

CrossMark
click for updatesCite this: *Chem. Sci.*, 2015, 6, 3044

Received 20th January 2015

Accepted 13th March 2015

DOI: 10.1039/c5sc00221d

www.rsc.org/chemicalscience

Iron(II)-catalyzed asymmetric intramolecular olefin aminochlorination using chloride ion†

Cheng-Liang Zhu,^{‡a} Jun-Shan Tian,^{‡a} Zhen-Yuan Gu,^{ab} Guo-Wen Xing^b
and Hao Xu^{*a}

An iron-catalyzed enantioselective and diastereoselective intramolecular olefin aminochlorination reaction is reported (ee up to 92%, dr up to 15 : 1). In this reaction, a functionalized hydroxylamine and chloride ion are utilized as nitrogen and chlorine sources, respectively. This new method tolerates a range of synthetically valuable internal olefins that are all incompatible with existing asymmetric olefin aminochlorination methods.

Introduction

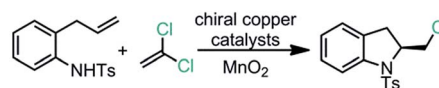
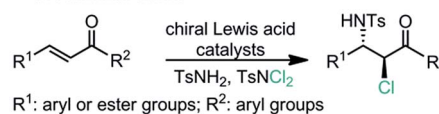
Enantioselective olefin halo-functionalization reactions constitute a range of synthetically valuable yet challenging transformations.¹ Although a variety of excellent asymmetric olefin halo-oxygenation reactions have been discovered,² there are much fewer asymmetric olefin aminohalogenation methods available.³ In particular, there have been just a few reported catalytic asymmetric olefin aminochlorination reactions.⁴ In one instance, Feng discovered the chiral Lewis acid-catalyzed aminochlorination of chalconic and other α,β -unsaturated olefins.^{4a,c} Also, Chemler reported copper-catalyzed aminochlorination of terminal olefins with chlorine radical donors in the presence of MnO_2 (Scheme 1A).^{4b} Despite these and other important discoveries, catalytic asymmetric aminochlorination methods for internal, non-chalconic olefins have yet to be developed. These methods would be synthetically valuable because they would readily provide vicinal amino chlorides, a class of important chiral building blocks. Moreover, asymmetric olefin aminochlorination that proceeds through an iron-nitrenoid intermediate has not yet been reported.⁵

We previously discovered $\text{Fe}(\text{BF}_4)_2$ -based catalysts for both diastereoselective and enantioselective intramolecular olefin aminofluorination reactions.⁶ Our initial attempts to apply these catalysts to olefin aminochlorination reactions led to either low diastereoselectivity or low yield, presumably due to the reason that chlorine and fluorine atom-transfer may proceed through

distinct mechanisms. Therefore, we explored a range of activating group–ligand combinations and discovered entirely new catalytic conditions for asymmetric olefin aminochlorination. Herein, we describe iron-catalyzed enantioselective and diastereoselective intramolecular aminochlorination for a range of internal, non-chalconic olefins (ee up to 92%, dr up to 15 : 1). In these reactions, a functionalized hydroxylamine and chloride ion were utilized as nitrogen and chlorine sources, respectively. This method tolerates a range of synthetically valuable internal olefins that are all incompatible with existing asymmetric olefin aminochlorination approaches; it also provides a new approach that is complementary to known methods for the asymmetric synthesis of amino chlorides with contiguous stereogenic centers.

Prior to this research, Bach reported an FeCl_2 -catalyzed racemic intramolecular olefin aminochlorination method using acyl azides, TMSCl , and EtOH under ligand-free conditions.⁷

A) previous work: asymmetric aminochlorination of chalconic and terminal olefins



B) current work: iron-catalyzed asymmetric aminochlorination of internal olefins with chloride ion



Scheme 1 Catalytic asymmetric olefin aminochlorination: summary of this work and other existing asymmetric methods.

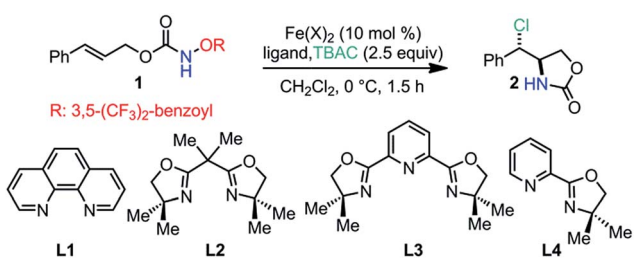
^aDepartment of Chemistry, Georgia State University, 100 Piedmont Avenue SE, Atlanta, Georgia, 30303, USA. E-mail: hxu@gsu.edu; Fax: +1-404-413-5505; Tel: +1-404-413-5553

^bDepartment of Chemistry, Beijing Normal University, Beijing, 100875, China

† Electronic supplementary information (ESI) available: Experimental procedure, characterization data for all new compounds, selected NMR spectra and HPLC traces. CCDC 1041826. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c5sc00221d

‡ These authors contributed equally.

Table 1 Catalyst discovery for the iron-catalyzed diastereoselective olefin aminochlorination reaction



Entry ^a	Fe(X) ₂	Ligand (mol%)	Conversion ^b	Yield ^c	dr ^b (anti : syn)
1	FeCl ₂	None	62%	45%	2 : 1
2	FeCl ₂	L1 (20)	>95%	80%	>20 : 1
3	Fe(NTf ₂) ₂	L1 (20)	>95%	86%	>20 : 1
4	Fe(NTf ₂) ₂	L2 (10)	>95%	82%	0.83 : 1
5	Fe(NTf ₂) ₂	L3 (10)	61%	34%	0.25 : 1
6	Fe(NTf ₂) ₂	L4 (20)	>95%	75%	1.8 : 1

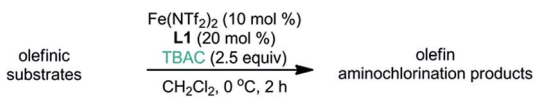
^a Unless stated otherwise, the reactions were carried out under a nitrogen atmosphere. TBAC: tetra-*n*-butylammonium chloride. ^b Conversion and dr were determined by ¹H NMR. ^c Isolated yield.

Excellent syn-selectivity was observed with styrenyl olefins (dr up to > 20 : 1). However, poor diastereoselectivity was recorded with non-styrenyl acyclic olefins (dr: 1 : 1). The new method presented here has a few unique features which complement the existing iron-catalyzed olefin aminochlorination method. First, excellent anti-selectivity has been observed across a wide range of styrenyl and non-styrenyl olefins. Second, good to excellent enantioselectivity has been achieved with a variety of internal, non-chalconic olefins (ee up to 92%). Finally, acyl azides are non-reactive under the described reaction conditions (*vide infra*), which suggests that iron-nitrenoid generation may proceed *via* different pathways compared with the known azide activation pathway.

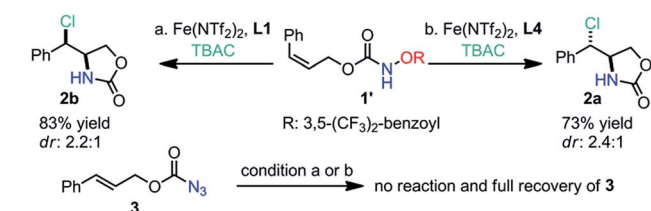
Results and discussion

A cinnamyl alcohol-derived acyloxy carbamate **1** was selected as the model substrate for catalyst discovery (Table 1).⁸ In the presence of tetra-*n*-butylammonium chloride (TBAC), we observed that FeCl₂ alone catalyzed a sluggish reaction under ligand-free conditions (entry 1, 45% yield, dr: 2 : 1).⁹ However, the FeCl₂-phenanthroline (**L1**) complex catalyzed the anti-

Table 2 Substrate scope of the iron-catalyzed diastereoselective olefin aminochlorination reaction



1	2	3
86% yield, dr >20:1 from <i>E</i> olefin 83% yield, dr: 0.46:1 from <i>Z</i> olefin	86% yield, dr >20:1 ^a	70% yield, dr: 7:1
4	5	6
67% yield, dr: 10:1	76% yield, dr: 10:1	76% yield, dr: 12:1
7	8	9
61% yield, dr >20:1 ^a	59%, dr >20:1	93% yield, dr: 4.7:1 from <i>E</i> olefin ^a 84% yield, dr: 7:1 from <i>Z</i> olefin ^a
10	11	12
50% yield, dr >20:1	76% yield	69% yield, dr >20:1 ^b
13	14	15
77% yield ^c	88% yield, dr: 1.7:1	64% yield, dr >20:1



Scheme 2 Iron-catalyzed aminochlorination with a *cis* olefin and an acyl azide. ^aReaction conditions: Fe(NTf₂)₂ (10 mol%), **L1** (20 mol%), TBAC (2.5 equiv.), CH₂Cl₂, 0 °C, 2 h. ^bReaction conditions: Fe(NTf₂)₂ (10 mol%), **L4** (20 mol%), TBAC (2.5 equiv.), CH₂Cl₂, 0 °C, 2 h.

^a Reaction conditions: −15 °C, 2 h. ^b Reaction conditions: 0 °C, 5 h.

^c Reaction conditions: 0 °C, 12 h.



aminochlorination with significantly improved yield and dr (entry 2, 80% yield, dr > 20 : 1). We also noted that the Fe(NTf₂)₂-L1 complex provided essentially the same reactivity and diastereoselectivity (entry 3, 86% yield, dr > 20 : 1). Interestingly, the Fe(NTf₂)₂-bisoxazoline (L2) complex resulted in a loss of diastereoselectivity (entry 4, 82% yield, dr: 0.83 : 1). Furthermore, the Fe(NTf₂)₂-L3 complex promoted the syn-aminochlorination with moderate yield and dr (entry 5, 34% yield, dr: 0.25 : 1). We also observed that the Fe(NTf₂)₂-L4 complex catalyzed the anti-aminochlorination with a modest dr (entry 6, 75% yield, dr: 1.8 : 1). Notably, an iron-L4 complex resulted in high dr and reaction rate in the previously reported olefin aminofluorination reaction.⁶ These observations suggest that ligands are involved in the diastereoselectivity-determining step and provide excellent opportunities for diastereo-control.

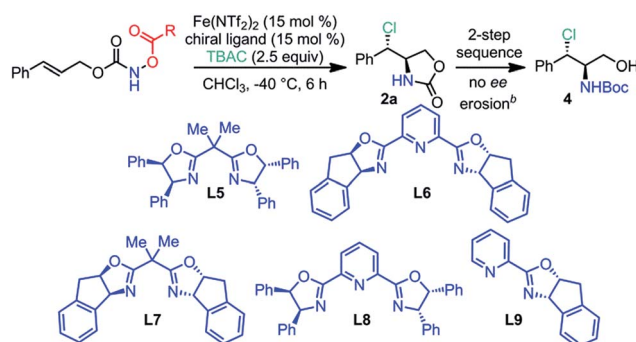
The observed ligand-enabled diastereo-control with *trans*-olefin **1** prompted us to evaluate *cis*-olefin **1'** (Scheme 2). To our surprise, the Fe(NTf₂)₂-L1 complex catalyzed syn-aminochlorination, while the Fe(NTf₂)₂-L4 complex promoted anti-aminochlorination with essentially the same dr (Scheme 2). The different reaction profiles for isomeric olefins **1** and **1'** suggest that the aminochlorination reaction is neither stereospecific nor fully stereo-convergent, which is significantly different from the iron-catalyzed olefin aminofluorination reaction.⁶

Furthermore, an acyl azide **3** was evaluated under the reaction conditions as a control experiment. Interestingly, the acyl azide **3** was fully recovered and no aminochlorination product

was detected. These results suggest that the activation of acyloxy carbamates (**1** and **1'**) may proceed *via* different pathways compared with the known azide activation pathway.⁷

We subsequently explored a range of olefins under the optimized conditions to evaluate the scope and limitations of this anti-aminochlorination method (Table 2). We discovered that di-substituted styrenyl olefins are generally good substrates; both electron-donating and electron-withdrawing substituents are compatible with this method (entries 1–4). Importantly, *ortho*-substituents and pyridyl groups are both tolerated (entries 5–6). Furthermore, extended aromatics, including naphthyl olefins, are reasonable substrates (entries 7–8). Moreover, isomeric ene-yne are both excellent substrates for the stereo-convergent and anti-selective method (entry 9). Additionally, we observed that both styrenyl and non-styrenyl tri-substituted olefins undergo aminochlorination smoothly with excellent dr (entries 10–11).¹⁰ We also discovered that a cyclohexyl-substituted olefin was an excellent substrate (entry 12, dr > 20 : 1). Further exploration revealed that both 1,1-disubstituted olefins and dienes are viable substrates with excellent regioselectivity (entries 13–14). Most notably, a cyclic olefin could also undergo highly diastereoselective anti-aminochlorination (entry 15, dr > 20 : 1), yielding a product which is difficult to obtain with known methods.¹¹ Since the FeCl₂-L1 complex provides essentially the same dr and yield in these diastereoselective reactions, FeCl₂ can be a convenient substitute for Fe(NTf₂)₂ in racemic reactions.

Table 3 Catalyst discovery for the iron-catalyzed asymmetric olefin aminochlorination reaction



Entry ^a	R	Ligand	Conversion ^c	Yield ^d	dr ^c (anti : syn)	ee ^e (anti)	ee ^e (syn)
1	3,5-(CF ₃) ₂ -Ph	L5	>95%	53%	9.9 : 1	84%	<5%
2	3,5-(CF ₃) ₂ -Ph	L6	>95%	68%	0.5 : 1	24%	79%
3	3,5-(CF ₃) ₂ -Ph	L7	88%	61%	1.7 : 1	<5%	<5%
4	3,5-(CF ₃) ₂ -Ph	L8	>95%	32%	2.5 : 1	47%	30%
5	3,5-(CF ₃) ₂ -Ph	L9	>95%	82%	0.5 : 1	8%	24%
6 ^f	3,5-(CF ₃) ₂ -Ph	L5	>95%	51%	11.0 : 1	90%	<5%
7 ^f	CH ₃	L5	>95%	42%	1.1 : 1	97%	<5%
8 ^f	CH ₂ Cl	L5	>95%	67%	9.6 : 1	89%	<5%
9 ^{f,g}	CH ₂ Cl	L5	>95%	58%	9.0 : 1	83%	<5%

^a Unless stated otherwise, the reactions were carried out under a nitrogen atmosphere with 4 Å molecular sieves. ^b Reaction conditions: Boc₂O, Et₃N, DMAP; then Cs₂CO₃, MeOH, 85% over two steps; see ESI for details. ^c Conversion and dr were determined by ¹H NMR. ^d Isolated yield. ^e Enantiomeric excess (ee) was measured by HPLC with chiral columns; the absolute stereochemistry was determined by X-ray crystallographic analysis of an analog of **2a**. ^f The reaction was carried out at -60 °C for 12 h. ^g The FeCl₂-L5 complex was used.



In order to fulfil the need for catalytic asymmetric olefin aminochlorination, we further explored asymmetric induction for internal, non-chalconic olefins with a variety of iron–chiral ligand complexes (Table 3).¹² First, we discovered that the iron–**L5** complex induced diastereoselective and enantioselective anti-aminochlorination, albeit with a low yield, mostly due to the competing aminohydroxylation reaction (entry 1, 53% yield, dr: 9.9 : 1). Interestingly, the anti-addition product **2a** was obtained with excellent ee (84% ee), while the syn-addition product **2b** was obtained essentially as a racemate (<5% ee).¹³ Additionally, a two-step procedure can convert **2a** to a chlorinated amino alcohol triad **4** without ee erosion.¹⁴ Next, we observed that the iron–**L6** complex induced moderately diastereoselective syn-aminochlorination (entry 2, 68% yield, dr: 0.48 : 1). To our surprise, the anti-addition product **2a** was obtained with moderate ee (24% ee), while the syn-addition product **2b** was isolated with significant ee (79% ee). Furthermore, we evaluated chiral ligands **L7** and **L8** and determined that they are less effective for asymmetric induction (entries 3–4). Additionally, chiral ligand **L9** induced fast yet non-selective aminochlorination with a high overall yield (entry 5).¹⁵ With the iron–**L5** complex in hand, we subsequently explored other reaction parameters. First, a decreased reaction temperature was found to benefit both dr and ee (entry 6, dr: 11 : 1 and 90% ee for **2a** at –60 °C). Next, replacing the 3,5-bis(trifluoromethyl) benzoyl activating group with a smaller acetyl group further enhanced the ee (entry 7, 97% ee for **2a**); however, much lower dr and yield were obtained (entry 7, dr: 1.1 : 1, 42% yield). Finally, a chloroacetyl activating group induced an effective balance between overall yield and stereoselectivity (entry 8, 67% yield, dr: 9.6 : 1 and 89% ee for **2a**). We also observed that the FeCl₂–**L5** complex induced a slightly less selective reaction with a lower yield (entry 9, 58% yield, dr: 9.0 : 1 and 83% ee for **2a**).

In order to evaluate the scope of this asymmetric method, we explored the asymmetric induction with a range of internal olefins (Table 4). The chiral catalyst provides excellent asymmetric induction with styrenyl olefins. A range of *para*-substituted styrenyl olefins with different electronic properties were converted to the corresponding aminochlorination products with high dr and ee (entries 1–6, dr: 9.6–15 : 1, ee: 86–91%). Additionally, *meta*-substituted styrenyl olefins are also good substrates but with slightly decreased ee (entries 7–9, dr: 10–15 : 1, ee: 80–87%). However, we discovered that *ortho*-substitution of styrenes has a deleterious effect on ee (entries 10–11, dr: 4.5–12 : 1, ee: 77–79%). Interestingly, both α - and β -naphthyl olefins are excellent substrates (entries 12–13, dr: 4.5–10 : 1, ee: 89–92%). To our delight, a 3-pyridyl olefin with a basic nitrogen atom is a reasonable substrate for the asymmetric aminochlorination (entry 14, dr: 1.8 : 1, ee: 70% for the anti-diastereomer). Moreover, we observed that the iron–**L5** complex can induce significant ee in the aminochlorination with non-styrenyl olefins (entry 15, dr: 2 : 1, ee: 54% for the anti-diastereomer). To our surprise, the iron–**L6** complex proved to be uniquely effective for the asymmetric induction with tri-substituted olefins, while the iron–**L5** complex was less effective (entry 16, dr: 2.3 : 1, ee: 86% for the anti-diastereomer).¹⁶

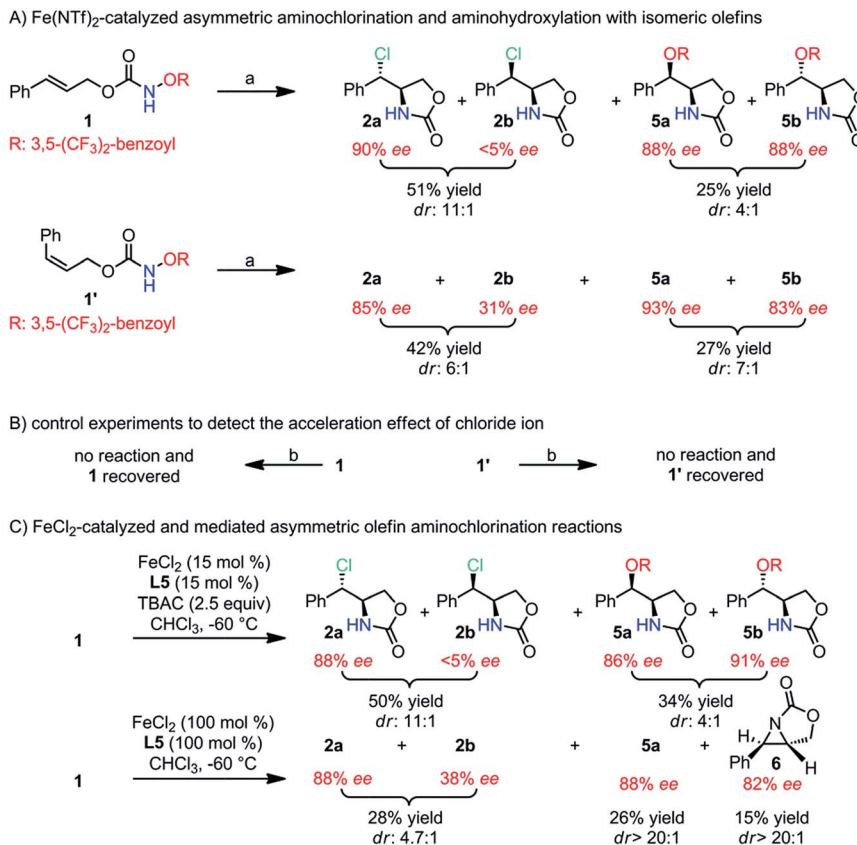
Table 4 Substrate scope for the iron-catalyzed asymmetric olefin aminochlorination reaction

olefinic substrates ^a		Fe(NTf ₂) ₂ (15 mol %) L5 (15 mol %) TBAC (2.5 equiv) CHCl ₃ , –60 °C, 12 h	olefin aminochlorination products ^a	
1			2	
67% yield, dr: 9.6:1 89% ee			65% yield, dr: 15:1 91% ee	
3			4	
69% yield, dr: 5.2:1 87% ee			84% yield, dr: 12:1 90% ee	
5			6	
62% yield, dr: 11:1 88% ee			71% yield, dr: 11:1 86% ee	
7			8	
75% yield, dr: 12:1 87% ee			63% yield, dr: 10:1 80% ee	
9			10	
71% yield, dr: 15:1 80% ee			78% yield, dr: 4.5:1 77% ee	
11			12	
55% yield, dr: 12:1 79% ee			63% yield, dr: 10:1 92% ee ^b	
13			14	
53% yield, dr: 4.5:1 89% ee ^b			51% yield, dr: 1.8:1 70% ee	
15			16	
66% yield, dr: 2:1 54% ee ^{b,c}			45% yield, dr: 2.3:1 86% ee ^{b,d}	

^a Unless stated otherwise, mono-chloroacetyl was selected as the activating group for asymmetric catalysis; the ee for all syn-aminochlorination products was less than 5%. ^b Bis(trifluoromethyl)-benzoyl was selected as the activating group. ^c The ee for the syn-addition product was 12%. ^d **L6** was used as the ligand for asymmetric induction; the ee for the syn-addition product was 50%.

During the exploration of substrate scope, it was surprising to observe completely different ee values for anti- and syn-diastereomers (e.g. **2a** and **2b**). In contrast, exactly the same ee for both diastereomeric products was observed in the iron-catalyzed aminofluorination of **1**.⁶ In order to obtain greater mechanistic insights, we carried out ee analysis for all isolable products using several control experiments (Scheme 3). First, in an Fe(NTf₂)₂-catalyzed reaction with *trans*-olefin **1**, two aminochlorination products were obtained (Scheme 3A, 90% ee for **2a**, <5% ee for **2b**, dr: 11 : 1).¹⁷ Simultaneously, diastereomers **5a** and **5b** were also isolated with the same ee as two competing olefin aminohydroxylation products (Scheme 3A, 88% ee for **5a** and **5b**, dr: 4 : 1). However, completely different selectivity (both dr and ee) was observed in an Fe(NTf₂)₂-catalyzed reaction with *cis*-olefin **1'** (Scheme 3A, 85% ee for **2a** and 31% ee for **2b**, dr:





Scheme 3 Control experiments to probe the mechanism. ^aReaction conditions: $\text{Fe}(\text{NTf}_2)_2$ (15 mol%), **L1** (15 mol%), TBAC (2.5 equiv.), CHCl_3 , -60°C , 12 h. ^bReaction conditions: $\text{Fe}(\text{NTf}_2)_2$ (15 mol%), **L1** (15 mol%), CHCl_3 , -60°C , 12 h.

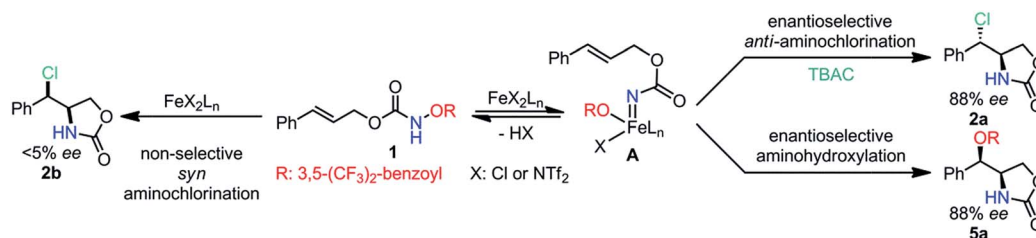
6 : 1; 93% ee for **5a** and 83% ee for **5b**, dr: 7 : 1). In both cases, **5a** and **5b** cannot be converted to **2a** under the reaction conditions.

These observations provide several important mechanistic insights. First, the non-stereospecificity observed in the iron-catalyzed olefin aminochlorination suggests that the formation of C–N and C–Cl bonds occurs in a stepwise fashion.¹⁸ Second, the lack of complete stereo-convergence between the reaction profiles of isomeric olefins (**1** and **1'**) suggests that C–N bond formation may be the rate- and ee-determining step.¹⁸ Furthermore, since essentially the same ee was observed for **2a**, **5a**, and **5b** from the reaction with *trans*-olefin **1**, it is likely that these products are derived from the same intermediate after the ee-determining step. Additionally, the fact that the syn-amino-chlorination product **2b** was isolated as a racemate suggests that **2b** may be derived from non-stereoselective pathways

which are distinct from the one leading to the formation of **2a**, **5a**, and **5b**.

The product divergence (**2a** vs. **5a/b**) after the ee-determining step is mechanistically interesting. Therefore, we studied the effect of external chloride ion. To our surprise, in the absence of TBAC, the $\text{Fe}(\text{NTf}_2)_2$ –**L5** complex alone was ineffective for the nitrogen atom-transfer at -60°C ; **1** and **1'** were both fully recovered (Scheme 3B). However, aminochlorination occurred as soon as a stoichiometric amount of TBAC was introduced. This observation suggests that the $\text{Fe}(\text{NTf}_2)_2$ –**L5** complex may serve as a pre-catalyst and it may be activated by chloride ion *in situ*.

In order to test this hypothesis, we further carried out the FeCl_2 -catalyzed reaction in the presence of TBAC (Scheme 3C). Notably, **2a** was isolated with essentially the same ee as that obtained under the standard conditions (88% ee for **2a** and <5%



Scheme 4 Proposed mechanistic working hypothesis for the iron-catalyzed asymmetric aminochlorination of *trans*-olefin **1**.



ee for **2b**). This result suggests that the catalytically relevant species may also be generated from the FeCl₂–**L5** complex.

To probe for more mechanistic details, we subsequently carried out the FeCl₂-promoted olefin aminochlorination in the absence of TBAC (100 mol% FeCl₂, 100 mol% **L5**, Scheme 3C). Under these conditions, FeCl₂ is the only available chlorine source. Surprisingly, we discovered that **2a** was obtained with essentially the same ee compared with the two previous control experiments (88% ee for **2a**). Furthermore, a syn-amino-hydroxylation product **5a** was isolated with excellent dr and ee (dr > 20 : 1, 88% ee). These observations suggest that Fe–Cl bond cleavage may be relevant for the chlorine atom-transfer step during the enantioselective anti-aminochlorination.¹⁹ In addition, we also identified a small amount of aziridine **6** (15% yield, 82% ee), and further discovered that it could not be converted to either **2a** or **5a** under the reaction conditions.

With the accumulated mechanistic evidence, we propose a plausible mechanistic working hypothesis for the iron-catalyzed asymmetric aminochlorination of *trans*-olefin **1** (Scheme 4). First, the iron catalyst reversibly cleaves the N–O bond in the acyloxyl carbamate **1**, generating iron-nitrenoid **A** with chloride as a counter ion. From there, **A** may participate in enantioselective and diastereoselective aminochlorination and amino-hydroxylation to afford **2a** and **5a**, respectively. Since the aminochlorination–aminohydroxylation competition occurs after the ee-determining step, **2a** is obtained with essentially the same ee as **5a**. At the same time, **1** may be converted to **2b** via a non-stereoselective pathway which is distinct from the one leading to the formation of **2a** and **5a**. Further mechanistic studies are required to elucidate the details.

Conclusions

In conclusion, we have described an iron-catalyzed enantioselective and diastereoselective aminochlorination method for internal, non-chalconic olefins. This method tolerates a range of synthetically valuable olefins that are all incompatible with existing asymmetric olefin aminochlorination methods. It also provides a complementary approach for the asymmetric synthesis of amino chlorides with contiguous stereogenic centers. Our preliminary mechanistic studies revealed that an FeCl₂-derived nitrenoid may be a feasible reactive intermediate and that Fe–Cl bond cleavage may be relevant for stereoselective chlorine atom-transfer. Our current efforts are focused on the mechanistic investigation of this new reaction and method development for the enantioselective intermolecular olefin aminochlorination.

Acknowledgements

This work was supported by the National Institutes of Health (GM110382) and Georgia State University. Z.-Y. G. was supported by NSFC (21272027) and a fellowship from China Scholarship Council.

Notes and references

- For selected reviews of asymmetric olefin halofunctionalization, see: (a) S. E. Denmark, W. E. Kuester and M. T. Burk, *Angew. Chem., Int. Ed.*, 2012, **51**, 10938; (b) S. R. Chemler and M. T. Bovino, *ACS Catal.*, 2013, **3**, 1076; (c) S. A. Snyder, D. S. Treitler and A. P. Brucks, *Aldrichimica Acta*, 2011, **44**, 27.
- For selected reports on catalytic asymmetric olefin halo-oxygenation, see: (a) S. H. Kang, S. B. Lee and C. M. Park, *J. Am. Chem. Soc.*, 2003, **125**, 15748; (b) G. E. Veitch and E. N. Jacobsen, *Angew. Chem., Int. Ed.*, 2010, **49**, 7332; (c) W. Zhang, S. Zheng, N. Liu, J. B. Werness, I. A. Guzei and W. Tang, *J. Am. Chem. Soc.*, 2010, **132**, 3664; (d) L. Zhou, C. K. Tan, X. Jiang, F. Chen and Y.-Y. Yeung, *J. Am. Chem. Soc.*, 2010, **132**, 15474; (e) K. Murai, T. Matsushita, A. Nakamura, S. Fukushima, M. Shimura and H. Fujioka, *Angew. Chem., Int. Ed.*, 2010, **49**, 9174; (f) S. E. Denmark and M. T. Burk, *Org. Lett.*, 2012, **14**, 256; (g) D. Huang, H. Wang, F. Xue, H. Guan, L. Li, X. Peng and Y. Shi, *Org. Lett.*, 2011, **13**, 6350; (h) R. Yousefi, D. C. Whitehead, J. M. Mueller, R. J. Staples and B. Borhan, *Org. Lett.*, 2011, **13**, 608; (i) R. Yousefi, K. D. Ashtekar, D. C. Whitehead, J. E. Jackson and B. Borhan, *J. Am. Chem. Soc.*, 2013, **135**, 14524; (j) D. H. Paull, C. Fang, J. R. Donald, A. D. Pansick and S. F. Martin, *J. Am. Chem. Soc.*, 2012, **134**, 11128; (k) M. C. Dobish and J. N. Johnston, *J. Am. Chem. Soc.*, 2012, **134**, 6068; (l) Y.-M. Wang, J. Wu, C. Hoong, V. Rauniyar and F. D. Toste, *J. Am. Chem. Soc.*, 2012, **134**, 12928; (m) V. Rauniyar, A. D. Lackner, G. L. Hamilton and F. D. Toste, *Science*, 2011, **334**, 1681; (n) T. Honjo, R. J. Phipps, V. Rauniyar and F. D. Toste, *Angew. Chem., Int. Ed.*, 2012, **51**, 9684; (o) J. Wu, Y.-M. Wang, A. Drljevic, V. Rauniyar, R. J. Phipps and F. D. Toste, *Proc. Natl. Acad. Sci. U. S. A.*, 2013, **110**, 13729; (p) H. Nakatsuji, Y. Sawamura, A. Sakakura and K. Ishihara, *Angew. Chem., Int. Ed.*, 2014, **53**, 6974; (q) L. Li, C. Su, X. Liu, H. Tian and Y. Shi, *Org. Lett.*, 2014, **16**, 3728.
- For selected reports on catalytic asymmetric olefin aminobromination and aminoiodination, see: (a) Y. Cai, X. Liu, Y. Hui, J. Jiang, W. Wang, W. Chen, L. Lin and X. Feng, *Angew. Chem., Int. Ed.*, 2010, **49**, 6160; (b) L. Zhou, J. Chen, C. K. Tan and Y.-Y. Yeung, *J. Am. Chem. Soc.*, 2011, **133**, 9164; (c) Y. F. Cai, X. H. Liu, J. Li, W. L. Chen, W. T. Wang, L. L. Lin and X. M. Feng, *Chem.-Eur. J.*, 2011, **17**, 14916; (d) A. Alix, C. Lalli, P. Retailleau and G. Masson, *J. Am. Chem. Soc.*, 2012, **134**, 10389; (e) D. Huang, X. Liu, L. Li, Y. Cai, W. Liu and Y. Shi, *J. Am. Chem. Soc.*, 2013, **135**, 8101; (f) C. S. Brindle, C. S. Yeung and E. N. Jacobsen, *Chem. Sci.*, 2013, **4**, 2100; (g) F. Chen, C. K. Tan and Y.-Y. Yeung, *J. Am. Chem. Soc.*, 2013, **135**, 1232. For mechanistically related asymmetric olefin sulfenofunctionalization, see: (h) S. E. Denmark and H. M. Chi, *J. Am. Chem. Soc.*, 2014, **136**, 8915; (i) S. E. Denmark, E. Hartmann, D. J. P. Kornfilt and H. Wang, *Nat. Chem.*, 2014, **6**, 1056.



- 4 For existing asymmetric olefin aminochlorination methods, see: (a) Y. F. Cai, X. H. Liu, J. Jiang, W. L. Chen, L. L. Lin and X. M. Feng, *J. Am. Chem. Soc.*, 2011, **133**, 5636; (b) M. T. Bovino and S. R. Chemler, *Angew. Chem., Int. Ed.*, 2012, **51**, 3923; (c) Y. Cai, X. Liu, P. Zhou, Y. Kuang, L. Lin and X. M. Feng, *Chem. Commun.*, 2013, **49**, 8054.
- 5 For catalytic olefin aminohydroxylation that proceeds through an iron-nitrenoid intermediate, see: (a) G.-S. Liu, Y.-Q. Zhang, Y.-A. Yuan and H. Xu, *J. Am. Chem. Soc.*, 2013, **135**, 3343; (b) Y.-Q. Zhang, Y.-A. Yuan, G.-S. Liu and H. Xu, *Org. Lett.*, 2013, **15**, 3910; (c) D.-F. Lu, C.-L. Zhu, Z.-X. Jia and H. Xu, *J. Am. Chem. Soc.*, 2014, **136**, 13186.
- 6 D.-F. Lu, G.-S. Liu, C.-L. Zhu, B. Yuan and H. Xu, *Org. Lett.*, 2014, **16**, 2912.
- 7 (a) T. Bach, B. Schlummer and K. Harms, *Chem. Commun.*, 2000, 287; (b) T. Bach, B. Schlummer and K. Harms, *Chem.-Eur. J.*, 2001, **7**, 2581; (c) H. Danielec, J. Klügge, B. Schlummer and T. Bach, *Synthesis*, 2006, 551.
- 8 See ESI† for details of substrate synthesis. Acyloxyl carbamates are reactive, while tosyloxyl and alkoxy carbamates are non-reactive and fully recovered under the reaction conditions.
- 9 The relative stereochemistry of **2a** was determined by comparison of the experimental NMR data with those reported in ref. 7. It was further corroborated by ¹H NMR and X-ray crystallographic analysis of a structural analog of **2a**. See ESI† for details.
- 10 The relative stereochemistry was assigned based on the ¹H NMR and X-ray crystallographic analysis of a structural analog described in ref. 6; see ESI† for details.
- 11 Complementary stereochemistry was achieved (in entry 15 of Table 2) compared with the known method reported in ref. 7, where the syn-aminochlorination product was isolated. This substrate did not undergo kinetic resolution with a chiral catalyst, the complex Fe(NTf₂)₂-**L5**. Both the starting material and product were isolated as racemates.
- 12 For leading references on chiral BOX and related ligands, see: (a) D. A. Evans, K. A. Woerpel, M. M. Hinman and M. M. Faul, *J. Am. Chem. Soc.*, 1991, **113**, 726; (b) H. Nishiyama, Y. Itoh, H. Matsumoto, S.-B. Park and K. Itoh, *J. Am. Chem. Soc.*, 1994, **116**, 2223; (c) Y. Nishikawa and H. Yamamoto, *J. Am. Chem. Soc.*, 2011, **133**, 8432.
- 13 The absolute stereochemistry of **2a** was determined by X-ray crystallographic analysis of a structural analog of **2a**. See ESI† for details.
- 14 For detailed procedure and HPLC traces of **4**, see ESI†.
- 15 For the synthesis of **L9**, see ref. 6.
- 16 The iron-**L5** complex catalyzed the reaction favoring the syn-addition product (dr (anti/syn): 0.47 : 1); ee for the anti-addition product was 60% and ee for the syn-addition product was <5%. The relative stereochemistry was assigned based on the ¹H NMR and X-ray crystallographic analysis of a structural analog described in ref. 6; see ESI† for details.
- 17 When a chloroacetyl group was used as the activating group, a different result was obtained. For details, see entry 8 of Table 3.
- 18 For an example of stepwise atom transfer reactions with different reaction profiles for *cis/trans* isomeric olefins, see: N. H. Lee and E. N. Jacobsen, *Tetrahedron Lett.*, 1991, **32**, 6533.
- 19 For the oxidation of a radical species by a high-valent metal through ligand transfer or electron transfer, see: (a) M. S. Kharasch and G. Sosnovsky, *J. Am. Chem. Soc.*, 1958, **80**, 756; (b) J. K. Kochi, *Science*, 1967, **155**, 415. For a relevant enzymatic C-H chlorination reaction of hydrocarbons catalyzed by iron-containing metalloenzymes, see: (c) F. H. Vaillancourt, J. Yin and C. T. Walsh, *Proc. Natl. Acad. Sci. U. S. A.*, 2005, **102**, 10111.

