Asymmetric Catalysis

DOI: 10.1002/anie.201407880

Asymmetric Synthesis of 2,3-Dihydropyrroles by Ring-Opening/Cyclization of Cyclopropyl Ketones Using Primary Amines**

Yong Xia, Xiaohua Liu, Haifeng Zheng, Lili Lin, and Xiaoming Feng**

Abstract: *The asymmetric ring-opening/cyclization of cyclopropyl ketones with primary amine nucleophiles was catalyzed by a chiral N,N′-dioxide/scandium(III) complex through a kinetic resolution process. A broad range of cyclopropyl ketones and primary amines are suitable substrates of this reaction. The corresponding products were afforded in excellent enantioselectivities and yields (up to 97% ee and 98% yield) under mild reaction conditions. This method provides a promising access to chiral 2,3-dihydropyrroles as well as an effective procedure for the kinetic resolution of 2-substituted cyclopropyl ketones.*

Chiral dihydropyrroles frameworks are a privileged structural unit in a number of natural compounds with important biological activities and also a key building block in the synthesis of complex molecules.[1,2] Versatile asymmetric approaches have been reported towards substituted pyrrolidine derivatives. For instance, asymmetric [3+2] cycloadditions of imines with allenes[3a–c] and of ynones with azomethine ylides[3d,e] have been developed to efficiently construct chiral 2,5-dihydropyrroles. Aside from the reactions starting from 2-pyrroline[4] and pyrrole[5] precursors, asymmetric [3+2] cycloadditions of 1-alkylallenylsilanes with α-imino esters[6a] and of isocyanoesters with nitroolefins[6b] were useful for the synthesis of chiral 2,3-dihydropyrroles. Tandem Michael/cyclization reactions also provide an efficient method to access such nitrogen heterocycles in an enantioenriched form.[7] Nevertheless, the development of an alternative method towards optically active 2,3-dihydropyrroles with various functional groups remains appealing.

In recent years, donor–acceptor cyclopropanes, as a useful class of building blocks, have been used as substrates in a series of organic transformations.[8–11] Extensive studies related to the formal [3+2] cycloaddition of cyclopropane-1,1-dicarboxylates with enol silyl ethers,[9a–c] aldehydes,[9d–g] aldimines,[9h,i] and indoles[9j–l] as well as the [3+3] cycloaddition of aromatic azomethine imines[10a,b] and nitrones[10c–g] have been conducted by the groups of Tang, Johnson, Kerr, and others. Furthermore, nucleophilic ring-opening reactions of cyclopropane derivatives with indoles,[11a,b] amines,[11c–h] or sodium azide[11i] were also reported to afford the corresponding acyclic products. However, asymmetric variants are rare; only one successful example on the use of secondary aliphatic amines as the nucleophiles for the construction of chiral γ-substituted γ-amino acid derivatives has been reported by Tang and co-workers.[11f] The France group found that the Lewis acid catalyzed ring-opening cyclization of cyclopropyl ketones with primary amines provided a milder approach to 2,3-dihydropyrroles bearing electron-withdrawing groups at the 4-position.[11g] Surprisingly, unlike for the reaction of cyclopropyl esters,[9c,f,i,k, 10b,e, 11b,f] an asymmetric variant of the reaction with cyclopropyl ketones has not been described. The carbonyl group of cyclopropyl ketones can coordinate to a chiral metal complex to enable enantioselective transformations,[10b,e, 11f] but also act as a functional group for further intramolecular condensation reactions. As part of our continuing work on exploring the use of metal complexes with a chiral *N,N′*-dioxide ligand in asymmetric catalysis,[12] we reported the [3+2] cycloaddition of aryl oxiranyl ketones with aldehydes and alkynes, which proceeds through the C–C bond cleavage of oxiranes.[12c,d] Herein, we describe a simple and highly enantioselective ring-opening/cyclization reaction of cyclopropyl ketones with primary amines that is catalyzed by a chiral *N,N′*-dioxide/Sc(III) complex. This transformation proceeds through a kinetic resolution process and generates chiral 2,4,5-trisubstituted 2,3-dihydropyrrole derivatives in good yields and enantioselectivities.

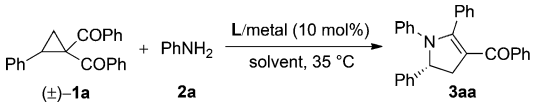
Initially, the ring-opening/cyclization reaction of racemic cyclopropyl ketone **1a** with aniline (**2a**) was selected as the model reaction. Several metal salts coordinated to *N,N′*-dioxide **L1**, which is derived from (*S*)-pipecolic acid, were tested in DCE at 35 °C. As shown in Table 1, $Sc(OTf)_3$ was able to accelerate this reaction, delivering the desired 2,3-dihydropyrrole **3aa** in promising enantioselectivity and moderate yield (73% *ee* and 30% yield; entry 3). Other metal salts, such as $Ni(ClO_4)_2 \cdot 6H_2O$, gave racemic product albeit in good yield (entry 1). To further improve the enantioselectivity of the reaction, a series of chiral *N,N′*-dioxides were examined. It was found that both the bulky amide subunits and the amino acid backbone of the ligands were crucial for the enantiocontrol. Increasing the steric bulk of the amide substituents benefited the enantioselectivity of the reaction (entries 3–5). Changing the chiral backbone of the ligand from (*S*)-pipecolic acid to (*S*)-proline and (*S*)-

[*] Y. Xia, Prof. Dr. X. H. Liu, H. F. Zheng, Dr. L. L. Lin, Prof. Dr. X. M. Feng
Key Laboratory of Green Chemistry & Technology, Ministry of Education, College of Chemistry, Sichuan University
Chengdu 610064 (China)
E-mail: liuxh@scu.edu.cn
xmfeng@scu.edu.cn
Prof. Dr. X. M. Feng
Collaborative Innovation Center of Chemical Science and Engineering, Tianjin (China)

[**] We thank the National Natural Science Foundation of China (21432006, 21321061, and 21172151), the National Basic Research Program of China (973 Program: 2011CB808600), and the Ministry of Education (NCET-11-0345) for financial support.

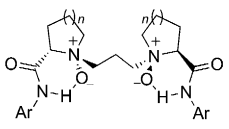
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201407880.

Table 1: Optimization of the reaction conditions.[a]

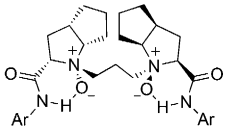


Entry	Metal salt	L	Solvent	Yield[b] [%]	*ee*[c] [%]
1	$Ni(ClO_4)_2 \cdot 6H_2O$	**L1**	DCE	71	0
2	$Yb(OTf)_3$	**L1**	DCE	60	58
3	$Sc(OTf)_3$	**L1**	DCE	30	73
4	$Sc(OTf)_3$	**L2**	DCE	49	63
5	$Sc(OTf)_3$	**L3**	DCE	41	87
6	$Sc(OTf)_3$	**L4**	DCE	39	73
7	$Sc(OTf)_3$	**L5**	DCE	39	76
8	$Sc(OTf)_3$	**L3**	DCM	51	84
9	$Sc(OTf)_3$	**L3**	THF	40	87
10	$Sc(OTf)_3$	**L3**	$CHCl_2CHCl_2$	39	89
11[d,e]	$Sc(OTf)_3$	**L3**	$CHCl_2CHCl_2$	82	91

[a] Unless otherwise noted, all reactions were performed with metal salt and ligand (10 mol%, 1:1), **1a** (0.40 mmol), and **2a** (0.10 mmol) in the specified solvent (0.5 mL) under N_2 atmosphere at 35 °C for 48 h. [b] Yield of isolated product. [c] Determined by HPLC analysis on a chiral stationary phase. [d] The reaction was performed in 1.0 mL of $CHCl_2CHCl_2$ for 96 h. [e] LiCl (1.0 equiv) was added. DCE = 1,2-dichloroethane, DCM = dichloromethane, OTf = trifluoromethanesulfonate.

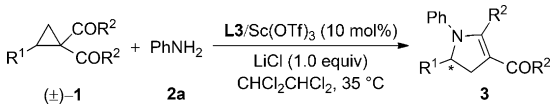


L1: R = 2,6-*i*Pr$_2$C$_6$H$_3$, *n* = 2
L2: R = 2,6-Et$_2$C$_6$H$_3$, *n* = 2
L3: R = 2,4,6-*i*Pr$_3$C$_6$H$_2$, *n* = 2
L4: R = 2,4,6-*i*Pr$_3$C$_6$H$_2$, *n* = 1



L5: R = 2,4,6-*i*Pr$_3$C$_6$H$_2$

Table 2: Variation of the cyclopropyl ketone.[a]



Entry	R^1, R^2	Yield[b] [%]	*ee*[c] [%]
1	Ph, Ph (**1a**)	82 (**3aa**)	91
2	4-MeC_6H_4, Ph (**1b**)	95 (**3ba**)	91
3	4-MeOC_6H_4, Ph (**1c**)	96 (**3ca**)	92
4	4-FC_6H_4, Ph (**1d**)	94 (**3da**)	95
5	4-ClC_6H_4, Ph (**1e**)	86 (**3ea**)	92
6	4-BrC_6H_4, Ph (**1f**)	88 (**3fa**)	95
7	3-MeC_6H_4, Ph (**1g**)	96 (**3ga**)	92
8	3-MeOC_6H_4, Ph (**1h**)	81 (**3ha**)	94
9	3-ClC_6H_4, Ph (**1i**)	67 (**3ia**)	95
10	3-BrC_6H_4, Ph (**1j**)	71 (**3ja**)	95
11	2-MeC_6H_4, Ph (**1k**)	92 (**3ka**)	94
12	2-MeOC_6H_4, Ph (**1l**)	95 (**3la**)	92
13	2,4-$Cl_2C_6H_3$, Ph (**1m**)	55 (**3ma**)	90
14	3,4-$Cl_2C_6H_3$, Ph (**1n**)	66 (**3na**)	96
15	2,3-$(MeO)_2C_6H_3$, Ph (**1o**)	76 (**3oa**)	90
16	3,4-$(MeO)_2C_6H_3$, Ph (**1p**)	98 (**3pa**)	92
17	1-naphthyl, Ph (**1q**)	98 (**3qa**)	96
18	2-naphthyl, Ph (**1r**)	97 (**3ra**)	94
19	$H_2C{=}CH$, Ph (**1s**)	43 (**3sa**)	91
20	Ph, 4-MeC_6H_4 (**1t**)	63 (**3ta**)	96
21	Ph, 4-FC_6H_4 (**1u**)	93 (**3ua**)	94
22	Ph, Me (**1v**)	59 (**3va**)	73
23[d]	Me, Ph (**1w**)	16 (**3wa**)	66

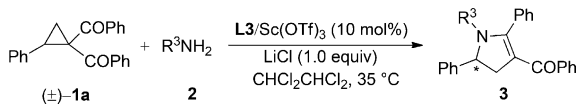
[a] Unless otherwise noted, all reactions were performed with **L3**/$Sc(OTf)_3$ (10 mol%, 1:1), LiCl (1.0 equiv), **1** (0.40 mmol), and **2a** (0.10 mmol) in $CHCl_2CHCl_2$ (1.0 mL) under N_2 atmosphere at 35 °C for 96 h. [b] Yield of isolated product. [c] Determined by HPLC analysis on a chiral stationary phase. [d] At 60 °C.

ramipril led to an obvious decrease in the enantioselectivity (entries 5–7). Then we focused on the optimization of solvent and additives. To our delight, when one equivalent of LiCl was added and the solvent changed to $CHCl_2CHCl_2$, the outcome of the reaction substantially improved, and the desired product was isolated in 82% yield and 91% *ee* (entries 8–11).[13] Therefore, the optimized conditions for the ring-opening/cyclization reaction entail the use of the **L3**/Sc^{III} complex (10 mol%) as the catalyst and LiCl as an additive in $CHCl_2CHCl_2$ at 35 °C for 96 hours (entry 11).

With the optimized reaction conditions in hand, the substrate scope was investigated by varying the cyclopropyl ketone partner. As shown in Table 2, a series of cyclopropyl ketone derivatives reacted smoothly with **2a**, providing the corresponding products in good to excellent enantioselectivities and poor to excellent yields (66–96% *ee*, 16–98% yield). Both electron-rich and electron-deficient aryl groups at the 2-position of the cyclopropyl ketones had a small effect on the enantioselectivity (entries 1–12). Dichloride-substituted ketones gave lower yields in comparison with dimethoxy-substituted ones (entries 13–16). Naphthyl-substituted cyclopropyl ketones were suitable substrates for this reaction, giving the desired products with excellent enantioselectivities and yields (94–96% *ee*, 97–98% yield; entries 17–18). Remarkably, a vinyl-substituted substrate was also compatible with this catalytic system, and the product was obtained with excellent enantioselectivity, albeit with moderate yield (entry 19). Then the effect of the electronic nature of the substituent at the *para* position of the benzoyl group of the cyclopropyl ketone was investigated. An electron-donating substituent decreased the reactivity, and a moderate yield was obtained compared with the substrate with an electron-withdrawing substituent (entries 20–21). When aliphatic ketone **1v** was used, the desired product was formed in 59% yield and 73% *ee* (entry 22). However, the reaction of methyl-substituted cyclopropyl ketone **1w** proceeded sluggishly even at elevated reaction temperatures (entry 23).

Subsequently, a range of primary amines were employed in this transformation. Substituted anilines with electron-rich or electron-deficient substituents at the *meta* or *para* position reacted smoothly with cyclopropyl ketone **1a**, and excellent results were achieved (85–96% *ee*, 85–98% yield; Table 3, entries 1–11). 2-Chloroaniline showed lower reactivity but higher enantioselectivity compared with 2-methoxyaniline (entries 12–13). Notably, cyclopropylamine also underwent the ring-opening reaction, affording the desired product with good enantioselectivity and acceptable yield (87% *ee*, 43% yield; entry 15). On the other hand, aliphatic amines, such as cyclopentanamine, 2-methylpropan-2-amine, and phenylmethanamine, did not provide the desired dihydropyrrole products. Furthermore, when the reaction of cyclopropyl ketone **1a** with aniline **2g** was carried out on a gram scale with 10 mol% of the chiral **L3**/Sc^{III} catalyst, good results were obtained (95% *ee*, 96% yield; entry 6).

Table 3: Variation of the primary amine.[a]



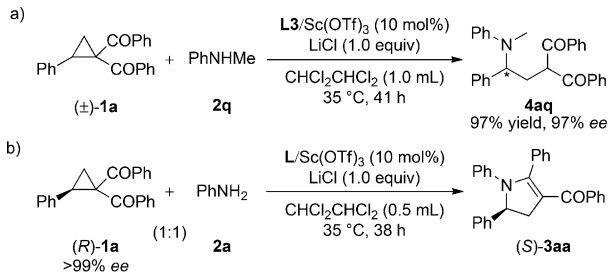
(±)-**1a** **2** **3**

Entry	R^3	Yield[b] [%]	*ee*[c] [%]
1	4-MeC_6H_4 (**2b**)	86 (**3ab**)	92
2	4-$MeOC_6H_4$ (**2c**)	89 (**3ac**)	85
3	4-FC_6H_4 (**2d**)	95 (**3ad**)	90
4	4-ClC_6H_4 (**2e**)	89 (**3ae**)	91
5[d]	4-BrC_6H_4 (**2f**)	85 (**3af**)	96
6[e]	4-$O_2NC_6H_4$ (**2g**)	96 (**3ag**)	95
7	3-MeC_6H_4 (**2h**)	89 (**3ah**)	87
8	3-FC_6H_4 (**2i**)	98 (**3ai**)	90
9	3-ClC_6H_4 (**2j**)	96 (**3aj**)	96
10	3-BrC_6H_4 (**2k**)	85 (**3ak**)	94
11	3-$F_3CC_6H_4$ (**2l**)	96 (**3al**)	95
12	2-$MeOC_6H_4$ (**2m**)	70 (**3am**)	90
13	2-ClC_6H_4 (**2n**)	46 (**3an**)	97
14	3,4-$(MeO)_2C_6H_3$ (**2o**)	81 (**3ao**)	92
15[f]	cyclopropyl (**2p**)	41 (**3ap**)	87

[a] Unless otherwise noted, all reactions were performed with **L3**/$Sc(OTf)_3$ (10 mol%, 1:1), LiCl (1.0 equiv), **1a** (0.4 mmol), and **2** (0.1 mmol) in $CHCl_2CHCl_2$ (1.0 mL) under N_2 atmosphere at 35 °C for 96 h. [b] Yield of isolated product. [c] Determined by HPLC analysis on a chiral stationary phase. [d] The absolute configuration of **3af** was determined to be *R* by X-ray analysis.[14] [e] The reaction was scaled up using **1a** (12.0 mmol) and **2g** (3.0 mmol) in 30.0 mL of $CHCl_2CHCl_2$. [f] Reaction time: 168 h.

Meanwhile, *N*-methylaniline (**2q**) was also subjected to this catalytic system, and the direct ring-opening product **4aq** was obtained with excellent enantioselectivity (97% *ee*) and yield (97%), which indicates that secondary anilines are also suitable nucleophiles (Scheme 1a).

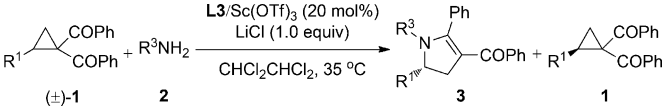
To gain insight into the origin of the enantioselectivity of the ring-opening reaction, we investigated the reaction of aniline (**2a**) and (*R*)-cyclopropane **1a**[14] with both enantiomeric forms of the *N*,*N*′-dioxide/Sc^{III} complex; the reactions were run for the same period of time. The matched reaction of (*R*)-**1a** and **2a** catalyzed by *ent*-**L3** derived from (*R*)-pipecolic acid provided the optically pure product (*S*)-**3aa** (>99% *ee*) in 40% yield. On the contrary, the reaction catalyzed by **L3** derived from (*S*)-pipecolic acid was unmatched, giving (*S*)-**3aa** in 82% *ee* and 9% yield. Therefore, a kinetic resolution process has occurred, and the reaction of (*S*)-**1a** proceeded significantly faster under the standard conditions with the **L3**/Sc^{III} complex catalyst. The *S* enantiomer is activated by the



L: *ent*–**L3**: 41% conv.; **3aa**: 40% yield, 99% *ee*; **1a** (recovered): 59% yield, 96% *ee*
L: **L3**: 9% conv.; **3aa**: 9% yield, 82% *ee*; **1a** (recovered): 87% yield, 99% *ee*

Scheme 1. a) Using a secondary amine as the substrate. b) Control experiments.

Table 4: Kinetic resolution of 2-substituted cyclopropanes with anilines.[a]



(±)-**1** **2** **3** **1**

Entry	**1**	**2**	*T* [h]	**3** Yield[b] [%]	**3** *ee*[c] [%]	**1** Yield[b] [%]	**1** *ee*[c] [%]	*s*[d]
1	**1a**	**2a**	22	51	80	48	85	24
2[e]	**1c**	**2a**	5	52	82	46	91	32
3	**1d**	**2a**	10	53	85	47	90	38
4	**1a**	**2g**	21	53	92	45	95	89
5	**1a**	**2j**	21	54	86	43	95	49

[a] Unless otherwise noted, all reactions were performed with **L3**/$Sc(OTf)_3$ (20 mol%, 1:1), LiCl (1.0 equiv), **1** (0.10 mmol), and **2** (0.30 mmol) in $CHCl_2CHCl_2$ (0.5 mL) under N_2 atmosphere at 35 °C. [b] Yield of isolated product. [c] Determined by HPLC analysis on a chiral stationary phase. [d] $s = \ln[(1-C)(1-ee^1)]/\ln[(1-C)(1+ee^1)]$; $C = ee^1/(ee^3+ee^1)$ where $ee^1 = ee$ of the recovered substrate, $ee^3 = ee$ of the product. [e] **2a** (0.075 mmol).

chiral Lewis acid catalyst. Then, the primary amine nucleophile attacks at the 2-position of the cyclopropane, which is followed by an intramolecular condensation to give the *R*-configured product,[11c,g] leaving predominantly the (*R*)-cyclopropyl ketone behind. However, the slightly decreased enantiopurity of the recovered cyclopropane indicates that some dynamic kinetic resolution might accompany the reaction.[9d,f,i,11b] Moreover, we can exclude that the reaction occurs through imine formation followed by a Cloke rearrangement,[11h,15] as we did not detect any imine intermediate under various conditions that generally benefit the generation of imines.

Consequently, the kinetic resolution of cyclopropyl ketones with amines was studied. When the catalyst loading was increased to 20 mol% and the amount of aniline was varied, the ring-opening/cyclization products **3** were obtained in 80–92% *ee* and 51–54% yield (Table 4, entries 1–5). Meanwhile, the cyclopropyl ketones **1** were recovered in 85–95% *ee* and 43–48 yield. Therefore, this method provides an easy access to both 2,3-dihydropyrroles and cyclopropyl ketones with high enantiopurities.

In conclusion, we have developed an asymmetric catalytic synthesis of chiral 2,4,5-trisubstituted 2,3-dihydropyrroles that proceeds through a ring-opening/cyclization reaction of cyclopropyl ketones with primary amine nucleophiles through a kinetic resolution process. With a chiral *N*,*N*′-dioxide/scandium(III) complex, the reaction provided the desired 2,3-dihydropyrroles in excellent enantioselectivities (up to 97% *ee*) and moderate to excellent yields (up to 98%). This method provides a promising access to chiral 2,3-dihydropyrroles as well as an effective kinetic resolution of 2-substituted cyclopropyl ketones. Further studies will focus on enantioselective ring-opening reactions with other nucleophiles.

Experimental Section

Typical procedure: *N*,*N*′-dioxide **L3** (0.01 mmol, 10 mol%), $Sc(OTf)_3$ (0.01 mmol, 10 mol%), and LiCl (0.10 mmol) were stirred in

$CHCl_2CHCl_2$ (1.0 mL) at 35 °C under N_2 atmosphere for 0.5 h; then **2a** (0.10 mmol) was added. The solution was stirred for 10 min at the same temperature, and then **1a** (0.4 mmol) was added. The mixture was stirred at 35 °C for 96 h. The reaction mixture was purified by flash column chromatography (petroleum ether/ethyl acetate = 4:1) on silica gel to afford the desired product as a yellow solid.

Received: August 2, 2014
Revised: September 8, 2014
Published online: ■■ ■■, ■■■■

Keywords: cyclization · kinetic resolution · *N*,*N*′-dioxides · ring opening · scandium

[1] a) D. E. Thurston, D. S. Bose, *Chem. Rev.* **1994**, *94*, 433 – 465; b) D. Antonow, M. Kaliszczak, G. D. Kang, M. Coffils, A. C. Tiberghien, N. Cooper, T. Barata, S. Heidelberger, C. H. James, M. Zloh, T. C. Jenkins, A. P. Reszka, S. Neidle, S. M. Guichard, D. I. Jodrell, J. A. Hartley, P. W. Howard, D. E. Thurston, *J. Med. Chem.* **2010**, *53*, 2927 – 2941; c) K. M. Rahman, H. Vassoler, C. H. James, D. E. Thurston, *ACS Med. Chem. Lett.* **2010**, *1*, 427 – 432; d) D. Antonow, D. E. Thurston, *Chem. Rev.* **2011**, *111*, 2815 – 2864; e) A. B. Smith III, A. K. Charnley, R. Hirschmann, *Acc. Chem. Res.* **2011**, *44*, 180 – 193; f) K. M. Rahman, C. H. James, T. T. T. Bui, A. F. Drake, D. E. Thurston, *J. Am. Chem. Soc.* **2011**, *133*, 19376 – 19385.

[2] a) E. A. Severino, C. R. D. Correia, *Org. Lett.* **2000**, *2*, 3039 – 3042; b) E. A. Severino, E. R. Costenaro, A. L. L. Garcia, C. R. D. Correia, *Org. Lett.* **2003**, *5*, 305 – 308; c) E. G. Occhiato, C. Prandi, A. Ferrali, A. Guarna, *J. Org. Chem.* **2005**, *70*, 4542 – 4545; d) U. Gross, M. Nieger, S. Bräse, *Org. Lett.* **2009**, *11*, 4740 – 4742.

[3] For selected examples of asymmetric syntheses of 2,5-dihydropyrroles, see: a) Y. Q. Fang, E. N. Jacobsen, *J. Am. Chem. Soc.* **2008**, *130*, 5660 – 5661; b) L. J. Yang, S. Wang, J. Nie, S. Li, J. A. Ma, *Org. Lett.* **2013**, *15*, 5214 – 5217; c) C. E. Henry, Q. Xu, Y. C. Fan, T. J. Martin, L. Belding, T. Dudding, O. Kwon, *J. Am. Chem. Soc.* **2014**, *136*, 11890 – 11893; d) G. Pandey, P. Banerjee, S. R. Gadre, *Chem. Rev.* **2006**, *106*, 4484 – 4517; e) F. Shi, S. W. Luo, Z. L. Tao, L. He, J. Yu, S. J. Tu, L. Z. Gong, *Org. Lett.* **2011**, *13*, 4680 – 4683.

[4] a) F. Ozawa, T. Hayashi, *J. Organomet. Chem.* **1992**, *428*, 267 – 277; b) L. F. Tietze, K. Thede, *Synlett* **2000**, 1470 – 1472; c) T. Tu, X. L. Hou, L. X. Dai, *Org. Lett.* **2003**, *5*, 3651 – 3653; d) C. Wu, J. Zhou, *J. Am. Chem. Soc.* **2014**, *136*, 650 – 652.

[5] R. Kuwano, M. Kashiwabara, M. Ohsumi, H. Kusano, *J. Am. Chem. Soc.* **2008**, *130*, 808 – 809.

[6] a) K. Daidouji, K. Fuchibe, T. Akiyama, *Org. Lett.* **2005**, *7*, 1051 – 1053; b) C. Guo, M. X. Xue, M. K. Zhu, L. Z. Gong, *Angew. Chem. Int. Ed.* **2008**, *47*, 3414 – 3417; *Angew. Chem.* **2008**, *120*, 3462 – 3465.

[7] a) G. Zhang, Y. H. Zhang, X. X. Jiang, W. J. Yan, R. Wang, *Org. Lett.* **2011**, *13*, 3806 – 3809; b) K. Oe, Y. Ohfune, T. Shinada, *Org. Lett.* **2014**, *16*, 2550 – 2553.

[8] For representative reviews, see: a) S. Danishefsky, *Acc. Chem. Res.* **1979**, *12*, 66 – 72; b) H. U. Reissig, R. Zimmer, *Chem. Rev.* **2003**, *103*, 1151 – 1196; c) T. P. Lebold, M. A. Kerr, *Pure Appl. Chem.* **2010**, *82*, 1797 – 1812; d) D. Zhang, H. Song, Y. Qin, *Acc. Chem. Res.* **2011**, *44*, 447 – 457; e) M. A. Cavitt, L. H. Phun, S. France, *Chem. Soc. Rev.* **2014**, *43*, 804 – 818; f) T. F. Schneider, J. Kaschel, D. B. Werz, *Angew. Chem. Int. Ed.* **2014**, *53*, 5504 – 5523; *Angew. Chem.* **2014**, *126*, 5608 – 5628.

[9] For selected examples of [3+2] annulations with enol silyl ethers, see: a) J. P. Qu, C. Deng, J. Zhou, X. L. Sun, Y. Tang, *J. Org. Chem.* **2009**, *74*, 7684 – 7689; b) J. P. Qu, Y. Liang, H. Xu, X. L. Sun, Z. X. Yu, Y. Tang, *Chem. Eur. J.* **2012**, *18*, 2196 – 2201; c) H. Xu, J. P. Qu, S. H. Liao, H. Xiong, Y. Tang, *Angew. Chem. Int. Ed.* **2013**, *52*, 4004 – 4007; *Angew. Chem.* **2013**, *125*, 4096 – 4099; for such transformations with aldehydes, see: d) P. D. Pohlhaus, J. S. Johnson, *J. Am. Chem. Soc.* **2005**, *127*, 16014 – 16015; e) P. D. Pohlhaus, S. D. Sanders, A. T. Parsons, W. Li, J. S. Johnson, *J. Am. Chem. Soc.* **2008**, *130*, 8642 – 8650; f) A. T. Parsons, J. S. Johnson, *J. Am. Chem. Soc.* **2009**, *131*, 3122 – 3123; g) S. Y. Xing, W. Y. Pan, C. Liu, J. Ren, Z. W. Wang, *Angew. Chem. Int. Ed.* **2010**, *49*, 3215 – 3218; *Angew. Chem.* **2010**, *122*, 3283 – 3286; with aldimines, see: h) S. K. Jackson, A. Karadeolian, A. B. Driega, M. A. Kerr, *J. Am. Chem. Soc.* **2008**, *130*, 4196 – 4201; i) A. T. Parsons, A. G. Smith, A. J. Neel, J. S. Johnson, *J. Am. Chem. Soc.* **2010**, *132*, 9688 – 9692; with indoles, see: j) D. B. England, T. D. O. Kuss, R. G. Keddy, M. A. Kerr, *J. Org. Chem.* **2001**, *66*, 4704 – 4709; k) H. Xiong, H. Xu, S. H. Liao, Z. W. Xie, Y. Tang, *J. Am. Chem. Soc.* **2013**, *135*, 7851 – 7854; l) J. Zhu, Y. Liang, L. J. Wang, Z. B. Zheng, K. N. Houk, Y. Tang, *J. Am. Chem. Soc.* **2014**, *136*, 6900 – 6903.

[10] For selected examples of [3+3] annulations with aromatic azomethine imines, see: a) C. Perreault, S. R. Goudreau, L. E. Zimmer, A. B. Charette, *Org. Lett.* **2008**, *10*, 689 – 692; b) Y. Y. Zhou, J. Li, L. Ling, S. H. Liao, X. L. Sun, Y. X. Li, L. J. Wang, Y. Tang, *Angew. Chem. Int. Ed.* **2013**, *52*, 1452 – 1456; *Angew. Chem.* **2013**, *125*, 1492 – 1496; for such transformations with nitrones, see: c) I. S. Young, M. A. Kerr, *Angew. Chem. Int. Ed.* **2003**, *42*, 3023 – 3026; *Angew. Chem.* **2003**, *115*, 3131 – 3134; d) M. P. Sibi, Z. H. Ma, C. P. Jasperse, *J. Am. Chem. Soc.* **2005**, *127*, 5764 – 5765; e) Y. B. Kang, X. L. Sun, Y. Tang, *Angew. Chem. Int. Ed.* **2007**, *46*, 3918 – 3921; *Angew. Chem.* **2007**, *119*, 3992 – 3995; f) D. A. Dias, M. A. Kerr, *Org. Lett.* **2009**, *11*, 3694 – 3697; g) W. J. Humenny, P. Kyriacou, K. Sapeta, A. Karadeolian, M. A. Kerr, *Angew. Chem. Int. Ed.* **2012**, *51*, 11088 – 11091; *Angew. Chem.* **2012**, *124*, 11250 – 11253.

[11] For selected examples of ring-opening reactions with indoles, see: a) M. R. Emmett, M. A. Kerr, *Org. Lett.* **2011**, *13*, 4180 – 4183; b) S. M. Wales, M. M. Walker, J. S. Johnson, *Org. Lett.* **2013**, *15*, 2558 – 2561; for such transformations with amines, see: c) R. P. Wurz, A. B. Charette, *Org. Lett.* **2005**, *7*, 2313 – 2316; d) O. Lifchits, A. B. Charette, *Org. Lett.* **2008**, *10*, 2809 – 2812; e) S. S. So, T. J. Auvil, V. J. Garza, A. E. Mattson, *Org. Lett.* **2012**, *14*, 444 – 447; f) Y. Y. Zhou, L. J. Wang, J. Li, X. L. Sun, Y. Tang, *J. Am. Chem. Soc.* **2012**, *134*, 9066 – 9069; g) M. C. Martin, D. V. Patil, S. France, *J. Org. Chem.* **2014**, *79*, 3030 – 3039; h) H. Nambu, M. Fukumoto, W. Hirota, T. Yakura, *Org. Lett.* **2014**, *16*, 4012 – 4015; with sodium azide, see: i) M. R. Emmett, H. K. Grover, M. A. Kerr, *J. Org. Chem.* **2012**, *77*, 6634 – 6637.

[12] a) X. H. Liu, L. L. Lin, X. M. Feng, *Acc. Chem. Res.* **2011**, *44*, 574 – 587; b) X. H. Liu, L. L. Lin, X. M. Feng, *Org. Chem. Front.* **2014**, *1*, 298 – 302; c) W. L. Chen, L. L. Lin, Y. F. Cai, Y. Xia, W. D. Cao, X. L. Liu, X. M. Feng, *Chem. Commun.* **2014**, *50*, 2161 – 2163; d) W. L. Chen, X. Fu, L. L. Lin, X. Yuan, W. W. Luo, J. H. Feng, X. H. Liu, X. M. Feng, *Chem. Commun.* **2014**, *50*, 11480 – 11483; e) M. S. Xie, X. X. Wu, G. Wang, L. L. Lin, X. M. Feng, *Acta Chim. Sinica* **2014**, *72*, 856 – 861.

[13] Using $ScCl_3 \cdot 6H_2O$ as the metal salt instead of $Sc(OTf)_3$ and no LiCl resulted in similar outcomes (65% yield, 95% *ee*). Thus, LiCl acts as a promoter for counterion exchange.

[14] The absolute configuration of the recovered **1a** was determined by comparing the circular-dichroism spectrum with that of **1i**. CCDC 1013667 (**3af**) and CCDC 1013674 (**1i**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

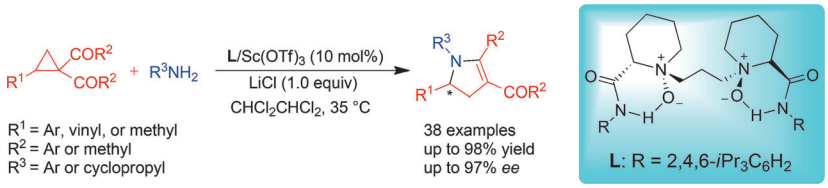
[15] I. Jabin, N. Monnier-Benoit, S. L. Gac, P. Netchitaïlo, *Tetrahedron Lett.* **2003**, *44*, 611 – 614.

Communications

Asymmetric Catalysis

Y. Xia, X. H. Liu,* H. F. Zheng, L. L. Lin, X. M. Feng* ——— ■■■■–■■■■

Asymmetric Synthesis of 2,3-Dihydropyrroles by Ring-Opening/Cyclization of Cyclopropyl Ketones Using Primary Amines



2,3-Dihydropyrroles are obtained in high yields and enantioselectivities through an enantioselective ring-opening/cyclization reaction of substituted cyclopropyl ketones with primary amine nucleophiles under mild reaction conditions. This method also provides an effective procedure for the kinetic resolution of2-substituted cyclopropyl ketones.