Asymmetric Catalysis

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Catalytic Asymmetric Intramolecular Homologation of Ketones with α-Diazoesters: Synthesis of Cyclic α-Aryl/Alkyl β-Ketoesters**

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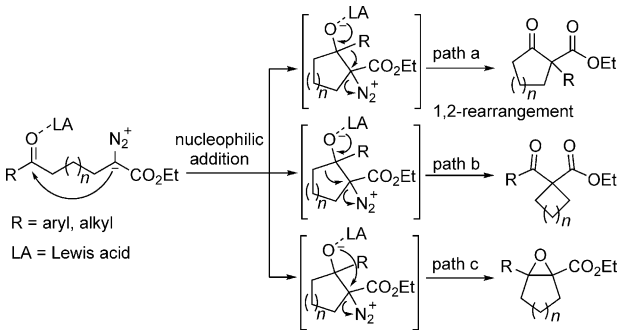
Abstract: *A catalytic asymmetric intramolecular homologation of simple ketones with α-diazoesters was firstly accomplished with a chiral N,N′-dioxide–Sc(OTf)$_3$ complex. This method provides an efficient access to chiral cyclic α-aryl/alkyl β-ketoesters containing an all-carbon quaternary stereocenter. Under mild conditions, a variety of aryl- and alkyl-substituted ketone groups reacted with α-diazoester groups smoothly through an intramolecular addition/rearrangement process, producing the β-ketoesters in high yield and enantiomeric excess.*

Lewis acid-catalyzed homologation of carbonyl compounds using α-diazoesters has become a popular and efficient method to achieve one-carbon unit insertion at the α-position of the carbonyl, thus synthesizing useful β-ketoesters (also known as a semipinacol rearrangement of in situ-formed α-diazo alcohols).[1–3] Particularly, chemists have applied this methodology to natural product synthesis.[4,5] In contrast, the asymmetric variation, which can directly introduce a chiral tertiary or quaternary stereocenter into the carbonyl compounds to get optically active molecules, has received much less attention so far. Examples of catalytic asymmetric Roskamp reaction (also known as Roskamp–Feng reaction) with aromatic and aliphatic aldehydes have recently been reported.[6] Enantioselective ring expansions of cyclohexanones[7] and isatins[8a] with diazo compounds could give access to seven-membered rings and 2-quinolone derivatives, respectively. Activated α-ketoesters underwent asymmetric intermolecular homologation to afford succinate derivatives with chiral quaternary centers.[8b] However, asymmetric homologation reactions involving unactivated acyclic ketones still remain an unsolved challenge; besides, no intramolecular asymmetric version has ever been achieved. The main reasons are low reactivity, complicated regiochemistry, and difficult stereocontrol for such ketones.[1]

Chiral cyclic β-ketoesters with an α-aryl/alkyl group are useful building blocks with the potential for diverse manipulations.[9] In contrast to numerous routes to chiral cyclic α-alkyl β-ketoesters,[9a,b] alternative strategies for the catalytic enantioselective construction of cyclic α-aryl β-ketoesters are much less developed and mainly based on C-acylations of silyl ketene acetals[10] and S_NAr reactions of β-ketoesters with activated aromatic compounds.[11] In connection to our work on the homologation reactions of carbonyl compounds with α-diazoesters,[6b,8] we envisioned that this framework can be achieved by designing a Lewis acid-catalyzed asymmetric intramolecular homologation of simple ketones and α-diazoesters through an addition/1,2-rearrangement process (Scheme 1, path a). This methodology would be more interesting because it leads to a catalytic construction of a chiral all-carbon quaternary stereocenter, which is a difficult challenge in asymmetric catalysis.[12] Nevertheless, complex regiochemical questions arise in this addition/rearrangement reaction, because there are at least two side-migration patterns of 1,2-alkyl shift (Scheme 1, path b) and epoxidation (Scheme 1, path c),[1,8] not to mention the difficulties on reactivity and enantioselectivity. We thought that a good design of the substrate structure as well as a suitable choice of the catalytic system will overcome these problems. Herein we reported the first asymmetric intramolecular homologation of simple ketones and α-diazoesters by a chiral *N*,*N*′-dioxide–Sc(OTf)$_3$ complex.[13]



Scheme 1. Regiochemistry of the intramolecular homologation.

With this idea in mind, we synthesized 2-diazo-6-ketoalkanoate **1a** containing both an α-diazoester group and a simple ketone group. Fortunately, in the presence of chiral *N*,*N*′-dioxide **L1**–Sc(OTf)$_3$ catalyst, the intramolecular reaction occurred through an asymmetric nucleophilic addition/1,2-aryl-shift route, giving cyclic α-phenyl-β-ketoester **2a** with a newly formed chiral all-carbon quaternary center in 83% yield and 92% *ee* (Table 1, entry 1). Other metal salts were also evaluated, but the results did not improve (entries 2–4). Next, we studied the effect of the chiral *N*,*N*′-dioxide ligands.

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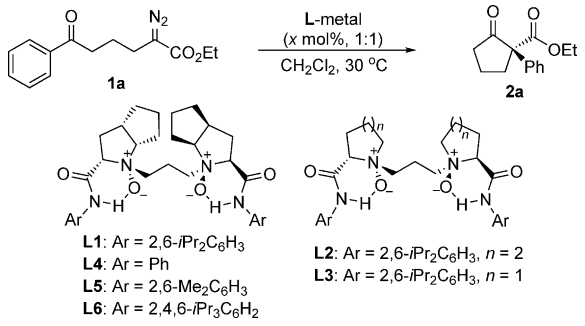
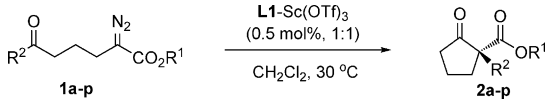
Table 1: Optimization of the reaction conditions.[a]



Entry	Ligand	Metal	*x*	t [h]	Yield [%][b]	*ee* [%][c]
1	**L1**	$Sc(OTf)_3$	10	3	83	92
2	**L1**	$Sn(OTf)_2$	10	10	33	5
3	**L1**	$Y(OTf)_3$	10	48	trace	n.d.
4	**L1**	$Yb(OTf)_3$	10	72	30	62
5	**L2**	$Sc(OTf)_3$	10	3	83	67
6	**L3**	$Sc(OTf)_3$	10	1.5	83	90
7	**L4**	$Sc(OTf)_3$	10	20	82	33
8	**L5**	$Sc(OTf)_3$	10	15	68	58
9	**L6**	$Sc(OTf)_3$	10	3	60	0
10[d]	**L1**	$Sc(OTf)_3$	0.5	5	81	93

[a] Reactions were performed with L–metal (*x* mol%, 1:1), **1a** (0.1 mmol) in 0.5 mL of CH_2Cl_2 at 30 °C. [b] Yield of the isolated product. [c] Determined by HPLC on a chiral stationary phase. [d] **L1**–$Sc(OTf)_3$ (0.5 mol%, 1:1), **1a** (0.2 mmol) in 1.0 mL of CH_2Cl_2. n.d. = not detectable.

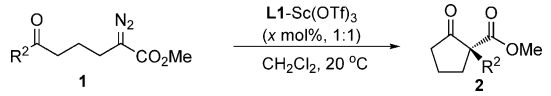
Table 2: Scope of ester and aromatic ketone groups.[a]



Entry	R^1	R^2	*t* [h]	Yield [%][b]	*ee* [%][c]
1	Et	Ph (**1a**)	5	81 (**2a**)	93
2[d]	Me	Ph (**1b**)	5	86 (**2b**)	95 (*S*)
3	*t*Bu	Ph (**1c**)	15	63 (**2c**)	92
4	Me	3-MeC_6H_4 (**1d**)	18	84 (**2d**)	96
5	Me	3-$MeOC_6H_4$ (**1e**)	15	88 (**2e**)	96
6	Me	3-$CH_2{=}CHC_6H_4$ (**1f**)	12	82 (**2f**)	95
7	Me	4-MeC_6H_4 (**1g**)	18	86 (**2g**)	92
8	Me	4-*t*BuC_6H_4 (**1h**)	6	88 (**2h**)	94
9	Me	4-$MeOC_6H_4$ (**1i**)	44	96 (**2i**)	92
10	Me	4-FC_6H_4 (**1j**)	18	85 (**2j**)	91
11	Me	4-ClC_6H_4 (**1k**)	15	85 (**2k**)	93
12	Me	4-BrC_6H_4 (**1l**)	18	80 (**2l**)	93
13	Me	3,5-$Me_2C_6H_3$ (**1m**)	20	65 (**2m**)	92
14	Me	2-naphthyl (**1n**)	12	87 (**2n**)	95
15	Me	2-furyl (**1o**)	20	95 (**2o**)	84
16	Me	2-thienyl (**1p**)	40	93 (**2p**)	80

[a] Reactions were performed with **1** (0.2 mmol), **L1**–$Sc(OTf)_3$ (0.5 mol%, 1:1), in 1.0 mL of CH_2Cl_2 at 30 °C. [b] Yield of isolated products. [c] Determined by HPLC on a chiral stationary phase. [d] The absolute configuration of **2b** was determined to be *S* by X-ray crystallographic analysis of the corresponding hydrazone (for details, see SI).

Table 3: Scope of aliphatic ketone groups.[a]



Entry	R^2	*x*	*t* [h]	Yield [%][b]	*ee* [%][c]
1[d]	Me (**1q**)	0.05	0.25	80 (**2q**)	66 (*R*)
2	*n*Bu (**1r**)	0.5	2	94 (**2r**)	86
3	*n*-hexyl (**1s**)	0.5	3	89 (**2s**)	85
4	cyclopropyl (**1t**)	2	8	92 (**2t**)	54
5	*t*Bu (**1u**)	10	24	0	–

[a] Reactions were performed with **1** (0.2 mmol), **L1**–$Sc(OTf)_3$ (*x* mol%, 1:1), in 1.0 mL of CH_2Cl_2 at 20 °C. [b] Yield of isolated products. [c] Determined by HPLC on a chiral stationary phase. [d] The absolute configuration was determined by comparing the optical rotation data to known literature values.

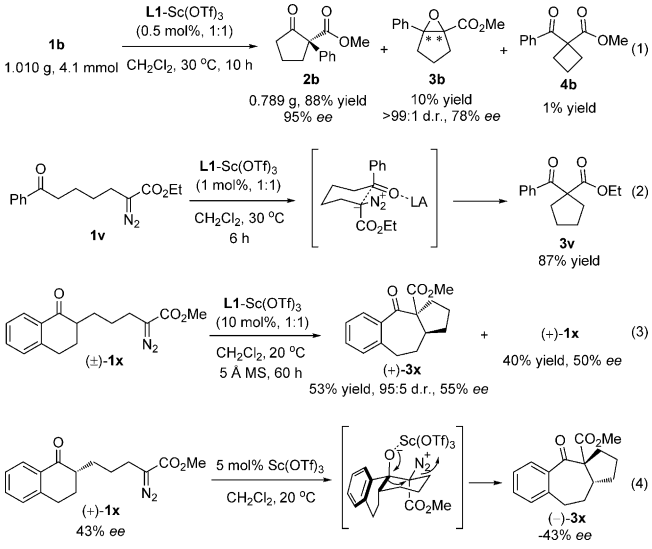
Upon changing the amino acid backbone, ligand **L2** derived from L-pipecolic acid afforded **2a** in 83% yield and 67% *ee* (entry 5), whereas L-proline-derived *N*,*N*′-dioxide **L3** gave **2a** in 83% yield and 90% *ee* (entry 6). Steric hindrance on the amide of the *N*,*N*′-dioxide ligand influences the reaction results greatly. Introducing bulky groups in the 2,6-position of the aniline benefited the enantioselectivity (entries 7 and 8 versus entry 1). However, racemic product was obtained when the steric hindrance at the *para*-position of the aniline was increased (entry 9). Remarkably, the catalyst loading could be reduced to 0.5 mol%, giving the similar enantioselectivity and yield (entry 10). In addition, the reaction did not have to be conducted under an inert atmosphere, and was unaffected by moisture and oxygen.

With the optimized conditions in hand (Table 1, entry 10), we examined the substrate generality of the reaction as shown in Table 2. Varying the ester group affected the enantioselectivity slightly. Meanwhile, the methyl ester gave better yield than the ethyl and *tert*-butyl ester (Table 2, entries 1–3). These results indicate that enhancing the steric hindrance on the ester group hampers the yield. The influence of position and electronic nature of substituents on the phenyl group was investigated. Almost all substrates with a substituent on the *meta*- or *para*-position of the phenyl group provided the β-ketoesters in excellent enantioselectivities (91–96% *ee*) and good yields (80–96%; entries 4–12). Particularly, a 96% yield was obtained when 4-$MeOC_6H_4$-substituted benzoyl group was employed, owing to the excellent regioselectivity of the transformation. Disubstituted substrate **1m** gave 92% *ee*, albeit with a lower yield (entry 13). Notably, condensed-ring and heteroaromatic ketone substrates were tolerated under the current system, producing the corresponding products with excellent yields and high *ee* values (entries 14–16).

We then explored the substrate scope of aliphatic ketones as shown in Table 3. Remarkably, the catalyst loading could even be reduced to 0.05 mol% with methyl-substituted substrate **1q** (Table 3, entry 1). The reaction was completed within 15 min, affording the product **2q** in 80% yield but only 66% *ee* for the (*R*)-isomer.[14] No obvious improvement of the enantioselectivity of **2q** was observed at a lower reaction temperature (−20 °C). Extending the alkyl length of the acyl group improved the results (entries 2 and 3). Secondary alkyl group was also tested and 92% yield and a moderate *ee* were obtained (entry 4). However, the *tert*-butyl group did not

show reactivity in this intramolecular homologation reaction (entry 5). This might be due to steric hindrance of the *tert*-butyl group inhibiting the nucleophilic addition of the diazoester. The electronic nature of the benzoyl substituent also affected the rate of the reaction, which was shown for ketone **1i** bearing an electron-donating 4-OMe group (Table 2, entry 9). The conversion of **1i** requires more time than other benzoyl substituted substrates. On the other hand, the intermolecular reaction of acetophenone and methyl 2-diazopropanoate gives no homologation product in the presence of 10 mol% **L1**–$Sc(OTf)_3$ (see the Supporting Information, SI). These experiments indicate that the first nucleophilic addition step is most likely the rate-limiting step for this homologation reaction.[15]

To demonstrate the utility of this process, the intramolecular homologation of **1b** was performed on a gram scale, furnishing the major product **2b** in 88% yield and 95% *ee* [Eq. (1) in Scheme 2]. Meanwhile, tetrasubstituted epoxide



Scheme 2. Scaled-up version of the asymmetric intramolecular homologation and the influence of the length of the tethering carbon-chain.

3b, formed through the attack of an oxygen anion, was obtained in 10% yield, >99:1 d.r., and 78% *ee*. Only 1% yield of the four-membered cyclic by-product **4b**, formed through an 1,2-alkyl migration, was obtained. Thus the detailed regioselectivity of the model reaction is 88:10:1. Next, the effect of the length of the carbon-chain tethering the α-diazoester and benzoyl group was probed. 2-Diazo-7-keto alkanoate **1v** dominantly reacted in an 1,2-alkyl migration pattern instead of 1,2-aryl shift [Eq. (2) in Scheme 2], giving the five-membered ring product **3v** in 87% yield. This process was likely controlled by stereoelectronic effects.[16,17] When the number of linking carbon units was further increased, no reaction occurred (see ethyl 2-diazo-8-oxo-8-phenyloctanoate in the SI). Additionally, a moderate kinetic resolution was observed with the racemic substrate **1x**. It underwent a highly diastereoselective addition/1,2-alkyl shift reaction, providing the desired product **3x** containing the octahydroazulen-4(1*H*)-one backbone, which is found in various synthetic intermediates and natural products [Eq. (3) in Scheme 2].[18] (+)-**1x** (43% *ee*) was converted to (−)-**3x** with −43% *ee* in the presence of $Sc(OTf)_3$ [Eq. (4) in Scheme 2]. The chirality of the rearranged group was maintained and no racemization of the substrate occurred in the process. Therefore, the intramolecular addition is diastereoselective and positions the alkyl group and the diazo moiety in an anti-periplanar relationship thus keeping the chirality unchanged following 1,2-migration.

In summary, we have realized the first intramolecular homologation of simple ketones with α-diazoesters. With a low loading of chiral *N*,*N*′-dioxide-scandium(III) catalyst, the intramolecular reaction performed well with a series of substrates, affording the corresponding cyclic β-ketoesters regioselectively with up to 96% yield and up to 96% *ee* under mild reaction conditions. Influence of various aromatic and aliphatic ketone groups as well as the linking-carbon-chain length were investigated. This methodology provides a novel and efficient method for the construction of α-aryl/alkyl-substituted 2-oxocyclopentanecarboxylates with a chiral all-carbon quaternary center. Further studies on related reactions are underway.

Experimental Section

200 μL of **L1**–$Sc(OTf)_3$ catalyst solution (0.005 M in THF) was added to a dry reaction tube. After removing THF in vacuum, CH_2Cl_2 (1.0 mL) were added, and the mixture was stirred at 30 °C for 0.5 h. Then, substrate **1** (0.20 mmol) was added, and the reaction was stirred at 30 °C for the indicated time. The crude mixture was purified by flash chromatography on silica gel (petroleum ether/dichloromethane/ethyl acetate = 20:2:1) to afford the desired product **2**.

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[1] For reviews, see: a) C. D. Gutsche, *Org. React.* **1954**, *8*, 364–429; b) T. Ye, M. A. McKervey, *Chem. Rev.* **1994**, *94*, 1091–1160; c) M. P. Doyle, M. A. McKervey, T. Ye, *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*, Wiley, New York, **1998**; d) Z. Zhang, J. Wang, *Tetrahedron* **2008**, *64*, 6577–6605; e) Y. Zhang, J. Wang, *Chem. Commun.* **2009**, 5350–5361; f) T. Hashimoto, K. Maruoka, *Bull. Chem. Soc. Jpn.* **2013**, *86*, 1217–1230; g) S.-H. Wang, B.-S. Li, Y.-Q. Tu, *Chem. Commun.* **2014**, *50*, 2393–2408; h) D. C. Moebius, V. L. Rendina, J. S. Kingsbury, *Top. Curr. Chem.* **2014**, *346*, 111–162.

[2] For recent examples of the Roskamp reaction with aldehydes and diazo compounds, see: a) C. R. Holmquist, E. J. Roskamp, *J. Org. Chem.* **1989**, *54*, 3258–3260; b) H. E. Bartrum, D. C. Blakemore, C. J. Moody, C. J. Hayes, *J. Org. Chem.* **2010**, *75*, 8674–8676; c) B. Morandi, E. M. Carreira, *Angew. Chem. Int. Ed.* **2011**, *50*, 9085–9088; *Angew. Chem.* **2011**, *123*, 9251–9254; d) Y. Xia, P. Qu, Z. Liu, R. Ge, Q. Xiao, Y. Zhang, J. Wang, *Angew. Chem. Int. Ed.* **2013**, *52*, 2543–2546; *Angew. Chem.* **2013**, *125*, 2603–2606; e) A. J. Wommack, J. S. Kingsbury, *J. Org. Chem.* **2013**, *78*, 10573–10587; f) D. M. Allwood, D. C. Blakemore, S. V. Ley, *Org. Lett.* **2014**, *16*, 3064–3067.

[3] For recent examples of ketone homologation reactions with diazo compounds, see: a) D. C. Moebius, J. S. Kingsbury, *J. Am. Chem. Soc.* **2009**, *131*, 878 – 879; b) J. A. Dabrowski, D. C. Moebius, A. J. Wommack, A. F. Kornahrens, J. S. Kingsbury, *Org. Lett.* **2010**, *12*, 3598 – 3601; c) T. Hashimoto, Y. Naganawa, K. Maruoka, *J. Am. Chem. Soc.* **2009**, *131*, 6614 – 6617; d) T. Hashimoto, Y. Naganawa, K. Maruoka, *Chem. Commun.* **2010**, *46*, 6810 – 6812; e) A. Gioiello, F. Venturoni, M. Marinozzi, B. Natalini, R. Pellicciari, *J. Org. Chem.* **2011**, *76*, 7431 – 7437; f) B. Alcaide, P. Almendros, C. Aragoncillo, G. Gómez-Campillos, M. Arnó, L. R. Domingo, *ChemPlusChem* **2012**, *77*, 563 – 569; and Ref. [2c].

[4] For recent examples of the Roskamp reaction in natural product synthesis, see: a) D. A. Evans, D. J. Adams, *J. Am. Chem. Soc.* **2007**, *129*, 1048 – 1049; b) J. Toueg, J. Prunet, *Org. Lett.* **2008**, *10*, 45 – 48; c) J. A. Marshall, P. M. Eidam, *Org. Lett.* **2008**, *10*, 93 – 96; d) K. L. Jackson, J. A. Henderson, H. Motoyoshi, A. J. Phillips, *Angew. Chem. Int. Ed.* **2009**, *48*, 2346 – 2350; *Angew. Chem.* **2009**, *121*, 2382 – 2386; e) J. Li, J. M. Suh, E. Chin, *Org. Lett.* **2010**, *12*, 4712 – 4715; f) G. Kumaraswamy, N. Jayaprakash, *Tetrahedron Lett.* **2010**, *51*, 6500 – 6502; g) H. Xue, J. Yang, P. Gopal, *Org. Lett.* **2011**, *13*, 5696 – 5699; h) M. Iqbal, R. J. G. Black, J. Winn, A. T. Reeder, A. J. Blake, P. A. Clarke, *Org. Biomol. Chem.* **2011**, *9*, 5062 – 5078; i) J. Yin, C. Wang, L. Kong, S. Cai, S. Gao, *Angew. Chem. Int. Ed.* **2012**, *51*, 7786 – 7789; *Angew. Chem.* **2012**, *124*, 7906 – 7909; j) D. A. Evans, D. J. Adams, E. E. Kwan, *J. Am. Chem. Soc.* **2012**, *134*, 8162 – 8170; k) J. S. Yadav, A. Haldar, T. Maity, *Eur. J. Org. Chem.* **2013**, 3076 – 3085; l) W. P. Unsworth, K. A. Gallagher, M. Jean, J. P. Schmidt, L. J. Diorazio, R. J. K. Taylor, *Org. Lett.* **2013**, *15*, 262 – 265; m) A. J. Catino, A. Sherlock, P. Shieh, J. S. Wzorek, D. A. Evans, *Org. Lett.* **2013**, *15*, 3330 – 3333.

[5] Z.-L. Song, C.-A. Fan, Y.-Q. Tu, *Chem. Rev.* **2011**, *111*, 7523 – 7556, and references therein.

[6] a) T. Hashimoto, H. Miyamoto, Y. Naganawa, K. Maruoka, *J. Am. Chem. Soc.* **2009**, *131*, 11280 – 11281; b) W. Li, J. Wang, X. L. Hu, K. Shen, W. T. Wang, Y. Y. Chu, L. L. Lin, X. H. Liu, X. M. Feng, *J. Am. Chem. Soc.* **2010**, *132*, 8532 – 8533; c) A. Hassner, I. Namboothiri in *Organic Syntheses Based on Name Reactions*, *3th ed.*, Elsevier, Oxford, **2011**, p. 408; d) L. Gao, B. C. Kang, G.-S. Hwang, D. H. Ryu, *Angew. Chem. Int. Ed.* **2012**, *51*, 8322 – 8325; *Angew. Chem.* **2012**, *124*, 8447 – 8450; for related regioselective examples, see: e) T. Hashimoto, Y. Naganawa, K. Maruoka, *J. Am. Chem. Soc.* **2008**, *130*, 2434 – 2435; f) L. Gao, B. C. Kang, D. H. Ryu, *J. Am. Chem. Soc.* **2013**, *135*, 14556 – 14559.

[7] a) T. Hashimoto, Y. Naganawa, K. Maruoka, *J. Am. Chem. Soc.* **2011**, *133*, 8834 – 8837; b) V. L. Rendina, D. C. Moebius, J. S. Kingsbury, *Org. Lett.* **2011**, *13*, 2004 – 2007.

[8] a) W. Li, X. H. Liu, X. Y. Hao, Y. F. Cai, L. L. Lin, X. M. Feng, *Angew. Chem. Int. Ed.* **2012**, *51*, 8644 – 8647; *Angew. Chem.* **2012**, *124*, 8772 – 8775; b) W. Li, X. H. Liu, F. Tan, X. Y. Hao, J. F. Zheng, L. L. Lin, X. M. Feng, *Angew. Chem. Int. Ed.* **2013**, *52*, 10883 – 10886; *Angew. Chem.* **2013**, *125*, 11083 – 11086; for a related example, see: c) W. Li, X. H. Liu, X. Y. Hao, X. L. Hu, Y. Y. Chu, W. D. Cao, S. Qin, C. W. Hu, L. L. Lin, X. M. Feng, *J. Am. Chem. Soc.* **2011**, *133*, 15268 – 15271.

[9] For selected reviews, see: a) B. M. Trost, M. L. Crawley, *Chem. Rev.* **2003**, *103*, 2921 – 2943; b) S. Shirakawa, K. Maruoka, *Angew. Chem. Int. Ed.* **2013**, *52*, 4312 – 4348; *Angew. Chem.* **2013**, *125*, 4408 – 4445; c) F. Bellina, R. Rossi, *Chem. Rev.* **2010**, *110*, 1082 – 1146.

[10] a) A. H. Mermerian, G. C. Fu, *J. Am. Chem. Soc.* **2003**, *125*, 4050 – 4051; b) A. H. Mermerian, G. C. Fu, *J. Am. Chem. Soc.* **2005**, *127*, 5604 – 5607; c) P. A. Woods, L. C. Morrill, R. A. Bragg, A. D. Smith, *Chem. Eur. J.* **2011**, *17*, 11060 – 11067; d) J. A. Birrell, J.-N. Desrosiers, E. N. Jacobsen, *J. Am. Chem. Soc.* **2011**, *133*, 13872 – 13875.

[11] a) M. Bella, S. Kobbelgaard, K. A. Jørgensen, *J. Am. Chem. Soc.* **2005**, *127*, 3670 – 3671; b) J. Alemán, B. Richter, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2007**, *46*, 5515 – 5519; *Angew. Chem.* **2007**, *119*, 5611 – 5615.

[12] For selected reviews on the construction of all-carbon quaternary stereocenters, see: a) K. Fuji, *Chem. Rev.* **1993**, *93*, 2037 – 2066; b) E. J. Corey, A. Guzman-Perez, *Angew. Chem. Int. Ed.* **1998**, *37*, 388 – 401; *Angew. Chem.* **1998**, *110*, 402 – 415; c) C. J. Douglas, L. E. Overman, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5363 – 5367; d) B. M. Trost, C. Jiang, *Synthesis* **2006**, 369 – 396; e) A. Y. Hong, B. M. Stoltz, *Eur. J. Org. Chem.* **2013**, 2745 – 2759.

[13] For reviews of chiral *N,N′*-dioxide-scandium(III), see: a) X. H. Liu, L. L. Lin, X. M. Feng, *Org. Chem. Front.* **2014**, *1*, 298 – 302; b) X. H. Liu, L. L. Lin, X. M. Feng, *Acc. Chem. Res.* **2011**, *44*, 574 – 587; c) "Chiral Scandium Complexes in Catalytic Asymmetric Reactions": X. M. Feng, X. H. Liu, *Scandium: Compounds, Productions and Applications* (Ed.: V. A. Greene), Nova Science, New York, **2011**, pp. 1 – 48.

[14] P. V. Ramachandran, G.-M. Chen, H. C. Brown, *J. Org. Chem.* **1996**, *61*, 88 – 94.

[15] The influence of the steric and electronic effect on the reactivity is consistent with the nature of the first nucleophilic addition. However, more studies are needed to unambiguously establish the reaction mechanism.

[16] A small amount of 1,2-aryl-shift byproduct and the epoxide could be detected by NMR and HRMS analysis.

[17] P. Deslongchamps, *Stereoelectronic Effects in Organic Chemistry*, Pergamon, New York, **1983**.

[18] For recent examples, see: a) A. Vasas, J. Hohmann, *Chem. Rev.* **2014**, *114*, 8579 – 8612; b) A. C. Jones, J. A. May, R. Sarpong, B. M. Stoltz, *Angew. Chem. Int. Ed.* **2014**, *53*, 2556 – 2591; *Angew. Chem.* **2014**, *126*, 2590 – 2628; c) S. J. McKerrall, L. Jørgensen, C. A. Kuttruff, F. Ungeheuer, P. S. Baran, *J. Am. Chem. Soc.* **2014**, *136*, 5799 – 5810.

