 3.87 (dd, *J* = 8.9, 3.0 Hz, 1 H), 1.87–1.74 (m, 2 H), 1.73–1.51 (m, 4 H), 1.47–1.07 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.8, 70.1, 65.0, 54.6, 39.7, 31.9, 27.2, 25.9, 25.9, 25.4.

S11b—Mp 71–74 °C.

IR (ATR, neat): 2925 (s), 2851 (s), 1759 (s), 1482 (w), 1375 (m), 1227(s), 1149 (s), 1035 (s), 820 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.58 (s, 1 H), 4.49 (t, *J* = 8.2 Hz, 1 H), 4.28–4.17 (m, 2 H), 3.90 (dd, *J* = 7.7, 3.9 Hz, 1 H), 1.84–1.74 (m, 2 H), 1.74–1.61 (m, 3 H), 1.53–1.13 (m, 7 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.1, 68.0, 65.8, 55.4, 40.6, 31.8, 28.7, 25.9, 25.9, 25.7.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{17}ClNO_2^+$ ($M + H^+$): 218.0942; found: 218.0937.

4-(Bromomethyl)-4-phenyloxazolidin-2-one (S12)

By following the General Procedure under the conditions described in Scheme 3, **S12** was obtained as a white solid; yield: 32 mg (63%); mp 94–96 °C.

IR (ATR, neat): 3252 (m), 2932 (w), 2853 (w), 1733 (s), 1376 (w), 1089 (s), 1061 cm^{-1} (w).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.28 (m, 5 H), 6.90 (s, 1 H), 4.68 (d, *J* = 8.8 Hz, 1 H), 4.49 (d, *J* = 8.8 Hz, 1 H), 3.80 (q, *J* = 11.0 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.7, 139.9, 129.3, 128.7, 124.8, 74.7, 63.5, 40.6.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{11}BrNO_2^+$ ($M + H^+$): 255.9973; found: 255.9965.

4-[(*E*)-1-Bromobut-2-en-1-yl]oxazolidin-2-one (S13a)

By following the General Procedure under the conditions described in Scheme 3, **S13a** and its *syn*-diastereomer **S13b** were obtained as a white foam; yield: 33 mg (73%); dr 1.2:1.

S13a—^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.23 (s, 1 H), 5.93–5.83 (m, 1 H), 5.59– 5.50 (m, 1 H),4.50 (t, *J* = 8.8 Hz, 1 H), 4.34 (dd, *J* = 9.8, 7.9 Hz, 1 H), 4.27 (dd, *J* = 9.3, 5.0 Hz, 1 H), 4.13–4.05 (m, 1 H), 1.78–1.76 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0, 133.8, 127.1, 68.7, 57.5, 56.6, 17.9.

S13b—IR (ATR, neat): 3276 (m), 2919 (w), 1751 (s), 1407 (w), 1233 (s), 1023 (m), 532 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.29 (s, 1 H), 5.93–5.83 (m, 1 H), 5.59– 5.50 (m, 1 H), 4.45–4.41 (m, 2 H), 4.18 (dd, *J* = 9.4, 4.7 Hz, 1 H), 4.11– 4.06 (m, 1 H), 1.76–1.74 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.8, 133.7, 126.3, 67.3, 57.2, 55.6, 17.8.

HRMS (ESI): *m*/*z* calcd for $C_7H_{11}BrNO_2^+$ (M + H^+): 219.9973; found: 219.9976.

4-Bromohexahydrobenzo[*d*]oxazol-2(3*H*)-one (S14)

By following the General Procedure under the conditions described in Scheme 3, **S14** was obtained as a white solid; yield: 27 mg (61%); dr >20:1; mp 115–117 °C.

IR (ATR, neat): 3272 (m), 2948 (w), 2885 (w), 1751 (s), 1201 cm^{-1} (w).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.71 (s, 1 H), 4.67–4.65 (m, 1 H), 3.90– 3.84 (m, 1 H), 3.78 (dd, *J* = 8.8, 5.9 Hz, 1 H), 2.27–2.23 (m, 2 H), 1.78– 1.58 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0, 77.0, 60.9, 53.8, 32.7, 25.9, 20.7.

HRMS (ESI): *m*/*z* calcd for $C_7H_{11}BrNO_2^+$ (M + H^+): 219.9973; found: 219.9972.

Asymmetric Olefinic Aminobromination; (*S*)-4-[(*R*)-Bromo(phenyl) methyl]oxazolidin-2-one (2a); Typical Procedure

To a flame-dried sealable 2-dram vial (vial **A**) equipped with a magnetic stir bar were added $Fe(NTf_2)_2$ (9.2 mg, 0.015 mmol, 15 mol%) and chiral ligand **L4** (7.3 mg, 0.015 mmol, 15 mol%). After the vial was evacuated and backfilled three times with N_2, anhydrous CH_2Cl_2 (1.0 mL) was added and the mixture was stirred at r.t. for 20 min. Meanwhile, a second flame-dried and N_2-protected 2-dram vial (vial **B**) with a magnetic stir bar was charged with **1** (0.1 mmol), anhydrous TOAB (137 mg, 0.24 mmol), freshly activated 4 Å molecular sieves, and anhydrous CH_2Cl_2 (3.0 mL). Both vials were degassed twice by brief evacuation and backfilling with N_2. Vial **B** was cooled down to −60 °C, and the catalyst solution in vial **A** was added to vial **B** dropwise via a syringe. The resulting solution was stirred at this temperature for 12 h and then gradually warmed up to r.t. The reaction was quenched with sat. aq $NaHCO_3$ (1 mL). The reaction mixture was extracted with CH_2Cl_2 (3 × 1.5 mL), and the combined organic phases were concentrated in vacuo. The residue was purified by a gradient silica gel flash column chromatography (hexanes–acetone, from 15:1 to 4:1) to afford **2a** as a white solid; yield: 17 mg (64%); dr >20:1; 89% ee. The dr was determined by crude ^{1}H NMR analysis and the ee was determined by Chiral HPLC analysis [Chiral AD-H column, 10% *i*-PrOH in hexanes, flow rate = 1.0 mL/min, UV detection at 205 nm; t_R (minor) = 17.45 min, t_R (major) = 21.20 min]; $[\alpha]_D^{20}$ + 77 (*c* = 0.65, CH_2Cl_2).

IR (ATR, neat): 3232 (m), 3133 (w), 2957 (w), 2853 (w), 1730 (s), 1236 (s), 1094 (s), 1022 (s), 650 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.32 (m, 5 H), 5.22 (s, 1 H), 4.76 (d, *J* = 9.4 Hz, 1 H), 4.69–4.58 (m, 1 H), 4.52–4.36 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.0, 137.0, 129.7, 129.4, 128.0, 69.5, 58.0, 54.5.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{10}BrNO_2Na^+$ [M + Na^+]: 277.9793; found: 277.9801.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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References

2. For selected reviews of enantioselective olefin halofunctionalization, see: Denmark SE, Kuester WE, Burk MT. Angew. Chem. Int. Ed. 2012; 51:10938. Zheng S, Schienebeck CM, Zhang W, Wang H-Y, Tang W. Asian J. Org. Chem. 2014; 3:366.

3. For selected references of catalytic asymmetric olefin bromooxygenation, see: Zhang W, Zheng S, Liu N, Werness JB, Guzei IA, Tang W. J. Am. Chem. Soc. 2010; 132:3664. [PubMed: 20192183] Zhou L, Tan CK, Jiang X, Chen F, Yeung Y-Y. J. Am. Chem. Soc. 2010; 132:15474. [PubMed: 20945837] Huang D, Wang H, Xue F, Guan H, Li L, Peng X, Shi Y. Org. Lett. 2011; 13:6350. [PubMed: 22092000] Denmark SE, Burk MT. Org. Lett. 2012; 14:256. [PubMed: 22145621] Paull DH, Fang C, Donald JR, Pansick AD, Martin SF. J. Am. Chem. Soc. 2012; 134:11128. [PubMed: 22726214] Murai K, Matsushita T, Nakamura A, Fukushima S, Shimura M, Fujioka H. Angew. Chem. Int. Ed. 2010; 49:9174. Wang Y-M, Wu J, Hoong C, Rauniyar V, Toste FD. J. Am. Chem. Soc. 2012; 134:12928. [PubMed: 22830953] Zhang W, Liu N, Schienebeck CM, Zhou X, Izhar II, Guzei IA, Tang W. Chem. Sci. 2013; 4:2652.

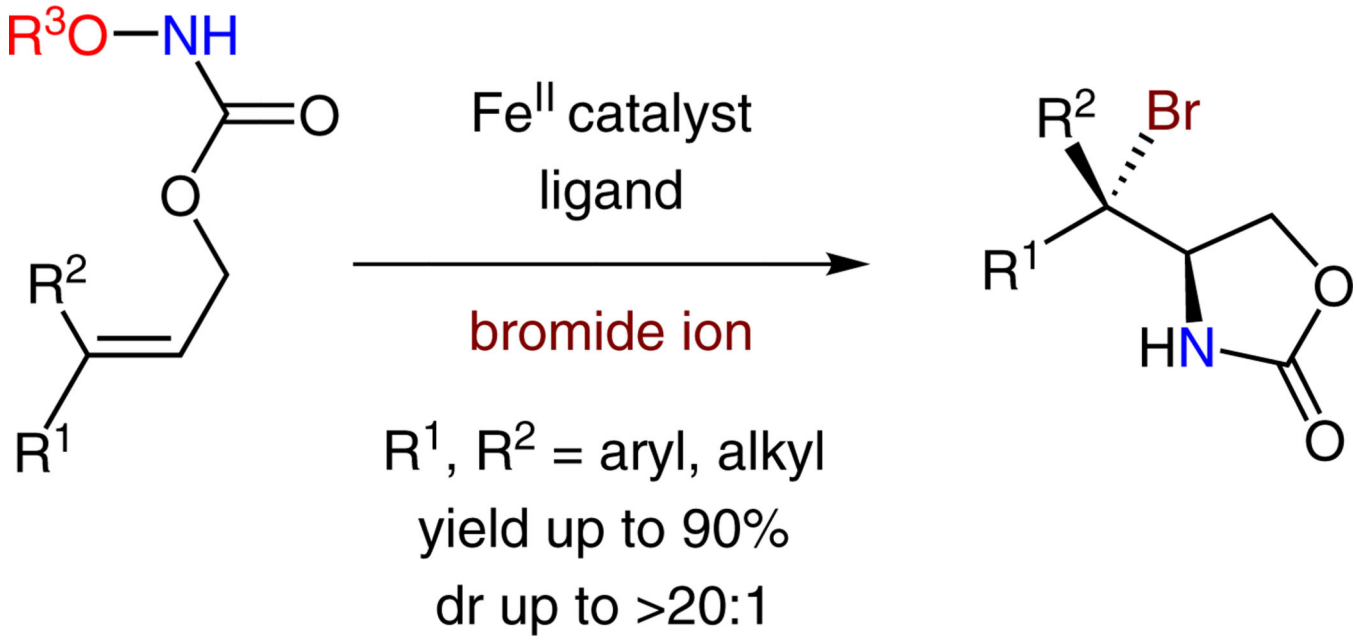
4. For selected reports on catalytic asymmetric olefin aminobromination via an electrophilic bromonium ion, see: Zhou L, Chen J, Tan CK, Yeung Y-Y. J. Am. Chem. Soc. 2011; 133:9164. [PubMed: 21539367] Alix A, Lalli C, Retailleau P, Masson G. J. Am. Chem. Soc. 2012; 134:10389. [PubMed: 22686436] Huang D, Liu X, Li L, Cai Y, Liu W, Shi Y. J. Am. Chem. Soc. 2013; 135:8101. [PubMed: 23659658] Cai Y, Liu X, Hui Y, Jiang J, Wang W, Chen W, Lin L, Feng X. Angew. Chem. Int. Ed. 2010; 49:6160. For a reference of asymmetric aminobromination of terminal olefins with bromine radical donors, see: Bovino MT, Chemler SR. Angew. Chem. Int. Ed. 2012; 51:3923.

5. For iron-catalyzed stereoselective olefin aminohydroxylation and aminofluorination that proceed through an iron-nitrenoid intermediate, see: Liu G-S, Zhang Y-Q, Yuan Y-A, Xu H. J. Am. Chem. Soc. 2013; 135:3343. [PubMed: 23402638] Zhang Y-Q, Yuan Y-A, Liu G-S, Xu H. Org. Lett. 2013; 15:3910. [PubMed: 23875702] Lu D-F, Zhu C-L, Jia Z-X, Xu H. J. Am. Chem. Soc. 2014; 136:13186. [PubMed: 25166591] Lu D-F, Liu G-S, Zhu C-L, Yuan B, Xu H. Org. Lett. 2014; 16:2912. [PubMed: 24829034]

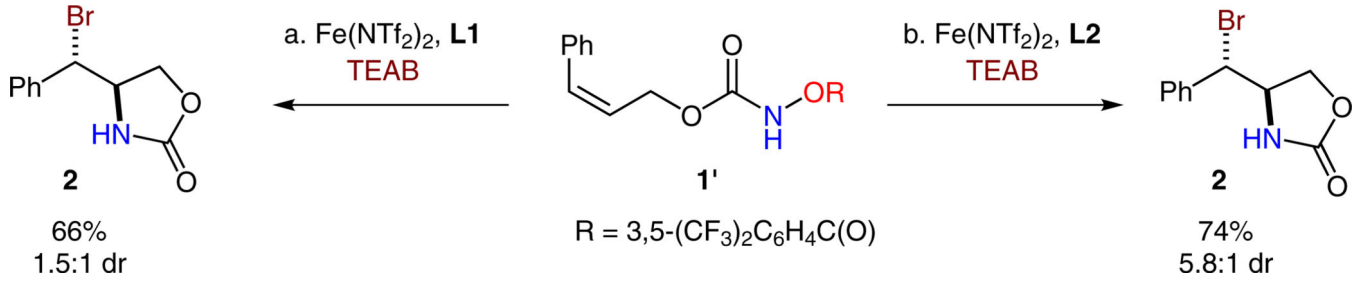
6. (a) Kamon T, Shigeoka D, Tanaka T, Yoshimitsu T. Org. Biomol. Chem. 2012; 10:2363. [PubMed: 22349660] (b) Shigeoka D, Kamon T, Yoshimitsu T. Beilstein J. Org. Chem. 2013; 9:860. [PubMed: 23766801]

7. For the synthesis of ligands see references 4c and 4d.

8. For the iron-catalyzed asymmetric aminochlorination method for internal olefins, see: Zhu C-L, Tian J-S, Gu Z-Y, Xing G-W, Xu H. Chem. Sci. 2015; 6:3044. For early work on ironcatalyzed racemic intramolecular olefin aminochlorination, see: Bach T, Schlummer B, Harms K. Chem. Commun. 2000:287.

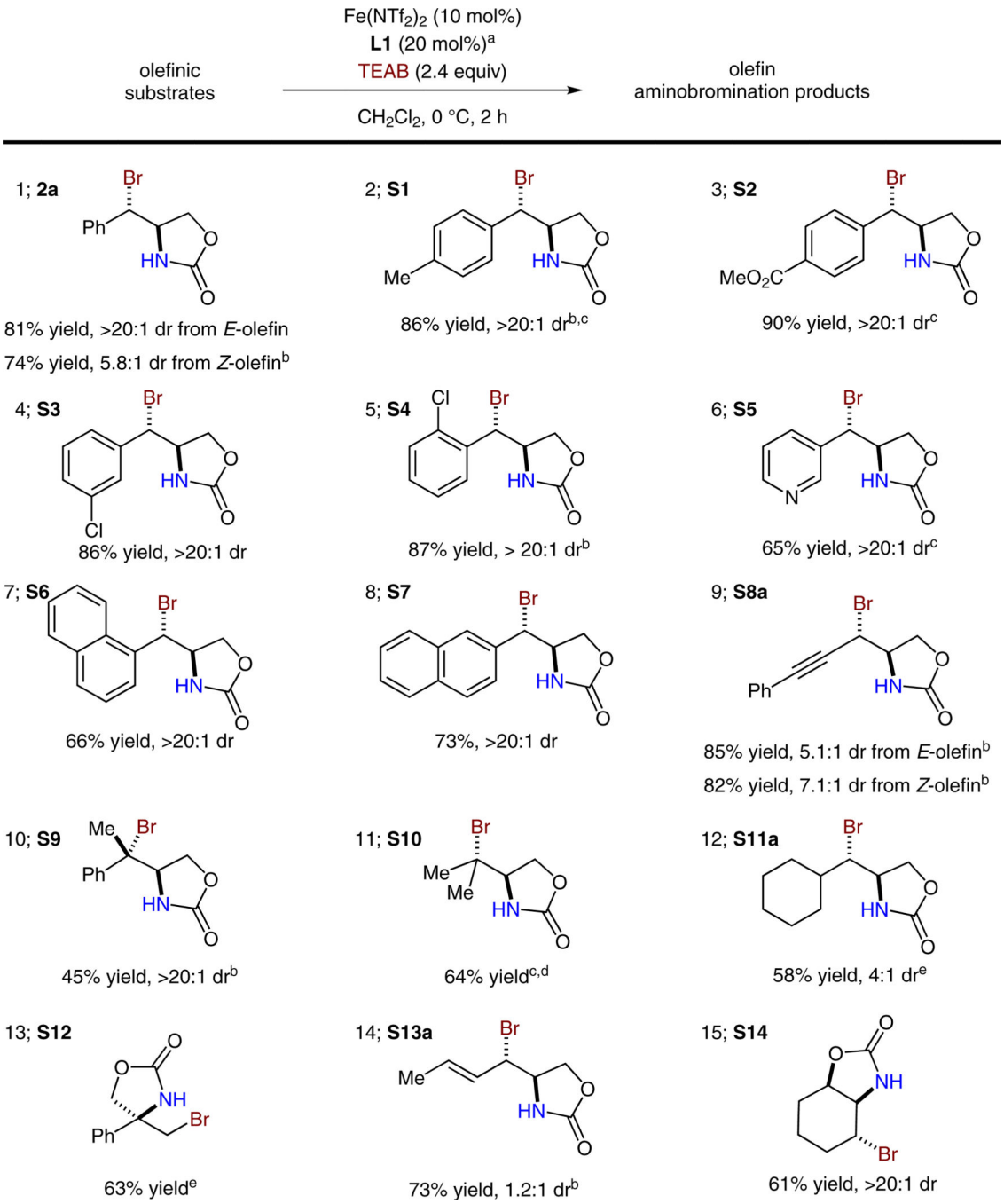


Scheme 1.
Iron-catalyzed diastereoselective olefin aminobromination with bromide ion



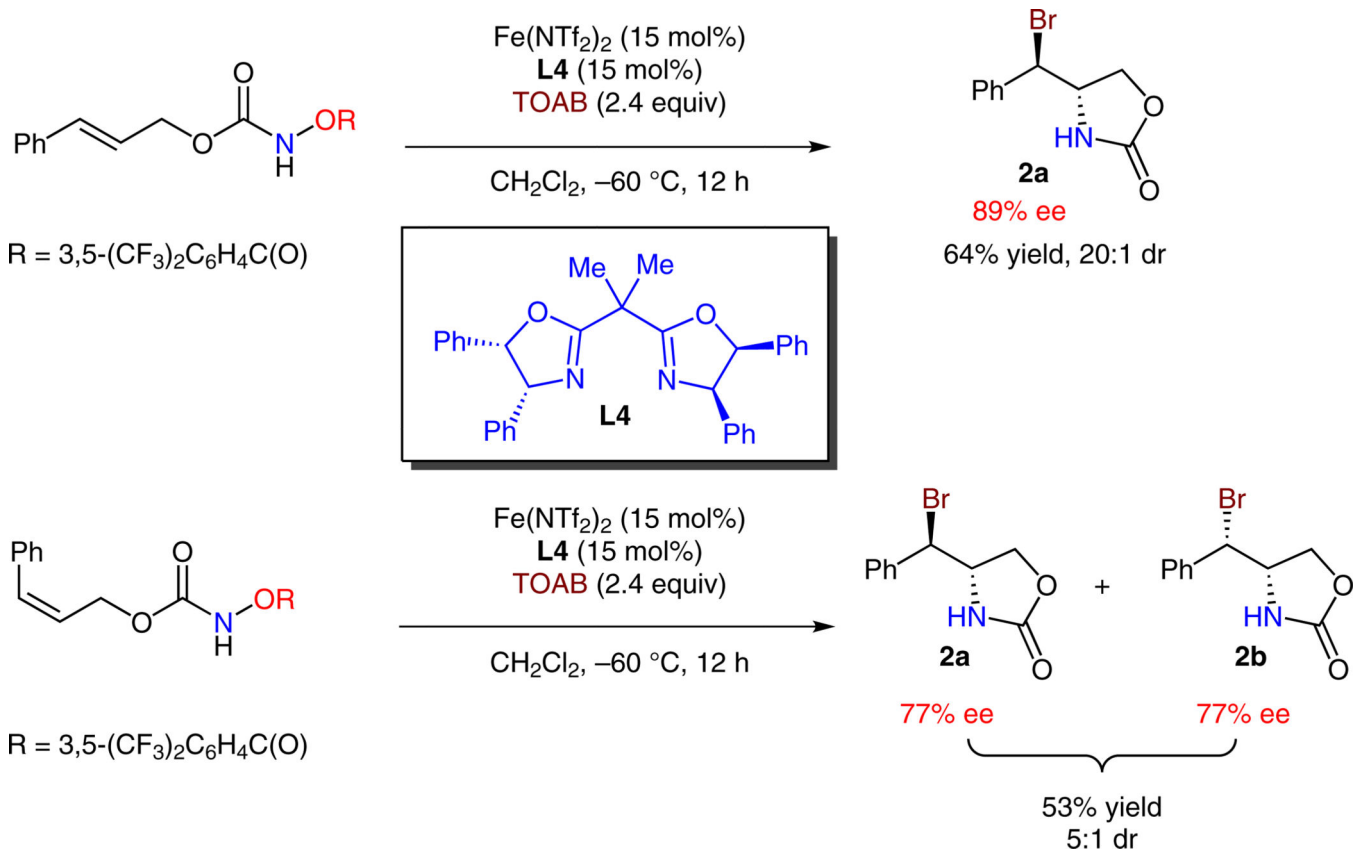
Scheme 2.

Ligand effect in the iron-catalyzed aminobromination of a *cis*-olefin. a) Reaction conditions: $Fe(NTf_2)_2$ (10 mol%), **L1** (20 mol%), TEAB (2.4 equiv), CH_2Cl_2, 0 °C, 2 h. b) Reaction conditions: $Fe(NTf_2)_2$ (10 mol%), **L2** (20 mol%), TEAB (2.4 equiv), CH_2Cl_2, 0 °C, 2 h.



Scheme 3.

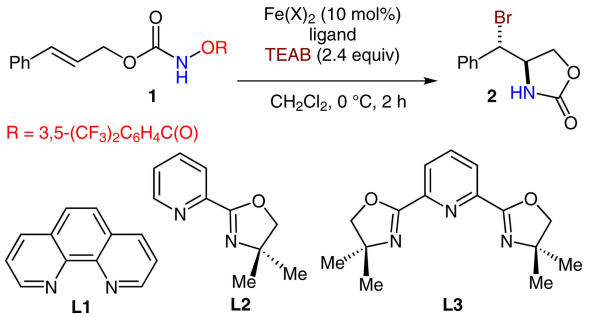
Substrate scope for the iron-catalyzed diastereoselective olefin aminobromination reaction. [a] Unless stated otherwise, the reactions were carried out under N_2 in the presence of 4 Å molecular sieves. [b] **L2** (20 mol%) was used as the ligand. [c] Reaction conditions: –15 °C, 6 h. [d] TOAB was used as the bromide source. [e] Reaction conditions: $Fe(NTf_2)_2 \cdot (\mathbf{L2})_2$ (15 mol %). TOAB: Tetraoctylammonium bromide.



Scheme 4.
Iron-catalyzed asymmetric aminobromination with isomeric olefins

Table 1

Catalyst Screening for the Iron-Catalyzed Diastereoselective Olefin Aminobromination



Entry[a]	$Fe(X)_2$	Ligand (mol%)	Conversion (%)[b]	Yield (%)[c]	dr (*anti/syn*)[b]
1	$FeBr_2$	none	>95	84	0.86:1
2	$FeBr_2$	**L1** (20)	>95	58	18:1
3	$Fe(OTf)_2$	**L1** (20)	>95	78	18:1
4	$Fe(NTf_2)_2$	**L1** (20)	>95	81	>20:1
5	$Fe(NTf_2)_2$	**L2** (20)	>95	78	12:1
6	$Fe(NTf_2)_2$	**L3** (20)	>95	75	13:1

[a] Unless stated otherwise, the reactions were carried out under N_2 in the presence of 4 Å molecular sieves.

[b] Conversion and dr were determined by ^1H NMR analysis.

[c] Isolated yield. TEAB: Tetraethylammonium bromide.