CHEMISTRY
A EUROPEAN JOURNAL

FULL PAPER

DOI: 10.1002/chem.201300478

Highly Enantioselective Aldol Reactions between Acetaldehyde and Activated Acyclic Ketones Catalyzed by Chiral Primary Amines

Yu-Hua Deng,[a] Jin-Quan Chen,[a] Long He,[a] Tai-Ran Kang,[a] Quan-Zhong Liu,*[a] Shi-Wei Luo,*[b] and Wei-Chen Yuan[c]

Abstract: Highly enantioselective cross-aldol reactions between acetaldehyde and activated acyclic ketones are reported for the first time. Various acyclic ketones, such as saturated and unsaturated keto esters, reacted with acetaldehyde in the presence of a chiral primary amine and a Brønsted acid to afford optically enriched tertiary alcohols in good yields and with excellent enantioselectivities. Trifluoromethyl ketones were tolerable under the reaction conditions, thereby affording the trifluoromethyl carbinol in good-to-excellent yields and enantioselectivities. Structural modification of the chiral amines from the same chiral source switched the stereoselectivity of the products. The utility of aldol chemistry was demonstrated in the brief synthesis of functionally enriched δ-lactones. Theoretical calculations on the transition-state structure indicated that the protonated tertiary amine could effectively activate the carbonyl group of a keto ester to promote the addition process through hydrogen-bonding interaction and, simultaneously, provide an appropriate attacking pattern for the approach of the keto ester to the enamine, which is formed from acetaldehyde and the chiral catalyst, on a particular face, resulting in high enantioselectivity.

Keywords: aldol reactions · amines · enantioselectivity · ketones · lactones

Introduction

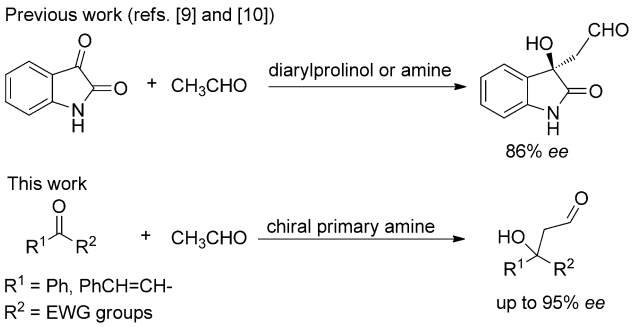
Asymmetric aminocatalysis[1] has received much attention and significant advancements have been made over the past few years. Organocatalytic asymmetric aldol reactions are still of use in C–C formation reactions that allow rapid access to β-hydroxycarbonyl compounds.[2] Despite this great success, direct asymmetric aldol reactions of acetaldehyde, the simplest aldehyde, as the nucleophile have received less attention[3] and the challenge of that very reactive acetaldehyde, which is highly prone to polymerization, still remains. Early in 1994, Harrie and Wong reported a stereospecific aldol reaction of acetaldehyde that was catalyzed by 2-deoxyribose-5-phosphate aldolase (DERA), but only a low yield was obtained;[4] the aldol product reacted further with dihydroxy ketone phosphate, thereby forming 5-deoxy-7-carbon carbohydrate derivatives in the presence of fructose-1,6-diphosphate aldolase from rabbit muscle (RAMA).[5] The first organocatalytic enantioselective self-aldol reaction of acetaldehyde was reported in 2002 by using proline as the catalyst.[6] Although good enantiomeric excess was obtained, the yield was too low to be practical. An alternative solution was a Mukayama-aldol reaction that employed the silyl enol ether of acetaldehyde with triflimide or a chiral phosphoramide as the catalyst.[7] Then, in 2008, the catalytic asymmetric direct aldol reaction between acetaldehyde and other aldehydes was accomplished, catalyzed by diarylprolinol, in moderate yields and good enantioselectivities.[8] Quite recently, Chen and co-workers reported that chiral primary amines were effective catalysts in enantioselective aldol reactions with acetaldehyde as the nucleophile.[9] To date, the cross-aldol reaction between acetaldehyde and ketones has seldom been explored. To the best of our knowledge, only isatin has been successfully applied in the enantioselective cross-aldol reaction with chiral amine catalysts.[9,10] In 2008, we developed a new family of chiral primary amines from optically pure binaphthol and amino acids. These chiral amines were found to be effective in asymmetric aldol reactions between acetone and aromatic aldehydes, keto esters, and unsaturated keto esters.[11] These direct cross-aldol reactions between acetaldehyde and ketones allowed rapid access to chiral tertiary alcohols, which are common scaffolds in many natural products (Scheme 1).[12] In our efforts toward achieving the cross-aldol reaction between acetaldehyde and ketones, we found that easily modified chiral primary amine catalysts with a binaphthyl backbone were effective in the reactions between

[a] Y.-H. Deng, J.-Q. Chen, Dr. L. He, Dr. T.-R. Kang, Prof. Q.-Z. Liu
Chemical Synthesis and Pollution Control
Key Laboratory of Sichuan Province and
College of Chemistry and Chemical Engineering
China West Normal University, Nanchong 637000 (P.R. China)
E-mail: quanzhongliu@cwnu.edu.cn

[b] Prof. S.-W. Luo
Department of Chemistry
University of Science and Technology of China
Hefei, 230026 (P.R. China)
E-mail: luosw@ustc.edu.cn

[c] Prof. W.-C. Yuan
Chengdu Institute of Organic Chemistry
Chengdu 610041 (P.R. China)

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201300478.



Scheme 1. Cross-aldol reactions between acetaldehyde and activated acyclic ketones. EWG = electron-withdrawing group.

acetaldehyde and activated acyclic ketones (Scheme 1). The structural modification of these chiral amines from the same chiral source allowed a switching of the stereoselectivity of the products. Herein, we report our results.

Results and Discussion

Based on the successful asymmetric aldol reaction between β,γ-unsaturated keto esters and ketones,[13] keto ester **1a** was initially chosen as the activated acyclic ketone for our enantioselective cross-aldol reaction with acetaldehyde. The hetero-Diels–Alder reaction between compound **1a** and acetaldehyde in the presence of proline-based catalysts has been reported previously, but the aldol reaction has never been described.[3f–h] In our investigation, proline-based organocatalysts **I** and **II** were screened first (Figure 1) and the aldol product was isolated in low yields and enantioselectivities (Table 1). For example, only 16% *ee* was obtained when proline was used as the catalyst. Diaryl-prolinol-based catalysts, such as catalysts **IIA**–**IID**, which have exhibited excellent efficiency in the asymmetric aldol reactions of aldehydes, even for acetaldehyde, were inefficient, thereby providing the corresponding product with only 20–22% *ee*.[10]

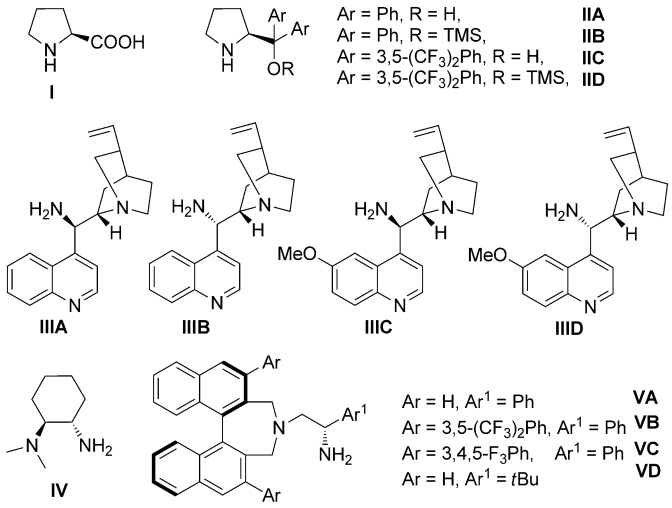
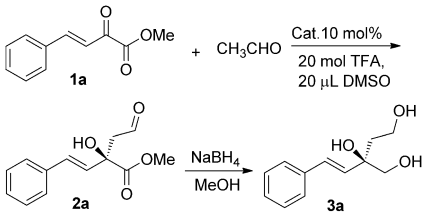


Figure 1. Catalysts that were screened in the work.

Table 1. Enantioselective cross-aldol reactions between acetaldehyde and unsaturated keto ester **1a**.[a]



Entry	Catalyst	Yield [%][b]	*ee* [%][c]
1[d]	**I**	32	16
2[d]	**IIA**	10	−20
3[d]	**IIB**	29	−22
4[d]	**IIC**	<5	–
5[d]	**IID**	<5	–
6	**IIIA**	26	−22
7	**IIIB**	58	4
8	**IIIC**	45	27
9	**IIID**	26	33
10	**IV**	74	22
11	**VA**	70	87
12	**VB**	76	−82.5
13	**VC**	60	−55
14	**VD**	60	77

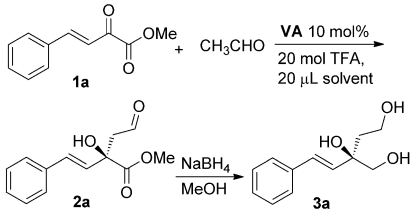
[a] Unless otherwise stated, the reaction was carried out with keto ester **1a** (0.1 mmol), acetaldehyde (10 equiv), catalyst (10 mol%), and trifluoroacetic acid (20 mol%) in DMSO (20 μL) at room temperature. [b] Yield of isolated product. [c] Determined by chiral HPLC after reduction of the product into the corresponding alcohol (**3a**). [d] No acid was added.

Very recently, cinchona-derived primary amines **III** have found application in asymmetric aldol reactions.[14] However, these catalysts provided similar results to those with catalysts **IIA**–**IID**. Chiral cyclohexanediamine catalyst **IV** was highly efficient in the enantioselective aldol reactions, thereby affording the product in good yield, but again only low enantioselectivity was obtained (74% yield, 22% *ee*). These results highlighted the difficulties in the enantioselective aldol reaction between acetaldehyde and acyclic ketones.

To our delight, the chiral amine catalysts that were developed by our group were found to be efficient in this reaction. For example, when amine **VA** was surveyed in the model reaction, both the enantioselectivity and yield were greatly enhanced: The corresponding tertiary alcohol was isolated in 70% yield and 87% *ee* (Table 1, entry 11). To the best of our knowledge, this result is the first example of an enantioselective aldol reaction between acetaldehyde and acyclic ketones. This catalyst was the most efficient among the organocatalysts that were surveyed in this work. Thus, other catalysts with this structure were investigated next. The introduction of substituents at the 3,3′-positions of the binaphthyl motif resulted in a switch in the stereoselectivity and the opposite configuration of the product was obtained. When catalyst **VB** was used, an inversion of the stereoselectivity was observed, with 82.5% *ee*. Thus, the stereochemical induction of the reaction greatly depended on the binaphthyl motif, but the *ee* values varied with the amine structure.

Further optimization of the reaction parameters, such as solvent, acid, and temperature, was carried out. Among the solvents that were surveyed, HMPA was the best in terms of yield and enantioselectivity (72% yield, 87% *ee*; Table 2,

Table 2. Solvent screen.[a]



Entry	Solvent	Yield [%][b]	*ee* [%][c]
1	DMSO	70	87
2	HMPA	72	87
3	DMF	50	36
4	THF	68	75
5	Et_2O	73	83
6	1,4-dioxane	48	74
7	CCl_4	64	81
8	$CHCl_3$	70	79
9	CH_2Cl_2	65	68
9	benzene	58	79
10	toluene	60	78
11	*n*-hexane	69	79
12	MeCN	60	78
13	neat	77	66

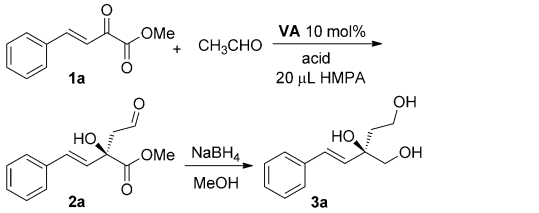
[a] Unless otherwise stated, the reaction was carried out with keto ester **1a** (0.1 mmol), acetaldehyde (10 equiv), catalyst **VA** (10 mol%), and trifluoroacetic acid (20 mol%) in DMSO (20 μL) at room temperature for 12 h. [b] Yield of isolated product. [c] Determined by chiral HPLC after reduction of the product into the corresponding alcohol. HMPA = hexamethylphosphoramide.

entry 2). The reaction was relatively slow when DMSO was used as the solvent and other solvents provided poorer results compared to those in polar aprotic solvents. Therefore, HMPA was chosen as the solvent for further investigations.

The selectivity of the reaction greatly depended on the strength of the acid that was used (Table 3). Among the acids that we investigated, triflic acid provided the highest yield and enantioselectivity (81% yield, 88% *ee*; Table 3, entry 5). The amount of acid has a slight impact on the reaction. Increasing the amount of acid to 30 mol% led to a marginal increase in enantioselectivity but the yield dropped (Table 3, entry 6). We found that the amount of catalyst had no effect on the reaction (Table 3, entry 7). Lowering the temperature to 0°C afforded the product in higher yield and enantioselectivity (81% yield, 92% *ee*; Table 3; entry 9); the reaction proceeded very slowly at −10°C, with no improvement in enantioselectivity.

With the optimal conditions for this reaction in hand, various keto esters were surveyed with acetaldehyde as the nucleophile. Among the keto esters that were screened, the corresponding products were obtained in good yields and good-to-excellent enantioselectivities. The electronic nature of aromatic ring of esters has little influence on the yield of the reaction. However, it seemed that the enantioselectivity

Table 3. Effects of the acid.[a]



Entry	Acid	*T* [°C]	Yield [%][b]	*ee* [%][c]
1	TFA	20	70	87
2	AcOH	20	68	51
3	*p*-$NO_2C_6H_4CO_2H$	20	66	72
4	$PhCO_2H$	20	48	61
5	TfOH	20	81	88
6[d]	TfOH	20	72	90
7[e]	TfOH	20	78	89
8[d]	TfOH	10	77	92
9[d]	TfOH	0	81	92
10[d]	TfOH	−10	72	90

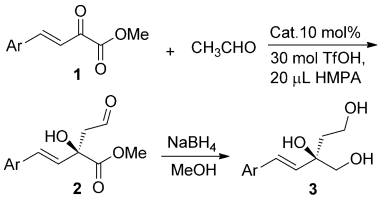
[a] Unless otherwise stated, the reaction was carried out by using keto ester **1a** (0.1 mmol) and acetaldehyde (10 equiv) in HMPA (20 μL) with **VA** (10 mol%) and acid (20 mol%) as the catalyst for 12 h at the indicated temperature. [b] Yield of isolated product. [c] Determined by chiral HPLC after reduction of the product into the corresponding alcohol. [d] TfOH (30 mol%) was used. [e] Catalyst (20 mol%) and TfOH (60 mol%) were used. TFA = trifluoroacetic acid, TfOH = trifluoromethanesulfonic acid, AcOH = acetic acid.

was heavily dependent on the electronic nature of the keto ester. Generally speaking, for substrates with the same substituted pattern, electron-deficient substrates provided higher selectivities compared to electron-rich substrates. For example, unsubstituted keto ester **1a** provided the product in 92% *ee*, whereas 4-methyl-substituted substrate **1b** provided the product in only 87% *ee* (Table 4, entries 1 and 2). For 4-substituted substrates, compounds **1c**, **1d**, and **1f**–**1h** provided their corresponding products in higher selectivities than compounds **1b** and **1e** (Table 4, entries 3, 4, and 6–9 vs. entries 2 and 5). Other substrates (compounds **1j**–**1m** and **1q**) also showed the same trend (Table 4, entries 10–13 and 17). It should be noted that the keto ester that was substituted with a furyl group was also tolerated under these conditions (Table 4, entry 16).

Although most of the aldol products (**2**) were oils, after reduction, the corresponding triols **3g** and **3i** were crystalline solids. Thus, the absolute configuration of compound **3g** was determined to be *R* by single-crystal X-ray diffraction analysis after recrystallization from *n*-hexane/Et_2O (Figure 2). The absolute configurations of other aldol products were tentatively assigned by analogy.

This procedure can be extended to the enantioselective aldol reaction between other activated acyclic ketones and acetaldehyde. The presence of fluorine atoms in pharmaceutical compounds often enhances their pharmacological activities.[15] With this fact in mind, trifluoromethyl-substituted keto ester **4a** was investigated in the enantioselective aldol reaction with acetaldehyde. The corresponding tertiary alcohol (**5a**) was obtained in 66% yield with 92% *ee*

Table 4. Enantioselective cross-aldol reactions between acetaldehyde and unsaturated keto esters.[a]



Entry	Ar	Keto ester	Yield [%][b]	*ee* [%][c]
1	C_6H_5	**1a**	81	92
2	4-MeC_6H_4	**1b**	80	87
3	4-$NO_2C_6H_4$	**1c**	55	89
4	4-CNC_6H_4	**1d**	84	94
5	4-$OMeC_6H_4$	**1e**	70	88
6	4-FC_6H_4	**1f**	70	91
7	4-ClC_6H_4	**1g**	83	91
8	4-$CF_3C_6H_4$	**1h**	90	94
9	4-BrC_6H_4	**1i**	81	87
10	3-ClC_6H_4	**1j**	73	89
11	3-BrC_6H_4	**1k**	74	85
12	3-$MeOC_6H_4$	**1l**	79	84
13	3-MeC_6H_4	**1m**	87	88
14	2-MeC_6H_4	**1n**	88	90
15	3,4,5-$(MeO)_3C_6H_2$	**1o**	78	94
16	furyl	**1p**	77	91
17	3-$NO_2C_6H_4$	**1q**	80	94

[a] Unless otherwise stated, the reaction was carried out with the keto ester (0.1 mmol), acetaldehyde (10 equiv), catalyst (10 mol%), and triflic acid (30 mol%) at 0°C. [b] Yield of isolated product. [c] Determined by chiral HPLC.

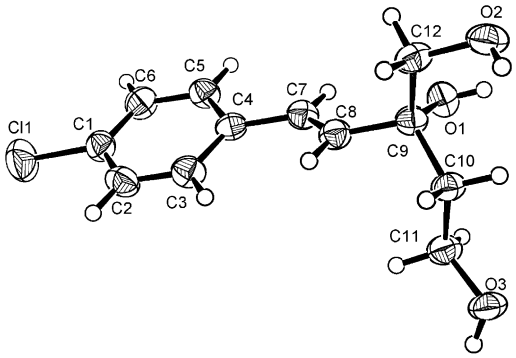
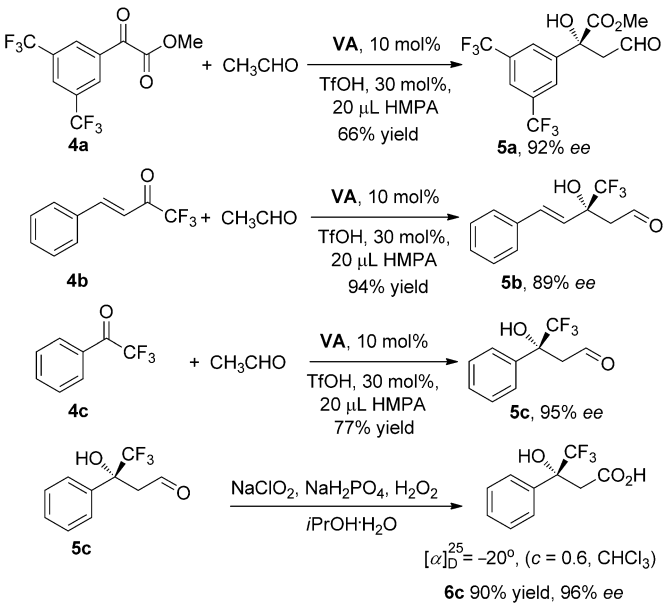


Figure 2. ORTEP drawing of compound **3g**; thermal ellipsoids are set at 45% probability.

(Scheme 2). Although CF_3-containing unsaturated ketone **4b** has been successfully employed in the asymmetric aldol reaction of acetone catalyzed by proline or prolinamide,[16] acetaldehyde has never been used as the nucleophile in the aldol reaction of compound **4b**. Under our conditions, compound **4b** reacted with acetaldehyde, thereby affording compound **5b** in 94% yield with 89% *ee*. Phenyl trifluoromethyl ketone **4c** also reacted with acetaldehyde and furnished optically enriched alcohol **5c** in 95% *ee*.[17] To the best of our knowledge, this is the first highly efficient asymmetric catalytic synthesis of a trifluoromethyl carbinol by using a trifluoromethyl ketone and acetaldehyde. It should be noted that compound **5c** can be easily transformed into the corresponding carboxylic acid (**6c**) without an erosion in enantioselectivity. Carboxylic acid **6c** has been found to be an important motif in pharmaceutical compounds[18] and was previously prepared by the diastereoselective reaction between a trifluoromethyl ketone and a chiral enolate[19] or by the alkenylation of the trifluoromethyl ketone, followed by a series of transformations, such as hydroboration and oxidation.[20]

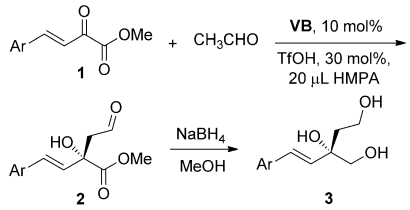


Scheme 2. Reactions between trifluoromethyl ketones and acetaldehyde.

Asymmetric transformations that can produce both enantiomers of a product in a specified reaction by using chiral catalysts with different substituents are desirable from a practical point of view. The absolute configuration of the enantioselective cross-aldol product can be switched to the *S* configuration by using catalyst **VB** under otherwise identical conditions (Table 5), although the *ee* values are slight lower. For example, compound **1a** reacted with acetaldehyde in the presence of 10 mol% of catalyst **VB** and 30 mol% of TfOH to afford compound (*S*)-**3a** in 88% yield with 84% *ee*. Other substrates provided their corresponding chiral tertiary alcohols in good yields with good enantioselectivities.

To obtain insight into the stereocontrol in this enantioselective nucleophilic addition reaction, theoretical calculations were performed on the plausible transition states (TS) by using the B3LYP/6-31(d) method,[21] as implemented in the Gaussian 03 program.[22] The located most stable TS structures are shown in Figure 3. The nitrogen atom of the tertiary amine in the key enamine intermediate, which is formed from the reaction of the amine catalyst with acetaldehyde, should be protonated during the reaction scheme under these conditions. The protonated amine could act as a hydrogen-bond (HB) donor to induce the keto ester into approaching the enamine through hydrogen-bonding interactions and simultaneously activate the carbonyl group of the keto ester to promote the nucleophilic addition of the en-

Table 5. Enantioselective aldol reactions between acetaldehyde and unsaturated keto esters catalyzed by catalyst **VB**.[a]



Entry	Ar	Keto ester	Yield [%][b]	*ee* [%][c]	Configuration
1	C_6H_5	**1a**	88	84	*S*
2	*p*-MeC_6H_4	**1b**	81	84	*S*
3	*p*-FC_6H_4	**1f**	80	82	*S*
4	*p*-$CF_3C_6H_4$	**1h**	90	81	*S*
5	*p*-ClC_6H_4	**1g**	91	85	*S*
6	3,4,5-$(OMe)_3C_6H_2$	**1o**	71	87	*S*

[a] Unless otherwise stated, the reaction was carried out with the keto ester (0.1 mmol), acetaldehyde (10 equiv), catalyst **VB** (10 mol%), and triflic acid (30 mol%) at 0°C. [b] Yield of isolated product. [c] Determined by chiral HPLC.

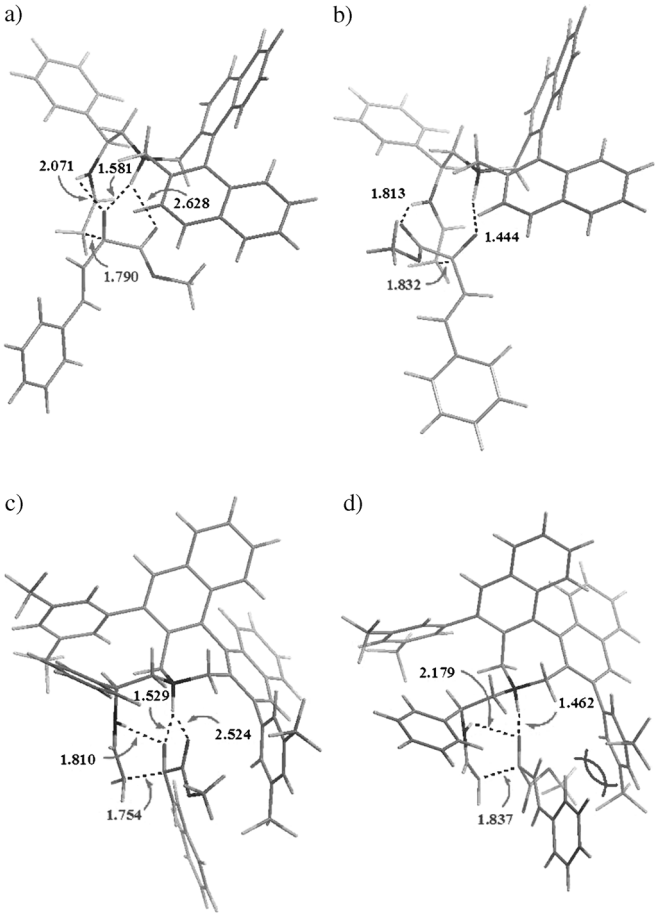


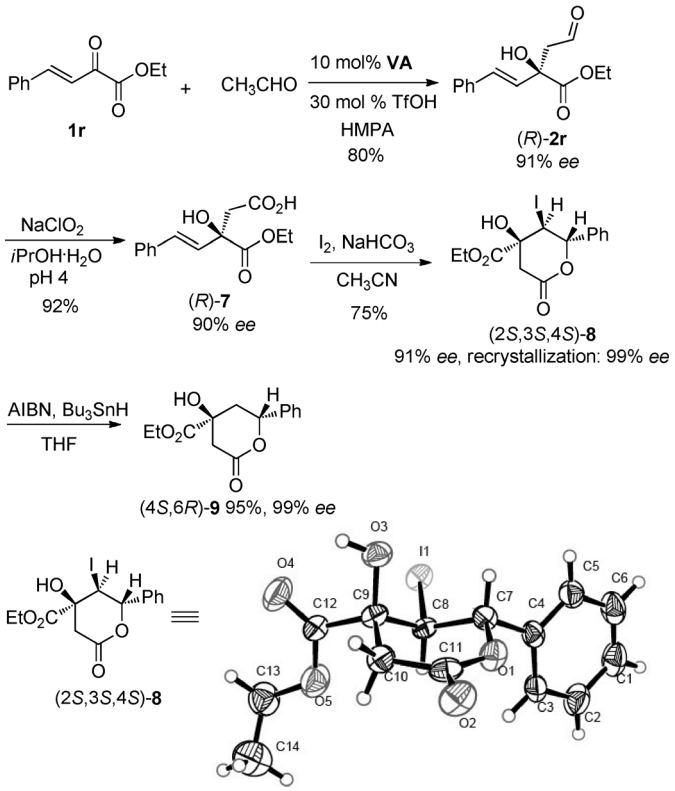
Figure 3. Located transition-state structures in the enantioselective aldol reaction by using the B3LYP/6-31(d) method; distances are in Å; relative enthalpies and Gibbs free energies [kcal mol^{-1}], respectively, are as follows: a) TS-**VA**-*R*, 0.00 and 0.00; b) TS-**VA**-*S*, 5.41 and 4.93; c) TS-**VB**-*S*, 0.00 and 0.00; d) TS-**VB**-*R*, 10.90 and 10.30.

amine to the carbonyl group of the keto ester. The keto ester may approach either the *Si* or *Re* faces of the enamine, with different HB patterns. The located TS structures indicated that transition state TS-**VA**-*R*, which corresponded to the main product that was experimentally observed with catalyst **VA**, was more favorable than transition state TS-**VA**-*S* by about 5 kcal mol^{-1} (Figure 3). The staggered conformation for the attack of the enamine onto the carbonyl group of the keto ester may contribute to the high stability of transition state TS-**VA**-*S*, whereas, in transition state TS-**VA**-*R*, there is an almost-eclipsed conformation for the addition. Conversely, when catalyst **VB** was used as the catalyst, the located TS structures indicate that transition state TS-**VB**-*S*, which generated the observed main product, was predicted to be more stable than transition state TS-**VB**-*R* by about 10 kcal mol^{-1} (Figure 3). The steric repulsion between the 3,5-$(CF_3)_2$Ph group on catalyst **VB** and the phenyl group of the keto ester in transition state TS-**VB**-*R* caused unfavorable interactions for the addition on the *Si* face of the keto ester. Appropriate matching of the bulky 3,3′-substituents of catalyst **VB** to the keto ester substrate should control the stereoselectivity of the addition process.

The aldol product can be easily transformed into a variety of functionally enriched compounds. To demonstrate the utility of this chemistry, keto ester **1r** was reacted with acetaldehyde, thereby affording tertiary alcohol **2r** in 80% yield with 91% *ee*. Compound **2r** was readily oxidized into the corresponding carboxylic acid with a pendent olefin (**7**) in 92% yield with 90% *ee*. The intramolecular substrate-controlled iodolactonization reaction in the presence of I_2 yielded a six-membered lactone (**8**) with 91% *ee* and excellent diastereoselectivity (>20:1);[23] the optical purity of compound **8** could be further increased to 99% *ee* after a single recrystallization step. The configuration of compound **8** was assigned as 2*S*,3*S*,4*S* by X-ray diffraction. Heating a mixture of compound **8** at reflux with azobisisobutyrontrile (AIBN) and Bu_3SnH in CH_2Cl_2 yielded optically pure δ-lactone **9** in 95% yield (Scheme 3).

Conclusion

In summary, we have developed an enantioselective cross-aldol reaction between acetaldehyde and activated acyclic ketones. The acyclic activated ketones reacted with acetaldehyde in the presence of a chiral primary amine and a Brønsted acid, thus yielding optically enriched tertiary alcohols in good yields and excellent enantioselectivities. The utility of this aldol chemistry was demonstrated in the brief synthesis of functionally enriched δ-lactones. Theoretical calculations on the transition-state structure were carried out to elucidate the catalytic mechanism.



Scheme 3. Utility of the enantioselective cross-aldol reaction and ORTEP drawing of compound (2*S*,3*S*,4*S*)-**8**; thermal ellipsoids are set at 40% probability.

Experimental Section

General procedure for the enantioselective cross-aldol reaction between acetaldehyde and ketones: To a solution of ketone **1a** (0.1 mmol) and catalyst **VA** (10 mol%) in HMPA (20 μL) in a test tube was added TfOH (4.5 mg, 2.7 μL, 30 mol%) at 0°C and the mixture was stirred for 15 min, followed by the addition of acetaldehyde (56 μL, 1 mmol). Then, the mixture was stirred at 0°C for 24–72 h until the reaction had been completed (by TLC). Excess acetaldehyde was removed under reduced pressure. The crude mixture was dissolved in MeOH (1.5 mL) at 0°C, reduced with $NaBH_4$ (114 mg, 3 mmol) for 1 h, and quenched with water (3 mL). The mixture was extracted with EtOAc (5×10 mL) and the combined organic extract was dried with anhydrous Na_2SO_4, filtered, concentrated under vacuum, and purified by flash chromatography on silica gel to afford the corresponding product (**3a**) as a white solid (81% yield). R_f= 0.22 (petroleum ether/EtOAc, 1:2); M.p. 85–87°C; $[\alpha]_D^{25}=+19.1$ ($c=0.3$, MeOH; 92% *ee*); ^{1}H NMR (400 MHz, [D$_6$]acetone): $\delta=7.48$–7.23 (m, 5H; Ar-H), 6.79 (d, $J=16.0$ Hz, 1H; CH=CH), 6.46 (d, $J=16.0$ Hz, 1H; CH=CH), 4.34 (s, 1H), 4.11–4.07 (m, 2H), 3.89–3.77 (m, 2H), 3.60–3.52 (m, 2H), 2.07–2.02 (m, 1H), 1.90–1.84 ppm (m, 1H); ^{13}C NMR (100 MHz, [D$_6$]acetone): $\delta=137.5$, 134.0, 128.6, 128.5, 127.1, 126.3, 75.7, 69.2, 58.5, 39.0 ppm; HRMS (ESI): *m*/*z* calcd for $C_{12}H_{16}O_3$: 231.0997 [*M*+Na]$^+$; found: 231.1003; IR (KBr): $\tilde{\nu}=3379$, 3310,3028, 2930, 2859, 1445, 1135, 1047, 978, 748, 694 cm^{-1}; HPLC (Daicel Chiralpak OD-H; *n*-hexane/isopropanol, 90:10; flow rate: 1.0 mL min^{-1}; $\lambda=254$ nm): t_R(major)=24.6 min, t_R(minor)=32.8 min.

(*R*,*E*)-Ethyl-2-hydroxy-2-(2-oxoethyl)-4-phenylbut-3-enoate (2r): To a solution of compound **1r** (72 μL, 0.4 mmol) and catalyst **VA** (16.8 mg, 10 mol%) in HMPA (20 μL) in a test tube was added TfOH (10.8 μL, 30 mol%) at 0°C and the mixture was stirred for 15 min, followed by the addition of acetaldehyde (56 μL, 1 mmol). Then, the mixture was stirred at 0°C for 37 h. The mixture was purified by flash column chromatography on silica gel (petroleum ether/EtOAc, 5:1) to afford compound **2r** (80 mg, 80% yield, including its hemiacetals) as a pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=9.77$ (t, $J=1.4$ Hz, 1H), 7.42–7.28 (m, 5H), 6.91 (d, $J=15.8$ Hz, 1H), 6.26 (d, $J=15.8$ Hz, 1H), 4.35–4.28 (m, 2H), 3.80 (s, 1H), 3.11 (dd, $J=0.4$ Hz, $J=16.9$ Hz), 2.97 (dd, $J=1.6$ Hz, $J=17.2$ Hz, 1H), 1.34 ppm (t, $J=7.2$ Hz, 3H). Owing to the instability of compound **2r**, the enantiomeric purity of **2r** was determined by HPLC analysis after reduction into its corresponding alcohol **3a**.

(*R*,*E*)-3-(Ethoxycarbonyl)-3-hydroxy-5-phenylpent-4-enoic acid (7): To a solution of crude compound **2r** (75 mg, 0.3 mmol) in *i*PrOH (3 mL) was added a 10% solution of NaH_2PO_4 buffer to adjust the pH to 4, followed by the addition of a 30% aqueous solution of H_2O_2 (24 μL) and 80% $NaClO_2$ (75 mg in 0.5 mL water, 2.2 equiv). The mixture was stirred at about 10°C until the reaction had been completed (monitored by TLC). Then, the reaction mixture was cooled to 0°C and Na_2SO_3 (50 mg) was added to remove the oxidant. The mixture was extracted with EtOAc (3×5 mL) and the organic layer was dried and concentrated. The residue was purified by flash column chromatography on silica gel (petroleum ether/EtOAc, 1:1) to afford compound **7** (73 mg, 92% yield, 90% *ee*) as a white solid. $R_f=0.36$ (petroleum ether/EtOAc, 1:2); M.p. 84–89°C; $[\alpha]_D^{25}=+28.2$ ($c=0.7$, $CHCl_3$; 90% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=$ 7.42–7.28 (m, 5H), 6.92 (d, $J=15.8$ Hz, 1H), 6.23 (d, $J=15.8$ Hz, 1H), 4.32 (q, $J=7.2$ Hz, 2H), 3.23 (d, $J=16.6$ Hz, 1H), 2.86 (d, $J=16.6$ Hz, 1H), 1.33 ppm (t, $J=7.2$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=$ 175.3, 173.4, 135.8, 131.3, 128.6, 128.2, 128.0, 126.8, 75.0, 62.8, 43.3, 14.0 ppm; HRMS (ESI): *m*/*z* calcd for $C_{14}H_{16}O_5$: 287.0895 [*M*+Na]$^+$; found: 287.0899; IR (KBr): $\tilde{\nu}=3488$, 2987, 2926, 1791, 1739, 1410, 1373, 1342, 1298, 1252, 1207, 1135, 1096, 980, 748, 696 nm; HPLC (Daicel Chiralpak OJ-H; *n*-hexane/isopropanol/TFA, 85:15:1; flow rate: 1.0 mL min^{-1}; $\lambda=254$ nm): t_R(major)=7.9 min, t_R(minor)=10.3 min.

(2*S*,3*S*,4*S*)-Ethyl-4-hydroxy-3-iodo-6-oxo-2-phenyltetrahydro-2H-pyran-4-carboxylate (8): To a solution of compound **7** (39.6 mg, 0.15 mmol) in dry MeCN (1.5 mL) was added $NaHCO_3$ (37.9 mg, 0.45 mmol) at 0°C and the resulting suspension was stirred for 15 min at 0°C. Then, iodine (113.8 mg, 0.45 mmol) was added and the mixture was stirred at 0°C for 2.5 days in the darkness until the reaction had been completed (monitored by TLC). The reaction mixture was quenched with water (1.5 mL) and extracted with $CHCl_3$ (4×10 mL). The organic layer was washed with a saturated aqueous solution of sodium thiosulfate to remove any excess iodine. The organic layer was dried over anhydrous sodium sulfate prior to concentration. Purification by column chromatography on silica gel (petroleum ether/EtOAc, 4:1) afforded iodolactone **8** (20:1 d.r., 75% yield, 91% *ee*). Recrystallization from *n*-hexane and Et_2O afforded enantiomerically pure iodolactone **8** (99.9% *ee*). $R_f=0.61$ (petroleum ether/ethyl acetate 2:1); M.p. 139–141°C; $[\alpha]_D^{25}=+40.5$ ($c=0.4$, CH_2Cl_2; 99.9% *ee*); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.42$(s, 5H), 5.71 (d, $J=11.3$ Hz), 4.64 (d, $J=11.3$ Hz), 4.46–4.32 (m, 2H), 3.23 (d, $J=16.6$ Hz, 1H), 3.31 (d, $J=17.4$ Hz, 1H), 3.06 (d, $J=17.4$ Hz), 1.40 ppm (t, $J=7.1$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=171.3$, 166.4, 136.7, 129.7, 128.6, 128.0, 83.0, 75.2, 64.0, 39.7, 34.2, 14.2 ppm; HRMS (ESI): *m*/*z* calcd for $C_{14}H_{15}IO_5$: 412.9862 [*M*+Na]$^+$; found: 412.9865; IR (KBr): $\tilde{\nu}=3396$, 2960, 2921, 1763, 1726, 1456,1433, 1396, 1353, 1244, 1201, 1115, 1093, 991, 733 nm; HPLC (Daicel Chiralpak OJ-H; *n*-hexane/isopropanol, 85:15, flow rate: 1.0 mL min^{-1}; $\lambda=210$ nm): t_R(minor)=16.2 min, t_R(major)= 17.6 min.

(4*S*,6*R*)-Ethyl-4-hydroxy-2-oxo-6-phenyltetrahydro-2H-pyran-4-carboxylate (9): The reaction was performed in a long-necked reaction tube that was equipped with a stirrer bar under a nitrogen atmosphere. Iodolactone **8** (20 mg, 0.05 mmol) was suspended in dry THF (1 mL) and treated with tri-*n*-butyltin hydride (15.3 μL, 0.06 mmol) in the presence of a catalytic amount of AIBN (1.2 mg, 10 mol%) as a free-radical initiator. The reaction was heated at reflux for 4 h. The reaction was cooled to ambient temperature and THF was removed under vacuum. The crude mixture was purified by flash column chromatography on silica gel (petroleum ether/EtOAc, 4:1) to afford δ-lactone **9** (12.6 mg, 95% yield, 99.8% *ee*). $R_f=0.57$ (petroleum ether/EtOAc, 2:1); M.p. 100–102°C; $[\alpha]_D^{25}=-4.8$ ($c=0.2$, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=7.42$–7.36 (m, 5H), 5.74 (dd, $J=3$ Hz, $J=11.9$ Hz, 1H), 4.35–4.30 (m, 2H), 3.62 (s, 1H), 3.07

(d, $J=17.5$ Hz, 1H), 2.84 (dd, $J=1.6$ Hz, $J=17.5$ Hz, 1H), 2.31 (q, $J=12.0$ Hz, 1H), 2.20–2.16 (m, 1H), 1.34 ppm (t, $J=7.1$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=173.8$, 168.3, 138.6, 128.7, 128.7, 125.9, 77.6, 71.5, 63.2, 40.8, 40.0, 14.1 ppm; ^{13}C DEPT-135 NMR (100 MHz, $[D_6]$acetone): $\delta=+128.8$, +128.7, +125.9, +77.6, −63.2, −40.8, −40.0, +14.1 ppm; HRMS (ESI): m/z calcd for $C_{14}H_{16}O_5$: 287.0895 $[M+Na]^+$; found: 287.0892; IR (KBr): $\tilde{\nu}=3508$, 3280, 3030, 2984, 2944, 1737, 1603, 1499, 1405, 1298, 1265, 1220, 1128, 1094, 1009, 904, 724, 644, 604 nm; HPLC (Daicel Chiralpak AD-H; *n*-hexane/isopropanol, 92:8; flow rate: 1.0 mL min^{-1}; $\lambda=210$ nm): t_R(major) = 22.9 min, t_R(minor) = 25.0 min.

CCDC-930397 ((*R*)-**3g**) and CCDC-930398 (**8**) contain 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

Acknowledgements

This work was financially supported by the NSFC (20772097, 21102116) and by Sichuan Province. We thank the Supercomputing Center of the USTC for the use of their computing resources.

[1] For insightful perspectives on the historical origins of aminocatalysis, see: a) C. F. Barbas III, *Angew. Chem.* **2008**, *120*, 44; *Angew. Chem. Int. Ed.* **2008**, *47*, 42; b) B. List, *Angew. Chem.* **2010**, *122*, 1774; *Angew. Chem. Int. Ed.* **2010**, *49*, 1730; c) G. Lelais, D. W. C. MacMillan, *Aldrichimica Acta* **2006**, *39*, 79; for reviews, see: d) A. Berkessel, H. Gröger, *Asymmetric Organo-catalysis: From Biomimetic Concepts to Applications in Asymmetric Synthesis*; Wiley-VCH, Weinheim, **2005**; e) *Enantioselective Organocatalysis* (Ed.: P. I. Dalko), Wiley-VCH, Weinheim, **2007**; f) P. Melchiorre, M. Marigo, A. Carlone, G. Bartoli, *Angew. Chem.* **2008**, *120*, 6232; *Angew. Chem. Int. Ed.* **2008**, *47*, 6138; g) P. I. Dalko, L. Moisan, *Angew. Chem.* **2004**, *116*, 5248; *Angew. Chem. Int. Ed.* **2004**, *43*, 5138; h) B. List, *Chem. Commun.* **2006**, 819; i) J. Seayad, B. List, *Org. Biomol. Chem.* **2005**, *3*, 719; j) X. H. Yu, W. Wang, *Org. Biomol. Chem.* **2008**, *6*, 2037; k) R. N. Butler, A. G. Coyne, *Chem. Rev.* **2010**, *110*, 6302; l) U. M. Lindström, *Chem. Rev.* **2002**, *102*, 2751; m) B. Alcaide, P. Almendros, *Angew. Chem.* **2008**, *120*, 4710; *Angew. Chem. Int. Ed.* **2008**, *47*, 4632; n) A. Dondoni, A. Massi, *Angew. Chem.* **2008**, *120*, 4716; *Angew. Chem. Int. Ed.* **2008**, *47*, 4638; o) S. E. Denmark, G. L. Beutner, *Angew. Chem.* **2008**, *120*, 1584; *Angew. Chem. Int. Ed.* **2008**, *47*, 1560; p) G. Guillena, C. Najera, D. J. Ramon, *Tetrahedron: Asymmetry* **2007**, *18*, 2249; q) B. List, J.-W. Yang, *Science* **2006**, *313*, 1584.

[2] For some representative examples, see: a) N. Mase, Y. Nakai, N. Ohara, H. Yoda, K. Takabe, F. Tanaka, C. F. Barbas III, *J. Am. Chem. Soc.* **2006**, *128*, 734; b) A. B. Northrup, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2002**, *124*, 6798; c) B. List, R. A. Lerner, C. F. Barbas III, *J. Am. Chem. Soc.* **2000**, *122*, 2395; d) A. Kumar, S. Singh, V. Kumar, S. S. Chimni, *Org. Biomol. Chem.* **2011**, *9*, 2731; e) Z. Q. Jiang, H. Yang, X. Han, J. Luo, M. W. Wong, Y. X. Lu, *Org. Biomol. Chem.* **2010**, *8*, 1368; f) M. Gruttadauria, A. M. P. Salvo, F. Giacalone, P. Agrigento, R. Noto, *Eur. J. Org. Chem.* **2009**, 5437; g) M. K. Zhu, X. Y. Xu, L. Z. Gong, *Adv. Synth. Catal.* **2008**, *350*, 1390; h) J. Huang, X. Zhang, D. W. Armstrong, *Angew. Chem.* **2007**, *119*, 9231; *Angew. Chem. Int. Ed.* **2007**, *46*, 9073; i) S. Guizzetti, M. Benaglia, L. Raimondi, G. Celentano, *Org. Lett.* **2007**, *9*, 1247; j) A. P. Brogan, T. J. Dickerson, K. D. Janda, *Angew. Chem.* **2006**, *118*, 8278; *Angew. Chem. Int. Ed.* **2006**, *45*, 8100; k) Y. Hayashi, *Angew. Chem.* **2006**, *118*, 8281; *Angew. Chem. Int. Ed.* **2006**, *45*, 8103; l) J. Casas, M. Engqvist, I. Ibrahem, B. Kaynak, A. Córdova, *Angew. Chem.* **2005**, *117*, 1367; *Angew. Chem. Int. Ed.* **2005**, *44*, 1343; m) A. B. Northrup, I. K. Mangion, F. Hettche, D. W. C. MacMillan, *Angew. Chem.* **2004**, *116*, 2204; *Angew. Chem. Int. Ed.* **2004**, *43*, 2152; n) N. Mase, F. Tanaka, C. F. Barbas III, *Angew. Chem.* **2004**, *116*, 2474; *Angew. Chem. Int. Ed.* **2004**, *43*, 2420; o) Y. Hayashi, S. Aratake, T. Okano, J. Takahashi, T. Sumiya, M. Shoji, *Angew. Chem.* **2006**, *118*, 5653; *Angew. Chem. Int. Ed.* **2006**, *45*, 5527; p) I. K. Mangion, A. B. Northrub, D. W. C. MacMillan, *Angew. Chem.* **2004**, *116*, 6890; *Angew. Chem. Int. Ed.* **2004**, *43*, 6722; q) R. Thayumanavan, F. Tanaka, C. F. Barbas, *Org. Lett.* **2004**, *6*, 3541; r) A. Córdova, W. Zou, P. Dziedzic, I. Ibrahem, E. Reyes, Y. Xu, *Chem. Eur. J.* **2006**, *12*, 5383; s) R. I. Storer, D. W. C. MacMillan, *Tetrahedron* **2004**, *60*, 7705.

[3] For asymmetric Mannich reactions of acetaldehyde, see: a) Y. Hayashi, T. Okano, T. Itoh, T. Urushima, H. Ishikawa, T. Uchimaru, *Angew. Chem.* **2008**, *120*, 9193; *Angew. Chem. Int. Ed.* **2008**, *47*, 9053; b) J. W. Wang, C. Chandler, M. Stadler, D. Kampen, B. List, *Nature* **2008**, *452*, 1012; c) T. Kano, Y. Yamaguchi, K. Maruoka, *Angew. Chem.* **2009**, *121*, 1870; *Angew. Chem. Int. Ed.* **2009**, *48*, 1838. For asymmetric Michael additions of acetaldehyde, see: d) P. García-García, A. Ladepeche, R. Halder, B. List, *Angew. Chem.* **2008**, *120*, 4797; *Angew. Chem. Int. Ed.* **2008**, *47*, 4719; e) Y. Hayashi, T. Itoh, M. Ohkubo, H. Ishkawa, *Angew. Chem.* **2008**, *120*, 4800; *Angew. Chem. Int. Ed.* **2008**, *47*, 4722; f) D. Xu, Y. Zhang, D. Ma, *Tetrahedron Lett.* **2010**, *51*, 3827; g) K. Juhl, K. A. Jorgensen, *Angew. Chem.* **2003**, *115*, 1536; *Angew. Chem. Int. Ed.* **2003**, *42*, 1498; h) J. Wang, F. Yu, X. Zhang, D. Ma, *Org. Lett.* **2008**, *10*, 2561.

[4] H. J. M. Gijsen, C. H. Wong, *J. Am. Chem. Soc.* **1994**, *116*, 8422.

[5] a) H. J. M. Gijsen, C. H. Wong, *J. Am. Chem. Soc.* **1995**, *117*, 2947; b) C. H. Wong, G.-J. Eduardo, C. Lihren, B. Olga, H. J. M. Gijen, D. H. Steensma, *J. Am. Chem. Soc.* **1995**, *117*, 3333; c) H. J. M. Gijsen, C. H. Wong, *J. Am. Chem. Soc.* **1995**, *117*, 7585.

[6] A. Córdova, W. Notz, C. F. Barbas, *J. Org. Chem.* **2002**, *67*, 301.

[7] a) M. B. Boxer, H. Yamamoto, *J. Am. Chem. Soc.* **2006**, *128*, 48; b) M. B. Boxer, H. Yamamoto, *J. Am. Chem. Soc.* **2007**, *129*, 2762; c) S. E. Denmark, T. Bui, *J. Org. Chem.* **2005**, *70*, 10190.

[8] a) Y. Hayashi, S. Samanta, T. Itoh, H. Ishikawa, *Org. Lett.* **2008**, *10*, 5581; b) Y. Hayashi, T. Itoh, S. Aratake, H. Ishikawa, *Angew. Chem.* **2008**, *120*, 2112; *Angew. Chem. Int. Ed.* **2008**, *47*, 2082; c) T. Urushima, Y. Yashui, H. Ishikawa, Y. Hayashi, *Org. Lett.* **2010**, *12*, 2966; d) A. Kinnell, T. Harman, M. Binham, A. Berry, A. Nelson, *Tetrahedron* **2012**, *68*, 7719.

[9] a) S. Hu, L. Zhang, J. Li, S. Z. Luo, J.-P. Chen, *Eur. J. Org. Chem.* **2011**, 3347; b) Q. Guo, J. C.-G. Zhao, *Tetrahedron Lett.* **2012**, *53*, 1768.

[10] a) Q. Guo, M. Bhanushali, C.-G. Zhao, *Angew. Chem.* **2010**, *122*, 9650; *Angew. Chem. Int. Ed.* **2010**, *49*, 9460; b) T. Itoh, H. Ishikawa, Y. Hayashi, *Org. Lett.* **2009**, *11*, 3854; c) N. Hara, S. Nakamura, N. Shibata, T. Toru, *Chem. Eur. J.* **2009**, *15*, 6790; d) W.-B. Chen, X.-L. Du, L.-F. Cun, X.-M. Zhang, W.-C. Yuan, *Tetrahedron* **2010**, *66*, 1441; e) S. Allu, N. Molleti, R. Panem, V. K. Singh, *Tetrahedron Lett.* **2011**, *52*, 4080.

[11] a) Q.-Z. Liu, X.-L. Wang, S.-W. Luo, B.-L. Zheng, D.-B. Qin, *Tetrahedron Lett.* **2008**, *49*, 7434; b) S.-S. Kan, J.-Z. Li, C.-Y. Ni, Q.-Z. Liu, T.-R. Kan, *Molecules* **2011**, *16*, 3778.

[12] a) A. B. Northrup, D. W. C. MacMillan, *Science* **2004**, *305*, 1752; b) I. K. Mangion, D. W. C. MicMillan, *J. Am. Chem. Soc.* **2005**, *127*, 3696.

[13] For reviews of application of keto esters in organic synthesis, see: a) M. Shiri, M. H. Heravi, B. Soleymanifard, *Tetrahedron* **2012**, *68*, 6593; for asymmetric aldol reactions of keto esters and ketones, see: b) L. Peng, L.-L. Wang, J.-F. Bai, L.-N. Jia, Y.-L. Guo, X.-Y. Luo, F.-Y. Wang, X.-Y. Xu, L.-X. Wang, *Org. Biomol. Chem.* **2011**, *9*, 4774; c) P. Li, J. Zhao, F. Li, A. S. C. Chan, F.-Y. Kwong, *Org. Lett.* **2010**, *12*, 5616; d) C. Zheng, Y. Wu, X. Wang, G. Zhao, *Adv. Synth. Catal.* **2008**, *350*, 2690; e) P. Li, S. H. Chan, A. S. Chan, F.-Y. Kwong, *Adv. Synth. Catal.* **2011**, *353*, 1179; f) C. Liu, X. W. Dou, Y. X. Lu, *Org. Lett.* **2011**, *13*, 5248; g) S. F. Viózquez, A. Bañón-Caballero, G. Guillena, C. Nájera, E. Gómez-Bengoa, *Org. Biomol. Chem.* **2012**, *10*, 4029; h) X. Zhu, A. Lin, L. Fang, W. Li, C. Zhu, Y. Cheng, *Chem. Eur. J.* **2011**, *17*, 8281; i) F. Wang, Y. Xiong, X. Liu, X. M. Feng, *Adv. Synth. Catal.* **2007**, *349*, 2665; j) M. Raj, G. S. Parashari, V. K. Singh, *Adv. Synth. Catal.* **2009**, *351*, 1284; k) S. A. Moteki, J. Han, S. Ari-

mitsu, M. Akakura, K. Nakayama, K. Maruoka, *Angew. Chem.* **2012**, *124*, 1213; *Angew. Chem. Int. Ed.* **2012**, *51*, 1187.
[14] a) S. Z. Luo, H. Xu, J.-Y. Li, L. Zhang, J.-P. Chen, *J. Am. Chem. Soc.* **2007**, *129*, 3074; b) J. Zhou, V. Wakchaure, P. Kraft, B. List, *Angew. Chem.* **2008**, *120*, 7768; *Angew. Chem. Int. Ed.* **2008**, *47*, 7656; c) J. Liu, Z.-G. Yang, Z. Wang, F. Wang, X.-H. Chen, X.-H. Liu, X.-M. Feng, Z.-S. Su, C.-W. Hu, *J. Am. Chem. Soc.* **2008**, *130*, 5654; d) Z.-Q. Jiang, Y.-X. Lu, *Tetrahedron Lett.* **2010**, *51*, 1884; e) S. H. McCooey, S. J. Connon, *Org. Lett.* **2007**, *9*, 599; f) B. Zheng, Q.-Z. Liu, C. Guo, X.-L. Wang, L. He, *Org. Biomol. Chem.* **2007**, *5*, 2913.
[15] S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320.
[16] D. Zhang, C. Yuan, *Tetrahedron* **2008**, *64*, 2480.
[17] a) N. Hara, R. Tamura, Y. Funahashi, S. Nakamura, *Org. Lett.* **2011**, *13*, 1662; b) L.-H. Qiu, Z.-X. Shen, C.-Q. Shi, Y.-H. Liu, Y.-W. Zhang, *Chin. J. Chem.* **2005**, *23*, 1641.
[18] E. Carceller, M. Merlos, M. Giral, C. Almansa, J. Bartrolf, J. Garcia-Rafanell, J. Forn, *J. Med. Chem.* **1993**, *36*, 2984.
[19] C. Mioskowski, G. Solladie, *Tetrahedron* **1980**, *36*, 227.
[20] R. Motoki, D. Tomita, M. Kanai, M. Shibasaki, *Tetrahedron Lett.* **2006**, *47*, 8083.
[21] P. M. W. Gill, B. G. Johnson, J. A. Pople, M. J. Frisch, *J. Chem. Phys. Lett.* **1992**, *197*, 499.
[22] Gaussian 03, Revision D.03, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, Jr., J. A. Montgomery, T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, Gaussian, Inc., Wallingford, CT, **2004**.
[23] a) P. Kaur, P. Singh, S. Kumar, *Tetrahedron* **2005**, *61*, 8231; b) A. R. Chamberlin, R. L. Mulholland, S. D. Kahn, W. J. Hehre, *J. Am. Chem. Soc.* **1987**, *109*, 672.

Received: February 6, 2013
Published online: April 4, 2013

