# Direct Organocatalytic Asymmetric Mannich Addition of 3-Substituted-2H -1,4-Benzoxazines: Access to Tetrasubstituted Carbon Stereocenters

**ARTICLE** *in* ADVANCED SYNTHESIS & CATALYSIS · NOVEMBER 2013

Impact Factor: 5.66 · DOI: 10.1002/adsc.201300654



**5 AUTHORS**, INCLUDING:

You-Qing Wang
Henan University
**17** PUBLICATIONS **416** CITATIONS
SEE PROFILE

Yongna Zhang
Henan University
**17** PUBLICATIONS **325** CITATIONS
SEE PROFILE

DOI: 10.1002/adsc.201300654

# Direct Organocatalytic Asymmetric Mannich Addition of 3-Substituted-2*H*-1,4-Benzoxazines: Access to Tetrasubstituted Carbon Stereocenters

You-Qing Wang,[a,*] Yongna Zhang,[b] Kun Pan,[a] Junxiong You,[a] and Jin Zhao[a]

[a] Provincial Key Laboratory of Natural Medicine and Immuno-Engineering, Henan University, Kaifeng, Henan 475004, People's Republic of China
Fax: (+86)-378-286-4665; e-mail: wyouqing@hotmail.com or wyouqing@foxmail.com
[b] Basic Experiment Teaching Center, Henan University, Kaifeng, Henan 475004, People's Republic of China

Received: July 25, 2013; Revised: September 9, 2013; Published online: November 13, 2013

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201300654.

**Abstract:** 3-Substituted-2*H*-1,4-benzoxazines undergo a highly enantioselective direct Mannich reaction with acetone in the presence of an L-proline catalyst at room temperature. The corresponding N-heterocycles with α-tetrasubstituted carbon stereocenters were obtained in good yields (48–92%) and excellent enantioselectivity (up to >99% *ee*). Furthermore, a novel modification involving the diastereoselective reduction of the Mannich adduct was carried out leading to the formation of a 1,3-amino alcohol with a chiral tetrasubstituted carbon stereocenter in high yield.

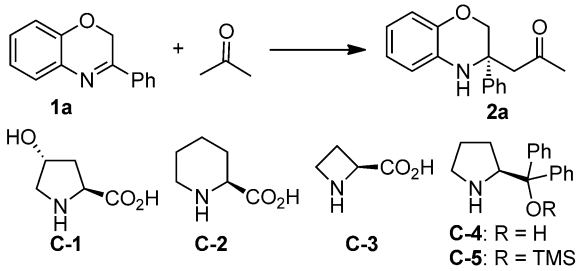
**Keywords:** asymmetric catalysis; Mannich reaction; nitrogen heterocycles; organocatalysis; tetrasubstituted carbon stereocenters

Catalytic enantioselective nucleophilic 1,2-additions to imines is one of the most efficient synthetic tools for obtaining a wide range of optically active amines.[1] The asymmetric addition to ketimines leading to the formation of chiral amines bearing an α-tetrasubstituted carbon stereocenter has rarely been explored compared to the corresponding aldimines, due to their lower electrophilicity and issues related to steroselectivity.[1,2] Therefore, the search for a catalytic enantioselective addition to ketimines[2] continues with the goal of increasing the diversity of possible substrates and reaction types.

The Mannich-type reaction[3] is an example in organic synthesis of an addition to C=N intermediates by a variety of nucleophiles such as enolized carbonyl compounds, resulting in new C–C bond formation adjacent to the nitrogen atom. In 2000, List reported the first proline-catalyzed asymmetric Mannich reaction of aldimines produced *in situ* from aldehydes and amines.[4] Over the last decade, the organocatalytic direct asymmetric Mannich reaction involving unmodified carbonyl compounds as nucleophile sources has become an area of active interest.[4] Excellent results with a variety of aldimines or their equivalents have been reported thereby.[4,5] Obviously, the Mannich adducts will be very important β-aminocarbonyl compounds bearing tetrasubstituted carbon stereocenters while ketimines were employed as electrophilic acceptors. However, unlike aldimines, a few successful examples have been appeared describing the catalytic asymmetric Mannich reaction of ketimines. In 2003, Jørgensen's group reported the first highly enantioselective Mannich reaction of α-ketimino esters anchored to the aryloxy formyl groups on the nitrogen atom with various silylketene acetals in the presence of a Zn Lewis acid catalyst, thus providing a direct access to optically active tetrasubstituted α-amino acid derivatives.[6a] Subsequently, the same activated ketimines were also employed for the organocatalytic enantioselective Mannich reaction of unmodified aldehydes.[6b] The proline-catalyzed asymmetric Mannich reaction of aryl trifluoromethyl ketimines was reported by Vovk et al.,[7a] and while only one example of an aryl trifluoromethyl ketimine was described by Nakamura and co-workers.[7b] A diamine-Brønsted acid-catalyzed asymmetric Mannich reaction of the cyclic trifluoromethyl *N*-acylketimine was described, in which a trifluoromethyldihydroquinazoline with a tetrasubstituted carbon stereocenter was formed.[8] An asymmetric Mannich addition of five-membered *C*-acylketimines was successfully carried out to afford the corresponding products catalyzed by proline with moderate to excellent region- and enantioselectivities.[9] Recently, the ketimines activated by two different ester groups were used in highly enantioselective Mannich reactions of aldehydes with secondary amine

**Table 1.** Optimization of the conditions for the Mannich reaction of imine **1a** and acetone.[a]




| Entry | Catalyst | Solvent | Additive | Yield [%][b] | *ee* [%][c] |
|---|---|---|---|---|---|
| 1 | L-proline | DMSO | – | 75 | 97 |
| 2 | L-proline | DMF | – | 58 | 95 |
| 3 | L-proline | $CH_3CN$ | – | 9 | 94 |
| 4 | L-proline | acetone | – | 21 | 95 |
| 5 | L-proline | MeOH | – | 32 | 27 |
| 6 | L-prolinamide | DMSO | – | 28 | 85 |
| 7 | L-proline methyl ester | DMSO | – | 78 | 75 |
| 8 | **C-1** | DMSO | – | 34 | 97 |
| 9 | **C-2** | DMSO | – | NR | N/A |
| 10 | **C-3** | DMSO | – | 78 | 87 |
| 11 | **C-4** | DMSO | – | NR | N/A |
| 12 | **C-5** | DMSO | – | NR | N/A |
| 13 | L-valine | DMSO | – | trace | N/A |
| 14 | L-proline | DMSO | 3 Å MS[d] | 73 | 97 |
| 15 | L-proline | DMSO | 4 Å MS[d] | 75 | 95 |
| 16 | L-proline | DMSO | 5 Å MS[d] | 25 | 97 |
| 17 | L-proline | DMSO | 50 mol% $CH_3CO_2H$ | 76 | 86 |
| 18 | L-proline | DMSO | 1.0 equiv. $H_2O$ | 79 | 96 |
| 19 | L-proline | DMSO | 5.0 equiv. $H_2O$ | 77 | 96 |
| 20 | L-proline | DMSO | 10.0 equiv. $H_2O$ | 72 | 97 |
| 21[e] | L-proline | DMSO | 55.5 equiv. $H_2O$ | NR | - |
| 22[f] | L-proline | DMSO | – | 37 | 31 |

[a] Unless otherwise specified, all reactions were carried out at room temperature with imine **1a** (0.1 mmol), acetone (1.0 mmol), and catalysts (0.03 mmol, 30 mol%) in the solvent (0.2 mL) for 5 days.
[b] Isolated yield.
[c] Determined by HPLC using a chiral column.
[d] 20.0 mg molecular sieves were added.
[e] 0.1 mL DMSO and 0.1 mL $H_2O$ were used.
[f] In an oil bath at 50 °C.

organocatalysts.[10] More recently, activated oxindole imines (isatin imines) were used as Mannich acceptors to construct 3-aminooxindole derivatives with excellent enantioselectivity.[11] However, all the aforementioned ketimines are activated by incorporating electron-withdrawing groups (carbonyl or trifluoromethyl). Therefore, unactivated ketimines still remain as unexplored substrates for the direct catalytic enantioselective Mannich reaction.[12] Moreover, the development of an efficient Mannich reaction of unactivated imines is still challenging and is in great demand as interest in the asymmetric synthesis of chiral molecules continues to grow.[13] Herein, we disclose the highly enantioselective organocatalytic direct Mannich reactions between 3-substituted-2*H*-1,4-benzoxazines and acetone to afford N-heterocycles with tetrasubstituted carbon stereocenters.

Based on our previous research on the phosphine-catalyzed [3+2]cycloaddition of allenoate and cyclic imines to afford the sulfamidate N-heterocycles,[14] we continue to explore the Mannich addition of cyclic imines. However, the use of cyclic imines as acceptors in the Mannich reaction has rarely been studied while much attention has been given to the corresponding acyclic imines.[6,8–10,15–16] Moreover, the cyclic imines would be more efficient alternative acceptors compared to the acyclic imines because the induced ring-strain increases the reactivity towards nucleophiles, and also rotational freedom is minimized by blocking *E/Z* isomerization of C=N bond.

In an initial experiment, the reaction of 3-phenyl-2*H*-1,4-benzoxazine **1a**[17] and acetone was carried out at room temperature using L-proline as a catalyst in dry DMSO. The progress of the reaction was monitored by TLC. One major new spot was observed along with a small amount unreacted imine **1a**. The desired Mannich addition product could be isolated in 75% yield with 97% *ee* in five days (Table 1, entry 1). The effect of different solvents was investigated (entries 1–5). The best result considering reactivity and enantioselectivity was obtained in DMSO. Different chiral amino acids and their derivatives were employed as the organocatalysts to test the efficiency of this reaction (entries 1, 6–13). Cyclic amino acids proved to be more effective in enhancing the reactivity and enantioselectivity. Only five-membered proline and four-membered azetidine gave good yields. The effect of additives was also studied (entries 14–21). Interestingly, in contrast to Ohsawa's report[15a] on the Mannich reaction of cyclic aldimines, water had no apparent effect on this reaction (entries 18 and 20). However, the reaction failed in the presence of excess water because of the insolubility of imine **1a** in the reaction mixture (entry 21). Moreover, the yield and enantioselectivity decreased significantly when the temperature was increased to 50 °C (entry 22).

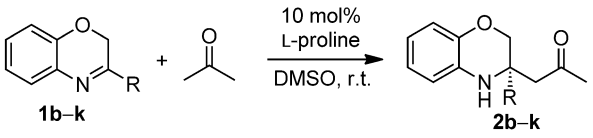
The course of the Mannich reaction with respect to the conversion and enantioselectivity was studied with time (Table 2). Aliquots from the reaction mixture were analyzed by HPLC at several intervals. The maximum conversion reached in about two days using proline (10 mol%) as the catalyst. A further increase in time and catalyst loadings[18] did not improve the yield. The enantioselectivity slightly gradually decreased with time.

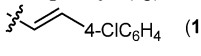
Next, the scope of the reaction was explored with respect to the substrate having different substituents (R of **1**) attached to the electrophilic carbon, as listed in Table 3. Under the optimized reaction conditions, the Mannich adducts **2** with a variety of aryl substituents at different positions on the aromatic ring, could be readily obtained with excellent enantioselectivity except for 4-methyl-substituted imine **1f** (entry 5), for which a slightly lower *ee* of 86% was obtained. Notably, the high 98% *ee* and 70% yield were also observed for imine **1j** containing a naphthyl group (entry 9). 4-Chlorostyryl substituted imine **1k**[17b] afforded the normal 1,2-addition Mannich product with significantly decreased enantioselectivity (entry 10).[19]

To further explore the scope of imines, the effect of a variety of substituents at different positions on the benzo-fused ring was investigated. As shown in Scheme 1, the corresponding Mannich products **4** with tetrasubstituted carbon stereocenters were obtained in 48–88% yields and excellent enantioselectivities (87 to >99% *ee*). This indicates that the *para*-substituents on the oxygen atom of the 2*H*-1,4-benzoxazine backbone exhibit some influence on the enantioselectivity, resulting in reduced enantioselectivities for Cl and F substituents (**4c** and **4d**). It seems that the *para*-substituents on the nitrogen atom of 2*H*-1,4-benzoxazine backbone exhibit a major influence only on the yield (**4e** and **4f**).[20]

The typical transformation of Mannich product **2a** was carried out, and the results are illustrated in Scheme 2. The carbonyl group of **2a** was smoothly reduced to a hydroxy group using $NaBH_4$, as the reducing reagent, in THF leading to the formation of 1,3-amino alcohol **5**. The single diastereoselective product

**Table 3.** Scope of the Mannich reaction.[a]




| Entry | R of **1** | Time [h] | Yield[b] [%] | *ee*[c] [%] |
|---|---|---|---|---|
| 1 | 4-$FC_6H_4$ (**1b**) | 48 | 82 | >99 |
| 2 | 4-$NO_2C_6H_4$ (**1c**) | 72 | 91 | >99 |
| 3 | 4-$ClC_6H_4$ (**1d**) | 72 | 78 | 98 |
| 4 | 4-$PhC_6H_4$ (**1e**) | 72 | 56 | 97 |
| 5 | 4-$MeC_6H_4$ (**1f**) | 48 | 71 | 86 |
| 6 | 3-$ClC_6H_4$ (**1g**) | 72 | 92 | 98 |
| 7 | 3-$BrC_6H_4$ (**1h**) | 60 | 94 | >99 |
| 8 | 3,4-$Cl_2C_6H_3$ (**1i**) | 72 | 78 | >99 |
| 9 | 2-naphthyl (**1j**) | 72 | 70 | 98 |
| 10 |  (**1k**) | 72 | 61 | 61 |



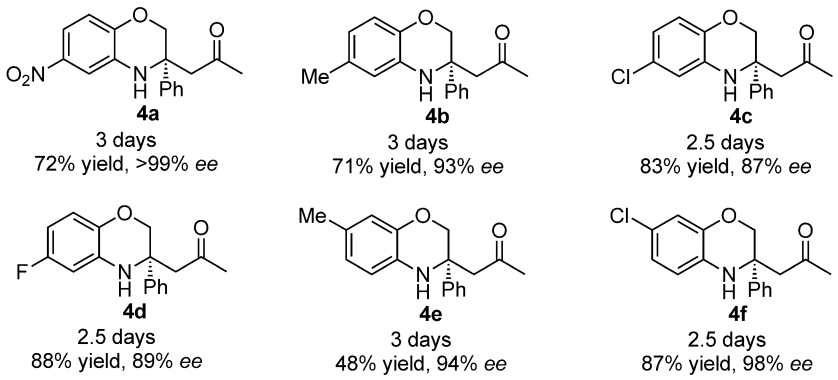
[a] *Reaction conditions:* imine **1** (0.2 mmol), acetone (2.0 mmol), proline (0.02 mmol, 10 mol%), and dry DMSO (0.4 mL).
[b] Isolated yield.
[c] Determined by HPLC using a chiral column.

**Table 2.** Mannich reaction of imine **1a** with acetone.[a]

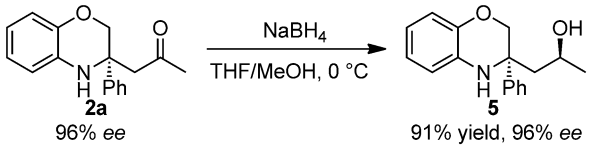
| Time [h] | 3 | 6 | 12 | 48 | 72 | 120 |
|---|---|---|---|---|---|---|
| Conv.[b] [%] | 12 | 27 | 50 | 72 | 69 | 68 |
| *ee* [%] | 98.7 | 98.4 | 98.0 | 97.4 | 97.1 | 96.5 |

[a] *Reaction conditions:* imine **1a** (0.2 mmol), acetone (2.0 mmol), L-proline (0.02 mmol, 10 mol%), and DMSO (0.4 mL) at room temperature.
[b] Calculated by HPLC analysis in 254 nm for the aliquots.




**Scheme 1.** Effect of a variety of substituents at different positions on the benzo-fused ring.




**Scheme 2.** Transformation of product **2a**.

**5** was easily isolated in 91% yield by column chromatography on silica gel, without any decrease in the optical purity as determined by HPLC analysis. Both the newly formed carbon stereocenters, one attached to a hydroxy group and the other in an adjacent tetrasubstituted carbon stereocenter, had the *S*-configuration.

The relative and absolute configurations of compound **5** were established by an X-ray diffraction study of its *O*-4-chlorobenzoyl ester **6** (Figure 1).[21] The stereochemistry of the adduct **2a** was assigned as being of the *S*-configuration. The absolute configurations of the other Mannich adducts were assigned by analogy (Table 3 and Scheme 1). This indicates that the cyclic ketimine is attacked on the *re*-face by the carbon nucleophile of an active enamine obtained from acetone in this Mannich addition.

In conclusion, we have described the highly enantioselective direct Mannich addition to 3-substituted-2*H*-1,4-benzoxazines using L-proline as the organocatalyst. This also represents the first demonstration of a catalytic asymmetric Mannich reaction to synthesize 3,4-dihydro-2*H*-1,4-benzoxazines, N-heterocycles with tetrasubstituted carbon stereocenters. Further studies on the reactions of ketimines with other nucleophiles are in progress.[22] The ring opening reactions of the 3,4-dihydro-2*H*-1,4-benzoxazines to the corresponding chiral amines with α-tetrasubstituted carbon stereocenters will also be investigated.

## Experimental Section

### Typical Procedure for the Mannich Reaction

To the mixture of ketimine (0.2 mmol) and L-proline (10 mol%, 0.02 mmol) in DMSO (0.4 mL) was added acetone (2 mmol) by a micro syringe. This reaction mixture was stirred at room temperature for the stated reaction time. Direct purification of the reaction mixture by chromatography on a silica gel column (petroleum ether/EtOAc: 20/1 to 10/1) gave the desired Mannich adducts. The enantiomeric

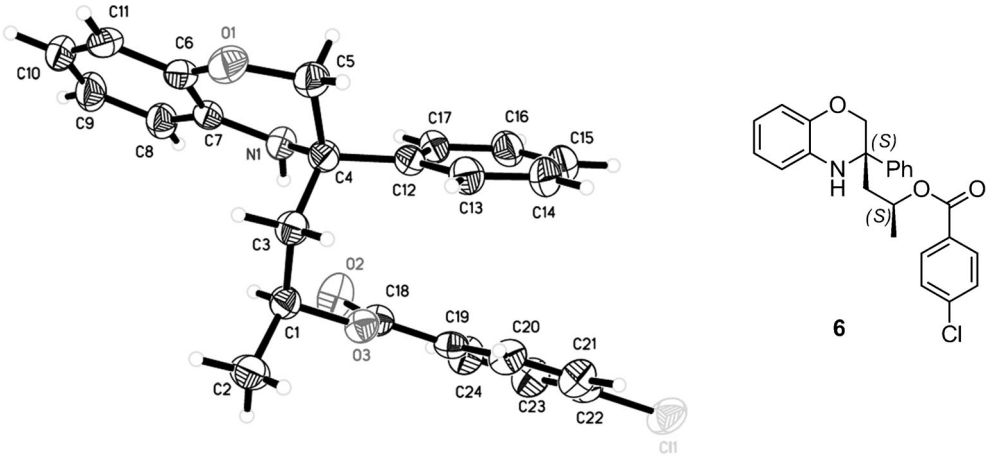



**Figure 1.** X-ray structure of *O*-4-chlorobenzoyl derivative **6**.

excess was determined by HPLC. Racemic Mannich adducts were obtained under catalysis with racemic proline.

### Work-Up for HPLC Analysis (Table 2)

An aliquot (1–2 drops) of the reaction mixture was filtered through a small silica gel column (petroleum ether/EtOAc: 4/1). After evaporation of the solvents, the residue was redissolved in isopropyl alcohol and subjected to HPLC analysis.

## Acknowledgements

*This project is financially supported by the National Natural Science Foundation of China (No. 21002022), Chinese Ministry of Education (the Scientific Research Foundation for the Returned Overseas Chinese Scholars), and the postdoctoral science foundation supports of Henan province in China. We thank Professor Yong-Gui Zhou (DICP, CAS, China) for a gift of imines **1**.*

## References

[1] a) S. Kobayashi, H. Ishitani, *Chem. Rev.* **1999**, *99*, 1069–1094; b) S. Kobayashi, Y. Mori, J. S. Fossey, M. M. Salter, *Chem. Rev.* **2011**, *111*, 2626–2704.

[2] O. Riant, J. Hannedouche, *Org. Biomol. Chem.* **2007**, *5*, 873–888.

[3] a) E. F. Kleinmann, in: *Comprehensive Organic Synthesis*, Vol. 2, (Eds.: B. M. Trost, I. Fleming), Pergamon, New York, **1991**, pp. 893–951; b) M. Arend, B. Westermann, N. Risch, *Angew. Chem.* **1998**, *110*, 1096–1122; *Angew. Chem. Int. Ed.* **1998**, *37*, 1044–1070.

[4] a) B. List, *J. Am. Chem. Soc.* **2000**, *122*, 9336–9337; b) B. List, P. Porjalev, W. T. Biller, H. J. Martin, *J. Am. Chem. Soc.* **2002**, *124*, 827–833.

[5] For reviews on direct asymmetric Mannich reactions, see : a) A. Córdova, *Acc. Chem. Res.* **2004**, *37*, 102–112; b) M. M. B. Marques, *Angew. Chem.* **2006**, *118*, 356–360; *Angew. Chem. Int. Ed.* **2006**, *45*, 348–352; c) A. Ting, S. E. Schaus, *Eur. J. Org. Chem.* **2007**, 5797–5815; d) J. M. M. Verkade, L. J. C. van Hemert, P. J. L. M. Quaedflieg, F. P. J. T. Rutjes, *Chem. Soc. Rev.* **2008**, *37*, 29–41; e) R. G. Arrayás, J. C. Carretero, *Chem. Soc. Rev.* **2009**, *38*, 1940–1948.

[6] a) S. Saaby, K. Nakama, M. A. Lie, R. G. Hazell, K. A. Jørgensen, *Chem. Eur. J.* **2003**, *9*, 6145–6154; b) W. Zhuang, S. Saaby, K. A. Jørgensen, *Angew. Chem.* **2004**, *116*, 4576–4578; *Angew. Chem. Int. Ed.* **2004**, *43*, 4476–4478.

[7] a) V. A. Sukach, N. M. Golovach, V. V. Pirozhenko, E. B. Rusanov, M. V. Vovk, *Tetrahedron: Asymmetry* **2008**, *19*, 761–764; b) N. Hara, R. Tamura, Y. Funahashi, S. Nakamura, *Org. Lett.* **2011**, *13*, 1662–1665.

[8] B. Jiang, J. J. Dong, Y. G. Si, X. L. Zhao, Z. G. Huang, M. Xu, *Adv. Synth. Catal.* **2008**, *350*, 1360–1366.

[9] L. Li, M. Han, M. Xiao, Z. Xie, *Synlett* **2011**, 1727–1730.

[10] T. Kano, S. Song, Y. Kubota, K. Maruoka, *Angew. Chem.* **2012**, *124*, 1217–1220; *Angew. Chem. Int. Ed.* **2012**, *51*, 1191–1194.

[11] a) X. Chen, H. Chen, X. Ji, H. Jiang, Z.-J. Yao, H. Liu, *Org. Lett.* **2013**, *15*, 1846–1849; b) Q.-X. Guo, Y.-W. Liu, X.-C. Li, L.-Z. Zhong, Y.-G. Peng, *J. Org. Chem.* **2012**, *77*, 3589–3594.

[12] Asymmetric Mannich reactions of ketimines with transition metal catalysts, see: a) Y. Suto, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2007**, *129*, 500–501; b) R. Yazaki, T. Nitabaru, N. Kumagai, M. Shibasaki, *J. Am. Chem. Soc.* **2008**, *130*, 14477–14479; c) Y. Du, L.-W. Xu, Y. Shimizu, K. Oisaki, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **2008**, *130*, 16146–16147; d) L. C. Wieland, E. M. Vieira, M. L. Snapper, A. H. Hoveyda, *J. Am. Chem. Soc.* **2009**, *131*, 570–576; e) G. Lu, T. Yoshino, H. Morimoto, S. Matsunaga, M. Shibasaki, *Angew. Chem.* **2011**, *123*, 4474–4477; *Angew. Chem. Int. Ed.* **2011**, *50*, 4382–4385.

[13] E. Gómez-Bengoa, J. Jiménez, I. Lapuerta, A. Mielgo, M. Oiarbide, I. Otazo, I. Velilla, S. Vera, C. Palomo, *Chem. Sci.* **2012**, *3*, 2949–2957.

[14] Y.-Q. Wang, Y. Zhang, H. Dong, J. Zhang, J. Zhao, *Eur. J. Org. Chem.* **2013**, 3764–3770.

[15] For asymmetric direct Mannich reactions of cyclic aldimines and ketones catalyzed by proline, see: a) T. Itoh, M. Yokoya, K. Miyauchi, K. Nagata, A. Ohsawa, *Org. Lett.* **2003**, *5*, 4301–4304; b) B. T. Hahn, R. Fröhlich, K. Harms, F. Glorius, *Angew. Chem.* **2008**, *120*, 10134–10137; *Angew. Chem. Int. Ed.* **2008**, *47*, 9985–9988; c) K. Schulz, L. Ratjen, J. Martens, *Tetrahedron* **2011**, *67*, 546–553; d) M. R. Monaco, P. Renzi, D. M. S. Schietroma, M. Bella, *Org. Lett.* **2011**, *13*, 4546–4549; e) D.-J. Cheng, S.-K. Tian, *Adv. Synth. Catal.* **2013**, *355*, 1715–1718.

[16] For related reactions of cyclic aldimines and methyl vinyl ketones, see: a) T. Itoh, M. Yokoya, K. Miyauchi, K. Nagata, A. Ohsawa, *Org. Lett.* **2006**, *8*, 1533–1535; b) K. Nagata, H. Ishikawa, A. Tanaka, M. Miyazaki, T. Kanemitsu, T. Itoh, *Heterocycles* **2010**, *81*, 1791–1798; c) M. P. Lalonde, M. A. McGowan, N. S. Rajapaksa, E. N. Jacobsen, *J. Am. Chem. Soc.* **2013**, *135*, 1891–1894; d) N. S. Rajapaksa, M. A. McGowan, M. Rienzo, E. N. Jacobsen, *Org. Lett.* **2013**, *15*, 706–709.

[17] The cyclic ketimines, 2*H*-1,4-benzoxazines, were used as the substrates of a catalytic asymmetric reduction, see: a) M. Rueping, A. P. Antonchick, T. Theissmann, *Angew. Chem.* **2006**, *118*, 6903–6907; *Angew. Chem. Int. Ed.* **2006**, *45*, 6751–6755; b) K. Gao, C.-B. Yu, D.-S. Wang, Y.-G. Zhou, *Adv. Synth. Catal.* **2012**, *354*, 483–488; c) Q.-A. Chen, K. Gao, Y. Duan, Z.-S. Ye, L. Shi, Y. Yang, Y.-G. Zhou, *J. Am. Chem. Soc.* **2012**, *134*, 2442–2448; d) J. Hu, D. Wang, Z. Zheng, X. Hu, *Chin. J. Chem.* **2012**, *30*, 2664–2668; e) J. L. Núñez-Rico, A. Vidal-Ferran, *Org. Lett.* **2013**, *15*, 2066–2069.

[18] Similar results (65% conversion in 24 h, 70% conversion in 48 h) were also observed in the presence of 30 mol% proline.

[19] The ketimines containing other saturated alkyl substituents (such as, R = Me, *t*-Bu) were unstable, and decomposed to a complex mixture even in the Mannich reaction.

[20] The Mannich reaction was also conducted between 3-phenyl-1,2-dihydroquinoxaline and acetone under the optimized reaction conditions, but no desired Mannich product was observed after two days and major product was 2-phenylquinoxaline. See the Supporting Information for details.
[21] The compound **6** was obtained on the treatment of alcohol **5** and 4-chlorobenzoyl chloride in pyridine, and a single crystal could be grown from its solution in dichloromethane and hexane. See the Supporting Information for more experimental details. CCDC 951533 contains the supplementary crystallographic data for this paper (compound **6**). These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.
[22] Other ketones such as 2-butanone and cyclohexanone were also tested, however, much lower reactivities were observed.