Asymmetric Catalysis

DOI: 10.1002/anie.201303119

Direct Catalytic Asymmetric Vinylogous Mannich-Type Reaction of γ-Butenolides with Ketimines**

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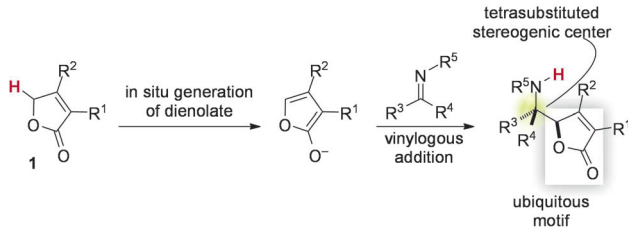
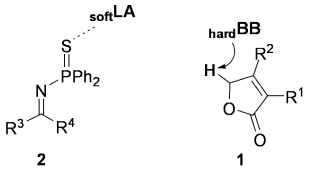
The construction of tetrasubstituted stereogenic centers through C–C-bond-forming reactions in a catalytic and enantioselective fashion has been studied intensively.[1] In particular, transformations that entail in situ catalytic generation of active nucleophiles allow for atom-economical access to this class of chemical entities.[2] γ-Butenolides **1** are an emerging class of pronucleophiles in direct catalytic asymmetric C–C-bond-forming reactions, because: 1) they bear relatively acidic protons that facilitate the generation of the corresponding dienolates, which engage in the subsequent vinylogous nucleophilic addition;[3–7] and 2) a rich chemical library containing the γ-butenolide motif is found in naturally occurring compounds (Scheme 1).[8] Despite its rapidly growing utility as a useful pronucleophile under proton-transfer conditions, **1** has not been used in direct catalytic asymmetric vinylogous Mannich-type reactions with ketimines to produce α-tetrasubstituted amines.[9–12] To date, the catalytic asymmetric vinylogous Mannich-type reaction of ketimines has only been addressed in an indirect manner utilizing 2-siloxyfuran as the preformed vinylogous enolate and electrophilically activated α-acyloxy ketimines.[13] Although recent advances in this field allowed the direct catalytic asymmetric Mannich-type reaction of ketimines, electrophilically activated ketimines, e.g., α-carbonyl or α-CF_3 ketimines, were generally used,[14] and only limited examples using ketimines without an electron-withdrawing group have been reported.[15] These circumstances and the synthetic utility of γ-butenolides led us to develop the direct catalytic asymmetric vinylogous Mannich-type reaction of γ-butenolide **1** with non-activated ketimines under proton-transfer conditions.



Scheme 1. Direct use of γ-butenolides **1** as pronucleophiles in the vinylogous Mannich-type reaction of ketimines under proton-transfer conditions.

We reasoned that the specific activation mode of ketimines is crucial to achieve this elusive reaction. Recently, we reported that *N*-thiophosphinoyl (-P(S)Ph_2) ketimines **2** were activated in situ with the aid of a soft Lewis acid as catalyst through soft–soft interaction, allowing for direct C–C bond formation with terminal alkynes.[16,17] In this context, a cooperative catalytic system containing a soft Lewis acid and a hard Brønsted base is a viable strategy,[18] in which the latter would promote the catalytic generation of dienolates from γ-butenolides **1** (Scheme 2). We initiated our study to identify



Scheme 2. Cooperative activation of ketimine electrophile **2** and γ-butenolide pronucleophile **1**.

feasible combinations of a soft Lewis acid and a hard Brønsted base by using γ-crotonolactone (**1a**) and *N*-thiophosphinoyl ketimine **2a** derived from acetophenone (Table 1). With a binary catalyst (10 mol%) comprised of [$Cu(CH_3CN_4)$]PF_6/(*R*,*R*)-Ph-BPE and Li(OC_6H_4-*p*-OMe),[19] the vinylogous Mannich-type reaction of ketimine **2a** proceeded to give the diastereomerically pure product **3a** in moderate yield and high enantioselectivity (Table 1, entry 1). Axially chiral bisphosphine ligands such as (*R*)-BINAP and (*R*)-DTBM-SEGPHOS afforded lower enantioselectivity (Table 1, entries 2,3). Among the chiral ligands screened, (R,R_P)-TANIAPHOS[20] outperformed in terms of both conversion and enantioselectivity (Table 1, entry 4).[21] When taking into account the relatively high acidity of **1a**, amine bases would be a reasonable option for the Brønsted base in

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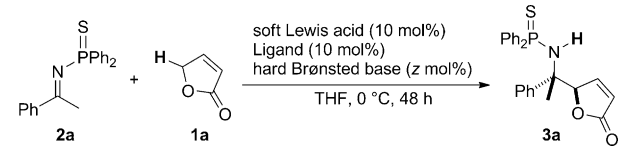
[**] This work was financially supported by JSPS KAKENHI (Grant Number 25713002) and JST, ACT-C. L.Y. thanks JSPS for a postdoctoral fellowship. Akinobu Matsuzawa is gratefully acknowledged for technical assistance in X-ray crystallographic analysis of **3a**. We thank Dr. Youmei Bao for technical support in spectral data collection.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201303119.

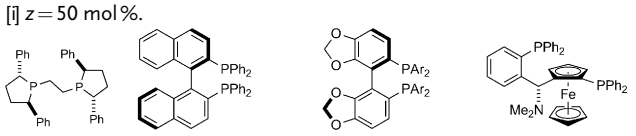
Table 1: Initial screening of the direct catalytic Mannich-type reaction of **1a** and **2a**.[a]



2a **1a** **3a**

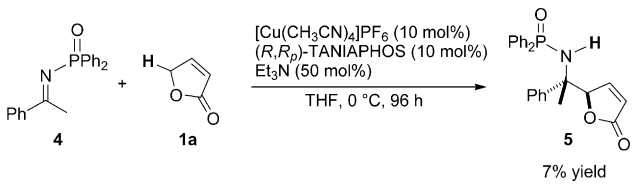
Entry	Soft[b] Lewis acid	Ligand	Hard Brønsted base	Yield [%][d]	d.r.[d]	*ee* [%][e]
1	$CuPF_6$	(*R*,*R*)-Ph-BPE	LiOAr[c]	44	>20:1	93
2	$CuPF_6$	(*R*)-BINAP	LiOAr[c]	51	>20:1	78[h]
3	$CuPF_6$	(*R*)-DTBM-SEGPHOS	LiOAr[c]	69	>20:1	84[h]
4	$CuPF_6$	(R,R_p)-TANIAPHOS	LiOAr[c]	71	>20:1	98
5	$CuPF_6$	(R,R_p)-TANIAPHOS	iPr_2NEt	17	>20:1	98
6	$CuPF_6$	(R,R_p)-TANIAPHOS	Cy_2NMe	46	>20:1	99
7	$CuPF_6$	(R,R_p)-TANIAPHOS	Et_3N	50	>20:1	99
8	$CuPF_6$	(R,R_p)-TANIAPHOS	Et_3N[i]	87[g]	>20:1	99
9	$AgPF_6$	(R,R_p)-TANIAPHOS	Et_3N[i]	33	>20:1	95
10[f]	$CuPF_6$	(R,R_p)-TANIAPHOS	–	0	–	–
11[f]	–	–	Et_3N[i]	0	–	–

[a] **1a**: 0.3 mmol, **2a**: 0.1 mmol, 0.2 M. $z = 10$ mol%, unless otherwise noted. [b] Acetonitrile complex $[Cu(CH_3CN)_4]PF_6$ was used. [c] Ar = C_6H_4-*p*-OMe. [d] Determined by ^1H NMR spectroscopy. [e] Determined by HPLC using a chiral stationary phase. [f] Reaction time was 96 h. [g] Yield of isolated product. [h] *ent*-**3a** was obtained in major. [i] $z = 50$ mol%.



(*R*,*R*)-Ph-BPE: (*R*)-BINAP Ar = 3,5-(tBu)$_2$-4-MeO-C_6H_2 (*R*)-DTBM-SEGPHOS (R,R_p)-TANIAPHOS

a cooperative catalytic system. Examination of the reaction using amine bases led us to identify Et_3N as a preferred base (Table 1, entries 5–7).[22] Intensive efforts to enhance the catalytic efficiency by changing other reaction parameters or the use of additives resulted in failure, and inexpensive Et_3N (50 mol%) afforded **3a** in 87% yield and with 99% *ee* (Table 1, entry 8). The catalyst containing silver instead of copper as a soft Lewis acid could promote the reaction, although inferior conversion and enantioselectivity were observed (Table 1, entry 9). No reaction took place in the absence of the soft Lewis acid or the hard Brønsted base even after 96 h, thus confirming that their cooperative function is critical to promote the reaction (Table 1, entries 10, 11). The reaction of oxygen analogue *N*-phosphinoyl ketimine **4** barely proceeded under the optimized reaction conditions, thereby proving that the S···Cu interaction was pivotal in activating the *N*-thiophosphinoyl ketimine **2a** (Scheme 3).

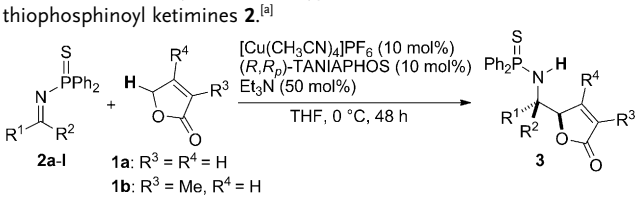


4 **1a** **5** 7% yield

Scheme 3. Application of optimized reaction conditions to *N*-phosphinoyl ketimine **4**.

The substrate scope of the direct catalytic asymmetric vinylogous Mannich-type reaction is summarized in Table 2. Uniformly high diastereo- and enantioselectivities were observed with a range of *N*-thiophosphinoyl ketimines **2**. Ketimines derived from *para*-halogenated acetophenones exhibited high reactivity to give the corresponding products in high yield (Table 2, entries 2–4). Catalyst loading could be reduced to 5 mol% in the reaction of a ketimine bearing a CF_3 group without any detrimental effect on the reaction efficiency (Table 2, entry 5). The reaction reached completion with 1.5 equivalents of **1a** (Table 2, entry 5). Substitution at the *ortho*- or *meta*-positions of the aromatic ring of ketimines

Table 2: Direct catalytic Mannich-type reaction of γ-butenolide **1** and *N*-thiophosphinoyl ketimines **2**.[a]



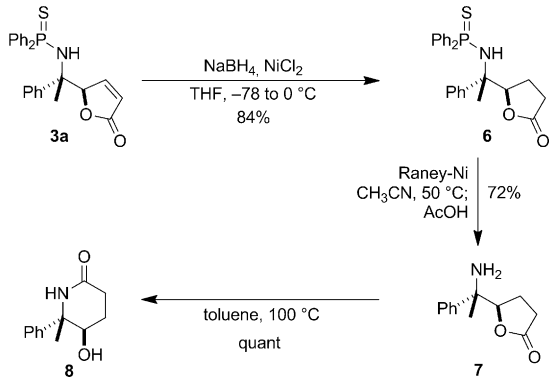
2a-l **1a**: $R^3 = R^4 = H$ **1b**: R^3 = Me, $R^4 = H$ **1c**: $R^3 = H$, R^4 = Me **3**

1. **3a**: 87%, 99% *ee* d.r. >20:1
2. **3b**: 92%, 99% *ee* d.r. >20:1
3. **3c**: 84%, 99% *ee* d.r. >20:1
4. **3d**: 91%, 99% *ee* d.r. >20:1
5. **3e** **5 mol% cat.**[b] 83%, 98% *ee* d.r. >20:1, 72 h **1.5 equiv of 1a:** 89%, 98% *ee* d.r. >20:1
6. **3f**: 88%, 98% *ee* d.r. >20:1
7. **3g**: 88%, 98% *ee* d.r. >20:1
8. **3h**: 80%, 98% *ee* d.r. >20:1
9. **3i**: 73%, 99% *ee* d.r. >20:1
10. **3j**: 70%, 98% *ee* d.r. >20:1, 96 h
11. **3k**: 63%, 99% *ee* d.r. >20:1
12. **3l**: 52%, 97% *ee* d.r. >20:1
13. **3m**: 61%, 98% *ee* d.r. >20:1, 96 h
14. **3n**: 55%, 99% *ee* d.r. >20:1

[a] **1**: 0.3 mmol, **2**: 0.1 mmol, 0.2 M. Yields of isolated products are presented. The diastereomeric ratio (d.r.) was determined by ^1H NMR analysis. *ee* values were determined by HPLC using a chiral stationary phase. [b] $[Cu(CH_3CN)_4]PF_6$ (5 mol%), (R,R_p)-TANIAPHOS (5 mol%), and Et_3N (25 mol%) were used. Reaction was conducted using 1 g of ketimine.

did not interfere with stereoselectivity (Table 2, entries 6,7). A marginal loss in reactivity was detected with ketimines bearing electron-donating substituents (Table 2, entries 8,9). Notably, excellent stereoselectivity was observed with more challenging ketimine substrates, e.g., ketimines derived from ethyl ketone and aliphatic ketones; albeit they were isolated with reduced yields (Table 2, entries 10–12). Methyl-substituted γ-crotonolactones **1b**,**c** were also applicable in the present catalytic system (Table 2, entries 13,14).

A transformation of the Mannich adduct is outlined in Scheme 4. 1,4-Reduction of an α,β-unsaturated lactone moiety was effected with $NiCl_2/NaBH_4$ to give the saturated



Scheme 4. Transformation of Mannich adduct **3a**.

product **6**.[23] Treatment of **6** with Raney-Ni, followed by the addition of AcOH, cleaved the N–P bond to give amine **7**. Heating of **7** in toluene led to the thermodynamically more-stable six-membered lactam **8** in quantitative yield.

In summary, a direct catalytic asymmetric vinylogous Mannich-type reaction of ketimines has been developed. Activation of the *N*-thiophosphinoyl group by a soft Lewis acid was key to achieve the enantioselective addition of the dienolate generated in situ to otherwise unreactive ketimine substrates. Application of this catalytic protocol to the enantioselective synthesis of biologically significant compounds is currently underway.

Received: April 14, 2013
Published online: May 29, 2013

Keywords: asymmetric catalysis · atom economy · cooperative catalysis · ketimines · synthetic methods

[1] Reviews: a) E. J. Corey, A. Guzman-Perez, *Angew. Chem.* **1998**, *110*, 402; *Angew. Chem. Int. Ed.* **1998**, *37*, 388; b) J. Christoffers, A. Mann, *Angew. Chem.* **2001**, *113*, 4725; *Angew. Chem. Int. Ed.* **2001**, *40*, 4591; c) C. J. Douglas, L. E. Overman, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5363; d) *Quaternary Stereocenters* (Eds.: J. Christoffer, A. Baro), Wiley, Weinheim, **2005**; e) B. M. Trost, C. Jiang, *Synthesis* **2006**, 369; f) I. Marek, G. Sklute, *Chem. Commun.* **2007**, 1683; g) P. G. Cozzi, R. Hilgraf, N. Zimmermann, *Eur. J. Org. Chem.* **2007**, 5969.

[2] B. M. Trost, *Science* **1991**, *254*, 1471.

[3] Early examples of the direct use of γ-butenolides as pronucleophiles in racemic aldol reactions: a) X. Franck, B. Figadére, *Tetrahedron Lett.* **2002**, *43*, 1449; b) K. Das Sarma, J. Zhang, T. T. Curran, *J. Org. Chem.* **2007**, *72*, 3311.

[4] For direct catalytic asymmetric Mannich reactions of γ-butenolides with aldimines, see: a) A. Yamaguchi, S. Matsunaga, M. Shibasaki, *Org. Lett.* **2008**, *10*, 2319; b) L. Zhou, L. Lin, J. Ji, M. Xie, X. Liu, X. Feng, *Org. Lett.* **2011**, *13*, 3056; c) Y.-L. Guo, J.-F. Bai, L. Peng, L.-L. Wang, L.-N. Jia, X.-Y. Luo, F. Tian, X.-Y. Xu, L.-X. Wang, *J. Org. Chem.* **2012**, *77*, 8338.

[5] For direct catalytic asymmetric aldol reactions of γ-butenolides with aldehydes, see: a) H. Ube, N. Shimada, M. Terada, *Angew. Chem.* **2010**, *122*, 1902; *Angew. Chem. Int. Ed.* **2010**, *49*, 1858; b) Y. Yang, K. Zheng, J. Zhao, J. Shi, L. Lin, X. Liu, X. Feng, *J. Org. Chem.* **2010**, *75*, 5382; c) S. V. Pansare, E. K. Paul, *Chem. Commun.* **2011**, *47*, 1027; d) S. V. Pansare, E. K. Paul, *Org. Biomol. Chem.* **2012**, *10*, 2119.

[6] For direct catalytic asymmetric Michael reactions of γ-butenolides with enones and nitroolefins: a) B. M. Trost, J. Hitce, *J. Am. Chem. Soc.* **2009**, *131*, 4572; b) Y. Zhang, C. Yu, Y. Ji, W. Wang, *Chem. Asian J.* **2010**, *5*, 1303; c) J. Wang, C. Qi, Z. Ge, T. Cheng, R. Li, *Chem. Commun.* **2010**, *46*, 2124; d) M. Terada, K. Ando, *Org. Lett.* **2011**, *13*, 2026.

[7] For a direct catalytic asymmetric Mannich reaction and a Michael reaction of α,β-unsaturated γ-butyrolactams: N. E. Shepherd, H. Tanabe, Y. Xu, S. Matsunaga, M. Shibasaki, *J. Am. Chem. Soc.* **2010**, *132*, 3666.

[8] Reviews: a) E.-I. Negishi, M. Kotora, *Tetrahedron* **1997**, *53*, 6707; b) G. Casiraghi, F. Zanardi, L. Battistini, G. Rassu, G. Appendino, *Chemtracts* **1998**, *11*, 803; c) F. Q. Alali, X.-X. Liu, J. L. McLaughlin, *J. Nat. Prod.* **1999**, *62*, 504; d) R. Bruckner, *Curr. Org. Chem.* **2001**, *5*, 679; e) T. Montagnon, M. Tofi, G. Vassilikogiannakis, *Acc. Chem. Res.* **2008**, *41*, 1001; f) T. M. Ugurchieva, V. V. Veselovsky, *Russ. Chem. Rev.* **2009**, *78*, 337.

[9] For general reviews on catalytic asymmetric Mannich-type reactions: a) S. Kobayashi, M. Ueno, in *Comprehensive Asymmetric Catalysis*, *Supplement 1* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **2003**, chap. 29.5, p. 143; b) G. K. Friestad, A. K. Mathies, *Tetrahedron* **2007**, *63*, 2541; c) S. Kobayashi, Y. Mori, J. S. Fossey, M. M. Salter, *Chem. Rev.* **2011**, *111*, 2626.

[10] Recent reviews on direct Mannich reactions: a) M. M. B. Marques, *Angew. Chem.* **2006**, *118*, 356; *Angew. Chem. Int. Ed.* **2006**, *45*, 348; b) A. Ting, S. E. Schaus, *Eur. J. Org. Chem.* **2007**, 5797; c) J. M. M. Verkade, L. J. C. van Hemert, P. J. L. M. Quaedflieg, F. P. J. T. Rutjes, *Chem. Soc. Rev.* **2008**, *37*, 29; d) R. Gómez Arrayás, J. C. Carretero, *Chem. Soc. Rev.* **2009**, *38*, 1940.

[11] Reviews on vinylogous Mannich reactions: a) S. K. Bur, S. F. Martin, *Tetrahedron* **2001**, *57*, 3221; b) S. F. Martin, *Acc. Chem. Res.* **2002**, *35*, 895; c) G. Casiraghi, L. Battistini, C. Curti, G. Rassu, F. Zanardi, *Chem. Rev.* **2011**, *111*, 3076.

[12] For an example of producing a tetrasubstituted stereogenic center in the direct catalytic asymmetric Mannich reaction of γ-substituted γ-butenolide and aldimines, see Ref. [4b].

[13] a) L. C. Wieland, E. M. Vieira, M. L. Snapper, A. H. Hoveyda, *J. Am. Chem. Soc.* **2009**, *131*, 570. After submission of this manuscript, a catalytic asymmetric vinylogous Mannnich-type reaction using 2-siloxyfuran and diphenylphosphinoyl ketimines was reported: b) M. Hayashi, M. Sano, Y. Funahashi, S. Nakamura, *Angew. Chem.* **2013**, *125*, 5667; *Angew. Chem. Int. Ed.* **2013**, *52*, 5557.

[14] For direct catalytic asymmetric Mannich reactions of ketimines bearing an α-carbonyl group, see: a) S. Saaby, K. Nakama, M. A. Lie, R. G. Hazell, K. A. Jørgensen, *Chem. Eur. J.* **2003**, *9*, 6145; b) W. Zhuang, S. Saaby, K. A. Jørgensen, *Angew. Chem.* **2004**, *116*, 4576; *Angew. Chem. Int. Ed.* **2004**, *43*, 4476; c) B. Jiang, J. J.

Dong, Y. G. Si, X. L. Zhao, Z. G. Huang, M. Xu, *Adv. Synth. Catal.* **2008**, *350*, 1360; d) N. Hara, S. Nakamura, M. Sano, R. Tamura, Y. Funahashi, N. Shibata, *Chem. Eur. J.* **2012**, *18*, 9276; e) W. Yan, D. Wang, J. Feng, P. Li, D. Zhao, R. Wang, *Org. Lett.* **2012**, *14*, 2512; f) T. Kano, S. Song, Y. Kubota, K. Maruoka, *Angew. Chem.* **2012**, *124*, 1217; *Angew. Chem. Int. Ed.* **2012**, *51*, 1191. For direct catalytic asymmetric Mannich reactions of ketimines bearing an α-CF_3 group, see: g) V. A. Sukach, N. M. Golovach, V. V. Pirozhenko, E. B. Rusanov, M. V. Vovk, *Tetrahedron: Asymmetry* **2008**, *19*, 761; h) N. Hara, R. Tamura, Y. Funahashi, S. Nakamura, *Org. Lett.* **2011**, *13*, 1662.

[15] For direct catalytic asymmetric Mannich reactions of non-activated ketimines (ketimines without adjacent electron-withdrawing groups): a) G. Lu, T. Yoshino, H. Morimoto, S. Matsunaga, M. Shibasaki, *Angew. Chem.* **2011**, *123*, 4474; *Angew. Chem. Int. Ed.* **2011**, *50*, 4382. For catalytic asymmetric Mannich reactions of nonactivated ketimines using organometallic reagents: b) Y. Suto, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2007**, *129*, 500; c) Y. Du, L.-W. Xu, Y. Shimiza, K. Oisaki, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2008**, *130*, 16146. For catalytic asymmetric self-coupling of ketone-derived enamides: d) C. Baudequin, A. Zamfir, S. B. Tsogoeva, *Chem. Commun.* **2008**, 4637. See also Ref. [13b].

[16] Synthesis of *N*-(thiophosphinoyl)imines: a) X. Xu, C. Wang, Z. Zhou, Z. Zeng, X. Ma, G. Zhao, C. Tang, *Lett. Org. Chem.* **2006**, *3*, 640; b) X. Xu, C. Wang, Z. Zhou, Z. Zeng, X. Ma, G. Zhao, C. Tang, *Heteroat. Chem.* **2008**, *19*, 238. Application of *N*-(thiophosphinoyl)imines as electrophiles: c) X. Ma, C. Wang, X. Xu, G. Zhao, Z. Zhou, C. Tang, *Lett. Org. Chem.* **2007**, *4*, 51; d) X. Ma, X. Xu, C. Wang, G. Zhao, Z. Zhou, C. Tang, *J. Organomet. Chem.* **2007**, *692*, 3685; e) X. Xu, C. Wang, Z. Zhou, X. Tang, Z. He, C. Tang, *Eur. J. Org. Chem.* **2007**, 4487; f) A. Lu, X. Xu, P. Gao, Z. Zhou, H. Song, C. Tang, *Tetrahedron: Asymmetry* **2008**, *19*, 1886; g) B. Zhang, Z. He, S. Xu, G. Wu, Z. He, *Tetrahedron* **2008**, *64*, 9471; h) K. Hu, C. Wang, X. Ma, Y. Wang, Z. Zhou, C. Tang, *Tetrahedron: Asymmetry* **2009**, *20*, 2178.

[17] L. Yin, Y. Otsuka, H. Takada, S. Mouri, R. Yazaki, N. Kumagai, M. Shibasaki, *Org. Lett.* **2013**, *15*, 698.

[18] Recent reviews on cooperative catalysis: Lewis acid/Brønsted base: a) M. Shibasaki, N. Yoshikawa, *Chem. Rev.* **2002**, *102*, 2187; b) N. Kumagai, M. Shibasaki, *Angew. Chem.* **2011**, *123*, 4856; *Angew. Chem. Int. Ed.* **2011**, *50*, 4760. Lewis acid/Lewis base: c) M. Kanai, N. Kato, E. Ichikawa, M. Shibasaki, *Synlett* **2005**, 1491; d) D. H. Paull, C. J. Abraham, M. T. Scerba, E. Alden-Danforth, T. Lectka, *Acc. Chem. Res.* **2008**, *41*, 655. Lewis acid/Brønsted acid and Lewis acid/Lewis acid: e) H. Yamamoto, K. Futatsugi, *Angew. Chem.* **2005**, *117*, 1958; *Angew. Chem. Int. Ed.* **2005**, *44*, 1924; f) H. Yamamoto, K. Futatsugi in *Acid Catalysis in Modern Organic Synthesis* (Eds.: H. Yamamoto, K. Ishihara), Wiley-VCH, Weinheim, **2008**.

[19] For representative examples in which this specific combination of soft Lewis acid/hard Brønsted base cooperative catalyst works efficiently, see: a) R. Yazaki, N. Kumagai, M. Shibasaki, *J. Am. Chem. Soc.* **2010**, *132*, 5522; b) M. Iwata, R. Yazaki, I.-H. Chen, D. Sureshkumar, N. Kumagai, M. Shibasaki, *J. Am. Chem. Soc.* **2011**, *133*, 5554.

[20] a) T. Ireland, G. Grossheimann, C. Wieser-Jeunesse, P. Knochel, *Angew. Chem.* **1999**, *111*, 3397; *Angew. Chem. Int. Ed.* **1999**, *38*, 3212; b) T. Ireland, K. Tappe, G. Grossheimann, P. Knochel, *Chem. Eur. J.* **2002**, *8*, 843; c) S. Fukuzawa, M. Yamamoto, M. Hosaka, S. Kikuchi, *Eur. J. Org. Chem.* **2007**, 5540.

[21] The absolute and relative configuration of **3a** was determined by X-ray crystallographic analysis. CCDC 932229 (**3a**) contains 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. A summary of the crystallographic analysis of **3a** is provided in the Supporting Information.

[22] A stronger base such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) induced polymerization of **1a** and resulted in a complicated reaction mixture, although the desired product **3a** was obtained with high yield.

[23] a) R. Paul, P. Buisson, N. Joseph, *Ind. Eng. Chem.* **1952**, *44*, 1006; b) C. W. Jefford, D. Jaggi, G. Bernardinelli, J. Boukouvalas, *Tetrahedron Lett.* **1987**, *28*, 4041.

