A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition

GDCh

Chemie

www.angewandte.org

Accepted Article

Title: Catalytic Radical Process for Enantioselective Amination of C(sp3)-H Bonds

Authors: Chaoqun Li, Kai Lang, Hongjian Lu, Yang Hu, Xin Cui, Lukasz Wojtas, and X. Peter Zhang

To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.201808923
Angew. Chem. 10.1002/ange.201808923

Link to VoR: http://dx.doi.org/10.1002/anie.201808923
http://dx.doi.org/10.1002/ange.201808923

WILEY-VCH

10.1002/anie.201808923

WILEY-VCH

COMMUNICATION

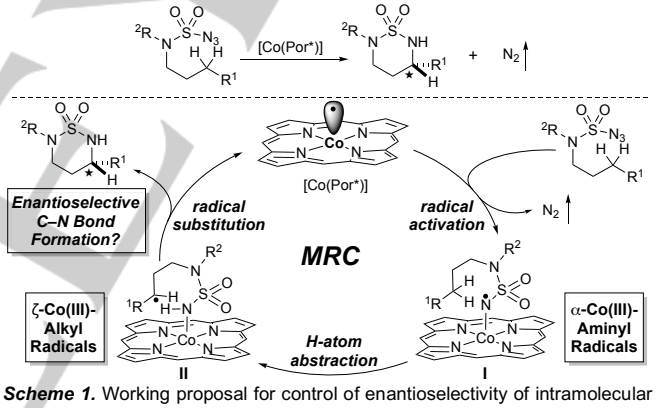
Catalytic Radical Process for Enantioselective Amination of C(sp^3)–H Bonds

Chaoqun Li,[b] Kai Lang,[a] Hongjian Lu,[b] Yang Hu,[b] Xin Cui,[b] Lukasz Wojtas,[b] and X. Peter Zhang*[a]

Abstract: A new catalytic radical system via Co(II)-based metalloradical catalysis is effective in activating sulfamoyl azides for enantioselective radical 1,6-amination of broad types of C(sp^3)–H bonds, affording six-membered chiral heterocyclic sulfamides in high yields with excellent enantioselectivities. The Co(II)-catalyzed C–H amination features an unusual degree of functional group tolerance and chemoselectivity. The unique profile of reactivity and stereoselectivity is attributed to the underlying stepwise radical pathway. The resulting optically active cyclic sulfamides can be readily converted to synthetically useful chiral 1,3-diamine derivatives with retention of the original enantiopurity.

Radical chemistry has the potential to offer new synthetic tools for construction of organic molecules with a unique profile of reactivity and selectivity that is complementary to ionic chemistry.[1,2] Despite significant progress in the field, the control of stereoselectivity, particularly enantioselectivity, presents a formidable task and has been largely unaddressed for many types of radical reactions. Among considerable efforts in surmounting this challenge,[3] metalloradical catalysis (MRC) represents a conceptually new approach in that metal-centered radicals are explored as open-shell catalysts for activating organic compounds to generate metal-supported radical species as well as for controlling their following homolytic radical reactions in a catalytic manner.[4,5] In this respect, Co(II) complexes of porphyrins, as stable 15e metalloradicals, have recently been demonstrated as efficient catalysts that homolytically activate diazo compounds and organic azides to generate α-Co(III)-alkyl radicals[6] and α-Co(III)-aminyl radicals,[7] respectively. These metal-stabilized organic radicals can serve as key intermediates to undergo subsequent radical reactions, such as radical addition to C=C bonds and H-atom abstraction of C–H bonds as well as radical substitution for C–C/C–N bond formation, leading to the development of new catalytic radical processes. Representative examples include radical olefin cyclopropanation,[8] radical olefin aziridination,[9] radical C–H alkylation,[10] and radical C–H amination.[11]

In addition to attaining controllable reactivity, the Co(II)-based metalloradical catalysis (Co(II)-MRC) enables the control of stereoselectivity through the use of D_2-symmetric chiral amidoporphyrins as the supporting ligands.[8,9b,9e,10] In particular, Co(II)-MRC was previously applied for homolytic activation of sulfamoyl azides to generate corresponding α-Co(III)-aminyl radicals **I** that could undergo 1,6-H-atom abstraction from C(sp^3)–H bonds to give ζ-Co(III)-alkyl radicals **II** (Scheme 1). Following intramolecular radical substitution, the C-centered radical intermediates **II** could be converted to six-membered cyclic sulfamides through C–N bond formation while regenerating the Co(II)-metalloradical catalyst (Scheme 1).[11a,11d-e,11g] Although substrate control of diastereoselectivity was previously demonstrated, whether the Co(II)-catalyzed radical amination could be rendered highly enantioselective is an unanswered important question that was not entirely clear due to the lack of information on the key C–N bond formation step. Does the intramolecular homolytic radical substitution proceed in a concerted fashion (S_H2 type) or a stepwise manner (S_H1 type) with first homolytic cleavage of the Co–N bond? Obviously, the former mechanism is the essential prerequisite for achieve asymmetric induction. Even under the operation of S_H2-type mechanism, realization of high enantiocontrol would entail the judicious identification of a D_2-symmetric chiral amidoporphyrin with a proper chiral environment that could effectively differentiate the two prochiral faces of the ζ-Co(III)-alkyl radicals **II** for the succeeding C–N bond formation (Scheme 1). If realized, it would establish the first asymmetric catalytic system for enantioselective intramolecular radical C(sp^3)–H amination of sulfamoyl azides to form six-membered chiral heterocyclic sulfamides, which are interesting heterocycles in their own right, but also serve as useful synthetic intermediates for preparation of valuable chiral 1,3-diamines (see Figure S1 in Supporting Information).[12]



Scheme 1. Working proposal for control of enantioselectivity of intramolecular 1,6-C(sp^3)–H radical amination of sulfamoyl azides via Co(II)-based MRC.

Catalytic intramolecular C–H amination provides an attractive approach for the construction of *N*-heterocycles.[4d,4e,13] Despite advancements, enantioselective variant of intramolecular C–H amination remains largely underdeveloped.[13e,f] We wish to report herein the development of the first asymmetric catalytic system for enantioselective 1,6-C(sp^3)–H amination of sulfamoyl azides via Co(II)-MRC. Under neutral and non-oxidative conditions, the Co(II) complex of a structure-optimized D_2-symmetric chiral amidoporphyrin allows for effective activation of sulfamoyl azides even at room temperature for intramolecular radical amination, forming the six-membered heterocyclic sulfamides in high yields with excellent enantioselectivities. In addition to benzylic C–H bonds, the Co(II)-based radical amination is also suitable for allylic, propargylic, non-activated, and even electron-deficient C–

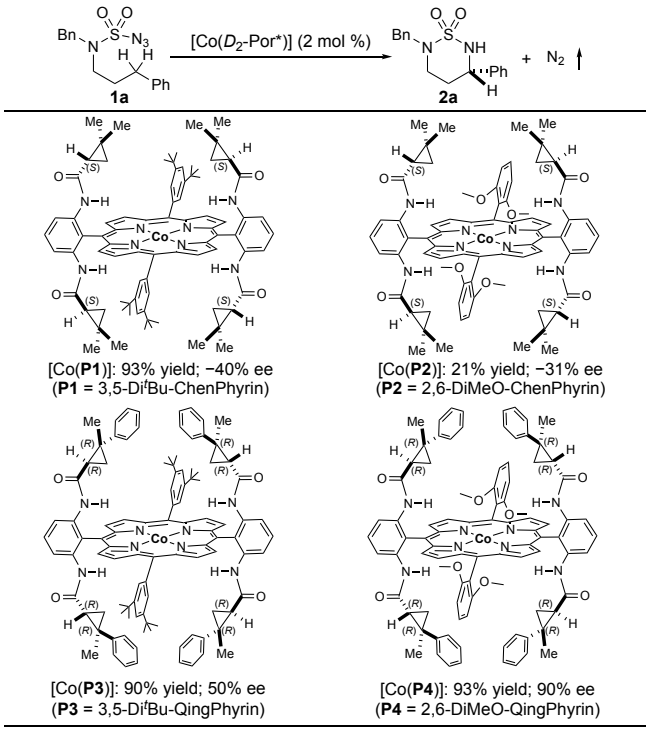
[a] Dr. K. Lang, Prof. Dr. X. P. Zhang
Department of Chemistry, Merkert Chemistry Center, Boston College, Chestnut Hill, Massachusetts 02467, United States
E-mail: peter.zhang@bc.edu
[b] Dr. C. Q. Li, Dr. H. J. Lu, Dr. Y. Hu, Dr. X. Cui, Dr. L. Wojtas, Department of Chemistry, University of South Florida, Tampa, FL 33620, United States.
Supporting information for this article is given via a link at the end of the document.

10.1002/anie.201808923

WILEY-VCH

COMMUNICATION

H bonds. Additional features of the C–H amination system include a remarkable degree of functional group tolerance, which is attributed to its underlying stepwise radical mechanism.

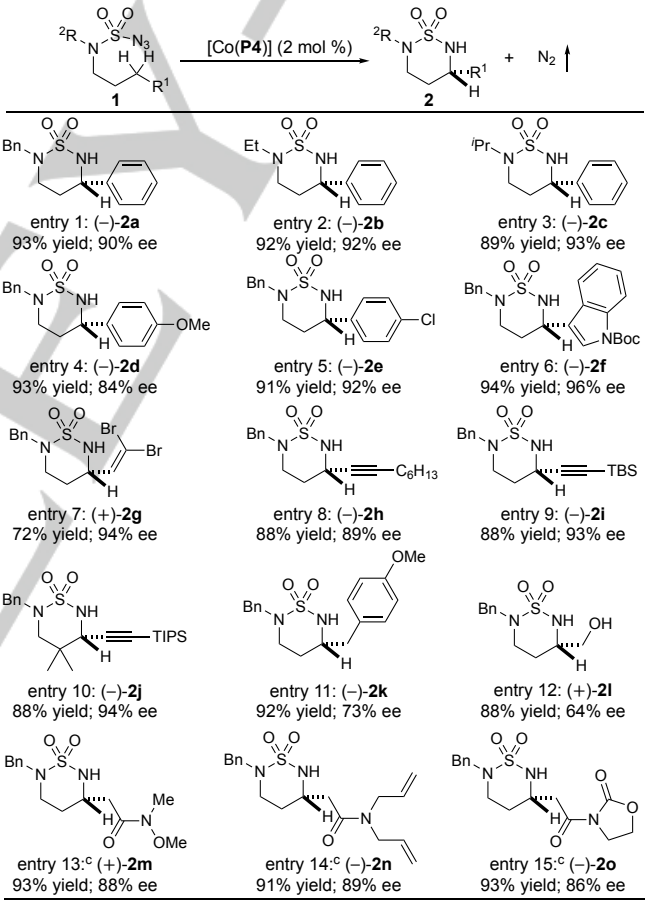


Scheme 2. Ligand effect on Co(II)-catalyzed enantioselective intramolecular C–H amination. [a] Carried out in MTBE at RT for 48 h on 0.10 mmol scale under N_2 in the presence of 4 Å MS; [azide **1a**] = 0.1 M. Isolated yields.

At the outset, sulfamoyl azide **1a** was selected as the model substrate for intramolecular 1,6-C(sp^3)–H radical amination via Co(II)-MRC (Scheme 2). After testing of different solvents, MTBE (methyl *tert*-butyl ether) was identified as the optimal reaction medium. The first-generation metalloradical catalyst [Co(**P1**)] (**P1** = 3,5-Di^{t}Bu-ChenPhyrin)[8a] was effective in catalyzing this reaction even at room temperature, affording the six-membered cyclic sulfamide **2a** in high yield with a low but significant level of enantioselectivity. Switching to the bulkier metalloradical catalyst [Co(**P2**)] (**P2** = 2,6-DiMeO-ChenPhyrin)],[8e] however, resulted in significant decrease in yield without improving enantioselectivity. When the second-generation catalyst [Co(**P3**)] (**P3** = 3,5-Di^{t}Bu-QingPhyrin)[8g,9e] was used, enhancement of asymmetric induction was observed with restoration of the high catalytic reactivity. Significant further increase in enantioselectivity was obtained with the employment of the more sterically hindered catalyst [Co(**P4**)] (**P4** = 2,6-DiMeO-QingPhyrin)], affording **2a** in 93% yield with 90% ee.

Under the optimized conditions, the [Co(**P4**)]-catalyzed system proved to be generally effective for intramolecular amination of various sulfamoyl azides with different types of C(sp^3)–H bonds (Table 1). In addition to *N*-benzyl sulfamoyl azide **1a** (Table 1; entry 1), this Co(II)-based C–H amination could tolerate sulfamoyl azides with varied *N*-substituents as shown for *N*-ethyl and *N*-isopropyl sulfamoyl azides **1b** and **1c** (Table 1; entries 2 and 3). Similarly, benzyl C–H bonds next to arenes with both electron-donating (**1d**) and -withdrawing (**1e**) substituents were suitable substrates for the amination (Table 1; entries 4 and 5). Additionally, sulfamoyl azide **1f** derived from indole could be aminated to form the heterocycle-containing cyclic sulfamide **2f** in 94% yield with 96% ee (Table 1; entry 6). Furthermore, this Co(II)-MRC could be extended for chemoselective amination of allylic and propargylic C–H bonds as demonstrated with sulfamoyl azide **1g–1j**. The corresponding cyclic sulfamides **2g–2j** were generated in high yields with excellent enantioselectivities without affecting the C=C and C≡C functionalities (Table 1; entries 7–10). Moreover, the amination worked equally well with non-activated C–H bonds. For example, the regioselective 1,6-amination of homobenzylic C–H bonds (**1k**) as well as of β-C–H bonds to functional groups such as hydroxyl (**1l**), Weinreb amide (**1m**), allylic amide (**1n**), and oxazolidinone imide (**1o**) could be achieved without reacting with the weaker benzylic or α-C–H bonds (Table 1; entries 11–15). This remarkable regioselectivity indicated that the corresponding α-Co(III)-aminyl radicals **I** (Scheme 1) had a strong preference for 1,6- over 1,7- or 1,5-H-atom abstraction. It is noteworthy that the metalloradical process features a remarkable level of functional group tolerance, encompassing a broad spectrum of functionalities such as alkene, alkyne, alcohol, indole, oxazolidinone, amide and other groups. This and the other unique attributes are in consistence with the underlying stepwise radical mechanism.

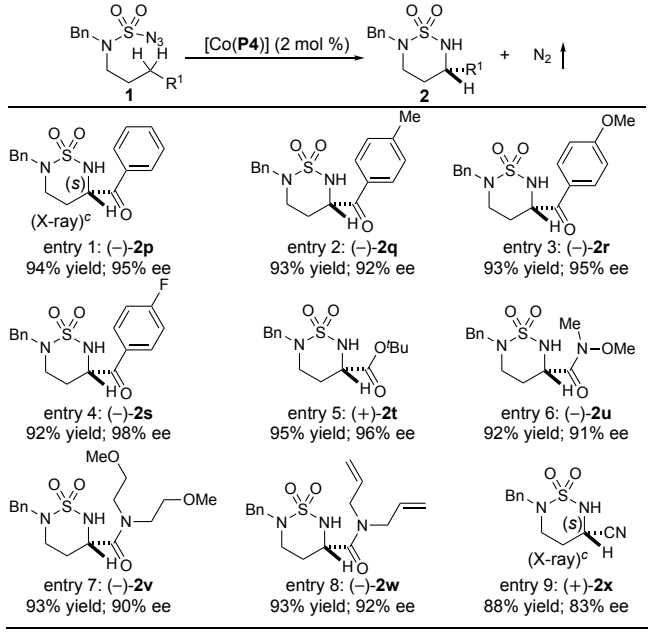
Table 1. [Co(**P4**)]-catalyzed 1,6-C–H amination of different sulfamoyl azides[a],[b]



[a] See footnote a of Scheme 2. [b] Isolated yields. [c] Performed in benzene.

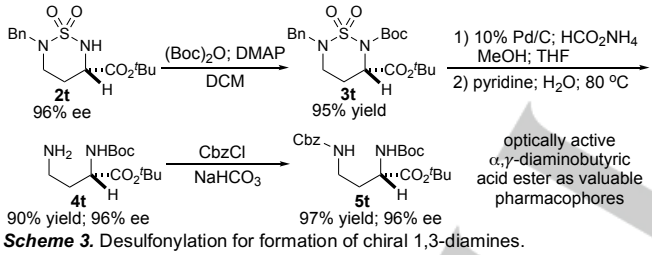
10.1002/anie.201808923

Table 2. [Co(**P4**)]-catalyzed amination of electron-deficient C–H bonds[a],[b]



[a] See footnote a of Scheme 2; performed in benzene. [b] Isolated yields. [c] [*S*] Absolute configuration.

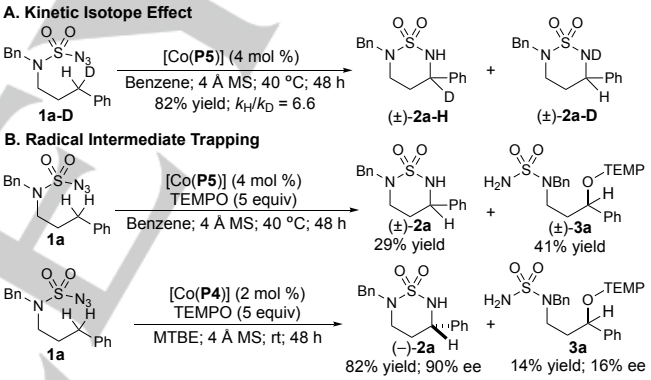
The [Co(**P4**)]-based system could also enable the enantioselective amination of various types of electron-deficient C–H bonds (Table 2). For instance, α-C–H amination of ketone azides **1p–1s** were efficiently achieved, affording optically active α,γ-diamino ketone derivatives **2p–2s** in high yields with excellent enantioselectivities (Table 2; entries 1–4). The absolute configuration of **2p** was established as (*S*). The electron-deficient C–H bond α to the ester in azide **1t** was also aminated smoothly, forming α,γ-diamino ester **2t** (Table 2; entry 5). Furthermore, this system could be applied to C–H bonds α to amides with varied *N*-substituents, producing α,γ-diamino amides **2u–2w** (Table 2; entries 6–8). Moreover, the C–H bonds α to cyano group could be enantioselectively aminated as shown with the formation of α,γ-diamino nitrile **2x** (Table 2; entry 9). The same (*S*) absolute configuration as **2p** was established for **2x**.



Scheme 3. Desulfonylation for formation of chiral 1,3-diamines.

To demonstrate the synthetic utility, the enantioenriched **2t** was selected as a model substrate to access chiral 1,3-diamine derivatives by desulfonylation and differential protection (Scheme 3). After Boc-protection, the resulting bis-protected cyclic sulfamide **3t** could proceed with selective debenzylation, followed by smooth desulfonylation, to afford the *N*-Boc-protected α,γ-diamino ester **4t** in high yield with full retention of the original enantiopurity. The primary amine in **4t** could be readily converted to the differentially *N,N′*-protected 1,3-diamine **5t** without erosion of the optical purity. Both 1,3-diamines **4t** and **5t** may serve as convenient chiral synthons for further transformations to prepare optically active α,γ-diamino acid derivatives.[12]

A set of experiments was conducted to probe the underlying mechanism (Scheme 4). First, the amination of mono-deuterated azide **1a-D** by the achiral catalyst [Co(**P5**)] (**P5** = 3,5-Di^{t}Bu-IbuPhyrin;[9a] see SI) was performed to determine the intramolecular kinetic isotope effect (KIE), obtaining a value of 6.6 (Scheme 4A). This large KIE agrees well with the proposed C–H bond cleavage via hydrogen-atom abstraction (Scheme 1). Second, as detailed in the Supporting Information, the α-Co(III)-aminyl radical **I** from the reaction of **1a** with [Co(**P5**)] could be directly detected by both EPR spectroscopy (Figure S2) and HRMS (Figure S3). Third, to trap the radical intermediate **II**, amination of **1a** by [Co(**P5**)] was carried out in the presence of TEMPO (Scheme 4B). While the yield of the amination product (±)-**2a** was significantly reduced, it concurrently generated TEMPO-containing sulfamide (±)-**3a** as a major product, which was ascribed to the trapping of the C-centered radical **II** by TEMPO. When the reaction was catalyzed by chiral catalyst [Co(**P4**)] under the standard conditions, the amination product (–)-**2a** was still formed as the major product with the same enantioselectivity (90% ee), albeit in a relatively lower yield than in the absence of TEMPO (from 93% to 82%). Meanwhile the TEMPO trapping product **3a** was obtained as a minor product in 14% yield with 16% ee. The difference in activity between [Co(**P4**)] and [Co(**P5**)] indicates that the more sterically hindered ligand environment of **P4** facilitated the radical substitution of intermediate **II** (Scheme 1). Collectively, these results support the proposed stepwise radical mechanism (Scheme 1).



Scheme 4. Mechanistic studies on Co(II)-catalyzed C–H amination.

In summary, metalloradical catalysis (MRC) has been successfully applied for the development of the first highly asymmetric catalytic system for intramolecular 1,6-C(sp^3)–H amination of sulfamoyl azides. Supported by the D_2-symmetric chiral amidoporphyrin, the Co(II)-based metalloradical system can effectively activate various sulfamoyl azides to aminate a broad range of C(sp^3)–H bonds. At room temperature under neutral and non-oxidative conditions, the six-membered cyclic sulfamides were produced in high yields with excellent enantioselectivities. The Co(II)-catalyzed amination exhibits a high degree of functional group tolerance and unusual level of chemoselectivity, which are attributed to the unique stepwise radical mechanism. The resulting optically active sulfamides can

be easily converted to synthetically useful 1,3-diamines with full retention of the original enantiopurity.

Acknowledgements

We are grateful for financial support by NIH (R01-GM098777) and in part by NSF (CHE-1624216).

Keywords: amination • cobalt • heterocycles • metalloradical catalysis • radicals

[1] a) Chatgilialoglu, C.; Studer, A. *Encyclopedia of Radicals in Chemistry, Biology and Materials*; John Wiley & Sons: Chichester, U.K., 2012. b) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions: Concepts, Guidelines, and Synthetic Applications*; Wiley-VCH: Weinheim, Germany, 2008.

[2] a) M. P. Sibi, S. Manyem, J. Zimmerman, *Chem. Rev*. **2003,** *103*, 3263; b) N. Kern, M. P. Plesniak, J. J. W. McDouall, D. J. Procter, *Nat. Chem*. **2017**, *9*, 1198.

[3] a) J. S. Lin, X. Y. Dong, T. T. Li, N. C. Jiang, B. Tan, X. Y. Liu, *J. Am. Chem. Soc.* **2016,** *138*, 9357; b) W. Zhang, F. Wang, S. D. McCann, D. Wang, P. Chen, S. S. Stahl, G. Liu, *Science* **2016,** *353*, 1014. c) J. S. Lin, F. L. Wang, X. Y. Dong, W. W. He, Y. Yuan, S. Chen, X. Y. Liu, *Nat. Commun.* **2017**, *8*, 14841.d) C. Morrill, C. Jensen, X. Just-Baringo, G. Grogan, N. J. Turner, D. J. Procter, *Angew. Chem. Int. Ed.* **2018**, *57*, 3692.

[4] a) H. Miyabe, A. Kawashima, E. Yoshioka, S. Kohtani, *Chem. Eur. J.* **2017**, *23*, 6225; b) A. Studer, D. P. Curran, *Angew. Chem. Int. Ed.* **2016**, *55*, 58; *Angew. Chem.* **2016**, 128, 58; c) H. Pellissier; H. Clavier, *Chem. Rev*. **2014,** *114*, 2775; d) H. Lu, X. P. Zhang, *Chem. Soc. Rev.* **2011,** *40*, 1899; e) T. G. Driver, *Org. Biomol. Chem.* **2010,** *8*, 3831; f) M. P. Doyle, *Angew. Chem. Int. Ed.* **2009,** *48*, 850; *Angew. Chem.* **2009,** *121*, 864.

[5] a) A. Gansäuer, T. Lauterbach, H. Bluhm, M. Noltemeyer, *Angew. Chem. Int. Ed.* **1999**, *38*, 2909; *Angew. Chem.* **1999,** *111*, 3112; b) A. Gansäuer, C.-A. Fan, F. Keller, J. Keil, *J. Am. Chem. Soc.* **2007**, *129*, 3484; c) A. Gansäuer, L. Shi, M. Otte, *J. Am. Chem. Soc.* **2010**,*132*,11858; d) S. Hildebrandt, A. Gansäuer, *Angew. Chem. Int. Ed*. **2016,** *55*, 9719; *Angew. Chem.* **2016,** *128*, 9871; e) N. Funken, F. Mühlhaus, A. Gansäuer, *Angew. Chem. Int. Ed*. **2016**, *55*, 12030; *Angew. Chem.* **2016,** *128*, 12209; f) W. Hao, X. Wu, J. Z. Sun, J. C. Siu, S. N. MacMillan, S. Lin, *J. Am. Chem. Soc.* **2017,** *139*, 12141; g) Y.-Q. Zhang, E. Vogelsang, Z.-W. Qu, S. Grimme,; A. Gansäuer, *Angew. Chem. Int. Ed.* **2017,** *56*, 12654; *Angew. Chem.* **2017,** *129*, 12828; h) W. Hao, J. H. Harenberg, X. Wu, S. N. MacMillan, S. Lin, *J. Am. Chem. Soc.* **2018,** *140*, 3514.

[6] a) W. I. Dzik, X. Xu, X. P. Zhang, J. N. H. Reek, B. de Bruin, *J. Am. Chem. Soc.* **2010,** *132*, 10891; b) J. L. Belof, C. R. Cioce, X. Xu, X. P. Zhang, B. Space, H. L. Woodcock, *Organometallics* **2011,** *30*, 2739; c) H. Lu, W. I. Dzik, X. Xu, L. Wojtas, B. de Bruin, X. P. Zhang, *J. Am. Chem. Soc.* **2011,** *133*, 8518.

[7] a) V. Lyaskovskyy, A. I. Olivos Suarez, H. Lu, H. Jiang, X. P. Zhang, B. de Bruin, *J. Am. Chem. Soc.* **2011,** *133*, 12264; b) A. I. Olivos Suarez, H. Jiang, X. P. Zhang, B. de Bruin, *Dalton Trans.* **2011,** *40*, 5697; c) K. H. Hopmann, A. Ghosh, *ACS Catal.* **2011,** *1*, 597; d) M. Goswami, V. Lyaskovskyy, S. R. Domingos, W. J. Buma, S. Woutersen, O. Troeppner, I. Ivanović-Burmazović, H. Lu, X. Cui, X. P. Zhang, E. J. Reijerse, S. DeBeer, M. M. van Schooneveld, F. F. Pfaff, K. Ray, B. de Bruin, *J. Am. Chem. Soc.* **2015,** *137*, 5468.

[8] a) Y. Chen, K. B. Fields, X. P. Zhang, *J. Am. Chem. Soc.* **2004,** *126*, 14718; b) Y. Chen, J. V. Ruppel, X. P. Zhang, *J. Am. Chem. Soc.* **2007**, *129*, 12074; c) S. Zhu, J. A. Perman, X. P. Zhang, *Angew. Chem. Int. Ed*. **2008,** *47*, 8460; *Angew. Chem.* **2008,** *120*, 8588; d) S. Fantauzzi, E. Gallo, E. Rose, N. Raoul, A. Caselli, S. Issa, F. Ragaini, S. Cenini, *Organometallics* **2008**, *27*, 6143; e) S. Zhu, J. V. Ruppel, H. Lu, L. Wojtas, X. P. Zhang, *J. Am. Chem. Soc.* **2008,** *130*, 5042; f) S. Zhu, X. Xu, J. A. Perman, X. P. Zhang, *J. Am. Chem. Soc.* **2010,** *132*, 12796; g) X. Xu, H. Lu, J. V. Ruppel, X. Cui, S. Lopez de Mesa, L. Wojtas, X. P. Zhang, *J. Am. Chem. Soc.* **2011,** *133*, 15292; h) X. Xu, S. Zhu, X. Cui, L. Wojtas, X. P. Zhang, *Angew. Chem. Int. Ed.* **2013,** *52*, 11857; *Angew. Chem.* **2013,** *125*, 12073; i) A. R. Reddy, F. Hao, K. Wu, C.-Y. Zhou, C. M. Che, *Angew. Chem. Int. Ed.* **2016**, *55*, 1810; *Angew. Chem.* **2016**, *128*, 1842; j) Y. Wang, X. Wen, X. Cui, L. Wojtas, X. P. Zhang, *J. Am. Chem. Soc.* **2017,** *139*, 1049; k) A. Chirila, B. G. Das, N. D. Paul, B. de Bruin, *ChemcatChem* **2017**, *9*, 1413; l) X. Xu, Y. Wang, H. X., Cui. Wojtas, X. P. Zhang, *Chem. Sci.* **2017,** *8*, 4347; m) S. Roy, S. K. Das, B. Chattopadhyay, *Angew. Chem. Int. Ed.* **2018**, *57*, 2238; *Angew. Chem.* **2018**, *130*, 2260.

[9] a) J. V. Ruppel, J. E.Jones, C. A. Huff, R. M. Kamble, Y. Chen, X. P. Zhang, *Org. Lett*. **2008,** *10*, 1995; b) V. Subbarayan, J. V. Ruppel, S. Zhu, J. A. Perman, X. P. Zhang, *Chem. Commun.* **2009,** 4266; c) L.-M. Jin, X. Xu, H. Lu, X. Cui, L. Wojtas, X. P. Zhang, *Angew. Chem. Int. Ed*. **2013,** *52*, 5309; *Angew. Chem.* **2013,** *125*, 5417; d) H. Jiang, K. Lang, H. Lu, L. Wojtas, X. P. Zhang, *Angew. Chem. Int. Ed.* **2016,** *55*, 11604; *Angew. Chem.* **2016,** *128*, 11776; e) H. Jiang, K. Lang, H. Lu, L. Wojtas, X. P. Zhang, *J. Am. Chem. Soc.* **2017,** *139*, 9164.

[10] a) X. Cui, X. Xu, L.-M. Jin, L. Wojtas, X. P. Zhang, *Chem. Sci.* **2015,** *6*, 1219; b) Y. Wang, X. Wen, X. Cui, X. P. Zhang, *J. Am. Chem. Soc.* **2018**, *140*, 4792; c) A. S. Karns, M. Goswami, B. de Bruin, *Chem. Eur. J.* **2018**, *24*, 5253; d) X. Wen, Y. Wang, X. P. Zhang, *Chem. Sci.* **2018,** *9*, 5082.

[11] a) H. Lu, H. Jiang, L. Wojtas,; X. P. Zhang, *Angew. Chem. Int. Ed*. **2010,** *49*, 10192; *Angew. Chem.* **2010,** *122*, 10390; b) H. Lu, V. Subbarayan, J. Tao, X. P. Zhang, *Organometallics* **2010,** *29*, 389; c) H. Lu, J. Tao, J. E. Jones, L. Wojtas, X. P. Zhang, *Org. Lett*. **2010,** *12*, 1248; d) H. Lu, H. Jiang, Y. Hu, L. Wojtas, X. P. Zhang, *Chem. Sci.* **2011,** *2*, 2361; e) H. Lu, Y. Hu, H. Jiang, L. Wojtas, X. P. Zhang, *Org. Lett*. **2012,** *14*, 5158; f) L.-M. Jin, H. Lu, Y. Cui, C. L. Lizardi, T. N. Arzua, L. Wojtas, X. Cui, X. P. Zhang, *Chem. Sci.* **2014,** *5*, 2422; g) H. Lu, C. Li, H. Jiang, C. L. Lizardi, X. P. Zhang, *Angew. Chem. Int. Ed*. **2014,** *53*, 7028; *Angew. Chem.* **2014,** *126*, 7148; h) O. Villanueva, N. M. Weldy, S. B. Blakey, C. E. MacBeth, *Chem. Sci*. **2015,** *6*, 6672; i) H. Lu, K. Lang, H. Jiang, L. Wojtas, X. P. Zhang, *Chem. Sci.* **2016,** *7*, 6934; j) P. F. Kuijpers, M. J. Tiekink, W. B. Breukelaar, D. L. J. Broere, N. P. van Leest, J. I. van der Vlugt, J. N. H. Reek, B. de Bruin, *Chem. Eur. J.* **2017,** *23*, 7945; k) Z.-Y. Gu, Y. Liu, F. Wang, X. Bao, S.-Y. Wang, S.-J. Ji, *ACS Catal.* **2017,** *7*, 3893.

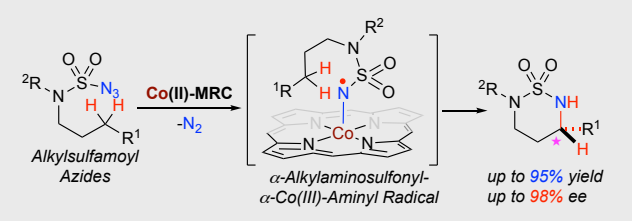
[12] a) J.-C. Kizirian, *Chem. Rev.* **2008**, *108*, 140; b) X. Ji, H. Huang, *Org. Biomol. Chem.* **2016**, *14*, 10557; c) G. Ronquist, R. Hugosson, B. J. Westermark, *Cancer Res. Clin. Oncol.* **1980**, *96*, 259.

[13] a) J. M. Alderson, J. R. Corbin, J. M. Schomaker, *Acc, Chem. Res.* **2017**, *50*, 2147; b) F. Collet, C. Lescot, P. Dauban, *Chem. Soc. Rev.* **2011**, *40*, 1926; c) Y. Liu, X. Guan, E. L.-M. Wong, P. Liu, J.-S. Huang, C.-M. Che, *J. Am. Chem. Soc.* **2013,** *135*, 7194; d) J. M. Alderson, A. M. Phelps, R. J. Scamp, N. S. Dolan, J. M. Schomaker, *J. Am. Chem. Soc*. **2014,** *136*, 16720; e) J.-L. Liang, S.-X. Yuan, J.-S. Huang, W.-Y. Yu, C.-M. Che, *Angew. Chem. Int. Ed.* **2002,** *41*, 3465; *Angew. Chem.* **2002,** *114*, 3615; f) E. Milczek, N. Boudet, S. Blakey, *Angew. Chem. Int. Ed.* **2008,** *47*, 6825; *Angew. Chem.* **2008,** *120*, 6931.

10.1002/anie.201808923

WILEY-VCH

COMMUNICATION



An enantioselective radical process has been established via cobalt(II)-based metalloradical catalysis for stereoselective amination of aliphatic C–H bonds at room temperature to form chiral 1,3-diamines under neutral and non-oxidative conditions.

*Chaoqun Li, Kai Lang, Hongjian Lu, Yang Hu, Xin Cui, Lukasz Wojtas, and X. Peter Zhang**

Page No. – Page No.

Catalytic Radical Process for Enantioselective Amination of C(sp^3)–H Bonds