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Expedient stereospecific Co-catalyzed tandem *C-N* and *C-O* bond formation of *N*-methylanilines with styrene oxides

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Cobalt(II)-catalyzed stereospecific coupling of *N*-methylanilines with styrene oxides is developed via a tandem *C-N* and *C-O* bond formation using *tert*-butyl hydroperoxide (TBHP) as an oxidant. Optically active epoxide can be reacted with high optical purities.

1,3-Oxazolidines[1] are unique class of heterocycles and found in numerous biologically important structural scaffolds[2] including quinocarcin, cyanocycline A and tetrazomine, which display antibacterial, antitubercular, antiproliferative and anticancer properties (Figure 1).[3] In addition, they are often utilized as the synthetic intermediates, auxiliaries, ligands and catalysts for organic transformation.[4] Considerable efforts are thus made on the development of effective synthetic methods for their construction.[5,6] Recently, Terada and co-workers reported a chiral organosuperbase-catalyzed coupling of epoxides with imines to produce chiral 1,3-oxazolidines (Scheme 1a).[7] Cobalt is less expensive, readily available, environmentally benign and active centre of a group of coenzymes. Much attention are thus devoted on the development of Co-based catalytic systems.[8,9] In addition, a catalytic C-H functionalization provides a powerful synthetic tool for the transformation of the simple substrates into complex molecules with structural diversity.[10,11] Herein, we present a stereospecific cobalt(II)-catalysed tandem *C-N* and *C-O* bonds formation of *N*-methylanilines with styrene oxides to furnish 1,3-oxazolidines in the presence of TBHP via a one-pot sequence of S_N2 ring opening of epoxide, C-H functionalization and cyclization. Optically active epoxide can be coupled with high enantiomeric purities.

First, we optimized the reaction employing *N*-methylaniline **1a** with styrene oxide **2a** as the model substrates using a series of Cu(II), Fe(II) and Co(II) salts at varied temperatures (Table 1). Gratifyingly, the coupling occurred to give 1,3-oxazolidine **3a** in 58% yield when the substrates were stirred with 10 mol% of $Cu(OTf)_2$ at 60 ˚C for 1 h in CH_2Cl_2, followed by treatment with TBHP and stirring for 2 h (entry 1). Subsequent screening of the catalysts revealed that Co(II) salts are superior to that of Cu(II) and Fe(II) salts (entries 2-7). The best results observed utilizing $Co(OAc)_2{\cdot}4H_2O$ with 67% yield (entry 6). $(CH_2Cl)_2$ was found to the solvent of choice, giving 73% yield, whereas toluene, acetonitrile and THF furnished 32-48% yields (entries 8-11). Screening of the oxidants such as DTBP, 30% H_2O_2 and O_2 led to inferior results (entries 12-14). Control experiments confirmed that the combination of $Co(OAc)_2{\cdot}4H_2O$ and TBHP is essential for this transformation (entries 15-16).

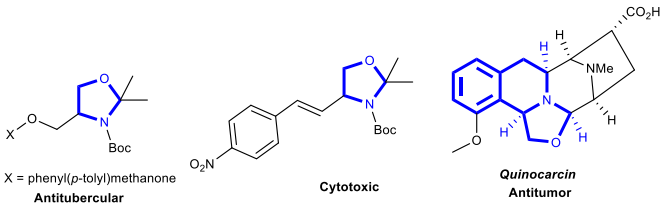
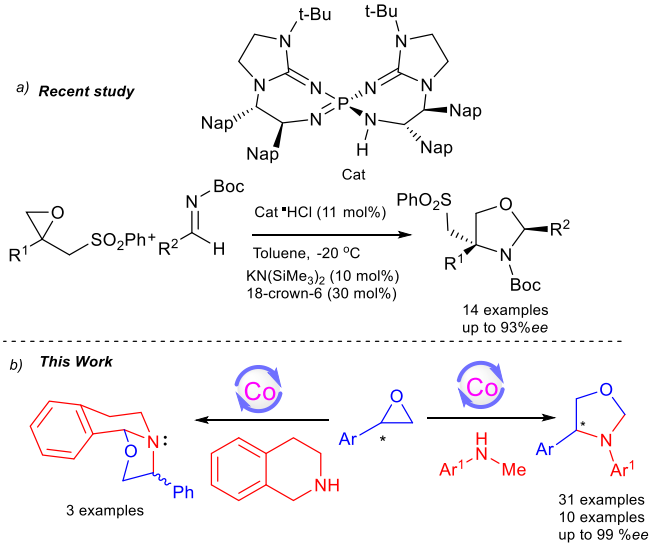


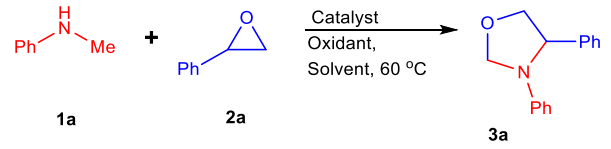
Figure 1. Some selected examples of biologically active 1,3-oxazolidine scaffolds.



Scheme 1. Recent methods for the synthesis of 1,3-oxazolidines from epoxides.

Having optimized the reaction condition, the scope of the procedure was inspected for a series of *N*-methylanilines **1b-q** with **2a** as a standard substrate (Table 2). *N*-Methylaniline bearing 2-methyl **1b** group underwent reaction to give the ring opening amino alcohol $\mathbf{A_1}$ in 81% yield and no cyclization was observed that may be to the steric hindrance of the methyl

Table 1 Optimization of the reaction conditions[a,b]



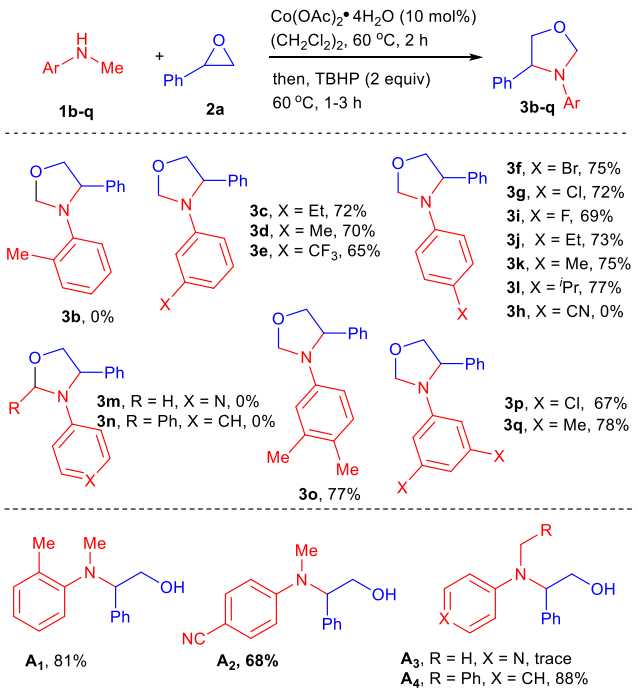
1a 2a 3a

Entry	Catalyst	Oxidant	Solvent	**3a** (%)[b]
1	$Cu(OTf)_2$	TBHP	CH_2Cl_2	34,[c] 42,[d] 48,[e] 58
2	$Cu(OAc)_2$	TBHP	CH_2Cl_2	45
3	$Fe(acac)_2$	TBHP	CH_2Cl_2	26
4	$Fe(OAc)_2$	TBHP	CH_2Cl_2	33
5	$Co(acac)_2$	TBHP	CH_2Cl_2	54
6	$Co(OAc)_2•4H_2O$	TBHP	CH_2Cl_2	67
7	$CoCl_2$	TBHP	CH_2Cl_2	60
8	$Co(OAc)_2•4H_2O$	TBHP	$(CH_2Cl)_2$	73
9	$Co(OAc)_2•4H_2O$	TBHP	Toluene	48
10	$Co(OAc)_2•4H_2O$	TBHP	CH_3CN	45
11	$Co(OAc)_2•4H_2O$	TBHP	THF	32
12	$Co(OAc)_2•4H_2O$	DTBP	$(CH_2Cl)_2$	48
13	$Co(OAc)_2•4H_2O$	30% H_2O_2	$(CH_2Cl)_2$	20
14	$Co(OAc)_2•4H_2O$	O_2	$(CH_2Cl)_2$	14
15	$Co(OAc)_2•4H_2O$	-	$(CH_2Cl)_2$	n.d.
16	-	TBHP	$(CH_2Cl)_2$	n.d.

[a]Reaction conditions. **1a** (0.50 mmol), **2a** (0.50 mmol), catalyst (10 mol %), solvent (2 mL), 60° C, 2 h, then oxidant (1 mmol), 60 °C, 1 h. [b]Isolated average yield of two runs. [c]Room temperature. [d]50° C. [e]1.5 eq. TBHP was used. n.d. = not detected.

functionality. However, the reaction of the substrates bearing 3-ethyl **1c**, 3-methyl **1d** and 3-trifluoromethyl **1e** substituents afforded the target heterocycles **3c-e** in 65-72% yields. Similar results observed with the substrates containing 4-bromo **1f**, 4-chloro **1g**, 4-fluoro **1i**, 4-ethyl **1j**, 4-methyl **1k** and 4-isopropyl **1l** substituents, giving **3f-g** and **3i-l** in 72-77% yields, whereas **1h** having 4-cyano group produced the ring opening amino alcohol $\mathbf{A_2}$ as a sole product **in** 68% yield, which may be due to the delocalization of nitrogen lone pair with aryl ring. Similarly, the reactions of *N*-methylpyridin-4-amine **1m** and *N*-benzylaniline **1n**, furnished the amino alcohols $\mathbf{A_3}$ and $\mathbf{A_4}$ in a trace amount and 88% yield, respectively, which could be presumably due to the steric hindrance to form the imine cation or the complex formation of Co species with pyridine nitrogen. However, the reaction of the substrates containing 3,4-dimethyl **1o**, 3,5-dichloro **1p** and 3,5-dimethyl **1q** substituents can be performed to afford **3o-q** in 67-78% yields.

Next, we studied the scope of the procedure for the reaction of styrene oxides **2b-l** with *N*-methylaniline **1a** as the standard substrate (Scheme 3). The reaction of styrene oxides having 2-chloro **2b**, 3-methoxy **2c,** 3-methyl **2d,** 3-fluoro **2e** and 3-nitro **2f** substituents occurred to afford the desired **3r-v** in 58-74% yields. Similarly, the epoxides bearing 4-acetoxy **2g**, 4-bromo **2h**, 4-chloro **2i** and 4-fluoro **2j** groups are well tolerated to furnish the oxazolidines **3w-z** in 75-80% yields, whereas the reaction of **2k** containing 4-cyano group yielded the uncyclized amino alcohol $\mathbf{A_5}$ in 82% yield. Furthermore, 2-ethylene oxide **2l** underwent the nucleophilic ring opening at the less hindered methylene carbon to give $\mathbf{A_6}$ in 90% yield, which showed no cyclization. However, the reaction of the epoxides **2g** and **2i** with *N*-methylanilines having 4-chloro **1g**, 4-methyl **1k** and 3-ethyl **1c** groups can be readily accomplished to furnish the oxazolidines **3ac-ae** in 71-76% yields.



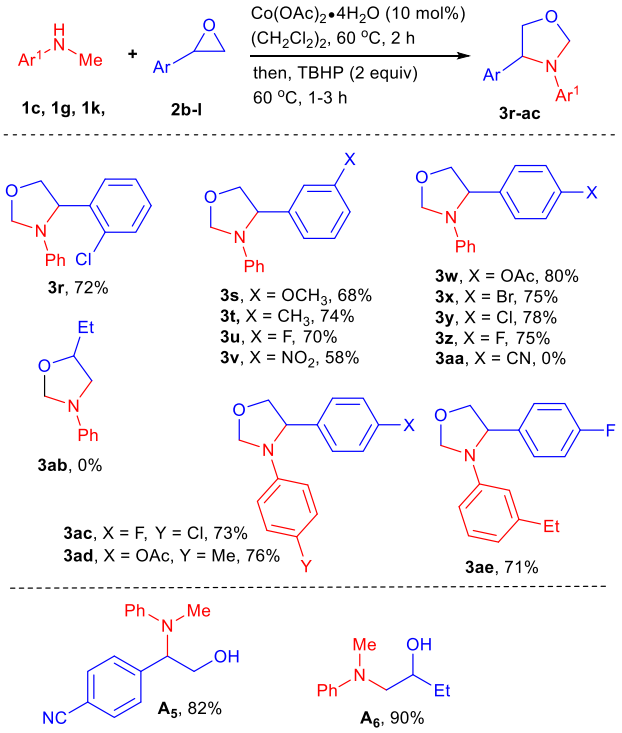
Scheme 2 Reaction of different *N*-methylanilines **1** with styrene oxide **2a**. Reaction conditions: **1b-q** (0.50 mmol), **2a** (0.50 mmol), $Co(OAc)_2·4H_2O$, $(CH_2Cl_2)_2$ (2 mL), 60 °C, 2 h, then TBHP (1 mmol), 60 °C, 1-3 h. Isolated yield.

The reaction condition was further extended to the coupling of tetrahydroisoquinoline **4** with styrene oxides (Scheme 4). Pleasingly, the reactions readily occurred to produce the tricylic heterocyclic scaffolds **5a-c** with good diasteroselectivity in 68-75 % yields.

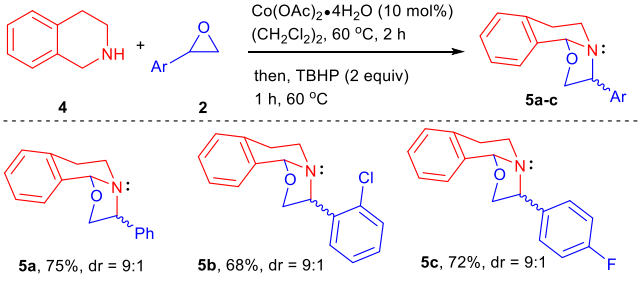
To reveal the stereoselectivity, we studied the reaction of (*R*)-styrene oxide **2a'** with a series of *N*-methylanilines (Scheme 5). To our delight, the reaction took place stereospecifically to give the 1,3-oxazolidines in high optical purities. For example, *N*-methylaniline having 3-ethyl group **1c** underwent reaction to give **3c'** in 98% ee and 75 % yield. Similar results observed with *N*-methylanilines containing 4-bromo **1f**, 4-chloro **1g**, 4-fluoro **1i**, 4-ethyl **1j**, 4-methyl **1k** and 4-isopropyl **1l** groups, providing **3f'**, **3g'** and **3i'-l'** in 95-98% ee and 70-76% yields. In addition, *N*-methylanilines having methyl groups at 3,4- **1o** and 3,5- **1q** positions could be coupled to give **3o'** and **3q'** in 97% ee and 73-76% yields. These results suggest that *N*-methylaniline reacts with epoxide presumably via a S_N2 pathway.[12]

To gain insight in the catalytic cycle, we studied the coupling of **1a** and **2a** as the representative example using BHT radical inhibitor (Scheme 6). ESI-Mass analysis of the reaction mixture revealed the formation BHT-adduct **6** and the amino alcohol $\mathbf{A_7}$ (see SI). The formation of **6** suggests that a radical intermediate may be involved. Our effort to isolate **6** was, however, failed due to the formation of a trace amount. When we reacted $\mathbf{A_7}$ using $Co(OAc)_2•4H_2O$ and TBHP, the oxidative cyclization occurred to give **3a** in 80% yield, which suggests that *N*-

methylaniline reacts with epoxide to give an amino alcohol that leads to a cyclization via C(sp^3)-H functionalization (Scheme 7).

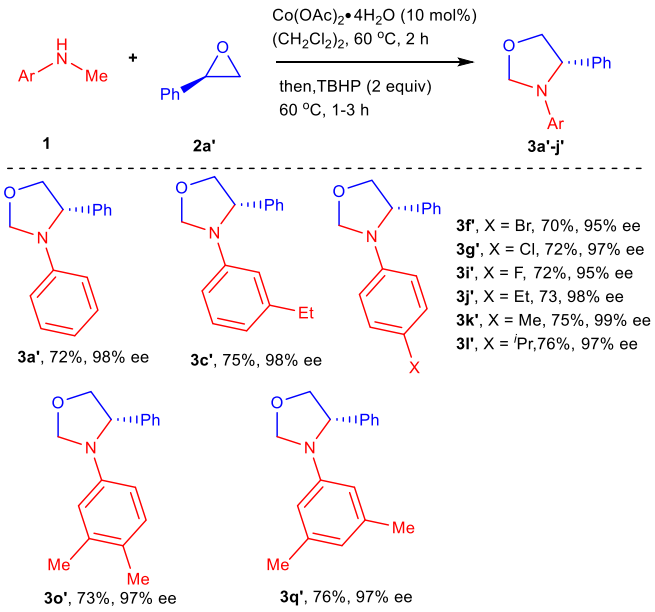


Scheme 3 Substrate scope of *N*-methylanilines **1** and styrene oxides **2b-l**. Reaction conditions: *N*-methylaniline (0.50 mmol), **2b-l** (0.50 mmol), $Co(OAc)_2{\cdot}4H_2O$, solvent (2 mL), 60° C, 2h, then TBHP (1 mmol), 60 °C, 1-3 h. Isolated yield.

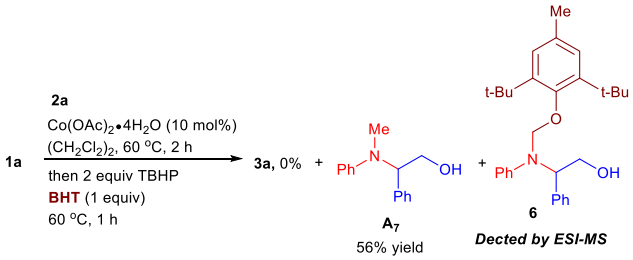


Scheme 4 Reaction of tetrahydroisoquinoline **4** with styrene oxides **2a**, **2c** and **2j**. Reaction conditions: **4** (0.50 mmol), **2** (0.50 mmol), $Co(OAc)_2{\cdot}4H_2O$, solvent (2 mL), 60° C, 2 h, then TBHP (1 mmol), 60 °C, 1 h. Isolated yield. *dr* calculated from 600 MHz ^{1}H NMR.

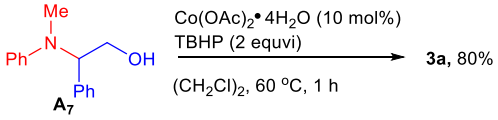
Based on these experimental results and the literature,[8,9] a proposed catalytic cycle is shown in Scheme 8. The chelation of Co(II) with epoxide oxygen ***a***, may facilitate the nucleophilic ring opening with *N*-methylanilines to give ***b*** via S_N2 pathway. The latter can convert into the radical cation ***c*** via a single electron transfer (SET) to Co(III) species, which can be produced from Co(II) with TBHP. Homolytic cleavage of the C-H bond in ***c*** using *t*-butoxy radical/ *t*-butylperoxy radical can give imine ion ***d*** that can lead to intramolecular cyclization to furnish the heterocycle **3**.[13] The Co(II)-Co(III) triggered cleavage of TBHP can be give the *t*-Butoxy radical. The proposed catalytic cycle also explains the requirement of an excess TBHP. Furthermore, the formation of the major diastereomer **5** can be exemplified through a chair like transition states (TS) ***e*** and ***f*** (Scheme 9). TS ***e*** is favoured because of the evading the undesired interaction, whereas TS ***f*** has 1,3-diaxial interaction.



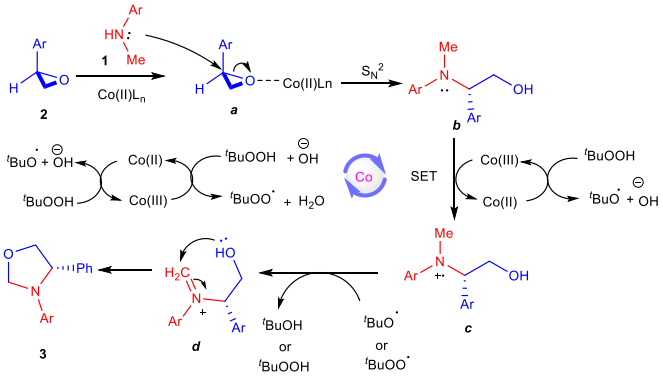
Scheme 5 Reaction of different *N*-methylanilines **1** with (*R*)-styrene oxide **2a'**. Reaction conditions: **1** (0.50 mmol), **2a'** (0.50 mmol), $Co(OAc)_2{\cdot}4H_2O$, solvent (2 mL), 60° C, 2 h, then TBHP (2 equvi), 60 °C, 1-3 h. Isolated yield.



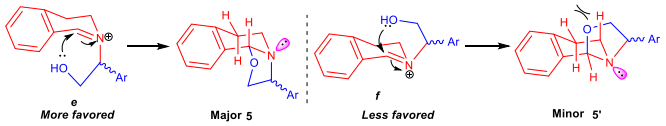
Scheme 6 Radical trapping experiment.



Scheme 7 Control experiment.



Scheme 8 Proposed reaction pathway.



Scheme 9 Stereochemical model.

In conclusion, we presented a Co(II)-catalyzed stereospecific coupling of *N*-methylanilines with styrene oxides to furnish 1,3-oxazolidines via a tandem *C-N* and *C-O* bonds formation in the presence of TBHP. Optically active epoxide can be coupled with high enantiomeric purities.

Notes and references

1 (a) E. D. Bergmann, *Chem. Rev.* 1953, **53**, 309; (b) S. Cicchi, F. M. Cordero and D. Giomi, (Eds. G. W. Gribble and J. A. Joule), *Progress in Heterocyclic Chemistry* 2009, **21**, 308.

2 J. D. Scott and R. M. Williams, *Chem. Rev.* 2002, **102**, 1669.

3 For biological properties, see: (a) F. Tomita, K. Takahashi and T. Tamaoki, *J. Antibiot.* 1984, **37**, 1268; (b) R. M. Williams, T. Glinka, M. E. Flanagan, R. Gallegos, H. Coffman and D. Pei, *J. Am. Chem. Soc.* 1992, **114**, 733; (c) R. S. B. Gonçalves, C. R. Kaiser, M. C. S. Lourenço, M. V. N. de Souza, J. L. Wardell, S. M. S. V. Wardell and A. D. da Silva, *Eur. J. Med. Chem*. 2010, **45**, 6095; (d) K. Ii, S. Ichikawa, B. Al-Dabbagh, A. Bouhss and A. Matsuda, *J. Med. Chem.* 2010, **53**, 3793; (e) L. Yu, W. Zhou and Z. Wang, *Bioorg. Med. Chem. Lett.* 2011, **21**, 1541; (f) R. S. B. Gonçalves, C. R. Kaiser, M. C. S. Lourenço, F. A. F.M. Bezerra, M. V. N. de Souza, J. L. Wardell, S. M. S. V. Wardell, M. G. M. O. Henriques and T. Costa, *Bioorg. Med. Chem.* 2012, **20**, 243; (g) S. F. Andrade, C. S. Teixeiraa, J. P. Ramosb, M. S. Lopesa, R. M. Páduaa, M. C. Oliveiraa, E. M. Souza-Fagundes and R. J. Alves, *Med. Chem. Commun.* 2014, **5**, 1693; (h) B. L. Barthel, E. L. Mooz, L. E. Wiener, G. G. Koch and T. H. Koch, *J. Med. Chem.* 2016, **59**, 2205; (i) S. F. Andrade, B. G. Oliveira, L. C. Pereira, J. P. Ramos, A. R. Joaquim, M. Steppe, E. M. Souza-Fagundes and R. J. Alves, *Eur. J. Med. Chem.* 2017, **138**, 13.

4 For synthetic application, see: (a) F. Fache, E. Schultz, M. L. Tommasino and M. Lemaire, *Chem. Rev.* 2000, **100**, 2159; (b) C. Agami and F. Couty, *Eur. J. Org. Chem.* 2004, 677; (c) H. Nakano, K. Osone, M. Takeshita, E. Kwon, C. Seki, H. Matsuyama, N. Takano and Y. Kohari, *Chem. Commun.* 2010, **46**, 4827; (d) C. Wolf and H. Xu, *Chem. Commun.* 2011, **47**, 3339; (f) H. Nakano, Y. Okuyama and E. Kwon, *Heterocycles* 2014, **89**, 1; (g) S. Raghavan and P. Senapati, *J. Org. Chem.* 2016, **81**, 6201; (h) A. Saleem, P. A. Kobielska, K. Harms, M. G. Katsikogianni, R. Telford, G. Novitchi and S. Nayak, *Dalton Trans*. 2018, **47**, 6156.

5 For examples of recent approaches for oxazolidine synthesis, see: (a) V. K. Yadav and V. Sriramurthy, *J. Am. Chem. Soc.* 2005, **127**, 16366; (b) D. J. Michaelis, C. J. Shaffer and T. P. Yoon, *J. Am. Chem. Soc.* 2007, **129**, 1866; (c) V. Sriramurthy, G. A. Barcan and O. Kwon, *J. Am. Chem. Soc.* 2007, **129**, 12928; (d) R. Maeda, R. Ishibashi, R. Kamaishi, K. Hirotaki, H. Furuno and T. Hanamoto, *Org. Lett.* 2011, **13**, 6240; (e) A. F. Ward and J. P. Wolfe, *Org. Lett.* 2011, **13**, 4728; (f) S. K. Nimmagadda, Z. Zhang and J. C. Antilla, *Org. Lett.* 2014, **16**, 4098; (g) L. Yang, A. Khan, R. Zheng, L. Y. Jin and Y. J. Zhang, *Org. Lett.* 2015, **17**, 6230; (h) Y. Toda, W. Kaku, M. Tsuruoka, S. Shinogaki, T. Abe, H. Kamiya, A. Kikuchi, K. Itoh and H. Suga, *Org. Lett.* 2018, **20**, 2659.

6 (a) C. Huo, R. Wei, W. Zhang, L. Yang and Z.-L. Liu, *Synlett* 2005, **1**, 161; (b) G. Bentabed-Ababsa, A. Derdour, T. Roisnel, J. A. Sáez, P. Pérez, E. Chamorro, L. R. Domingo and F. Mongin, *J. Org. Chem.* 2009, **74**, 2120; (c) M. B. Shaghafi, R. E. Grote and E. R. Jarvo, *Org. Lett.* 2011, **13**, 5188; (d) A. Kondoh, K. Odaira and M. Terada, *Angew. Chem. Int. Ed.* 2015, **54**, 11240.

7 A. Kondoh, S. Akahira, M. Oishi and M. Terada, *Angew. Chem. Int. Ed.* 2018, **57**, 6299.

8 For recent examples of Co(II)-catalyzed C-H functionalization, see: (a) M. O. Ratnikov and M. P. Doyle, *J. Am. Chem. Soc.* 2013, **135**, 1549; (b) X.-J. Shang and Z.-Q. Liu, *Tetrahedron Lett.* 2015, **56**, 482; (c) X. Wu, K. Yang, Y. Zhao, H. Sun, G. Li and H. Ge, *Nat. Commun.* 2015, **6**, 6462; (d) M. Moselage, J. Li and L. Ackermann, *ACS Catal.* 2016, **6**, 498; (e) Y. Li, M. Wang, W. Fan, F. Qian, G. Li and H. Lu, *J. Org. Chem.* 2016, **81**, 11743; (f) X. Wang, B. Lei, L. Ma, L. Zhu, X. Zhang, H. Zuo, D. Zhuang and Z. Li, *Chem. Asian J.* 2017, **12**, 2799; (g) Q. Li, W. Hu, R. Hu, H. Lu and G. Li, *Org. Lett.* 2017, **19**, 4676; (h) M. S. Segundo, I. Guerrero and A. Correa, *Org. Lett.* 2017, **19**, 5288; (i) Q. Yang, S. Li and J. Wang, *Org. Chem. Front.* 2018, **5**, 577; (j) M. R. Patil, N. P. Dedhia, A. R. Kapdi and A. Vijay Kumar, *J. Org. Chem.* 2018, **83**, 4477; (k) B. Lin, S. Shi, R. Lin, Y. Cui, M. Fang, G. Tang and Y. Zhao, *J. Org. Chem.* 2018, **83**, 6754; (l) M. Tan, K. Li, J. Yin and J. You, *Chem. Commun.* 2018, **54**, 1221.

9 For Co(II)-catalyzed epoxide ring opening, see: (a) J. Iqbal, M. Mukhopadhyay and A. K. Mandal, *Synlett* 1997, 876; (b) H. Pellissier and H. Clavier, *Chem. Rev.* 2014, **114**, 2775; (c) L. Liu and H. Sun, *Angew. Chem. Int. Ed.* 2014, **53**, 9865; (d) Y. Zhang, J. Ji, X. Zhang, S. Lin, Q. Pan and L. Jia, *Org. Lett.* 2014, **16**, 2130; (e) G. P. Cerai and B. Morandi, *Chem. Commun.* 2016, **52**, 9769; (f) M. L. Jamieson, N. Z. Brant, M. A. Brimble and D. P. Furkert, *Synthesis* 2017, **49**, 3952.

10 For reviews, see: (a) K. R. Campos, *Chem. Soc. Rev.* 2007, **36**, 1069; (b) C.-J Li, *Acc. Chem. Res.* 2009, **42**, 335; (c) S. H. Cho, J. Y. Kim, J. Kwak and S. Chang, *Chem. Soc. Rev*. 2011, **40**, 5068; (d) Hu Li, Bi-Jie Li and Z.-J. Shi, *Catal. Sci. Technol.* 2011, **1**, 191; (e) C. Zhang, C. Tang and N. Jiao, *Chem. Soc. Rev.* 2012, **41**, 3464; (f) T. A. Ramirez, B. Zhao and Y. Shi, *Chem. Soc. Rev.* 2012, **41**, 931; (g) J. Miao and H. Ge, *Eur. J. Org. Chem.* 2015, 7859; (h) T. Gensch, M. N. Hopkinson, F. Glorius and J. Wencel-Delord, *Chem. Soc. Rev.* 2016, **45**, 2900; (i) R. R. Karimov and J. F. Hartwig, *Angew. Chem. Int. Ed.* 2018, **57**, 4234.

11 For recent examples, see: (a) M. L. Deb, S. S. Dey, I. Bento, M. T. Barros and C. D. Maycock, *Angew. Chem. Int. Ed.* 2013, **52**, 9791; (b) A. Modak, U. Dutta, R. Kancherla, S. Maity, M. Bhadra, S. M. Mobin and D. Maiti, *Org. Lett.* 2014, **16**, 2602; (c) F.-L. Zhang, K. Hong, T.-J. Li, H. Park and J.-Q. Yu, *Science* 2016, **351**, 6270; (d) G. Li and H. Nakamura, *Angew. Chem. Int. Ed.* 2016, **55**, 6758; (e) T. Huang, X. Liu, J. Lang, J. Xu, L. Lin, and X. Feng, *ACS Catal.* 2017, **7**, 5654; (f) C. Zhu, R. Zhu, H. Zeng, F. Chen, C. Liu, W. Wu and H. Jiang, *Angew. Chem. Int. Ed.* 2017, **56**, 13324; (g) Y. Lan, P. Fan, X.-W. Liu, F.-F. Meng, T. Ahmad, Y.-H. Xu and T.-P. Loh, *Chem. Commun.* 2017, **53**, 12353; (h) J. Wang, R. Sang, X. Chong, Y. Zhao, W. Fan, Z. Lia and J. Zhao, *Chem. Commun.* 2017, **53**, 7961; (i) S. K. Singh, N. Chandna and N. Jain, *Org. Lett.* 2017, **19**, 1322; (j) H. Long, G. Wang, R. Lu, M. Xu, K. Zhang, S. Qi, Y. He, Y. Bu and L. Liu, *Org. Lett.* 2017, **19**, 2146; (k) J. Xie, Y. Huang, H. Song, Y. Liu and Q. Wang, *Org. Lett.* 2017, **19**, 6056; (l) X. Pang, M. Wu, J. Ni, F. Zhang, J. Lan, B. Chen and R. Yan, *J. Org. Chem.* 2017, **82**, 10110; (m) L. Mendive-Tapia, A. Albornoz-Grados, A. Bertran, F. Albericio and R. Lavilla, *Chem. Commun.* 2017, **53**, 2740; (n) B. Lin, S. Shi, R. Lin, Y. Cui, M. Fang, G. Tang and Y. Zhao, *J. Org. Chem.* 2018, **83**, 6754.

12 R. E. Parker and N. S. Isaacs, *Chem. Rev.* 1959, **59**, 737.

13 E. Spier, U. Neuenschwander and I. Hermans, *Angew. Chem. Int. Ed.* 2013, **52**, 1581.

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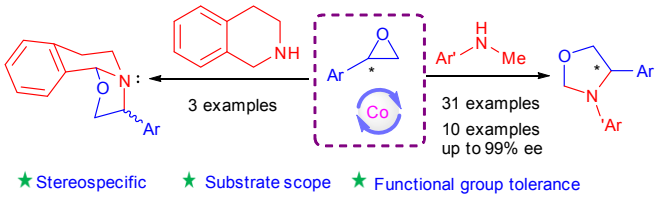

A Co(II)-catalyzed stereospecific sequential *C-N* and *C-O* bond formation of styrene oxides with *N*-methylanilines has been developed. Optically active epoxide can be coupled with high enantiomeric purities.