Radical Group Transfer

How to cite:
International Edition: doi.org/10.1002/anie.202017175
German Edition: doi.org/10.1002/ange.202017175

Iron-Catalyzed Radical Asymmetric Aminoazidation and Diazidation of Styrenes

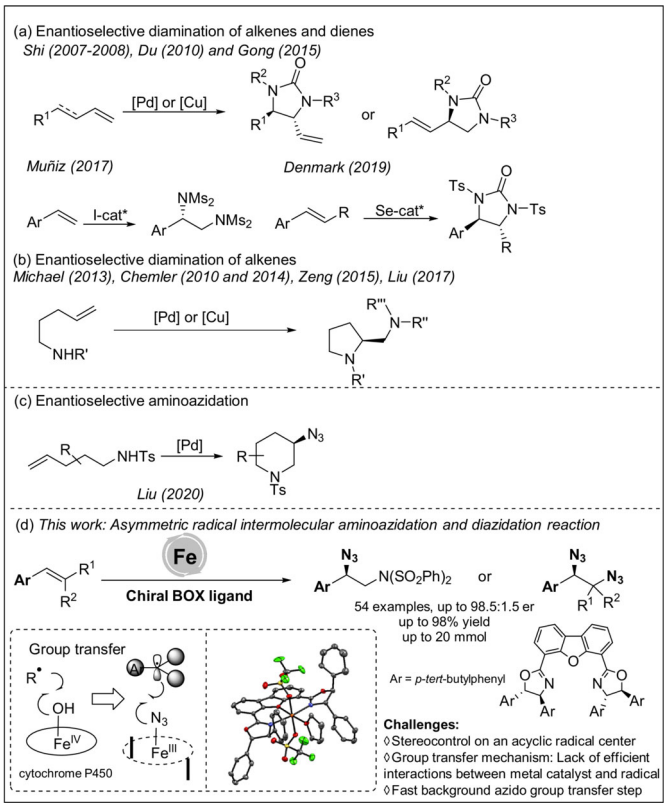
*Daqi Lv, Qiao Sun, Huan Zhou, Liang Ge, Yanjie Qu, Taian Li, Xiaoxu Ma, Yajun Li, and Hongli Bao**

In memory of Professor Kilian Muñiz

Abstract: *Asymmetric aminoazidation and diazidation of alkenes are straightforward strategies to build value-added chiral nitrogen-containing compounds from feedstock chemicals. They provide direct access to chiral organoazides and complement enantioselective diamination. Despite the advances in non-asymmetric reactions, asymmetric aminoazidation or diazidation based on acyclic systems has not been previously reported. Here we describe the iron-catalyzed intermolecular asymmetric aminoazidation and diazidation of styrenes. The method is practically useful and requires relatively low loading of catalyst and chiral ligand. With mild reaction conditions, the reaction can be completed on a 20 mmol scale. Studies of the mechanism suggest that the reaction proceeds via a radical pathway and involves stereocontrol of an acyclic free radical which probably takes place through a group transfer mechanism.*

Introduction

Enantioenriched, vicinal diamines are found in many natural products, drugs, and other biologically active molecules, and are also privileged chiral ligands widely used in asymmetric synthesis and catalysis.[1] While C–C bond formation involving reductive coupling of aldimines[2] and/or imines[3] is effective for the synthesis of chiral diamines, the catalytic asymmetric diamination of alkenes or dienes is the most straightforward and convenient approach to production of these structures (Scheme 1). Shi,[1d,4] Du,[5] Gong,[6] Muñiz[7] and Denmark[8] have established powerful palladium-, aryliodine- and organoselenium-catalyzed intermolecular diamination of alkenes or dienes, respectively. Michael,[9] Chemler,[10] Zeng[11] and Liu[12] developed palladium or copper catalyzed inter/intramolecular diamination with one external amination reagent and the other derived from alkene substrates, producing useful chiral indolines and pyrrolidines.



Scheme 1. State of the art in catalytic asymmetric diamination and aminoazidation, and this work.

Aminoazidation and diazidation of alkenes are also promising strategies because they not only provide methods complementary to diamination, but also have additional potential due to the rich chemistry of the azido group. Organoazides are familiar as versatile reactants in numerous reactions including the Curtius rearrangement,[13] Regitz diazo transfer,[14] Staudinger ligation,[15] Aza-Wittig reaction,[16] Boyer rearrangement,[17] Huisgen "click" reaction[18] and many other reactions.[15a,19] The azide group is an important synthon and is also found in many drugs and bioactive molecules.[15b,20] With the significance of organic azides and diamines, there is continuing interest in the development of aminoazidation[21] and diazidation[22] of alkenes and many novel methods have been developed.

In spite of the advances in related non-asymmetric reactions,[21a–k,23] enantioselective aminoazidation and diazi-

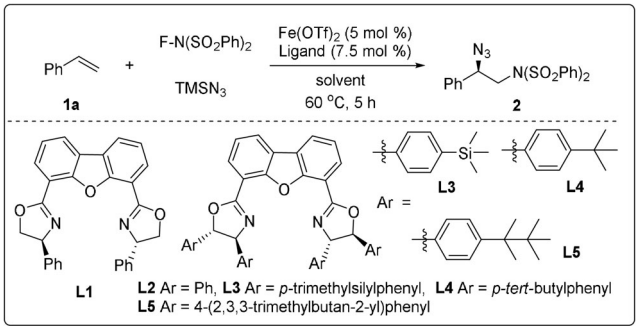
[*] D. Lv, Dr. Q. Sun, Dr. H. Zhou, L. Ge, Y. Qu, T. Li, X. Ma, Dr. Y. Li, Prof. H. Bao
Key Laboratory of Coal to Ethylene Glycol and Its Related Technology, State Key Laboratory of Structural Chemistry, Center for Excellence in Molecular Synthesis, Fujian Institute of Research on the Structure of Matter, Chinese Academy of Sciences
155 Yangqiao Road West, Fuzhou, Fujian 350002 (P. R. China)
E-mail: hlbao@fjirsm.ac.cn
Prof. H. Bao
University of Chinese Academy of Sciences
Beijing 100049 (P. R. China)
Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under: https://doi.org/10.1002/anie.202017175.

dation are underdeveloped. There is only one example of a successful enantioselective aminoazidation, an intra/ intermolecular aminoazidation leading to structurally diverse substituted piperidines (Scheme 1c).[24] There is a need for asymmetric aminoazidation/diazidation reactions but those based on the intermolecular mode on an acyclic system remain a challenge. Previous studies on azidation reactions showed that the metal-catalyzed radical azidation often involves an intermolecular group transfer mechanism.[25] Our studies on the mechanism of iron-catalyzed carboazidation of alkenes also have suggested an azido group transfer pathway.[26] In general, covalent, dative, ionic and hydrogen bonds between a chiral metal catalyst and a radical reaction partner in a metal-catalyzed intermolecular group transfer reaction are usually absent. Consequently, interactions between these two species tend to be inefficient. Stereocontrol of untethered radicals in a group transfer radical reaction is therefore highly challenging and successful examples of such reactions are uncommon (vide infra).[27] The enantioselective Kharasch addition reaction reported by Ready et al.[27a] is probably the first successful example of intermolecular asymmetric radical group transfer reaction dealing with untethered radicals. Zhang et al. recently reported the elegant enantioselective intermolecular radical C–H amination,[27d] and we[27c] and Liu[27e] independently developed asymmetric carboazidation of styrenes and acrylamides. Despite these recent breakthroughs, asymmetric aminoazidation and diazidation remain important unsolved problems. Herein, we report our results of the iron-catalyzed radical asymmetric aminoazidation and diazidation of styrenes.

Results and Discussion

Our study began with screening of the conditions of the Fe-catalyzed asymmetric aminoazidation of styrene (**1a**) using *N*-fluorobenzenesulfonimide (NFSI) as the *N*-radical precursor, trimethylsilyl azide ($TMSN_3$) as the N_3 source and a ligand. An initial trial with 5 mol% $Fe(OTf)_2$ and 7.5 mol% of a ligand (**L1**) in Et_2O at 60 °C for 5 h afforded the desired aminoazidation product (**2**) in 8% yield with a 64:36 enantiomeric ratio (er) (Table 1, entry 1). The ligand (**L1**) contains a large planar aromatic system that could support interactions with π electrons, and two phenyl groups that may protect the radicals from non-selective azidation. Bulkier ligands (**L2**–**L5**) were designed. Ligand **L2**, with four phenyl groups was found to deliver the product in 29% yield and 80.5:19.5 er (entry 2). Ligand **L4** which has a *t*-Bu group at the *para*-position of each of the phenyl groups in **L2** was found to increase the yield of the product (**2**) to 55% and the er to 91.5:8.5 (entry 4). With a more sterically-hindered ligand (**L5**), the yield fell to 4% and the er slightly decreased to 91:9 (entry 5). Several Box ligands (**L6**–**L10**) were also examined, and these reactions gave lower yields and enantioselectivities (see Table S1† in Supplementary Information—SI). A series of metal catalysts including various iron compounds were tested, and $Fe(OTf)_2$ was found to be the best catalyst (see SI, Table S2†). Solvent effects were investigated (entries 6–13), and it was found that use of $CHCl_3$ rather than Et_2O significantly improved the yield to 96% albeit with a decreased er of 87:13 (entry 12). Upon reducing the temperature from 60 °C to room temperature (rt) and extending the reaction time to 48 h, the product was obtained in a yield of 90% and with 91:9 er (entry 14). Further lowering the temperature failed to improve the reaction yield (entry 15). By reducing the catalyst and ligand loading to 1 mol% and 1.2 mol%, respectively (entry 16), the yield could be further increased to 98% without affecting the enantioselectivity. Using the conditions in entry 16 and replacing **L4** with **L5** afforded the product in 96% yield with 93:7 er (entry 17).

Table 1: Reaction optimization using styrene as a substrate.[a]



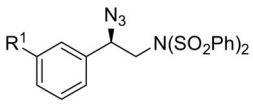
Entry	Ligand	Solvent	Yield [%][b]	er[c]
1	**L1**	Et_2O	8	64:36
2	**L2**	Et_2O	29	80.5:19.5
3	**L3**	Et_2O	0	–
4	**L4**	Et_2O	55	91.5:8.5
5	**L5**	Et_2O	4	91:9
6	**L4**	DME	48	89:11
7	**L4**	THF	trace	–
8	**L4**	PhMe	16	89:11
9	**L4**	CH_3CN	5	65.5:34.5
10	**L4**	DCE	25	82:18
11	**L4**	DCM	46	85.5:14.5
12	**L4**	$CHCl_3$	96	87:13
13	**L4**	CCl_4	66	88:12
14[d]	**L4**	$CHCl_3$	90	91:9
15[e]	**L4**	$CHCl_3$	14	90.5:9.5
16[d,f]	**L4**	$CHCl_3$	98	91:9
17[d,g]	**L5**	$CHCl_3$	96	93:7

[a] The reaction was performed with styrene (0.1 mmol), NFSI (0.25 mmol), $TMSN_3$ (0.25 mmol), $Fe(OTf)_2$ (5 mol%), ligand (7.5 mol%), solvent (2 mL), 60 °C, 5 h. [b] Yield of isolated product. [c] Determined by HPLC analysis on a chiral stationary phase. [d] rt, 48 h. [e] 10 °C, 48 h. [f] $Fe(OTf)_2$ (1 mol%), **L4** (1.2 mol%). [g] $Fe(OTf)_2$ (1 mol%), **L5** (1.2 mol%).

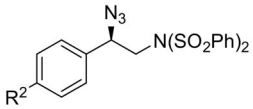
With the optimized conditions in hand, we explored the scope of the aminoazidation reaction and obtained the results shown in Scheme 2. Styrenes with one or more substituents on the phenyl groups were examined and were found to provide the corresponding products (**3**–**32**) with good yields and er. Most of the reactions were performed with **L4** or **L5**, and it was found that **L4** afforded products with better enantioselectivity in most cases with the exception of reactions forming products **5**, **16** and **32**.

Electron-donating groups such as methoxyl, methyl, isopropyl or *n*-octyl, and electron-withdrawing groups, including F, Cl, Br, CF_3, or CHF_2 are all tolerated. When vinyl

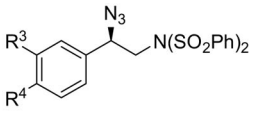
Scope of aminoazidation



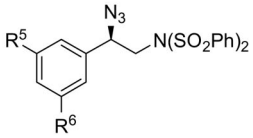
2, R^1 = H, 96% yield; 93:7 er (**L5**)
3, R^1 = OMe, 62% yield; 90:10 er (**L4**)
4, R^1 = Me, 75% yield; 90:10 er (**L4**)
5, R^1 = ^{i}Pr, 93% yield; 93:7 er (**L5**)
6, R^1 = ^{n}C_8H_{17}, 87% yield; 90:10 er (**L4**)
7, R^1 = F, 90% yield; 93:7 er (**L4**)
9, R^1 = Br, 60% yield; 95:5 er (**L4**)
10, R^1 = CF_2H, 86% yield; 93:7 er (**L4**)
11, R^1 = CF_3, 86% yield; 93:7 er (**L4**)



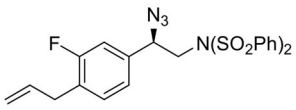
12, R^2 = F, 70% yield; 89:11 er (**L4**)
13, R^2 = Cl, 85% yield; 92:8 er (**L4**)
14, R^2 = CH_2Cl, 82% yield; 92:8 er (**L4**)
15, R^2 = CF_3, 70% yield; 89:11 er (**L4**)



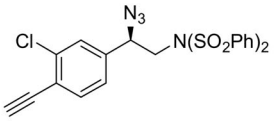
16, R^3 = Me, R^4 = Me, 60% yield; 92:8 er (**L5**)
17, R^3 = Cl, R^4 = Me, 92% yield; 94:6 er (**L4**)
18, R^3 = Me, R^4 = F, 81% yield; 94:6 er (**L4**)
19, R^3 = F, R^4 = F, 72% yield; 92:8 er (**L4**)
20, R^3 = Cl, R^4 = F, 85% yield; 97:3 er (**L4**)
22, R^3 = Cl, R^4 = Cl, 80% yield; 93:7 er (**L4**)
23, R^3 = Me, R^4 = Br, 60% yield; 89:11 er (**L4**)
24, R^3 = Br, R^4 = F, 61% yield; 91:9 er (**L4**)



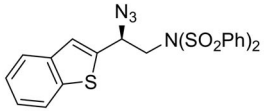
27, R^5 = Me, R^6 = OMe, 83% yield; 90:10 er (**L4**)
28, R^5 = Me, R^6 = Me, 70% yield; 92:8 er (**L4**)
29, R^5 = F, R^6 = F, 50% yield; 91:9 er (**L4**)
30, R^5 = Br, R^6 = Br, 88% yield; 92:8 er (**L4**)
31, R^5 = F, R^6 = Br, 67% yield; 90:10 er (**L4**)
32, R^5 = CF_3, R^6 = CF_3, 85% yield; 90:10 er **(L5)**



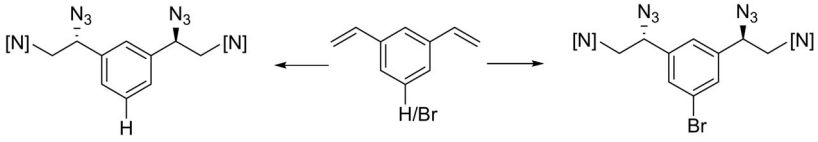
25, 68% yield; 89:11 er (**L4**)



26, 80% yield; 90:10 er (**L4**)



33, 90% yield; 88:12 er (**L4**)

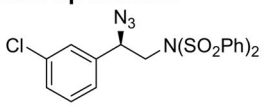


34,[c] 95% yield
80:20 dr, 98:2 er (**L4**)

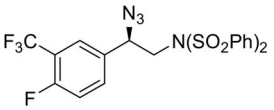
[N] = $N(SO_2Ph)_2$

35,[c] 85% yield
79:21 dr, 98.5:1.5 er (**L4**)

Scale-up reaction

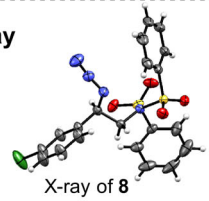


8, 98% yield; 94:6 er (**L4**)
10 mmol scale: 97% yield 94:6 er
with 0.75 mol% iron catalyst

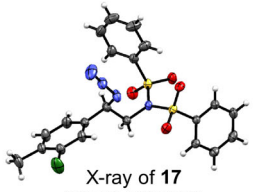


21, 72% yield; 92:8 er (**L4**)
20 mmol scale, 70% yield, 97:3 er
(after recystallization)
with 0.75 mol% iron catalyst

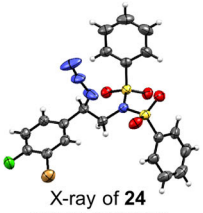
X-ray



X-ray of **8**
CCDC 2038969

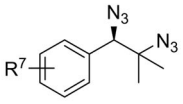


X-ray of **17**
CCDC 2038972

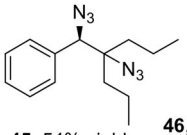


X-ray of **24**
CCDC 2038970

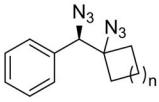
Scope of diazidation with L4 as the ligand



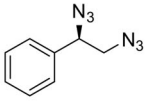
37, R^7 = 3-H, 64% yield; 97:3 er
38, R^7 = 3-CF_3, 55% yield; 93:7 er
39, R^7 = 3-Cl, 58% yield; 97:3 er
40, R^7 = 3-F, 58% yield; 95:5 er
41, R^7 = 3-Br, 75% yield; 95:5 er
42, R^7 = 3-CH_3, 60% yield; 85:15 er
43, R^7 = 3,5-diBr, 55% yield; 88:12 er
44, R^7 = 3,4-diCl, 54% yield; 89:11 er



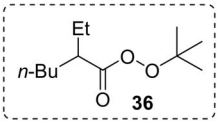
45, 54% yield
92:8 er



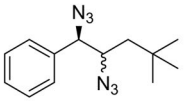
46, n= 1, 75% yield; 95:5 er
47, n= 2, 55% yield; 93:7 er
48, n= 3, 72% yield; 92:8 er
49, n= 5, 80% yield; 92:8 er



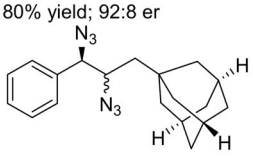
50, 61% yield, 73:27 er



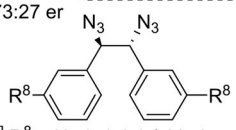
36



51, dr 2:1, 60% yield
major 85:15 er
minor 93:7 er



52, dr 3:2, 61% yield
major 85:15 er
minor 92:8 er



53,[d] R^8 = H, dr 1.4:1 (chiral:meso),
73% yield, 92:8 er
54, R^8 = F, dr 1.3:1 (chiral:meso),
78% yield, 90:10 er
55, R^8 = Cl, dr 1:1 (chiral:meso),
67% yield, 88:12 er
56,[d] R^8 = Br, dr 1:1.2 (chiral:meso),
67% yield, 91:9 er

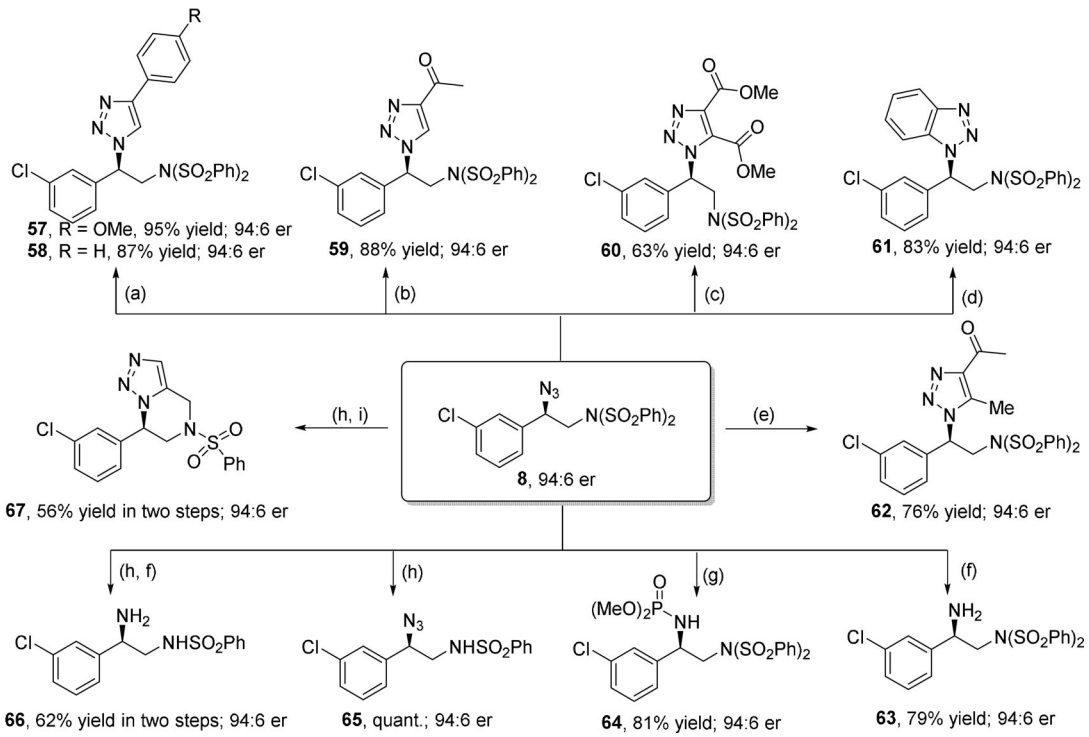
Scheme 2. Scope of iron-catalyzed intermolecular asymmetric aminoazidation and diazidation of styrenes.[a,b] [a] The aminoazidation reactions were performed with styrene (0.1 mmol), NFSI (2.5 equiv), $TMSN_3$ (2.5 equiv), $Fe(OTf)_2$ (1 mol%), **L4**/**L5** (1.2 mol%), $CHCl_3$ (2 mL), rt, 48 h. The diazidation reaction was performed with alkene (0.2 mmol), alkyl perester **36** (3.5 equiv),$TMSN_3$ (3.5 equiv), $Fe(OTf)_2$ (5 mol%), **L4** (6 mol%), $CHCl_3$ (2 mL), rt, 72 h. [b] Yields of isolated products. [c] Olefin (0.1 mmol), NFSI (5.0 equiv), $TMSN_3$ (5.0 equiv), $Fe(OTf)_2$ (2 mol%), **L4** (2.4 mol%), $CHCl_3$ (4 mL), rt, 48 h. [d] Toluene as solvent.

and allyl/alkynyl groups are present in the same molecule the aminoazidation occurs selectively at the vinyl group, affording products **25** and **26**. 2-Vinylbenzo[*b*]thiophene was also compatible with the reaction and afforded the desired product (**33**) in 90% yield and 88:12 er. By doubling the amount of reagents and the catalytic loading, 1,3-divinylbenzene and 1-bromo-3,5-divinylbenzene underwent double reactions affording the products **34** and **35**, respectively, with moderate diastereoselective ratios and high er. The absolute stereochemistry of products **8**, **17** and **24** has been confirmed as *R* by single crystal X-ray crystallography. It should be noted that the results of this reaction when performed on a scale of up to 20 mmol with 0.75 mol% of iron catalyst remained excellent.

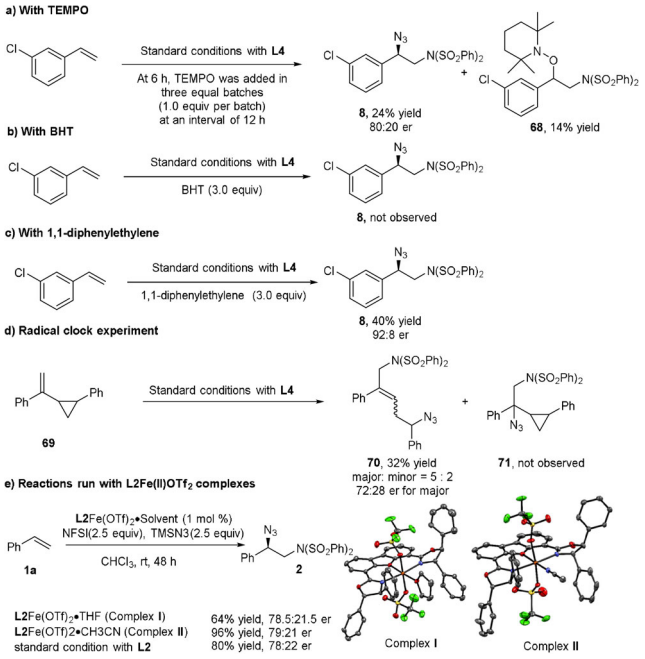
Diazidation of alkenes is a powerful strategy with which to incorporate two azido groups. Asymmetric diazidation however has not been reported. We explored the diazidation of styrenes with this catalytic system and found the chiral iron catalyst is suitable for disubstituted and trisubstituted styrenes and produces the otherwise inaccessible chiral diazidation products. With trisubstituted styrenes, products **37**–**49** with up to 97:3 er were obtained. Products **51** and **52**, which contain two asymmetric centers were produced from unsymmetric styrenes, each isomer with a moderate er. Diazide compounds **53**–**56** were delivered from symmetrical styrenes. The chiral products delivered er as high as 97:3. Diazidation of styrene afforded the corresponding product (**50**) in moderate yield but with low er.

To demonstrate the synthetic utility of the reaction, different transformations of the aminoazidation product (**8**) were performed (Scheme 3). Click reactions of **8** with terminal[21d,28] or internal alkynes,[29] a benzyne precursor,[30] or acetylacetone[31] afforded the corresponding triazoles (**57**–**62**) with good yields and without loss of enantioselectivity. The chiral azide (**8**) was reduced in 79% yield to the corresponding chiral primary amine (**63**) by refluxing the chlorophenyl compound (**8**) with indium powder in MeOH.[32] Compound **8** could be further reduced with $P(OMe)_3$ to afford a chiral phosphoramide (**64**) in 81% yield.[21f] Besides azide transformations, compound **8** undergoes mono-desulfonylation upon treatment with *n*-Bu_4NF[33] to afford a product (**65**) in a quantitative yield. Further reduction of **65** with indium gave the monoprotected 1,2-diamine (**66**) in 62% yield.[32] One-pot propargylation/intramolecular [3+2] cycloaddition of compound **66** afforded a novel triazolopyrazine derivative (**67**).[34]

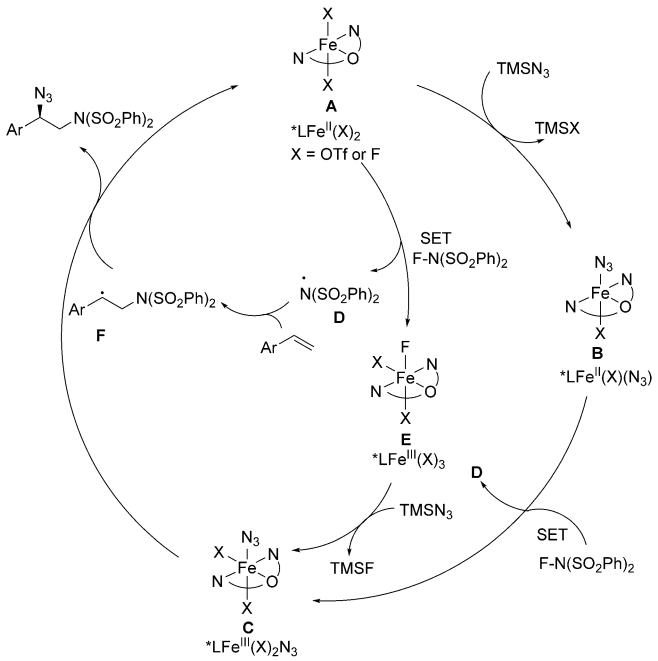
To gain insight into the radical nature and mechanism of the reaction, control experiments were performed. In radical trap experiments, the reaction was significantly inhibited by the addition of TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl), and the desired product (**8**) was formed in only 24% yield (Scheme 4a). An aminooxygenated product (**68**) was



Scheme 3. Synthetic applications of the aminoazidation products. Reaction conditions: a) **8** (0.2 mmol), aryl alkyne (2.0 equiv), $CuSO_4 \cdot 5H_2O$ (20 mol%), Na-ascorbate (0.4 equiv), *t*-BuOH/H_2O/DCM (2:1:0.2), rt, 24 h; b) **8** (0.2 mmol), but-3-yn-2-one (1.2 equiv), $Cu(OAc)_2$ (10 mol%), 2-aminophenol (5 mol%), DCM/H_2O (1:1), rt, 18 h; c) **8** (0.2 mmol), DMAD (1.1 equiv), *t*-BuOH/H_2O/DCM (2:1:0.25), 70°C, 18 h; d) **8** (0.2 mmol), 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (2.0 equiv), CsF (2.0 equiv), CH_3CN, rt, 4 h; e) **8** (0.2 mmol), acetylacetone (2.0 equiv), K_2CO_3 (0.2 equiv), DMF, 40°C, 17 h; f) **8** (0.2 mmol), In powder (1.5 equiv), NH_4Cl (1.5 equiv), MeOH, reflux, 5 h; g) **8** (0.2 mmol), $P(OMe)_3$ (1.5 equiv), PhMe, 80°C, 12 h; h) **8** (0.5 mmol), TBAF (1.1 equiv, 1 M in THF), THF, 70°C, 1.5 h; i) **8** (0.5 mmol), propargyl bromide (1.1 equiv), K_2CO_3 (2.0 equiv), CH_3CN, 60°C, 4 h. DMAD = dimethyl acetylenedicarboxylate.



Scheme 4. Mechanistic studies.



Scheme 5. Proposed mechanism.

isolated from this reaction in 14% yield. This suggests the existence of a benzyl radical, generated from the addition of a disulfonimidyl radical to the alkene. The radical inhibitor BHT (2,6-di-*tert*-butyl-4-methylphenol) was found to completely inhibit the aminoazidation reaction (Scheme 4b). The addition of 1,1-diphenylethylene severely suppressed the reaction, the yield of the desired product (**8**) decreasing to 40% (Scheme 4c). A radical clock experiment with (2-phenylcyclopropyl)styrene (**69**) was conducted and the ring-opened product (**70**) was formed in 32% yield with no aminoazidation product (**71**) (Scheme 4d). These results are consistent and suggest that the reaction proceeds via a radical pathway and that a benzyl radical may be an intermediate.

To identify the catalytically active species in this reaction, two complexes, **L2**-$Fe^{II}OTf_2$·THF and **L2**-$Fe^{II}OTf_2$·CH_3CN were synthesized and their structures were established by X-ray crystallography (Scheme 4e). The complexes catalyze the model reaction in terms of both the yield and enantioselectivity. This suggests that an **L**-$Fe^{II}OTf_2$ complex may serve as the catalytically active species. Based on the above studies of the mechanism, a catalytic cycle is proposed in Scheme 5 for the iron-catalyzed asymmetric aminoazidation of styrenes. Coordination of the iron catalyst with the ligand affords an iron(II) complex (**A**), which undergoes ligand exchange with $TMSN_3$ to afford an iron(II) azide complex (**B**). A single electron transfer (SET) process between NFSI and **B** affords an iron(III) azide species (**C**) and a bis-sulfonylamidyl radical (**D**). Alternatively, the SET process could proceed prior to the ligand exchange with $TMSN_3$. Complex **A** participates in a SET with NFSI to afford an oxidized iron species (**E**) and a radical (**D**) and **E** reacts with $TMSN_3$ to generate the iron(III) azide species (**C**). Addition of the bis-sulfonylamidyl radical (**D**) to the styrene gives a benzyl radical (**F**), which can participate in a group transfer mechanism with species **C** to afford the final product regenerating the active catalyst species **A**.[26,27c]

Conclusion

We are reporting the first iron-catalyzed radical asymmetric aminoazidation and diazidation of styrenes. The reaction proceeds under mild reaction conditions, with low catalyst loading and broad styrene scope. A range of chiral aminative organoazides and diazides have been synthesized, and can be readily further transformed into various useful nitrogen-containing compounds. Studies on the mechanism of the reaction suggest the involvement of a benzyl radical, and a radical pathway has been proposed for the transformation.

Acknowledgements

We thank Professor Daqiang Yuan from our institute for X-ray crystallography analysis. This work was supported by the National Key R&D Program of China (Grant No. 2017YFA0700103), the NSFC (Grant Nos. 21871258, 21922112, and 22001251), the Strategic Priority Research Program of the Chinese Academy of Sciences (Grant No. XDB20000000), Scientific Research Foundation of Fujian Normal University in China and Innovative Research Teams Program II of Fujian Normal University in China (IRTL1703).

Conflict of interest

The authors declare no conflict of interest.

Keywords: aminoazidation · asymmetric catalysis · iron catalysis · radical group transfer

[1] a) S. R. Saibabu Kotti, C. Timmons, G. Li, *Chem. Biol. Drug Des.* **2006**, *67*, 101 – 114; b) F. Cardona, A. Goti, *Nat. Chem.* **2009**, *1*, 269 – 275; c) R. I. McDonald, G. Liu, S. S. Stahl, *Chem. Rev.* **2011**, *111*, 2981 – 3019; d) Y. Zhu, R. G. Cornwall, H. Du, B. Zhao, Y. Shi, *Acc. Chem. Res.* **2014**, *47*, 3665 – 3678.

[2] X. Shao, K. Li, S. J. Malcolmson, *J. Am. Chem. Soc.* **2018**, *140*, 7083 – 7087.

[3] M. Zhou, K. Li, D. Chen, R. Xu, G. Xu, W. Tang, *J. Am. Chem. Soc.* **2020**, *142*, 10337 – 10342.

[4] a) H. Du, W. Yuan, B. Zhao, Y. Shi, *J. Am. Chem. Soc.* **2007**, *129*, 11688 – 11689; b) H. Du, B. Zhao, Y. Shi, *J. Am. Chem. Soc.* **2008**, *130*, 8590 – 8591; c) H. Du, B. Zhao, W. Yuan, Y. Shi, *Org. Lett.* **2008**, *10*, 4231 – 4234.

[5] X. Hu, Z. Cao, Z. Liu, Y. Wang, H. Du, *Adv. Synth. Catal.* **2010**, *352*, 651 – 655.

[6] M.-S. Wu, T. Fan, S.-S. Chen, Z.-Y. Han, L.-Z. Gong, *Org. Lett.* **2018**, *20*, 2485 – 2489.

[7] K. Muñiz, L. Barreiro, R. M. Romero, C. Martínez, *J. Am. Chem. Soc.* **2017**, *139*, 4354 – 4357.

[8] Z. Tao, B. B. Gilbert, S. E. Denmark, *J. Am. Chem. Soc.* **2019**, *141*, 19161 – 19170.

[9] E. L. Ingalls, P. A. Sibbald, W. Kaminsky, F. E. Michael, *J. Am. Chem. Soc.* **2013**, *135*, 8854 – 8856.

[10] a) B. W. Turnpenny, S. R. Chemler, *Chem. Sci.* **2014**, *5*, 1786 – 1793; b) F. C. Sequeira, B. W. Turnpenny, S. R. Chemler, *Angew. Chem. Int. Ed.* **2010**, *49*, 6365 – 6368; *Angew. Chem.* **2010**, *122*, 6509 – 6512.

[11] S. Fu, H. Yang, G. Li, Y. Deng, H. Jiang, W. Zeng, *Org. Lett.* **2015**, *17*, 1018 – 1021.

[12] G. Qiu, Q. Wang, J. Zhu, *Org. Lett.* **2017**, *19*, 270 – 273.

[13] T. Curtius, *Ber. Dtsch. Chem. Ges.* **1890**, *23*, 3023 – 3033.

[14] M. Regitz, *Angew. Chem. Int. Ed. Engl.* **1967**, *6*, 733 – 749; *Angew. Chem.* **1967**, *79*, 786 – 801.

[15] a) E. F. V. Scriven, K. Turnbull, *Chem. Rev.* **1988**, *88*, 297 – 368; b) S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem. Int. Ed.* **2005**, *44*, 5188 – 5240; *Angew. Chem.* **2005**, *117*, 5320 – 5374.

[16] T. Yakura, H. Nambu, *Tetrahedron Lett.* **2018**, *59*, 188 – 202.

[17] J. H. Boyer, J. Hamer, *J. Am. Chem. Soc.* **1955**, *77*, 951 – 954.

[18] a) S. G. Agalave, S. R. Maujan, V. S. Pore, *Chem. Asian J.* **2011**, *6*, 2696 – 2718; b) W. Xi, T. F. Scott, C. J. Kloxin, C. N. Bowman, *Adv. Funct. Mater.* **2014**, *24*, 2572 – 2590; c) R. Huisgen, *Proc. Chem. Soc.* **1964**, 385 – 434.

[19] D. Intrieri, P. Zardi, A. Caselli, E. Gallo, *Chem. Commun.* **2014**, *50*, 11440 – 11453.

[20] a) L. Ge, M.-F. Chiou, Y. Li, H. Bao, *Green Synth. Catal.* **2020**, *1*, 86 – 120; b) P. Thirumurugan, D. Matosiuk, K. Jozwiak, *Chem. Rev.* **2013**, *113*, 4905 – 4979; c) P.-G. Ding, X.-S. Hu, F. Zhou, J. Zhou, *Org. Chem. Front.* **2018**, *5*, 1542 – 1559; d) P. Sivaguru, Y. Ning, X. Bi, *Chem. Rev.* **2021**, https://doi.org/10.1021/acs.chemrev.0c01124.

[21] a) K. Wu, Y. Liang, N. Jiao, *Molecules* **2016**, *21*, 352; b) Q. Li, G. Li, S. Ma, P. Feng, Y. Shi, *Org. Lett.* **2013**, *15*, 2601 – 2603; c) J. Li, M. Liu, Q. Li, H. Tian, Y. Shi, *Org. Biomol. Chem.* **2014**, *12*, 9769 – 9772; d) B. Zhang, A. Studer, *Org. Lett.* **2014**, *16*, 1790 – 1793; e) C. E. Hendrick, K. J. Bitting, S. Cho, Q. Wang, *J. Am. Chem. Soc.* **2017**, *139*, 11622 – 11628; f) K. Shen, Q. Wang, *J. Am. Chem. Soc.* **2017**, *139*, 13110 – 13116; g) Y. Li, Y. Liang, J. Dong, Y. Deng, C. Zhao, Z. Su, W. Guan, X. Bi, Q. Liu, J. Fu, *J. Am. Chem. Soc.* **2019**, *141*, 18475 – 18485; h) L. Wang, X. Wang, G. Zhang, S. Yang, Y. Li, Q. Zhang, *Org. Chem. Front.* **2019**, *6*, 2934 – 2938; i) P. Wang, Y. Luo, S. Zhu, D. Lu, Y. Gong, *Adv. Synth. Catal.* **2019**, *361*, 5565 – 5575; j) D. Wu, S.-S. Cui, Y. Lin, L. Li, W. Yu, *J. Org. Chem.* **2019**, *84*, 10978 – 10989; k) F. Foschi, C. Loro, R. Sala, J. Oble, L. Lo Presti, E. M. Beccalli, G. Poli, G. Broggini, *Org. Lett.* **2020**, *22*, 1402 – 1406; l) S. Makai, E. Falk, B. Morandi, *J. Am. Chem. Soc.* **2020**, *142*, 21548 – 21555.

[22] a) G. Fumagalli, P. T. Rabet, S. Boyd, M. F. Greaney, *Angew. Chem. Int. Ed.* **2015**, *54*, 11481 – 11484; *Angew. Chem.* **2015**, *127*, 11643 – 11646; b) M. Z. Lu, C. Q. Wang, T. P. Loh, *Org. Lett.* **2015**, *17*, 6110 – 6113; c) Y. A. Yuan, D. F. Lu, Y. R. Chen, H. Xu, *Angew. Chem. Int. Ed.* **2016**, *55*, 534 – 538; *Angew. Chem.* **2016**, *128*, 544 – 548; d) N. Fu, G. S. Sauer, A. Saha, A. Loo, S. Lin, *Science* **2017**, *357*, 575 – 579; e) H. Peng, Z. Yuan, P. Chen, G. Liu, *Chin. J. Chem.* **2017**, *35*, 876 – 880; f) H. Zhou, W. Jian, B. Qian, C. Ye, D. Li, J. Zhou, H. Bao, *Org. Lett.* **2017**, *19*, 6120 – 6123; g) S. J. Shen, C. L. Zhu, D. F. Lu, H. Xu, *ACS Catal.* **2018**, *8*, 4473 – 4482; h) L. Xu, J. Chen, L. Chu, *Org. Chem. Front.* **2019**, *6*, 512 – 516.

[23] a) H. Su, W. Li, Z. Xuan, W. Yu, *Adv. Synth. Catal.* **2015**, *357*, 64 – 70; b) P. Zhang, W. Sun, G. Li, L. Hong, R. Wang, *Chem. Commun.* **2015**, *51*, 12293 – 12296.

[24] X. Li, X. Qi, C. Hou, P. Chen, G. Liu, *Angew. Chem. Int. Ed.* **2020**, *59*, 17239 – 17244; *Angew. Chem.* **2020**, *132*, 17392 – 17397.

[25] a) X. Huang, T. M. Bergsten, J. T. Groves, *J. Am. Chem. Soc.* **2015**, *137*, 5300 – 5303; b) L. Zhang, S. Liu, Z. Zhao, H. Su, J. Hao, Y. Wang, *Chem. Sci.* **2018**, *9*, 6085 – 6090.

[26] M. F. Chiou, H. Xiong, Y. Li, H. Bao, X. Zhang, *Molecules* **2020**, *25*, 1224.

[27] a) B. Chen, C. Fang, P. Liu, J. M. Ready, *Angew. Chem. Int. Ed.* **2017**, *56*, 8780 – 8784; *Angew. Chem.* **2017**, *129*, 8906 – 8910; b) Y. Zeng, M. F. Chiou, X. Zhu, J. Cao, D. Lv, W. Jian, Y. Li, X. Zhang, H. Bao, *J. Am. Chem. Soc.* **2020**, *142*, 18014 – 18021; c) L. Ge, H. Zhou, M.-F. Chiou, H. Jiang, W. Jian, C. Ye, X. Li, X. Zhu, H. Xiong, Y. Li, L. Song, X. Zhang, H. Bao, *Nat. Catal.* **2021**, *4*, 28 – 35; d) L. M. Jin, P. Xu, J. Xie, X. P. Zhang, *J. Am. Chem. Soc.* **2020**, *142*, 20828 – 20836; e) L. Wu, Z. Zhang, D. Wu, F. Wang, P. Chen, Z. Lin, G. Liu, *Angew. Chem. Int. Ed.* **2021**, *60*, 6997 – 7001; *Angew. Chem.* **2021**, *133*, 7073 – 7077.

[28] F. Broghammer, D. Brodbeck, T. Junge, R. Peters, *Chem. Commun.* **2017**, *53*, 1156 – 1159.

[29] X. Sun, X. Li, S. Song, Y. Zhu, Y.-F. Liang, N. Jiao, *J. Am. Chem. Soc.* **2015**, *137*, 6059 – 6066.

[30] S. Chandrasekhar, M. Seenaiah, C. L. Rao, C. R. Reddy, *Tetrahedron* **2008**, *64*, 11325 – 11327.

[31] E. P. J. Ng, Y.-F. Wang, B. W.-Q. Hui, G. Lapointe, S. Chiba, *Tetrahedron* **2011**, *67*, 7728 – 7737.

[32] X. Geng, F. Lin, X. Wang, N. Jiao, *Org. Lett.* **2017**, *19*, 4738 – 4741.

[33] A. Yasuhara, M. Kameda, T. Sakamoto, *Chem. Pharm. Bull.* **1999**, *47*, 809 – 812.

[34] R. Li, D. J. Jansen, A. Datta, *Org. Biomol. Chem.* **2009**, *7*, 1921 – 1930.

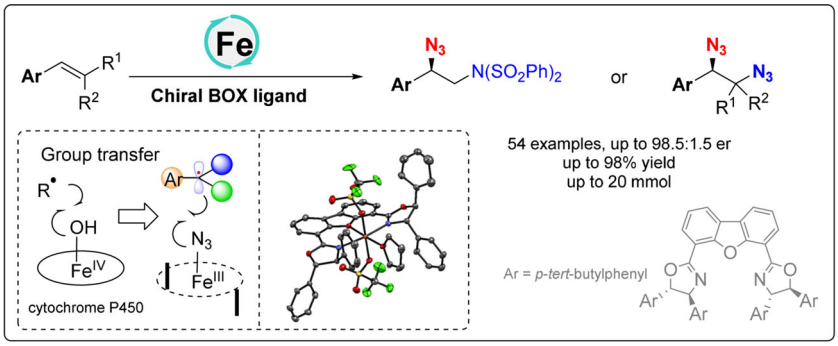
Manuscript received: December 26, 2020
Accepted manuscript online: March 22, 2021
Version of record online: ■■ ■■, ■■■■

Research Articles

Radical Group Transfer

D. Lv, Q. Sun, H. Zhou, L. Ge, Y. Qu, T. Li, X. Ma, Y. Li, H. Bao* ——— ■■■■–■■■■

Iron-Catalyzed Radical Asymmetric Aminoazidation and Diazidation of Styrenes



Biologically accessible hydroxylation in nature often proceeds through a radical rebound process. However, such a radical rebound usually leads to non-stereoselectivity. Rendering the radical rebound enantioselective is quite challenging. Herein, the first radical asymmetric aminoazidation and diazidation on acyclic systems via radical rebound is reported.