Asymmetric Catalysis

DOI: 10.1002/anie.201304561

Switchable Diastereoselectivity in Enantioselective [4+2] Cycloadditions with Simple Olefins by Asymmetric Binary Acid Catalysis**

Jian Lv, Long Zhang, Sanzhong Luo, and Jin-Pei Cheng*

Chiral 3,4-dihydro-2*H*-pyrans and tetrahydropyrans are versatile structural motifs of a number of bioactive natural products (e.g. epicalyxin F and sugiresinol),[1,2] fragrances (doremox),[3] and foodstuff flavorings (Figure 1).[4] A straightforward approach to access this type of products is the catalytic asymmetric inverse-electron-demand Diels–Alder reaction between α,β-unsaturated carbonyl compounds and alkenes.[5–8] Though extensively explored in asymmetric catalysis,[9] this reaction has been limited to electron-rich alkenes, such as enol ethers, enamines, and cyclopentadienes.[10] Reactions with electronically unbiased simple alkenes would give the illustrated compounds directly (Figure 1), but have been rather unsuccessful. In fact, as a consequence of the intrinsic electronic/orbital constraints, intermolecular Diels–Alder reactions with simple olefins are generally difficult to achieve and require harsh conditions and long reaction times.[11] Hence, achieving a catalytic asymmetric version of the reaction with simple olefins remains elusive, despite the tremendous advances in Diels–Alder chemistry.

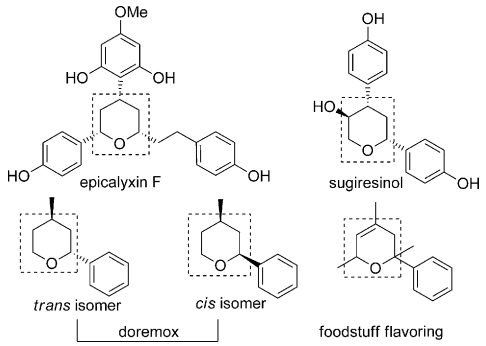
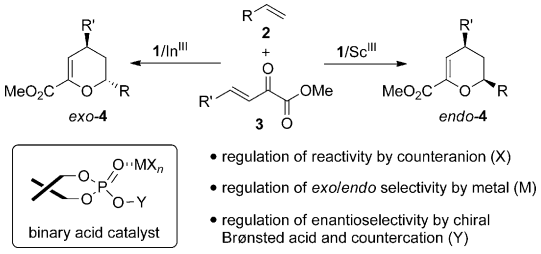


Figure 1. Examples of chiral tetrahydropyran derivatives in bioactive compounds.

This is also true for inverse-electron-demand Diels–Alder reactions, for which asymmetric catalysis with simple olefins has not been achieved so far.[9n,12]

We describe herein an asymmetric hetero-Diels–Alder reaction of simple olefins with electron-deficient enones (e.g. β,γ-unsaturated α-ketoesters **3**). The reaction is mediated by a chiral binary acid complex that synergistically combines a chiral phosphoric acid[13] with a metal salt (In^{III} or Sc^{III}; Scheme 1).[14] Interestingly, simply using a different metal



Scheme 1. Diastereoselective and enantioselective [4+2] cycloaddition.

center can lead to either the *endo* or the *exo* adduct with good diastereo- and enantioselectivity. This catalyst-dependent diastereoselectivity is quite unexpected, because Diels–Alder reactions tend to be *endo*-selective as a consequence of orbital constraints,[15] and substrate-independent diastereoselectivity remains a challenging issue in Diels–Alder reactions, particularly in the context of asymmetric catalysis.[16,17]

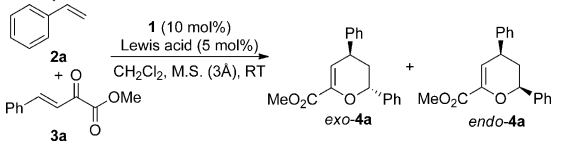
Previously, we have developed *endo*-selective and enantioselective hetero-Diels–Alder reactions of cyclopentadienes catalyzed by a unique binary acid **1a**/$InBr_3$.[18–20] Taking advantage of the synergistic feature as well as the combinatorial flexibility,[21] we tested this binary acid catalysis in reactions with simple olefins such as styrenes. Unfortunately, when styrene **2a** was employed instead of cyclopentadienes in the reaction catalyzed by **1a**/$InBr_3$, no reaction was observed under otherwise identical conditions, not even by increasing the temperature from −70 °C to RT (Table 1, entry 1). Subsequently, we found that an enhanced cationic nature of the indium center (by using the $BArF^-$ salt instead of the Br^- salt; $BArF = [3,5\text{-}(CF_3)_2C_6H_3]_4B$) is essential for both the reactivity and stereoselectivity. Accordingly, the binary acid complex $InBr_3$/**1a** was first treated with three equivalents of Ag(BArF) before the substrates were added. In the presence of $In(BArF)_3$/**1a**, the reaction between styrene **2a** and ketoester **3a** proceeded smoothly to afford [4+2] adduct **4a**

[*] Dr. J. Lv, Dr. L. Zhang, Prof. Dr. S. Luo, Prof. Dr. J.-P. Cheng
Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Molecular Recognition and Function Institute of Chemistry, Chinese Academy of Sciences
Beijing 100190 (China)
E-mail: luosz@iccas.ac.cn
Homepage: http://luosz.iccas.ac.cn

[**] We gratefully acknowledge the Natural Science Foundation of China (21025208 and 21202170) and the Ministry of Science and Technology (2012CB821600) for financial support.

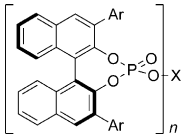
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201304561.

Table 1: Optimization of reaction conditions.[a]



Entry	**1**/Lewis acid	Yield [%][b]	*exo*/*endo* **4a**[c]	*ee* [%][d] *exo*-**4a**	*ee* [%][d] *endo*-**4a**
1[e]	**1a**/$InBr_3$	NR	–	–	–
2	**1a**/$In(BArF)_3$	77	70:30	80	77
3	**1b**/$In(BArF)_3$	**82**	**97:3**	**99**	–
4	**1b**/$In(BF_4)_3$	61	90:10	81	–
5	**1b**/$In(PF_6)_3$	NR	–	–	–
6	**1c**/$In(BArF)_3$	NR	–	–	–
7	**1b**/$Au(BArF)_3$	NR	–	–	–
8	**1b**/Ag(BArF)	NR	–	–	–
9	**1b**/$Sc(BArF)_3$	81	29:71	50	6
10	**1c**/$Sc(BArF)_3$	95	4:96	–	87
11	**1d**/$Sc(BArF)_3$	89	25:75	42	10
12	**1e**/$Sc(BArF)_3$	90	20:80	38	22
13[f]	**1f**/$Sc(BArF)_3$	**99**	**<1:99**	**–**	**>99**

[a] General conditions: **2a** (0.3125 mmol), **3a** (0.0625 mmol), **1** (10 mol%), Lewis acid (5 mol%), and 3 Å M.S. (10 mg) at RT in CH_2Cl_2 (0.5 mL) for 12 h. [b] Yields of isolated products. [c] Determined by ^1H NMR analysis. [d] Determined by HPLC analysis on a chiral stationary phase. [e] Reaction tested at −70 °C and at RT. [f] 2.5 mol% of **1f**. Entries in bold mark optimized reaction conditions. BArF = $[3,5\text{-}(CF_3)_2C_6H_3]_4B]$, NR = no reaction.



1a: Ar=4-$(C_6F_5)C_6H_4$, *n*=1, X=H
1b: Ar=4-$(C_6H_5)C_6H_4$, *n*=1, X=H
1c: Ar=2,4,6-(*i*Pr)$_3C_6H_4$, *n*=1, X=H
1d: Ar=4-$(C_6H_5)C_6H_4$, *n*=1, X=Li
1e: Ar=4-$(C_6H_5)C_6H_4$, *n*=2, X=Ca
1f: Ar=2,4,6-(*i*Pr)$_3C_6H_4$, *n*=2, X=Ca

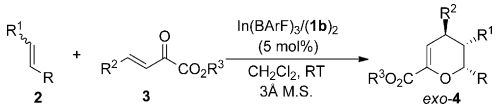
in high yield and moderate diastereo- and enantioselectivity (Table 1, entry 2). More surprisingly, the reaction gave mainly the *exo* product instead of the *endo* product, which is usually observed in the reaction with cyclopentadiene.[9,18] This unexpected finding led us to further explore the diastereoselectivity in this type of reaction.

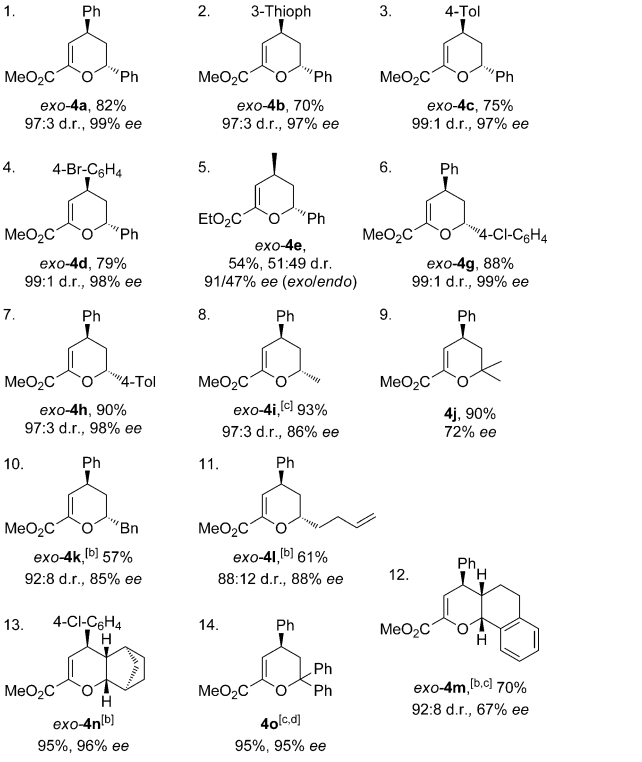
Different Lewis acids, counteranions, chiral phosphoric acids, and combinations thereof were then examined in the model reaction of styrene **2a** with ketoester **3a** (Table 1). The use of different Lewis acids had dramatic impacts on both the reactivity and diastereoselectivity of the reaction. Significantly improved stereoselectivity can be observed with chiral phosphoric acid **1b** in combination with $In(BArF)_3$, and the reaction gave 97:3 *exo*/*endo* selectivity and 99% *ee* (Table 1, entry 3). The use of other indium salts resulted in either low reactivity or poor stereoselectivity (Table 1, entries 1, 4, and 5). Other BArF salts were also examined (Table 1, entries 2 and 7–9). Although a number of metals, such as Au^{III} and Ag^{I}, could not catalyze the reaction (Table 1, entries 7 and 8), the change of the metal ion from In^{III} to Sc^{III} changed the diastereoselectivity of adduct **4a**. In the latter case, the use of $Sc(BArF)_3$ gave the *endo* product with moderate diastereoselectivity, but poor enantioselectivity (Table 1, entry 9). The *endo* selectivity of this reaction can be readily improved by a quick screening of different chiral phosphoric acid ligands. In this regard, **1f**, the calcium salt of phosphoric acid **1c**,[22,23] was found to be the optimal ligand, delivering the product with more than 99:1 *endo*/*exo* and 99% *ee* (Table 1, entry 13). The use of other phosphoric acid ligands, such as free acid **1c** and the lithium or calcium salts of **1b** (**1d** and **1e**, respectively), gave inferior results in terms of both reactivity and stereoselectivity (Table 1, entries 10–12).

Thus, $In(BArF)_3$/**1b** and $Sc(BArF)_3$/**1f** were identified as the optimal catalysts for *exo*- and *endo*-selective [4+2] cycloadditions, respectively, with excellent diastereoselective and enantioselective control in both cases.

Next, the substrate scope of the *exo*-selective reaction with binary acid $In(BArF)_3$/**1b** was explored. In the presence of $InBr_3$/**1a**/Ag(BArF), the reaction between styrene **2a** and a variety of ketoesters proceeded smoothly to afford [4+2] adducts **4a–d** in high yield, excellent *exo* selectivity and enantioselectivity (up to 99:1 d.r., 99% *ee*, Table 2). An aliphatic α-ketoester afforded the cyclic adduct **4e** with good enantioselectivity, but with low diastereoselectivity (51:49 d.r. and 91% *ee* for the *exo* product). Substituted styrenes and 1,2-dihydronaphthalene gave *exo* adducts **4g**, **4h**, and **4m** in high yields and with excellent enantioselectivity (up to 99:1 d.r., 99% *ee*). The reaction did not work with highly electron-

Table 2: Substrate scope of the *exo*-selective reaction with simple olefins.[a]





[a] General conditions: **2** (0.3125 mmol), **3** (0.0625 mmol), **1b** (10 mol%), $InBr_3$ (5 mol%), Ag(BArF) (15 mol%), and 3 Å M.S. (10 mg) at RT in CH_2Cl_2 (0.5 mL) for 2–72 h. [b] 10 mol% of catalyst. [c] With **1a**. [d] 1 mol% of catalyst. All diastereomeric ratios (d.r.) refer to *exo*/*endo*. Thioph = thiophene, Tol = 4-methylphenyl.

rich 4-methoxy-styrene, because this olefin is prone to polymerization under the conditions. To our delight, industrial feedstock olefins, such as propene and isobutene, can be used in this reaction, affording products **4i** and **4j** with up to 97:3 d.r. and 86% *ee*. The reaction also worked well with 2,5-hexadiene (product **4l**) and allylbenzene (product **4k**). Moreover, ring-strained norbornene also worked very well to give the *exo* adduct **4n** exclusively in high yield and good enantioselectivity (95% yield, 96% *ee*).

The scope of the *endo*-selective hetero-Diels–Alder reaction was then examined with Sc(BArF)$_3$/**1f**. Most of the reactions showed excellent *endo* selectivity and enantioselectivity (Tables 3 and 4). The substrate scope of the reaction is similar to that of the *exo* process with a few exceptions: 1) the highly electron-rich 4-methoxy-styrene, which is not tolerated in the *exo* process, can be used as substrate in this case (Table 3, entry 6); 2) the *endo*-selective reactions did not work with simple linear olefins, such as propene, 2,5-hexadiene, and allylbenzene, and ring-strained norbornene, 3) the *endo*-selective reactions worked well with α-methyl-substituted styrenes to give the desired *endo* adducts **6a–i**, which bear quaternary stereogenic centers in good yields and with good diastereoselectivity (up to >98:2 *endo*/*exo*) and high enantioselectivity (up to 97% *ee* for *endo* adduct; Table 4). In comparison, the reactions with α-methyl styrene under the *exo*-selective conditions gave rather complicated product mixtures, probably as a result of the various by-pathways, such as ene and carbonyl-ene processes under these conditions. A larger substituted styrene, 1,1-diphenylethylene, which worked well with In(BArF)$_3$/**1b** (95% yield, 95% *ee*, Table 2, product **4o**), turned out to be a rather sluggish substrate with Sc(BArF)$_3$/**1f** (<10% yield, racemic), indicating the space-demanding nature of the *endo* pathway; 4) a tri-substituted styrene has also been tested as substrate in the *endo*-selective reaction. In this case, the inseparable mixture of α,β-dimethyl styrene regioisomers ($Z/E = 2:5$) were directly subjected to the catalytic reaction. Remarkably, the reaction proceeded smoothly with only one isomer (*E* isomer), affording a single adduct (**6j**) in good yield and with excellent diastereoselectivity and enantioselectivity (99:1 d.r., 98% *ee*, Table 4, entry 9).

Based on the determined absolute configuration of (2*S*,4*S*)-*endo*-**4a**,[24] a tentative *endo* transition state that accounts for the stereoselectivity can be proposed (Figure 2). In this model, the 2,4,6-(*i*Pr)$_3$C$_6$H$_2$ moieties of a neutral phosphate ligand in complex with Ca/Sc constitute a well-defined chiral space that channels the orbital-favored and less-space-demanding *endo* transition state, and the reaction occurs through bidentate activation of the ketoester by the cationic scandium metal center. The *endo*-selective Diels–Alder pathway seems to be intrinsically favored in this case, as the same reactions catalyzed by other achiral Lewis acids also showed *endo* selectivity.[11,12]

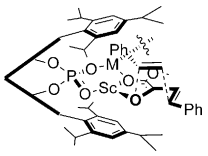
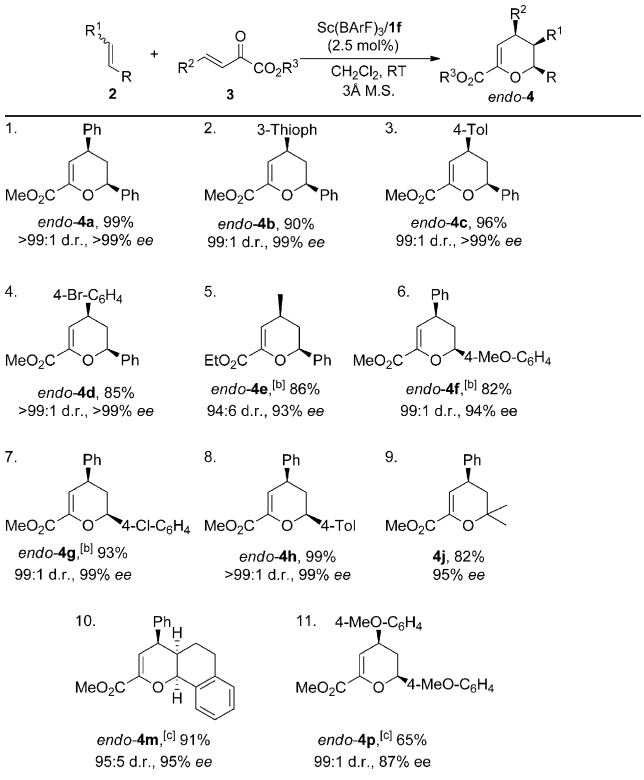


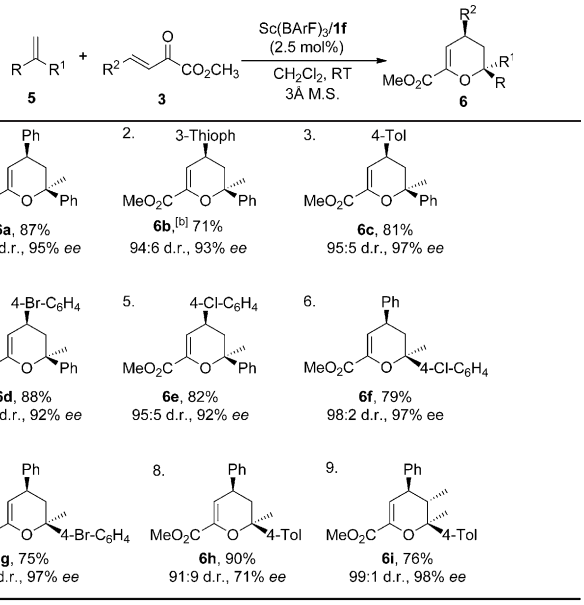
Figure 2. Proposed *endo* transition state for catalysis with Sc(BArF)$_3$/**1f**.

Table 3: Substrate scope of the *endo*-selective reaction with simple olefins.[a]



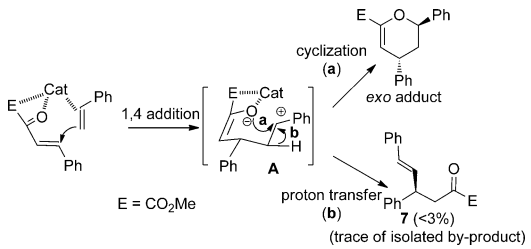
[a] General conditions: **2** (0.3125 mmol), **3** (0.0625 mmol), **1f** (2.5 mol%), $ScBr_3$ (2.5 mol%), AgBArF (7.5 mol%), and 3 Å M.S. (10 mg) at RT in CH_2Cl_2 (0.5 mL) for 2–24 h. [b] 5 mol% of catalyst. [c] 10 mol% of catalyst. All d.r. values refer to *endo*/*exo*.

Table 4: Substrate scope of the *endo*-selective reaction with α-methyl olefins.[a]



[a] General conditions: **2** (0.3125 mmol), **5** (0.0625 mmol), **1f** (2.5 mol%), $ScBr_3$ (2.5 mol%), Ag(BArF) (7.5 mol%), and 3 Å M.S. (10 mg) at RT in CH_2Cl_2 (0.5 mL) for 2–24 h. [b] 5 mol% of catalyst. All d.r. values refer to *endo*/*exo*.

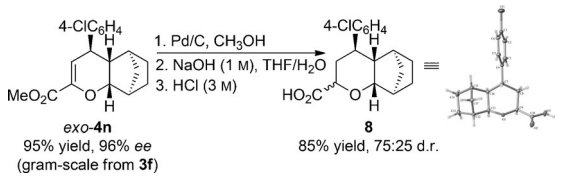
On the other hand, this result seems paradoxical because the exchange of Sc with In in the chiral binary acid complex would lead exclusively to *exo* selectivity. Usually, steric hindrance, imposed by either the substrate or the catalyst, has been proposed to account for the observed *exo* selectivity in Diels–Alder reactions.[25] However, the *endo* selectivity in similar reactions of cyclopentadienes with the same In^{III}/**1b** catalyst strongly suggests that the steric model is not applicable in the current case.[18a] In this case, a stepwise pathway is invoked to explain the *exo* selectivity. In this scenario, the reaction occurs through direct 1,4-nucleophilic addition of the olefin to the enone followed by an intramolecular substitution (pathway a, Figure 2) to afford the cyclic [4+2] *exo* product. A similar mechanism of stepwise addition has also been proposed for *exo*-selective hetero-Diels–Alder reactions with enol ethers.[17a] Experimentally, we have been able to isolate a trace of a by-product, characterized as vinyl addition product **7**. This observation is consistent with the proposed zwitterionic intermediate **A** undergoing proton transfer to generate vinylation adduct **7**, a typical Friedel–Crafts-type process. At this stage, the catalytic mode in the proposed reaction pathway (Scheme 2) remains obscure. Further mechanistic studies are clearly warranted for reactions with the indium binary acid catalyst with its superior performance and exceptional *exo* selectivity.



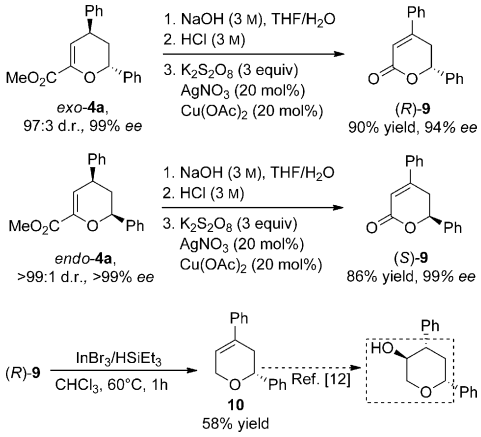
Scheme 2. Stepwise [4+2] cycloaddition.

The developed *exo*-selective [4+2] cycloaddition could also be performed on a gram scale. The reaction of an β,γ-unsaturated α-ketoester (1.0 g) with norbornene, catalyzed by binary acid $In(BArF)_3$/**1b** (5 mol%) afforded adduct **4n** in 95% yield with 96% *ee*. Hydrogenation of the double bond in **4n** could be successfully performed using Pd/C as the catalyst to nearly quantitatively afford the α-methoxycarbonyl tetrahydropyran, which was next saponified to the free acid **8**. The absolute configuration of **4** was determined through the X-ray crystal structure of **8** (Scheme 3). Further applications were focused on the decarboxylation of 3,4-dihydro-2*H*-pyran-6-carboxylic acids, obtained by saponification of **4a**, to afford δ-lactones **9** in good yield under oxidative conditions (Scheme 4). Lactone (*R*)-**9** could be chemoselectively reduced to 3,6-dihydro-2*H*-pyran **10**. This transformation sequence can be readily applied to the asymmetric synthesis of sugiresinol and doremox, starting from *endo*-**4e** and *endo*-**4p**, respectively.

In summary, a highly diastereoselective and enantioselective [4+2] cycloaddition of simple olefins with β,γ-unsaturated α-ketoesters has been realized with a unique binary acid, in which a chiral phosphoric acid is synergistically combined with a metal salt. A simple exchange of the metal ion from In^{III} to Sc^{III} leads to a switch from the *exo*- to the *endo*-selective [4+2] cycloaddition, which both occur with excellent diastereoselectivity and enantioselectivity. We also found that in the presence of a Lewis acid the use of a metal salt of the chiral phosphoric acid instead of the free phosphoric acid led to a much improved stereoselectivity, thus providing two Lewis acid combinations in asymmetric binary acid catalysis. These results underline the synergistic and combinatorial features of asymmetric binary acid catalysts in influencing chemo-, diastereo-, and enantioselectivity. Detailed mechanistic studies are ongoing and will be reported in due course.



Scheme 3. Transformation of *exo*-**4n**.



Scheme 4. Transformation of **4a**.

Received: May 27, 2013
Published online: July 29, 2013

Keywords: asymmetric catalysis · binary catalysts · diastereoselectivity · Diels–Alder reaction · olefins

[1] a) M. B. Gewali, Y. Tezuka, A. H. Banskota, M. S. Ali, I. Saiki, H. Dong, S. Kadota, *Org. Lett.* **1999**, *1*, 1733–1736; b) Y. Tezuka, M. B. Gewali, M. S. Ali, A. H. Banskota, S. Kadota, *J. Nat. Prod.* **2001**, *64*, 208–213.
[2] D. A. Whiting, *Nat. Prod. Rep.* **1987**, *4*, 499–525.
[3] a) Firmenich SA, Geneva, Switzerland, US005219836A, **1993**; b) Firmenich SA, Geneva, Switzerland, EP0581052A1, **1994**.
[4] International Flavors & Fragrances Inc., New York, N.Y. US4070491A, **1977**.

[5] For selected examples of natural and bioactive unnatural products that contain dihydropyran and tetrahydropyran moieties, see: D. G. Kang, D. H. Choi, J. K. Lee, Y. J. Lee, M. K. Moon, S. N. Yang, T. O. Kwon, J. W. Kwon, J. S. Kim, H. S. Lee, *Planta Med.* **2007**, *73*, 1436 – 1440.

[6] C. Olier, M. Kaafarani, S. Gastaldi, M. P. Bertrand, *Tetrahedron* **2010**, *66*, 413 – 445.

[7] a) K. C. Nicolaou, S. A. Synder, *Classics in Total Synthesis*, Wiley-VCH, Weinheim, **2003**; b) A. B. Smith III, R. J. Fox, T. M. Razler, *Acc. Chem. Res.* **2008**, *41*, 675 – 687.

[8] L. F. Tietze, G. Kettschau, J. A. Gewart, A. Schuffenhauer, *Curr. Org. Chem.* **1998**, *2*, 19 – 62.

[9] For examples of catalysis by chiral oxazoline/$Cu^{(II)}$ complexes, see; a) D. A. Evans, J. S. Johnson, *J. Am. Chem. Soc.* **1998**, *120*, 4895 – 4896; b) D. A. Evans, E. J. Olhava, J. S. Johnson, J. M. Janey, *Angew. Chem.* **1998**, *110*, 3553 – 3557; *Angew. Chem. Int. Ed.* **1998**, *37*, 3372 – 3375; c) D. A. Evans, J. S. Johnson, E. J. Olhava, *J. Am. Chem. Soc.* **2000**, *122*, 1635 – 1649; d) J. Thorhauge, M. Johansen, K. A. Jørgensen, *Angew. Chem.* **1998**, *110*, 2543 – 2546; *Angew. Chem. Int. Ed.* **1998**, *37*, 2404 – 2406; e) H. Audrain, J. Thorhauge, R. G. Hazell, K. A. Jørgensen, *J. Org. Chem.* **2000**, *65*, 4487 – 4497; f) W. Zhuang, J. Thorhauge, K. A. Jørgensen, *Chem. Commun.* **2000**, 459 – 460; g) H. Audrain, K. A. Jørgensen, *J. Am. Chem. Soc.* **2000**, *122*, 11543 – 11544; catalysis by chiral Schiff base/Cr^{III} complexes: h) K. Gademann, D. E. Chavez, E. N. Jacobsen, *Angew. Chem.* **2002**, *114*, 3185 – 3187; *Angew. Chem. Int. Ed.* **2002**, *41*, 3059 – 3061; i) X. Gao, D. G. Hall, *J. Am. Chem. Soc.* **2003**, *125*, 9308 – 9309; catalysis by chiral Lewis acid/Sc^{III} complexes: j) G. Desimoni, G. Faita, M. Mella, F. Piccinini, M. Toscanini, *Eur. J. Org. Chem.* **2007**, 1529 – 1534; k) G. Desimoni, G. Faita, M. Toscanini, M. Boiocci, *Chem. Eur. J.* **2007**, *13*, 9478 – 9485; catalysis by chiral Lewis acid/Er^{III} complexes: l) Y. Zhu, M. Xie, S. Dong, X. Zhao, L. Lin, X. Liu, X. Feng, *Chem. Eur. J.* **2011**, *17*, 8202 – 8208; catalysis by other chiral Lewis acid/Cu^{II} complexes: J. Zhou, Y. Tang, *Org. Biomol. Chem.* **2004**, *2*, 429 – 433; m) Y. Zhu, X. Chen, M. Xie, S. Dong, Z. Qiao, L. Lin, X. Liu, X. Feng, *Chem. Eur. J.* **2010**, *16*, 11963 – 11968; a review on asymmetric hetero-Diels – Alder reactions: n) X. Jiang, R. Wang, *Chem. Rev.* **2013**, *113*, 5515 – 5546; for inverse-electron-demand aza-Diels – Alder reactions, see: o) T. Akiyama, H. Morita, K. Fuchibe, *J. Am. Chem. Soc.* **2006**, *128*, 13070 – 13071; p) H. Liu, G. Dagousset, G. Masson, P. Retailleau, J. Zhu, *J. Am. Chem. Soc.* **2009**, *131*, 4598 – 4599; q) M. Xie, X. Chen, Y. Zhu, B. Gao, L. Lin, X. Liu, X. Feng, *Angew. Chem.* **2010**, *122*, 3887 – 3890; *Angew. Chem. Int. Ed.* **2010**, *49*, 3799 – 3802; r) G. Dagousset, J. Zhu, G. Masson, *J. Am. Chem. Soc.* **2011**, *133*, 14804 – 14813; s) F. Shi, G.-J. Xing, R.-Y. Zhu, W. Tan, S. Tu, *Org. Lett.* **2013**, *15*, 128 – 131.

[10] a) G. Catherine, D. Robert, C. Teddy, M. Vicent, D. Gilles, *J. Org. Chem.* **2004**, *69*, 4192 – 4202; b) G. Frederic, B. Keltoum, F. Djibril, G. Catherine, M. Vincent, D. Gilles, D. Robert, *Org. Lett.* **2007**, *9*, 211 – 214; c) G. Florian, H. Hidayat, M. Arnaud, D. Gilles, K. Andreas, *Org. Lett.* **2009**, *11*, 3060 – 3063.

[11] a) C. Fehr, J. Galindo, G. Ohloff, *Helv. Chim. Acta* **1981**, *64*, 1247 – 1256; b) A. Sera, M. Ohara, H. Yamada, E. Egashira, N. Ueda, J.-i. Setsune, *Chem. Lett.* **1990**, 2043 – 2046; c) G. Dujardin, M. Maudet, E. Brown, *Tetrahedron Lett.* **1994**, *35*, 8619 – 8622; d) S. Leconte, G. Dujardin, E. Brown, *Eur. J. Org. Chem.* **2000**, 639 – 643; e) L. Maingot, S. Leconte, I. Chataigner, A. Martel, G. Dujardin, *Org. Lett.* **2009**, *11*, 1619 – 1622.

[12] For an example of a Diels – Alder reaction of styrene mediated by a chiral auxiliary, see: E. Brown, G. Dujardin, M. Maudet, *Tetrahedron* **1997**, *53*, 9679 – 9694.

[13] For reviews on chiral phosphoric acids, see: a) T. Akiyama, J. Itoh, K. Fuchibe, *Adv. Synth. Catal.* **2006**, *348*, 999 – 1010; b) T. Akiyama, *Chem. Rev.* **2007**, *107*, 5744 – 5788; c) J. Yu, F. Shi, L. Z. Gong, *Acc. Chem. Res.* **2011**, *44*, 1156 – 1171; d) M. Rueping, A. Kuenkel, L. Atodiresei, *Chem. Soc. Rev.* **2011**, *40*, 4539 – 4549.

[14] For reviews on catalysis with a combination of a chiral phosphoric acid and a metal, see: a) M. Rueping, R. M. Koenigs, I. Atodiresei, *Chem. Eur. J.* **2010**, *16*, 9350 – 9365; b) R. J. Phipps, G. L. Hamilton, F. D. Toste, *Nat. Chem.* **2012**, *4*, 603 – 614; c) M. Mahlau, B. List, *Angew. Chem.* **2013**, *125*, 540 – 556; *Angew. Chem. Int. Ed.* **2013**, *52*, 518 – 533; d) K. Brak, E. N. Jacobsen, *Angew. Chem.* **2013**, *125*, 558 – 588; *Angew. Chem. Int. Ed.* **2013**, *52*, 534 – 561.

[15] a) N. Çelebi-Ölçüm, D. H. Ess, V. Aviyente, K. N. Houk, *J. Am. Chem. Soc.* **2007**, *129*, 4528 – 4529; b) N. Çelebi-Ölçüm, D. H. Ess, V. Aviyente, K. N. Houk, *J. Org. Chem.* **2008**, *73*, 7472 – 7480.

[16] A. Barba, S. Barroso, G. Blay, L. Cardona, M. Melegari, J. R. Pedro, *Synlett* **2011**, 1592 – 1596.

[17] For examples on tuning diastereoselectivity by achiral Lewis acids, see: a) A. Martel, S. Leconte, G. Dujardin, E. Brown, V. Maisonneuve, R. Retoux, *Eur. J. Org. Chem.* **2002**, 514 – 525; b) L. F. Tietze, S. Christoph, G. Andrea, *Chem. Eur. J.* **1996**, *2*, 139 – 148.

[18] a) J. Lv, L. Zhang, S. Hu, J.-P. Cheng, S. Luo, *Chem. Eur. J.* **2012**, *18*, 799 – 803; b) J. Lv, X. Zhong, S. Luo, J.-P. Cheng, *Acta Chim. Sin.* **2012**, *70*, 1518 – 1522.

[19] For a review on combined acid catalysis, see: H. Yamamoto, K. Futatsugi, *Angew. Chem.* **2005**, *117*, 1958 – 1977; *Angew. Chem. Int. Ed.* **2005**, *44*, 1924 – 1942.

[20] For a review on asymmetric catalysis with multimetallic systems, see: M. Shibasaki, M. Kanai, *Acc. Chem. Res.* **2009**, *42*, 1117 – 1127.

[21] a) J. Lv, S. Luo, *Chem. Commun.* **2013**, *49*, 847 – 858; b) J. Lv, X. Li, L. Zhang, S. Luo, J.-P. Cheng, *Org. Lett.* **2010**, *12*, 1096 – 1099; c) J. Lv, L. Zhang, Y. Zhou, Z. Nie, S. Luo, J.-P. Cheng, *Angew. Chem.* **2011**, *123*, 6740 – 6744; *Angew. Chem. Int. Ed.* **2011**, *50*, 6610 – 6614.

[22] For a review on catalysis with chiral phosphate salts, see: Y. Yamashita, T. Tsubogo, S. Kobayashi, *Chem. Sci.* **2012**, *3*, 967 – 975.

[23] For selected examples of the use of chiral calcium phosphate salts as catalysts, see: a) M. Hatano, K. Moriyama, T. Maki, K. Ishihara, *Angew. Chem.* **2010**, *122*, 3911 – 3914; *Angew. Chem. Int. Ed.* **2010**, *49*, 3823 – 3826; b) A. Alix, C. Lalli, P. Retailleau, G. Masson, *J. Am. Chem. Soc.* **2012**, *134*, 10389 – 10392; c) M. Rueping, T. Bootwicha, E. Sugiono, *Synlett* **2011**, 323 – 326; d) M. Rueping, T. Bootwicha, S. Kambutong, E. Sugiono, *Chem. Asian J.* **2012**, *7*, 1195 – 1198; e) W. Zheng, Z. Zhang, M. J. Kaplan, J. C. Antilla, *J. Am. Chem. Soc.* **2011**, *133*, 3339 – 3341; f) Z. Zhang, W. Zhang, J. C. Antilla, *Angew. Chem.* **2011**, *123*, 1167 – 1170; *Angew. Chem. Int. Ed.* **2011**, *50*, 1135 – 1138; g) F. Drouet, C. Lalli, H. Liu, G. Masson, J. Zhu, *Org. Lett.* **2011**, *13*, 94 – 97.

[24] Determined by comparing the optical rotation with that of the known compound, see Ref. [12].

[25] Y.-h. Lam, P. H.-Y. Cheong, J. M. B. Mata, S. J. Stanway, V. Gouverneur, K. N. Houk, *J. Am. Chem. Soc.* **2009**, *131*, 1947 – 1957.

