

Heterocycles

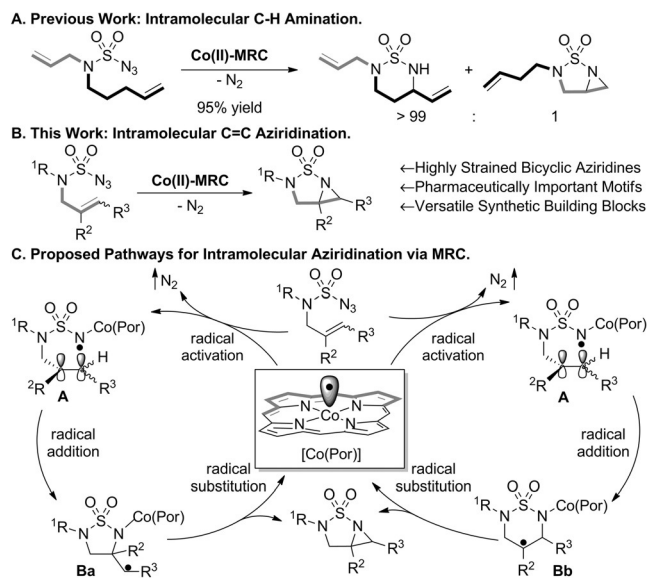
Deutsche Ausgabe: DOI: 10.1002/ange.201605238
Internationale Ausgabe: DOI: 10.1002/anie.201605238

Intramolecular Radical Aziridination of Allylic Sulfamoyl Azides by Cobalt(II)-Based Metalloradical Catalysis: Effective Construction of Strained Heterobicyclic Structures

Huiling Jiang, Kai Lang, Hongjian Lu, Lukasz Wojtas, and X. Peter Zhang*

Abstract: Cobalt(II)-based metalloradical catalysis (MRC) has been successfully applied for effective construction of the highly strained 2-sulfonyl-1,3-diazabicyclo[3.1.0]hexane structures in high yields through intramolecular radical aziridination of allylic sulfamoyl azides. The resulting [3.1.0] bicyclic aziridines prove to be versatile synthons for the preparation of a diverse range of 1,2- and 1,3-diamine derivatives by selective ring-opening reactions. As a demonstration of its application for target synthesis, the metalloradical intramolecular aziridination reaction has been incorporated as a key step for efficient synthesis of a potent neurokinin 1 (NK₁) antagonist in 60% overall yield.

Radical chemistry has displayed vast potential in modern organic synthesis as it has many attractive features which are complementary to ionic chemistry.^[1] To address the existing challenges in the field,^[2] metalloradical catalysis (MRC) presents a new approach to achieving controllable reactivities and selectivities through catalytic generation of metal-stabilized organic radicals, such as the fundamentally new α -Co^{III}-alkyl and α -Co^{III}-aminyl radicals.^[3,4] For example, the α -Co^{III}-aminyl radicals (also known as cobalt(III) nitrene radicals), which can be generated through a unique radical-transfer process from the cobalt-centered radicals of cobalt(II) porphyrins [Co(Por)] to organic azides upon metalloradical activation,^[3e-g] have demonstrated controlled reactivities for both hydrogen atom abstraction of C–H bonds and radical addition to C=C bonds to furnish a catalytic radical amination^[5] and aziridination,^[6] respectively, with high levels of selectivity. In particular, the cobalt(II)-based MRC system exhibits remarkable chemoselectivity, as exemplified by the selective transformation of the sulfamoyl azide containing both *N*-allyl and *N*-bis(homoallyl) groups (Scheme 1A). Exclusive intramolecular 1,6-radical amination of the allylic C–H bonds was reported and there was no observation of the potential intramolecular radical aziridination of the C=C



Scheme 1. Cobalt(II)-based metalloradical catalysis (MRC) for intramolecular C–H amination versus intramolecular C=C aziridination of allylic sulfamoyl azides

bonds.^[5e] In the absence of the more reactive *N*-bis(homoallyl) group, however, it was unclear if intramolecular aziridination of *N*-allylic sulfamoyl azides was possible in view of the high strain associated with the resulting 2-sulfonyl-1,3-diazabicyclo[3.1.0]hexane structure (Scheme 1B).^[7] This type of catalytic process (Scheme 1C) would require the corresponding α -Co^{III}-aminyl radical **A** to undergo efficient intramolecular addition to the olefin unit to generate either the γ -Co^{III}-alkyl radical intermediate **Ba** (Scheme 1C; left: 5-*exo-trig* cyclization) or the γ -Co^{III}-alkyl radical **Bb** (Scheme 1C; right: 6-*endo-trig* cyclization), followed by 3-*exo-tet* radical cyclization to deliver the aziridine product with regeneration of the [Co(Por)] catalyst. If successful, this catalytic transformation would be highly useful as the resulting [3.1.0] heterobicyclic structures are the key motifs in compounds of medicinal importance, and can also serve as versatile building blocks for the preparation of functionalized diamines.^[8–11]

A number of catalytic systems have been successfully developed for intramolecular aziridination of olefins.^[12–15] While several types of [*n*.1.0] heterobicyclic structures have been synthesized,^[13–15] there is no previous report on the synthesis of [3.1.0] bicyclic sulfamoyl aziridines by catalytic intramolecular aziridination (Scheme 1B).^[7] This lack of

[*] Dr. K. Lang, Prof. Dr. X. P. Zhang
Department of Chemistry, Merkert Chemistry Center, Boston College
Chestnut Hill, Massachusetts 02467 (USA)
E-mail: peter.zhang@bc.edu

Dr. H. Jiang, Prof. Dr. H. Lu, Dr. L. Wojtas, Prof. Dr. X. P. Zhang
Department of Chemistry, University of South Florida
Tampa, FL 33620 (USA)

Prof. Dr. H. Lu
The Institute of Chemistry & Biomedical Sciences
Nanjing University, Nanjing, 210093 (P.R. China)

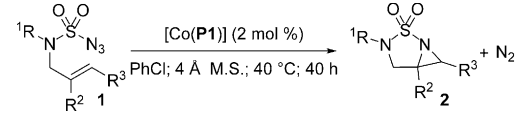
Supporting information for this article can be found under:
<http://dx.doi.org/10.1002/anie.201605238>.

precedent is presumably due to the high ring strain of the bicyclic transition state associated with the concerted asynchronous mechanism of most intramolecular catalytic systems involving metallonitrenes as the key intermediates. We envisioned that the cobalt(II)-based MRC could potentially address this challenge by constructing the bicyclic structure through a stepwise ring formation in two separate radical cyclization steps (Scheme 1 C). Herein we report the development of the first catalytic system for intramolecular aziridination with allylic sulfamoyl azides by cobalt(II)-based MRC, thus allowing effective construction of the highly strained 2-sulfonyl-1,3-diazabicyclo[3.1.0]hexane structure in high yields. By taking advantage of the high strain, the resulting sulfonylated [3.1.0] bicyclic diaza aziridine products can be efficiently utilized as a new synthon for the preparation of 1,2- and 1,3-diamine derivatives by selective ring-opening reactions in an *exo*- and *endo*-fashion, respectively.

At the outset of this project, *N*-benzyl-*N*-allyl-sulfamoyl azide (**1a**), which was prepared from the corresponding amine in one step,^[5d] was selected as a model substrate to explore the possibility of cobalt(II) MRC for intramolecular aziridination of allylic sulfamoyl azides and to establish effective catalytic conditions (Scheme 2). While the metalloradical catalyst [Co(TPP)] (TPP = tetraphenylporphyrin) was ineffective, [Co(**P1**)], in which the *D*_{2h}-symmetric porphyrin 3,5-di-*t*-Bu-IbuPhyrin **P1** has amide functionalities at the *ortho*-positions of the meso-phenyl groups,^[6b] could effectively catalyze the intramolecular aziridination reaction under mild reaction conditions without the need for other reagents or additives, thus affording the desired sulfonylated [3.1.0] bicyclic diaza aziridine **2a** in 92 % yield with N₂ as the sole byproduct. The dramatic difference in catalytic activity between [Co(TPP)] and [Co(**P1**)] is a remarkable demonstration of ligand-accelerated catalysis and could be rationalized as the outcome of hydrogen-bonding stabilization of a cobalt(III) aminyl radical intermediate.^[3f]

Under the optimized reaction conditions (2 mol % of [Co(**P1**)] in PhCl at 40 °C for 40 h), the cobalt(II)-based intramolecular aziridination was found to have a broad substrate scope for a wide range of allylic sulfamoyl azides (Table 1). In addition to the *N*-benzyl group (Bn) in **1a** (entry 1), the metalloradical system could tolerate a variety of *N*-substituted functionalities because of its neutral and non-

Table 1: Intramolecular aziridination of allylic sulfamoyl azides by [Co(**P1**)].^[a,b]



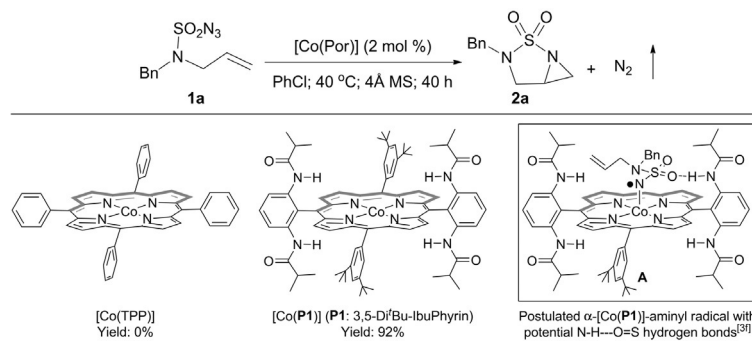
entry 1: 92% (2a)	entry 2: 84% (2b)	entry 3: 87% (2c) ^[c]	entry 4: 99% (2d)
entry 5: 96% (2e)	entry 6: 86% (2f)	entry 7: 98% (2g)	entry 8: 70% (2h) ^[d]
entry 9: 95% <i>c/t</i> > 20:1 [(±)- 2i]	entry 10: 30% <i>t/c</i> > 20:1 [(±)- 2j] ^[e,f]	entry 11: 99% (2k) ^[g]	
entry 12: >99% (2l) ^[g]	3: 99%	entry 13: >99% (2m) ^[g]	entry 14: 87% <i>c/t</i> > 20:1 (2n)

[a] Performed under N₂; [azide **1**]: 0.08 M. [b] Yield of isolated product.

[c] PCB = *para*-chlorobenzyl. [d] with 30 % azide recovered.

[e] PMB = *para*-methoxybenzyl. [f] In PhCl at 80 °C; with 60 % azide recovered. [g] 0.5 mol % [Co(**P1**)] for 8 h. Boc = *tert*-butoxycarbonyl.

oxidative conditions, as demonstrated by the high-yielding aziridination reactions of the allylic sulfamoyl azides **1b–e** which contain 4-methoxybenzyl (PMB), 4-chlorobenzyl (PCB), allyl, and propargyl groups, respectively (entries 2–5). It is worth noting that these electron-rich *N*-substituents could be oxidatively degraded in other catalytic systems which require the use of a stoichiometric amount of oxidant, such as PhI(OAc)₂ or PhI=O.^[15] Similarly, allylic sulfamoyl azides bearing electron-withdrawing groups were also suitable substrates for the catalytic system. For example, azides bearing *N*-ethoxycarbonyl (**1f**) and *N*-Boc (**1g**) groups underwent intramolecular aziridination to generate the corresponding bicyclic aziridines **2f** and **2g** in 86 and 98 % yields, respectively (entries 6 and 7). Besides the tolerance of various functional groups, the cobalt(II)-catalyzed aziridination process shows interesting regioselectivity. For example, when the azide **1h**, containing both internal and terminal olefins, was utilized as the substrate, the aziridine **2h** was isolated in 70 % yield as the sole product, thus indicating preferred reactivity of less sterically hindered terminal olefins over internal olefins (entry 8). In the absence of terminal olefins, however, both *cis* and *trans* internal olefins could also successfully undergo aziridination with stereospecificity (entries 9 and 10). Presumably also because of the steric effect, the *cis*-olefin-derived azide **1i** (entry 9) was found to be more reactive than the *trans*-olefin-derived azide **1j** (entry 10), thus resulting in stereospecific formation of the corresponding aziridines **2i** and **2j** in 95 and 30 % yields, respectively. Interestingly, it

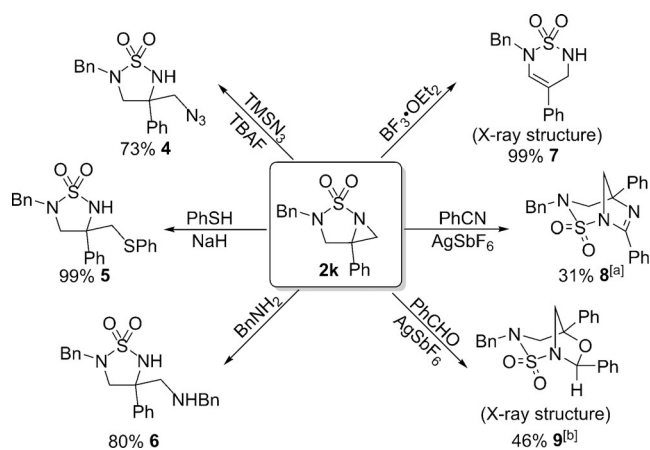


Scheme 2. Ligand effect on [Co(Por)]-catalyzed intramolecular aziridination of allylic sulfamoyl azide: Importance of potential hydrogen-bonding interactions. M.S. = molecular sieves.

was found that allylic azides derived from disubstituted terminal olefins exhibited even higher reactivity. For example, at a catalyst loading as low as 0.5 mol % and in much shorter reaction time (8 h), the

2-phenyl allylic azide **1k** effectively underwent aziridination by [Co(**P1**)], thus affording the desired sulfonylated [3.1.0] bicyclic diaza aziridine **2k** in nearly quantitative yield (entry 11). It is worth noting the exceedingly high strain of the 2-sulfonyl-1,3-diazabicyclo[3.1.0]hexane structure in **2k** where the two bridgeheads are a quaternary carbon center and a tertiary nitrogen center, respectively. As an additional example, the intramolecular aziridination reaction of the 2-chloro-allylic azide **1l** could be readily catalyzed by [Co(**P1**)] to afford the corresponding chloro-[3.1.0] bicyclic diaza aziridines **2l** in full conversion (entry 12). Although the tertiary alkyl chloride **2l** could be characterized by both ^1H and ^{13}C NMR spectroscopy (see the Supporting Information), it underwent a subsequent ring-opening reaction during the purification, thus affording the ketone product **3** in nearly quantitative yield (entry 12). The ready formation of **3** is presumably a result of the unusual kinetic susceptibility of the bridgehead quaternary amino halide units to halide substitution by water and subsequent rearrangement. Similarly, the 2-bromo-allylic azide **1m** could also be converted into **3** in an excellent yield, presumably via the initial aziridination product bromo-[3.1.0] bicyclic diaza aziridines **2m** (entry 13). Remarkably, even the cyclohexene-derived azide **1n** could be successfully employed as the substrate for the cobalt(II)-based intramolecular aziridination, thus allowing construction of the highly strained tricyclic aziridine **2n** in 87% yield with excellent control of diastereoselectivity (entry 14). It is noted that **2n** and related fused tricyclic aziridine compounds may serve as useful precursors for preparation of the valuable 1,2,3-cyclohexanetriamine motif which has been found in a number of biologically and pharmaceutically important compounds.^[9]

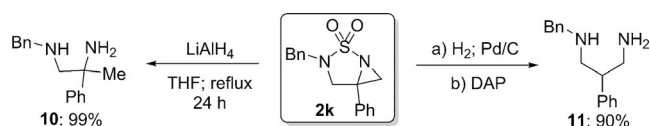
In view of the high ring strain associated with the 2-sulfonyl-1,3-diazabicyclo[3.1.0]hexane structure, we then turned our attention to explore further transformations of **2**. In particular, we were interested in the possibility of regioselectively opening the bicyclic rings of these compounds. By using **2k** as a representative example, the three-membered aziridine ring of the bicyclo[3.1.0] structure was regioselectively opened at the *exo*-position by various nucleophiles (Scheme 3). For example, **2k** could be effectively opened by trimethylsilyl azide, thiophenol, and benzylamine under mild reaction conditions to afford the corresponding five-membered thiadiazolidine dioxide derivatives **4–6** in good to excellent yields. In addition to *exo*-ring opening reactions by nucleophiles, we also demonstrated the selective *endo*-ring opening at the bridgehead position of the bicyclo[3.1.0] structure in the presence of Lewis acids.^[10] When treated with $\text{BF}_3\cdot\text{OEt}_2$, **2k** was regioselectively opened to form the thiadiazine dioxide **7** in quantitative yield, presumably via a 1,3-dipole intermediate.^[10] The structure of **7** was confirmed by X-ray crystallographic analysis (see the Supporting Information). In the presence of AgSbF_6 , the resulting 1,3-dipole intermediate from **2k** could be partially trapped by dipolarophiles such as benzonitrile and benzaldehyde to form



Scheme 3. Regioselective ring-opening reactions of the [3.1.0] bicyclic diaza aziridine **2k** by various reagents. [a] Isolated together with 59% of **7**. [b] Isolated together with 34% of **7**. TBAF = tetra-*n*-butylammonium fluoride, TMS = trimethylsilyl.

the tricyclic compounds **8** and **9**, respectively, in addition to the formation of **7**. X-ray crystallographic analysis (see the Supporting Information) established the unique [3.2.1] tricyclic structure of **9** as having four heteroatoms with tertiary nitrogen and quaternary carbon bridgeheads.

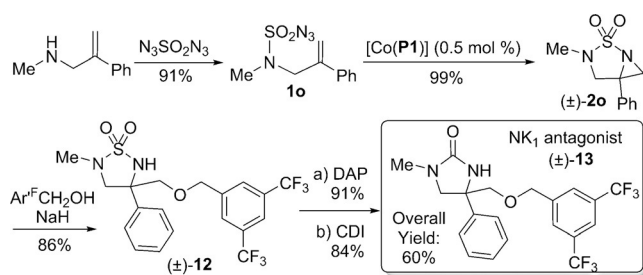
Considerable effort has been dedicated to the development of efficient methods for the preparation of diamines, which are prevalent motifs in biologically active molecules and can also function as chelating ligands for complexing transition metals.^[11] Given that cyclic sulfamides can serve as precursors of diamines,^[16] we show that the aziridines **2** can be efficiently desulfonylated for selective formation of either 1,2-diamines or 1,3-diamines, depending on the specific reaction conditions, as demonstrated with the reactions of **2k** (Scheme 4). When treated with LiAlH_4 in THF, **2k** was



Scheme 4. Selective reductive desulfonylation of bicyclic aziridine structure. THF = tetrahydrofuran.

selectively opened at the *exo*-position through facile removal of the sulfonyl group, thus producing the 1,2-diamine **10**, containing a quaternary chiral carbon center, in 99% yield. Alternatively, **2k** could be selectively converted into the 1,3-diamine **11** in 90% yield, by aziridine ring opening (*endo*) under $\text{H}_2/\text{Pd/C}$ reduction conditions and subsequent desulfonylation by transamination with 1,3-diaminopropane (DAP).

To showcase the application of [Co(**P1**)]-catalyzed intramolecular aziridination of allylic sulfamoyl azides and the subsequent transformations of the resulting sulfonylated [3.1.0] bicyclic diaza aziridines for target synthesis, we developed a concise and high-yielding synthetic route to the bioactive compound **13** (Scheme 5),^[17] one member of a family of potent Neurokinin 1 (NK_1) receptor antago-



Scheme 5. Application of the cobalt(II)-catalyzed intramolecular aziridination for the efficient synthesis of the potent NK₁ antagonist **13**. CDI = 1,1'-carbonyldiimidazole.

nists.^[18] The compound **13** consists of a core structure of *N*-methylimidazolidin-2-one with a quaternary carbon center bearing phenyl and (3,5-bis(trifluoromethyl)benzyloxy)-methyl groups. Starting from *N*-methyl-2-phenylallylamine, the allylic sulfamoyl azide **10** was readily prepared in 91 % yield. The catalytic intramolecular aziridination of **10** proceeded smoothly in the presence of only 0.5 mol % of [Co(**P1**)], thus affording the desired [3.1.0] bicyclic sulfamoyl aziridine **20** in 99 % yield on a gram scale. Upon treatment with bis(trifluoromethyl)benzyl alcohol (Ar'^FCH₂OH) in the presence of NaH, **20** was regioselectively opened to give **12** in 86 % yield. The cyclic sulfamide **12** was successfully transformed into the final cyclic urea analogue **13** through straightforward desulfonation with DAP in 91 % yield, and subsequent carbonylation with 1,1'-carbonyldiimidazole (CDI) in 84 % yield. The five-step synthesis of **13** was achieved in an overall yield of 60 %.^[19]

In summary, we have developed the first synthetic tool for efficient construction of highly strained 2-sulfonally-1,3-diazabicyclo[3.1.0]hexane structures through intramolecular radical aziridination by cobalt(II)-based MRC. The [Co(**P1**)]-catalyzed aziridination system, which operates under neutral and nonoxidative conditions, is generally applicable to a wide range of allylic sulfamoyl azides, thus allowing high-yielding synthesis of the bicyclic aziridine molecules with various substitution patterns. By taking advantage of the high strain associated with the unique heterobicyclic structure, we have demonstrated a series of synthetic applications of the resulting [3.1.0] bicyclic diaza aziridines as intermediates for preparation of valuable 1,2- and 1,3-diamines, and related derivatives. The catalytic method was also showcased as a key step in the high-yielding synthesis of the NK₁ antagonist **13**. Efforts are underway to study the detailed catalytic mechanism of this cobalt(II)-based radical intramolecular aziridination, as well as to develop an asymmetric variant.

Acknowledgements

We are grateful for the financial support by the NIH (R01-GM102554) and, in part, by the NSF (CHE-1624216).

Keywords: aziridination · cobalt · heterocycles · metalloradical catalysis · radicals

How to cite: *Angew. Chem. Int. Ed.* **2016**, *55*, 11604–11608
Angew. Chem. **2016**, *128*, 11776–11780

- [1] a) B. Quiclet-Sire, S. Z. Zard, *Pure Appl. Chem.* **2011**, *83*, 519–551; b) J. M. R. Narayanam, C. R. J. Stephenson, *Chem. Soc. Rev.* **2011**, *40*, 102–113; c) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322–5363.
- [2] For recent successful examples, see: a) J. Du, K. L. Skubi, D. M. Schultz, T. P. Yoon, *Science* **2014**, *344*, 392–396; b) J. M. Hoyt, V. A. Schmidt, A. M. Tondreau, P. J. Chirik, *Science* **2015**, *349*, 960–963; c) J. L. Jeffrey, J. A. Terrett, D. W. C. MacMillan, *Science* **2015**, *349*, 1532–1536; d) Q. M. Kainz, C. D. Matier, A. Bartoszewicz, S. L. Zultanski, J. C. Peters, G. C. Fu, *Science* **2016**, *351*, 681–684.
- [3] For detailed studies on the involvement of α -Co^{III}-alkyl radical intermediates (also known as cobalt(III) carbene radicals) for catalytic cyclopropanation and C–H alkylation, see: a) W. I. Dzik, X. Xu, X. P. Zhang, J. N. H. Reek, B. de Bruin, *J. Am. Chem. Soc.* **2010**, *132*, 10891–10902; b) J. L. Belof, C. R. Cioce, X. Xu, X. P. Zhang, B. Space, H. L. Woodcock, *Organometallics* **2011**, *30*, 2739–2746; c) H. Lu, W. I. Dzik, X. Xu, L. Wojtas, B. de Bruin, X. P. Zhang, *J. Am. Chem. Soc.* **2011**, *133*, 8518–8521; d) X. Cui, X. Xu, L.-M. Jin, L. Wojtas, X. P. Zhang, *Chem. Sci.* **2015**, *6*, 1219–1224. For detailed studies on the involvement of related α -Co^{III}-aminyl radical intermediates (also known as cobalt(III) nitrene radicals) for catalytic aziridination and C–H amination, see: e) V. Lyaskovskyy, A. I. Olivos Suarez, H. Lu, H. Jiang, X. P. Zhang, B. de Bruin, *J. Am. Chem. Soc.* **2011**, *133*, 12264–12273; f) A. I. Olivos Suarez, H. Jiang, X. P. Zhang, B. de Bruin, *Dalton Trans.* **2011**, *40*, 5697–5705; g) 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*, 5468–5479. For a recent review on nitrogen-centered radical ligands, see: h) A. I. Olivos Suarez, V. Lyaskovskyy, J. N. H. Reek, J. I. van der Vlugt, B. de Bruin, *Angew. Chem. Int. Ed.* **2013**, *52*, 12510–12529; *Angew. Chem.* **2013**, *125*, 12740–12760.
- [4] For a recent review on titanium(III)-based MRC, see: a) A. Gansäuer, S. Hildebrandt, E. Vogelsang, R. A. Flowers II, *Dalton Trans.* **2016**, *45*, 448–452. For the first demonstration of titanium(III)-based, metalloradical noncatalytic process, see: b) W. A. Nugent, T. V. RajanBabu, *J. Am. Chem. Soc.* **1988**, *110*, 8561–8562. For select examples of catalytic processes via Ti^{III}-based MRC c) A. Gansäuer, B. Rinker, M. Pierobon, S. Grimme, M. Gerenkamp, C. Mück-Lichtenfeld, *Angew. Chem. Int. Ed.* **2003**, *42*, 3687–3690; *Angew. Chem.* **2003**, *115*, 3815–3818; d) A. Gansäuer, C.-A. Fan, F. Keller, J. Keil, *J. Am. Chem. Soc.* **2007**, *129*, 3484–3485; e) A. Gansäuer, A. Fleckhaus, M. A. Lafont, A. Okkel, K. Kotsis, A. Anoop, F. Neese, *J. Am. Chem. Soc.* **2009**, *131*, 16989–16999; f) A. Gansäuer, S. Hildebrandt, A. Michelmann, T. Dahmen, D. von Laufenberg, C. Kube, G. D. Fianu, R. A. Flowers II, *Angew. Chem. Int. Ed.* **2015**, *54*, 7003–7006; *Angew. Chem.* **2015**, *127*, 7109–7112.
- [5] For select examples of C–H amination by cobalt(II)-based MRC, see: a) S. Cenini, E. Gallo, A. Penoni, F. Ragaini, S. Tollari, *Chem. Commun.* **2000**, 2265–2266; b) J. D. Harden, J. V. Ruppel, G.-Y. Gao, X. P. Zhang, *Chem. Commun.* **2007**, 4644–4646; c) H. Lu, J. Tao, J. E. Jones, L. Wojtas, X. P. Zhang, *Org. Lett.* **2010**, *12*, 1248–1251; d) H. Lu, H. Jiang, L. Wojtas, X. P. Zhang, *Angew. Chem. Int. Ed.* **2010**, *49*, 10192–10196; *Angew. Chem.* **2010**, *122*, 10390–10394; e) H. Lu, H. Jiang, Y. Hu, L. Wojtas, X. P. Zhang, *Chem. Sci.* **2011**, *2*, 2361–2366; f) H. Lu, Y. Hu, H. Jiang, L. Wojtas, X. P. Zhang, *Org. Lett.* **2012**, *14*, 5158–5161; g) L.-M. Jin, H. Lu, Y. Cui, C. L. Lizardi, T. N. Arzua, L. Wojtas, X. Cui, X. P. Zhang, *Chem. Sci.* **2014**, *5*, 2422–2427; h) H. Lu, C. Li, H. Jiang, C. L. Lizardi, X. P. Zhang, *Angew.*

- Chem. Int. Ed.* **2014**, *53*, 7028–7032; *Angew. Chem.* **2014**, *126*, 7148–7152. For a review on C–H amination by cobalt(II)-based MRC, see: i) H. Lu, X. P. Zhang, *Chem. Soc. Rev.* **2011**, *40*, 1899–1909.
- [6] Cobalt(II)-based MRC has been applied for catalytic intermolecular aziridination with different organic azides. For phosphoril azides, see: a) J. E. Jones, J. V. Ruppel, G.-Y. Gao, T. M. Moore, X. P. Zhang, *J. Org. Chem.* **2008**, *73*, 7260–7265; b) J. R. Tao, L.-M. Jin, X. P. Zhang, *Beilstein J. Org. Chem.* **2014**, *10*, 1282–1289. For arylsulfonyl azides, see: c) J. V. Ruppel, J. E. Jones, C. A. Huff, R. M. Kamble, Y. Chen, X. P. Zhang, *Org. Lett.* **2008**, *10*, 1995–1998. For trichloroethoxysulfonyl azide, see: d) V. Subbarayan, J. V. Ruppel, S. Zhu, J. A. Perman, X. P. Zhang, *Chem. Commun.* **2009**, 4266–4268. For fluoroaryl azides, see: e) L.-M. Jin, X. Xu, H. Lu, X. Cui, L. Wojtas, X. P. Zhang, *Angew. Chem. Int. Ed.* **2013**, *52*, 5309–5313; *Angew. Chem.* **2013**, *125*, 5417–5421. For aryloxysulfonyl azides, see: f) V. Subbarayan, L.-M. Jin, X. Cui, X. P. Zhang, *Tetrahedron Lett.* **2015**, *56*, 3431–3434.
- [7] Only one example was reported for synthesis of 2-sulfonyl-1,3-diazabicyclo[3.1.0]hexane structure by a noncatalytic process. See: a) N. Khettache, M. Berredjem, Z. Régaïnia, N. E. Aouf, *Heterocycles* **2008**, *75*, 2243–2250. The related intramolecular aziridination of sulfamate derived from an allyl alcohol failed to give the [3.1.0] bicyclic aziridine product presumably because of the high ring strain. See: b) F. Duran, L. Leman, A. Ghini, G. Burton, P. Dauban, R. H. Dodd, *Org. Lett.* **2002**, *4*, 2481–2483.
- [8] For synthetic applications for aziridination, see: a) P. M. Wehn, J. Du Bois, *Angew. Chem. Int. Ed.* **2009**, *48*, 3802–3805; *Angew. Chem.* **2009**, *121*, 3860–3863; b) C. Mößner, C. Bolm, *Catalyzed Asymmetric Aziridination in Transition Metals for Organic Synthesis: Building Blocks and Fine Chemicals*, 2nd ed., Wiley-VCH, Weinheim, **2008**.
- [9] a) C. Robert, Patent, WO02060859 (A2), **2008**; b) B. Wuensch, D. Schepmann, C. Bourgeois, Patent, WO2009080745 (A2), **2009**.
- [10] a) P. A. Wender, D. Strand, *J. Am. Chem. Soc.* **2009**, *131*, 7528–7529; b) P. Dauban, G. Malik, *Angew. Chem. Int. Ed.* **2009**, *48*, 9026–9029; *Angew. Chem.* **2009**, *121*, 9188–9191.
- [11] S. K. Liew, Z. He, J. D. St. Denis, A. K. Yudin, *J. Org. Chem.* **2013**, *78*, 11637–11645.
- [12] For select reviews on aziridination by transition-metal catalysis, see: a) P. Müller, C. Fruit, *Chem. Rev.* **2003**, *103*, 2905–2920; b) S. Fantauzzi, A. Caselli, E. Gallo, *Dalton Trans.* **2009**, 5434–5443; c) H. Pellissier, *Tetrahedron* **2010**, *66*, 1509–1555; d) “Oxidation: C–N Bond Formation by Oxidation (Aziridines)”: H. Jiang, X. P. Zhang in *Comprehensive Chirality*, Vol. 5 (Eds.: E. M. Carreira, H. Yamamoto), Elsevier, Amsterdam, **2012**, pp. 168–182.
- [13] For the synthesis of [3.1.0] and [4.1.0] bicyclic sulfonyl aziridines by catalytic intramolecular aziridination, see: a) P. Müller, C. Baud, Y. Jacquier, *Can. J. Chem.* **1998**, *76*, 738–750; b) P. Dauban, R. H. Dodd, *Org. Lett.* **2000**, *2*, 2327–2329; c) P. Dauban, L. Sanier, A. Tarrade, R. H. Dodd, *J. Am. Chem. Soc.* **2001**, *123*, 7707–7708; d) J. L. Liang, S. X. Yuan, P. W. H. Chan, C.-M. Che, *Org. Lett.* **2002**, *4*, 4507–4510; e) J. L. Liang, S. X. Yuan, P. W. H. Chan, C.-M. Che, *Tetrahedron Lett.* **2003**, *44*, 5917–5920; f) J. L. Liang, S. X. Yuan, J. S. Huang, C.-M. Che, *J. Org. Chem.* **2004**, *69*, 3610–3619; g) A. Padwa, A. C. Flick, C. A. Leverett, T. Stengel, *J. Org. Chem.* **2004**, *69*, 6377; h) P. Liu, E. L.-M. Wong, A. W.-H. Yuen, C.-M. Che, *Org. Lett.* **2008**, *10*, 3275–3278; i) L. Kiefer, T. Gorojankina, P. Dauban, H. Faure, M. Ruat, R. H. Dodd, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 7483–7487.
- [14] For the synthesis of [4.1.0] and [5.1.0] bicyclic sulfonated aziridines by catalytic intramolecular aziridination, see: a) K. Guthikonda, J. Du Bois, *J. Am. Chem. Soc.* **2002**, *124*, 13672–13673; b) P. M. Wehn, J. H. Lee, J. Du Bois, *Org. Lett.* **2003**, *5*, 4823–4826; c) K. Guthikonda, P. M. Wehn, B. J. Caliendo, J. Du Bois, *Tetrahedron* **2006**, *62*, 11331–11342; d) A. Esteoule, F. Duran, P. Retailleau, R. H. Dodd, P. Dauban, *Synthesis* **2007**, 1251–1260; e) M. E. Harvey, D. G. Musaev, J. Du Bois, *J. Am. Chem. Soc.* **2011**, *133*, 17207–17216; f) G. Malik, A. Esteoule, P. Retailleau, P. Dauban, *J. Org. Chem.* **2011**, *76*, 7438–7448; g) M. S. Valle, M. F. Saraiva, P. Retailleau, M. V. de Almeida, R. H. Dodd, *J. Org. Chem.* **2012**, *77*, 5592–5599. Also see ref. [7b].
- [15] For the synthesis of [4.1.0] and [5.1.0] bicyclic sulfamoyl aziridines by catalytic intramolecular aziridination, see: T. Kurokawa, M. Kim, J. Du Bois, *Angew. Chem. Int. Ed.* **2009**, *48*, 2777–2779; *Angew. Chem.* **2009**, *121*, 2815–2817.
- [16] a) R. M. de Figueiredo, *Angew. Chem. Int. Ed.* **2009**, *48*, 1190–1193; *Angew. Chem.* **2009**, *121*, 1212–1215; b) K. Muñiz, J. Streuff, C. H. Hövelmann, A. Núñez, *Angew. Chem. Int. Ed.* **2007**, *46*, 7125–7127; *Angew. Chem.* **2007**, *119*, 7255–7258; c) R. I. McDonald, S. S. Stahl, *Angew. Chem. Int. Ed.* **2010**, *49*, 5529–5532; *Angew. Chem.* **2010**, *122*, 5661–5664.
- [17] a) H.-J. Shue, X. Chen, N.-Y. Shih, D. J. Blythin, S. Paliwal, L. Lin, D. Gu, J. H. Schwerdt, S. Shah, G. A. Reichard, J. J. Piwinski, R. A. Duffy, J. E. Lachowicz, V. L. Coffin, F. Liu, A. A. Nomeir, C. A. Morgan, G. B. Varty, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3896–3901; b) H.-J. Shue, X. Chen, J. H. Schwerdt, S. Paliwal, D. J. Blythin, L. Lin, D. Gu, C. Wang, G. A. Reichard, H. Wang, J. J. Piwinski, R. A. Duffy, J. E. Lachowicz, V. L. Coffin, A. A. Nomeir, C. A. Morgan, G. B. Varty, N.-Y. Shih, *Bioorg. Med. Chem. Lett.* **2006**, *16*, 1065–1069.
- [18] a) G. B. Varty, M. E. Cohen-Williams, J. C. Hunter, *Behav. Pharmacol.* **2003**, *14*, 87–95; b) G. B. Varty, M. E. Cohen-Williams, C. A. Morgan, U. Pylak, R. A. Duffy, J. E. Lachowicz, G. J. Carey, V. L. Coffin, *Neuropsychopharmacology* **2002**, *27*, 371–379; c) P. J. Hesketh, *Supported Care Cancer* **2004**, *12*, 550–554.
- [19] For a recent synthesis of analogous compounds by copper(I)-catalyzed diamination, see: Y. Wen, B. Zhao, Y. Shi, *Org. Lett.* **2009**, *11*, 2365–2368.

Received: May 29, 2016

Revised: June 25, 2016

Published online: August 11, 2016