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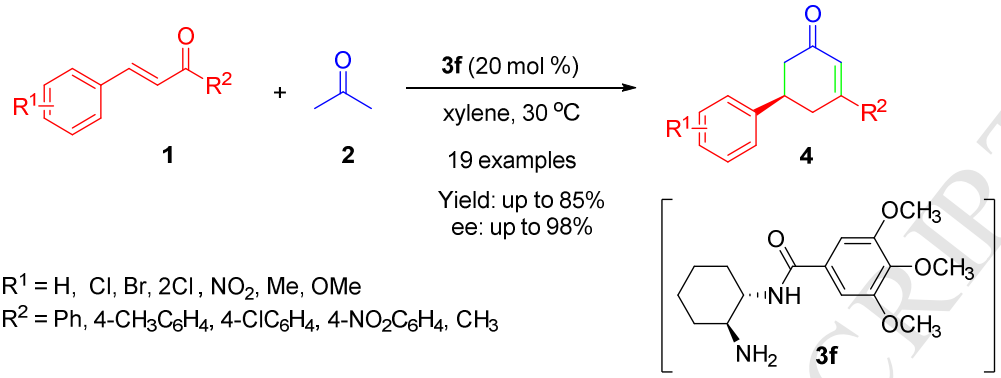
Graphical Abstract



R^1 = H, Cl, Br, 2Cl, NO_2, Me, OMe

R^2 = Ph, 4-$CH_3C_6H_4$, 4-ClC_6H_4, 4-$NO_2C_6H_4$, CH_3

Highly Enantioselective Michael-Aldol-Dehydration Reaction for the Synthesis of Chiral 3,5-Diaryl-Cyclohexenones Catalyzed by Primary Amine

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Abstract: A simple organocatalytic Michael-aldol-dehydration domino approach to chiral 3,5-diaryl-cyclohexenones from acetone and α,β-unsaturated ketones was developed for the first time using a simple chiral primary amine as a catalyst. Moderate to good yields (up to 85%) and excellent enantioselectivities (88-98% *ee*) were obtained.

Keywords: organocatalysis; domino reaction; 3,5-diaryl-cyclohexenones; enantioselective synthesis

Introduction

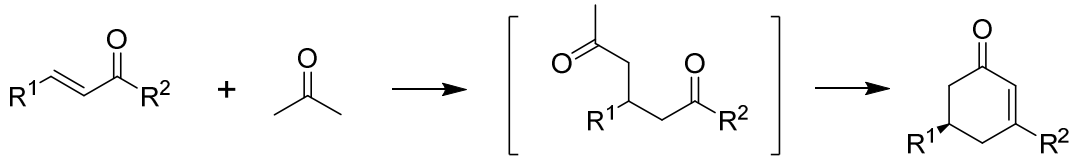
Chiral cyclohexenones are important chiral scaffolds which have been widely used in the synthesis of asymmetric natural products and a broad spectrum of biologically active molecules.[1] Therefore, many useful strategies have been developed for the synthesis of this kind of compounds, including various multistep synthesis,[2] intramolecular aldol condensation reactions,[3] kinetic resolution of racemic substituted cyclohexenones by asymmetric catalytic reactions,[4] and enantioselective Robinson annulation, which consists of three consecutive processes: (I) the

asymmetric Michael addition of a carbonyl compound to an α, β-unsaturated ketone/aldehyde, (II) an intramolecular aldol reaction, and (III) dehydration. Low cost starting materials are advantages for Robinson annulation strategy.[5]

In recent 20 years, asymmetric organocatalysis has emerged as a versatile strategy for the stereoselective preparation of valuable chiral compounds. Pure organic molecules are utilized as chiral catalysts providing a valuable complement to the traditional organometallic and biological approaches to asymmetric catalysis.[6] These stereo-controlled methods offer a practical pathway for the construction of a variety of enantio-enriched cyclohex-2-enones.[5] For instance, Jorgensen et al.[7] and Hayashi et al.[8] successfully used diarylprolinol silyl ether as an organocatalyst, and α,β-unsaturated aldehydes as the Michael acceptors to prepare various chiral cyclohexenones with excellent enantioselectivities. Deng and coworkers reported an asymmetric Michael addition for the synthesis of chiral cyclohexenones catalyzed by 9-amino-9-deoxyepiquinine.[9] Zhao et al. applied chiral primary-secondary diamine catalysts to catalyze the Michael-aldol-dehydration reaction between benzoylacetates, β-ketoamides and α,β-unsaturated ketones to form chiral cyclohexenones in high enantioselectivities with excellent yields.[10] However, the reports about synthesis of chiral 3,5-diaryl-cyclohexenones are very rare. In 2000, the Corey group reported the preparation of (**S**)-3,5-diaryl-cyclohexenones via a five step synthesis.[2c] Two straightforward procedures for the preparation of non-chiral 3,5-diaryl-cyclohexenones via Robinson annulation reaction of chalcones and acetone have been revealed. In 1998, Inanaga et al. synthesized non-chiral 3,5-diaryl-cyclohexenones via the reaction of chalcones and acetone catalyzed by lanthanoid salts.[11] In 2014, the Ghosh group reported the pyrrolidine-catalyzed direct synthesis of non-chiral 3,5-diaryl-cyclohexenones from acetone and chalcones.[12] However, to the best of our

knowledge, the asymmetric version of the Robinson annulation of chalcones with acetone for the preparation of chiral 3,5-diaryl-cyclohexenones has not been reported yet.

In asymmetric catalysis, chiral secondary amines have been widely studied as highly versatile and extremely powerful catalysts. However, chiral primary amines as organocatalysts are relatively underutilized. In consideration of the advantage of primary amine catalysis for successfully dealing with major challenges in various sterically hindered carbonyl compounds, which many approaches hardly handle,[13] it is greatly desirable to develop more chiral primary amine catalysts in asymmetric organocatalysis. Moreover, for the choice of chiral catalysts for asymmetric synthesis, a combination of efficiency, availability, and economy is the core consideration. Enantiomerically pure *trans*-1,2-diaminocyclohexane is a structurally simple molecule which fits the requirements very well. As described in a review by Hanessian and coworker:[14] *trans*-1,2-diaminocyclohexane was first reported by Wieland *et al*. in 1926,[15] who prepared it from hexahydrophthalic acid through conversion to the hydrazide followed by a Curtius reaction. Nowadays, this diamine is readily available because it is a component in a byproduct amine stream produced during the purification of 1,6-hexanediamine, which is one of the materials for the manufacture of Nylon 66.[16] Its optical resolution can be easily done in aqueous medium by utilization of D- or L-tartaric acid to obtain the (R,R)- or the (S,S)-enantiomer in enantiopure form, respectively.[17] Fascinated by its features of ready availability and structural simplicity, our group has been paying much attention on development of new trans-1,2-diaminocyclohexane derived chiral catalysts for asymmetric organocatalysis.[18]



Scheme 1 Robinson annulation reaction

Although there are numerous asymmetric aldol reactions reported, aliphatic ketones and aldehydes are mainly concerned; to the best of our knowledge, there is scarcely any reported example for the aromatic ketones without any other assisted functional group participating asymmetric (domino) aldol reactions with other aliphatic ketones. For the Robinson annulation reaction (the sequential asymmetric Michael addition/intramolecular aldol reaction/dehydration) as shown in **Scheme 1**, generally when R^1 and R^2 are both aliphatic groups or R^1 aromatic while R^2 aliphatic, the initial (metal free organocatalytic) Michael reaction and subsequent aldol reactions may readily take place, while when both R^1 and R^2 are aromatic substituted groups such as chalcone, the enantioselectivity and reactivity of the first Michael addition is difficultly to be controlled due to steric hindrance and the minor differences between the two groups. To the best of our knowledge, there has been only one example on the asymmetric Michael addition of acetone to chalcone which was reported in 2014 and a chiral benzoylthiourea–pyrrolidine was used as a catalyst; only 53% yield with 50% *ee* was obtained without subsequent aldol reaction.[19]

Based on double catalysis: enamine/imine-hydrogen bonding mechanism such as Noyori's chiral ligand N-[(1R,2R)-2-amino-1,2-diphenylethyl]-4-methylbenzenesulfonamide (Ts-DPEN), [20] a chiral primary amine bifunctional catalyst, which has been successfully used for the highly enantioselective Michael addition of acetone to nitroalkenes,[21] (1S,2S)-diaminocyclohexane and its benzoyl derivatives were chosen as very simple bifunctional organocatalysts. In this work, a highly enantioselective Robinson annulation of chalcones with acetone was developed using a

chiral primary amine as a catalyst to construct (R)-3,5-diaryl-cyclohexenones.

Results and discussion

Initially, the domino reaction of chalcone **1a** and acetone **2** was used as a model reaction at 30 ^{o}C in PhMe, and a variety of optically active primary amines shown in **Figure 1** were screened as catalysts. As can be seen from the results in **Table 1**, when **3a** was used in the reaction, only a trace amount of product **4a** was detected (**Table 1**, entry 1). Catalysts **3b-3f** could promote the model reaction, giving the desired product with high enantioselectivities (92-96% *ee*, the absolute configuration of **3a** was determined as **R** by comparison of HPLC with literature.[3e, 10a]) but in low yields (10-31%) (**Table 1**, entries 2-6). Taking into consideration of both yield and enantiomeric excess, **3f** was chosen as the catalyst for the cascade reaction. We speculated that the low yields may be due to the evaporation of acetone. Thus, we attempted to improve the yield by adding acetone (20 eq.) in two portions (10 eq. each portion) at the beginning and after 2 days into the reaction mixture, which gave the product in a better yield of 42% with 96% *ee* (**Table 1,** entry 7). Therefore, the amount of acetone (10 equiv. + 10 equiv./2d) was adopted in the following investigation.

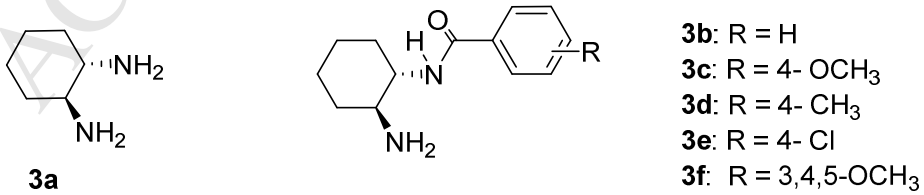
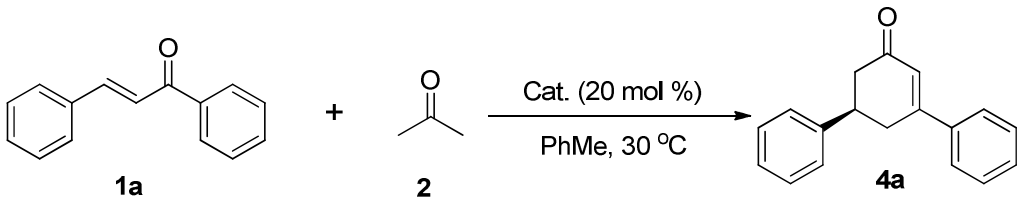


Figure 1. Structures of the catalysts

Table 1. Screening of chiral primary amine catalysts **3a-3f**.[a]



1a + **2** → **4a**

Entry	Catalyst	Yield (%)[b]	*ee* (%)[c] (**R**)
1	**3a**	trace	n.d
2	**3b**	15	92
3	**3c**	27	94
4	**3d**	24	94
5	**3e**	10	92
6	**3f**	31	96
7[d]	**3f**	42	96

[a] The reactions were carried out using **1a** (0.20 mmol), **2** (10 equiv., 0.15 mL), and catalyst (20 mol %) in PhMe (1.0 mL) at 30 °C for 4 days.

[b] Isolated yield after column chromatography on silica gel.

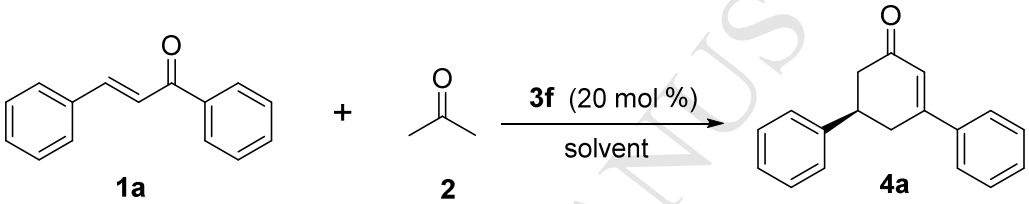
[c] Determined by chiral HPLC analysis (AS-H).

[d] Acetone **2** (10 equiv., 0.15 mL) was used when setting the reaction, and another portion of acetone **2** (10 equiv., 0.15 mL) was added into the reaction mixture after 2 days.

Different solvents were tested for the model reaction catalyzed by **3f** at 30 °C (Table 2). The results revealed that the solvent had a significant effect on the rate and the enantioselectivity of the reaction. In polar solvents, such as DMF, MeCN, MeOH, and EtOH, the reaction resulted in poor yields (Table 2, entries 1-4). By contrast, in non-polar solvents or solvents with low polarity, such as PhMe, PhBr, and xylene, the reaction gave better yields (42-56%) and better enantioselectivities (90-97% *ee*, Table 2, entries 10-12). Among them, the reaction in xylene provided product with an excellent enantioselectivity (96% *ee*) in a relatively good yield (52%) (Table 2, entry 12). Thus, xylene was selected for further optimization. Next, the influence of

temperature on the model reaction in xylene was investigated at 20, 40, and 50 ^{o}C, respectively. The results indicated that the yield improved from 36% to 60% when the temperature was increased from 20 to 50 ^{o}C (Table 2, entries 12-15), however the enantioselectivity decreased from 96% *ee* to 90% *ee*. Therefore, in view of both yield and stereoselectivity, 30 ^{o}C was selected as the suitable temperature for the domino reaction.

Table 2. Effect of solvents and temperature on the reaction.[a]



Entry	Solvent	Temp. (^{o}C)	Time (d)	Yield (%)[b]	*ee* (%)[c] (**R**)
1	DMF	30	6	trace	n.d.
2	MeCN	30	6	trace	n.d.
3	MeOH	30	6	18	86
4	EtOH	30	6	25	84
5	Ethyl acetate	30	4	48	88
6	MTBE	30	6	28	86
7	Acetone	30	6	38	84
8	$CHCl_3$	30	4	48	84
9	CH_2Cl_2	30	4	42	82
10	PhMe	30	4	42	97
11	PhBr	30	4	56	90
12	xylene	30	4	52	96
13	xylene	20	4	36	96
14	xylene	40	4	54	94
15	xylene	50	4	60	90

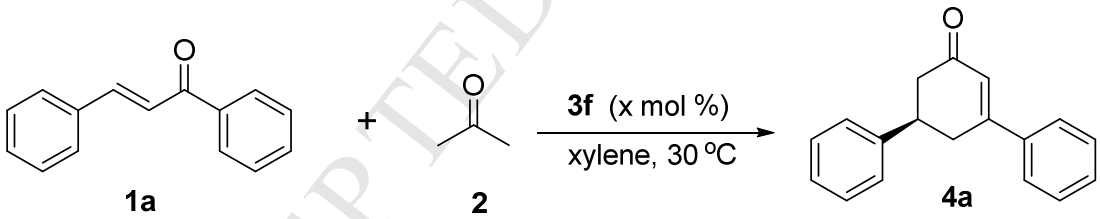
[a] The reactions were carried out using **1a** (0.20 mmol), **2** (10 equiv. + 10 equiv./2d), and **3f** (20 mol %) in solvent (1.0 mL).

[b] Isolated yield after column chromatography on silica gel.

[c] Determined by chiral HPLC analysis (AS-H).

Other parameters, including the amount of acetone, the catalyst loading and the volume of solvent, were also investigated (Table 3). No superior results were obtained by screening of the amount of acetone and catalyst loading (Table 3, entries 1-7). However, when the volume of the solvent (xylene) was reduced from 1.0 mL to 0.50 mL, the reaction gave a better yield of 62% with high stereoselectivity of 94% *ee* after 4 d (**Table 3**, entry 9). Through these screenings, the optimized reaction conditions were found to be a combination of **3f** (20 mol %), acetone (10 equiv. + 10 equiv./2d), and 0.5 mL of xylene as the solvent (for 0.20 mmol scale of chalcone **1a**) at 30 ^{o}C. In addition, the effect of some additives, such as AcOH, CF_3CO_2H and $PhCO_2H$ etc, was also investigated, but no positive results were obtained.

Table 3. Effect of the amount of acetone, catalyst loading and volume of solvent on the reaction. [a]



Entry	**2** (x equiv.)	**3f** (mol %)	Xylene (mL)	Yield (%)[b]	*ee* (%)[c] (**R**)
1	5	20	1.0	41	96
2	10	20	1.0	52	96
3	15	20	1.0	54	90
4	20	20	1.0	54	88
5	10	10	1.0	36	96
6	10	15	1.0	45	96
7	10	30	1.0	53	95
8	10	20	2.0	42	96
9	10	20	0.5	62	94

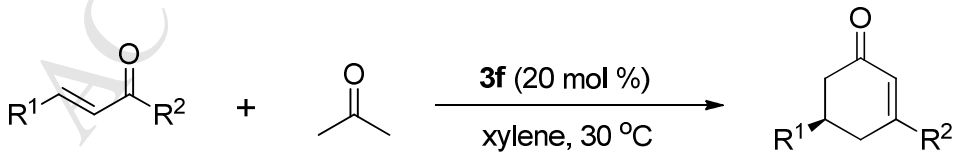
[a] The reactions were carried out using **1a** (0.20 mmol), **2** (x equiv. + x equiv./2d), and catalyst **3f** in xylene at 30 ^{o}C for 4 d.

[b] Isolated yield after column chromatography on silica gel.

[c] Determined by chiral HPLC analysis (AS-H).

Under the optimized reaction conditions, the scope and the limitations of this domino reaction were examined with different chalcones **1** (Table 4). As can be seen from the table, catalyst **3f** showed good catalytic activity for the cascade reaction. The product yields of up to 85% and enantioselectivities of up to 98% *ee* were achieved with various chalcones bearing either electron-withdrawing or electron-donating substituents in the *ortho*, *meta* or *para* position of the aromatic ring (Table 4**,** entries 1-18). The position of substituent in the aromatic ring had obvious effect on the yields. For instance, the reaction with 2-Cl substituted chalcone gave better yield than that with 3- or 4-Cl substituted chalcone (Table 4, entries 2-4). Besides chalcones, 4-phenylbut-3-en-2-one was also tested, giving the product in 80% yield and 88% *ee* (Table 4, entry 19). In addition, some ketones other than acetone, were also surveyed, such as butanone, 3-methylbutanone, 3-pentanone, 1-chloroacetone, ethyl acetoacetate and 1,3-diphenylpropan-2-one, under the present reaction conditions, but no desired products were detected.

Table 4. Substrate scope.[a]



1 **2** **4**

Entry	R^1	R^2	Product	Time (d)	Yield (%)[b]	*ee* (%)[c] (**R**)
1	Ph	Ph	**4a**	4	62	94
2	2-ClC_6H_4	Ph	**4b**	2	82	96
3	3-ClC_6H_4	Ph	**4c**	4	62	94
4	4-ClC_6H_4	Ph	**4d**	6	54	94

5	3-BrC_6H_4	Ph	**4e**	4	60	95
6	4-BrC_6H_4	Ph	**4f**	4	56	95
7	2,3-$Cl_2C_6H_3$	Ph	**4g**	4	74	95
8	2,4-$Cl_2C_6H_3$	Ph	**4h**	2	85	96
9	2,6-$Cl_2C_6H_3$	Ph	**4i**	2	72	98
10	4-$NO_2C_6H_4$	Ph	**4j**	6	52	92
11	4-$CH_3C_6H_4$	Ph	**4k**	6	41	91
12	4-$CH_3OC_6H_4$	Ph	**4l**	6	32	96
13	Ph	4-$CH_3C_6H_4$	**4m**	6	48	97
14	2-ClC_6H_4	4-$CH_3C_6H_4$	**4n**	4	67	96
15	Ph	4-ClC_6H_4	**4o**	6	50	94
16	2-ClC_6H_4	4-ClC_6H_4	**4p**	2	76	96
17	4-ClC_6H_4	4-ClC_6H_4	**4q**	4	71	94
18	Ph	4-$NO_2C_6H_4$	**4r**	2	64	95
19	Ph	CH_3	**4s**	4	80	88

[a] The reactions were carried out using **1a** (0.20 mmol), **2** (10 equiv. + 10 equiv./2d, except for entries 2, 8, 9, 16 and 18, in which only 10 equiv. of **2** was used), and catalyst **3f** (20 mol %) in xylene (0.50 mL) at 30 °C.

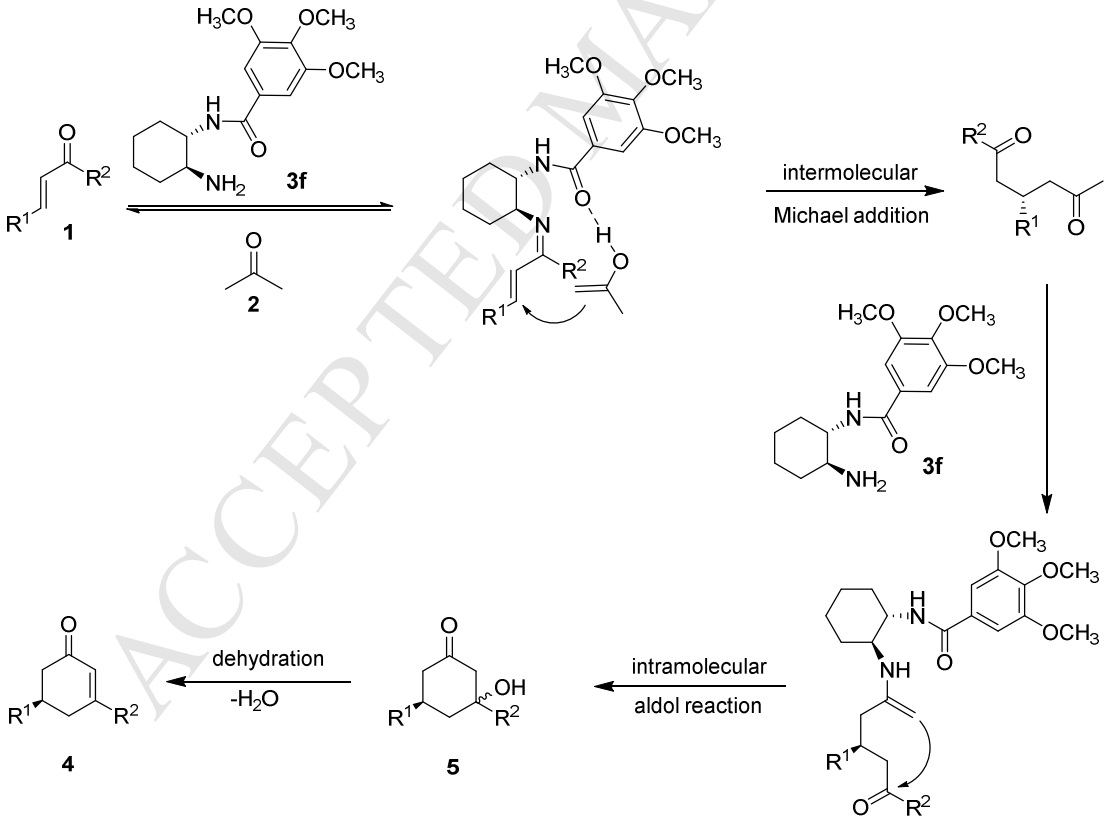
[b] Isolated yield after column chromatography on silica gel.

[c] Determined by chiral HPLC analysis (AS-H, AD-H).

Finally, the mechanism of the primary amine catalyzed tandem Michael-aldol-dehydration reaction was explored. To investigate the interplay between catalyst **3f** and substrates, some NMR control experiments were conducted. Chalcone (**1a**) and acetone (**2**) were separately mixed with catalyst **3f** to test their ^{1}H NMR in DMSO-d_6. It was found that the ^{1}H NMR for the mixture of acetone+**3f** showed some interesting changes: The signals of aromatic protons and methoxyl groups of **3f** were obviously split, revealing that acetone must have certain interaction with the amide part which directly connects to the benzene ring in catalyst **3f**. However, in the mixture of chalcone+**3f**, the chemical shifts for the aromatic protons and methoxyl groups of **3f** didn't show obvious changes, but the chemical shifts of protons from the cyclohexyl of **3f** moved to downfield slightly; on the contrary, the chemical shifts of protons from chalcone moved to upfield slightly. This suggested that chalcone did not affect the amide part of **3f**, and instead it may have some

interaction with NH_2 of catalyst **3f**. This is probably due to the steric hindrance of chalcone. (For the ^1H NMR spectra of these NMR control experiments, please see the Supporting information).

Based on the above control experiments and previous reports,[3e,9,10a,13] a possible mechanism was proposed (**Scheme 2**): Firstly, chalcone **1** is activated by catalyst **3f** *via* the formation of imine, and acetone **2** is activated by the amide of **3f** through the formation of enol and hydrogen bond with amide carbonyl oxygen. The enol attacks the α,β-unsaturated imine from *Si* face to generate the Michael adduct. Secondly, catalyst **3f** further activates the Michael adduct *via* the formation of chiral enamine intermediate, and an intramolecular aldol addition occurs which gave the cyclohexane ring **5.** Finally, product chiral cyclohexenone **4** is generated by the dehydration of **5**.



Scheme 2 Possible mechanism for the primary amine catalyzed domino reaction.

Conclusion

In conclusion, a highly enantioselective organocatalytic domino Michael-aldol-dehydration reaction for the synthesis of 3,5-disubstituted chiral cyclohexenones was developed for the first time. Easily available acetone and chalcones were used as starting materials, and a simple chiral primary amine was used as a catalyst. The various products were obtained in moderate to good yields of up to 85% with excellent enantioselectivities of 91-98% *ee*. This procedure provided a simple and straightforward method to construct 3,5-disubstituted chiral cyclohexenones.

Experimental

General

NMR data were obtained for ^{1}H at 300 MHz, 600 MHz and for ^{13}C at 75 MHz, 150 MHz. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard in $CDCl_3$ or $(CD_3)_2SO$ solution. In each case, the enantiomeric excess was determined by chiral HPLC analysis on chiralpak AD-H and AS-H in comparison with authentic racemates. All optical rotations $[\alpha]_{20}^{D}$ were obtained from a polarimeter (WZZ-2S 2SS). High-resolution mass spectra were obtained by using ESI ionization sources (Varian 7.0T FTICR-MS). All chemical reagents (include **3a**) and solvents were purchased from commercial vendors, and used without any further purification unless otherwise stated. All the reactions were monitored by thin-layer chromatography (TLC) with Haiyang GF254 silica gel plates. Flash column chromatography was carried out using 200–300 mesh silica gel at increased pressure.

General procedure for the synthesis of catalysts 3b-3f.

Catalysts **3a** was purchased from commercial vendors; **3b-3f** were synthesized following previous

procedures.[21]

General procedure for the Michael-aldol-dehydration reactions.

A mixture of catalyst **3f** (12 mg, 20 mol %), chalcone **1** (0.20 mmol) and acetone **2** (10 equiv. + 10 equiv./2d) in xylene (0.50 mL) was stirred at 30 ^{o}C. Upon completion of the reaction (monitored by TLC), the solvent was evaporated under reduced pressure. The residue was purification by flash column chromatography (EtOAc/hexane = 1/3-1/10, v/v) to afford the corresponding products.

Acknowledgements

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References

1 (a) Hareau, G. P. J.; Koiwa, M. S.; Sato, F. *J. Am. Chem. Soc.* **1999**, *121*, 3640. (b) Mohr, P.; Halcomb, J. R. L.; *J. Am. Chem. Soc.* **2003**, *125*, 1712. (c) Lakshmi, R.; Bateman, T. D.; McIntosh, M. C.; *J. Org. Chem.* **2005**, *70*, 5313. (d) Baran, P. S. Richter, J. M. Lin, D. W. *Angew. Chem. Int. Ed.* **2005**, *44*, 609. (e) Goeke, A.; Mertl, D.; Brunner, G. *Angew. Chem. Int. Ed.* **2005**, *44*, 99. (f) Yamashita, S.; Iso, K.; Hirama, M. *Org. Lett.* **2008**, *10*, 3413. (g) Klunder, A. J. H.; Zhu, J.; Zwanenburg, B. *Chem. Rev.* **1999**, *99*, 1163.

2 For selected examples, see: (a) Hareau, V. G.; Hikichi, S.; Sato, F. *Angew. Chem. Int. Ed.* **1998**, *37*, 2099. (b) Hikichi, S.; Hareau, G. P. J.; Sato, F.; *Tetrahedron Lett.* **1997**, 38, 8299. (c) Sarakinos, G.; Corey, E. J.; *Org. Lett.* **1999**, *1* , 811. (d) Hareau, G. P. J.; Koiwa, M.; Hikichi, S.; Sato, F. *J. Am. Chem. Soc.* **1999**, *121*, 3640. (e) Hanazawa, T.; Koiwa, M.; Hareau, G. P. J.; Sato, F. *Tetrahedron Lett.* **2000**, *41*, 2659.

3 (a) Pidathala,C.; Hoang, L.; Vignola, N.; List, B. *Angew. Chem. Int. Ed.* **2003**, *42*, 2785. (b) Hayashi, Y.; Sekizawa, H.; Yamaguchi, J.; Gotoh, H. *J. Org. Chem.* **2007**, *72*, 6493. (c) Itagaki, N.; Kimura, M.; Sugahara, T.; Iwabuchi, Y. *Org. Lett.* **2005**, *7*, 4185. (d) Itagaki, N.; Sugahara, T.;

Iwabuchi, Y.; *Org. Lett.* **2005**, *7*, 4181. (e) Chen, L.; Luo, S.; Li, J.; Li, X.; Cheng, J. P. *Org. Biomol. Chem.* **2010**, *8*, 2627.

4 Naasz, R.; Arnold, L. A.; Minnaard, A. J.; Feringa, B. L.; *Angew. Chem. Int. Ed.* **2001**, *40*, 927.

5 Yang, X.; Wang, J.; Li, P. F. *Org. Biomol. Chem.* **2014**, *12*, 2499.

6 Paolo, M.; Mauro, M.; Armando, C.; Giuseppe, B. *Angew. Chem. Int. Ed.* **2008**, *47*, 6138.

7 (a) Carlone, A.; Marigo, M.; North, C.; Landa, A.; Jørgensen, K. A. *Chem. Commun.* **2006**, 4928. (b) Bolze, P.; Dickmeiss, G.; Jørgensen, K. A.; *Org. Lett.* **2008**, *10*, 3753. (c) Albrecht, Ł.; Richter, B.; Vila, C.; Krawczyk, H.; Jørgensen, K. A.; *Chem. Eur. J.* **2009**, *15*, 3093.

8 Hayashi, Y.; Toyoshima, M.; Gotoh, H.; Ishikawa, H.; *Org. Lett.* **2009**, *11*, 45.

9 Xie, J. W.; Chen, W.; Li, R.; Zeng, M.; Du, W.; Yue, L.; Chen, Y. C.; Wu, Y.; Zhu, J.; Deng, J. G.; *Angew. Chem. Int. Ed.* **2007**, *46*, 389.

10 (a) Yang, Y. Q.; Chai, Z.; Wang, H. F.; Chen, X. K.; Cui, H. F.; Zheng, C. W.; Xiao, H.; Li, P.; Zhao, G. *Chem.–Eur. J.* **2009**, *15*, 13295. (b) Huang, Y. M.; Zheng, C. W.; Zhao, G. *J. Org. Chem.* **2015**, *80*, 3798.

11 Kamaura, M.; Daikai, K.; Hanamoto, T.; Inanaga, J. *Chem. Lett.* **1998**, 697.

12 Wagh, S. J.; Chowdhury, R.; Ghosh, S. K. *Current Organocatalysis*, **2014**, *1(2)*, 71.

13 Paolo, M. *Angew. Chem. Int. Ed.* **2012**, *51*, 9748 .

14 Youssef, L. B.; Stephen, H. *Chem. Rev.* **1997**, *97*, 3161.

15 Wieland, H.; Schlichtung, O.; Langsdorf, W. V. Z. *Phys. Chem.* **1926**, *161*, 74.

16 (a) Whitney, T. A. *U.S. Patent 4* 085138, **1978**; Chem. Abstr. 1978, 89, 108356x. (b) Whitney, T. A. *J. Org. Chem.* **1980**, *45*, 4214.

17 Glasbol, F.; Steenbol, P.; Sorenson, S. B. *Acta Chem. Scand.* **1980**, *26*, 3605.

18 (a) Yang, Y.; He, Y. H.; Guan, Z.; Huang W. D. *Adv. Synth. Catal.* **2010**, *352*, 2579. (b) Zhong, J.; Guan, Z.; He, Y. H. *Catalysis Communications 32* (**2013**) 18. (c) Guan, Z.; Luo, Y.; Zhang, B. Q.; Heinen, K.; Yang, D. C.; He, Y. H. *Tetrahedron: Asymmetry 25* (**2014**) 802.

19 Ban, S. R.; Zhu, X. X.; Zhang, Z. P.; Li, Q. S. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 2517.

20 Shohei, H.; Akio, F.; Jun, T.; Takao, I.; Ryoji, N. *J. Am. Chem. Soc.* **1995**, *117*, 7562.

21 Peng, L.; Xu, X. Y.; Wang, L. L.; Huang, J.; Bai, J. F.; Huang, Q. C.; Wang, L. X. *Eur. J. Org. Chem.* **2010**, 1849.