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PAPER

Asymmetric *syn*-selective direct aldol reaction of protected hydroxyacetone catalyzed by primary amino acid derived bifunctional organocatalyst in the presence of water†

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A new series of water compatible primary-tertiary diamine catalysts derived from natural primary amino acids bearing a hydrophobic side chain have been synthesized. These new primary-tertiary diamine-Brønsted acid conjugates bifunctional organocatalysts efficiently catalyzes the asymmetric direct *syn* selective cross-aldol reaction of different protected hydroxyacetone with various aldehydes in high yield (94%) and high enantioselectivity (up to 97% ee of *syn*) and dr of 91 : 9 (*syn*/*anti*) under mild reaction conditions.

Introduction

Chiral 1,2-diols are common structural motifs found in a huge array of natural and biologically active molecules.[1] The monoprotected optically active 1,2-diol units have a considerable strategic value in multistep synthesis, thus, making them an extremely attractive target for synthetic organic chemistry. Several approaches have been reported for the construction of optically active monoprotected 1,2-diols unit. One of the approaches for synthesis of this unit is the Mukayama aldol reaction involving enol silyl ether.[2] Another approach for the synthesis of monoprotected 1,2-diols consists of regioselective monoprotection of a less hindered hydroxyl group in unsymmetrical 1,2-diols.[3] Unfortunately, the selective protection of a more hindered hydroxy group is very difficult, which limits the scope of this methodology. Recent emergence of organocatalysis[4] has provided convenient access to these chiral monoprotected 1,2-diol units in a single step using protected hydroxyacetone as a donor in direct aldol reactions.[5,7,8]

The direct enantioselective organocatalytic aldol reactions of protected hydroxyacetone with aldehydes produce both *anti* and *syn* configured monoprotected 1,2-diols. The organocatalytic methods using proline and proline derived organocatalysts preferably produce *anti* configured monoprotected 1,2-diols.[5] In 2007, Barbas *et al.*[6] discovered the catalytic potential of primary amine based organocatalysts for the enantioselective synthesis of *syn* 1,2-diols, around the same time Wu *et al.*[7] reported the enantioselective synthesis of monoprotected *syn* 1,2-diols using threonine based primary amine catalysts. Since then, literature records few reports on the enantioselective synthesis of monoprotected *syn* 1,2-diols.[8] Therefore, the development of new and efficient catalysts for this transformation still remains an important goal.

In addition, the use of water in organocatalytic reactions is of great current interest due to its unique properties as compared to commonly employed organic solvents.[9] Our research group have a keen interest in developing organocatalytic asymmetric reactions in water.[10] We have successfully developed organocatalysts for asymmetric direct *anti* selective aldol reactions using water as reaction medium. As part of our ongoing programme to develop water compatible organocatalysts for direct aldol reactions, we were interested in designing chiral primary amine organocatalysts, since primary amines have been shown to form a *Z*-enamine intermediate, which, leads to *syn* stereoselectivity in the aldol adduct.[11]

We planned to explore the use of primary amino acid based chiral diamine organocatalysts for the reaction of protected hydroxyacetone with aromatic aldehydes in water. Therefore, we selected hydrophobic primary amino acids like L-isoleucine, L-leucine, L-valine and L-phenylalanine for synthesis of primary-tertiary diamines, which on protonation with an acid co-catalyst produce bifunctional organocatalysts.[12] We envisaged that the hydrophobic alkyl chain of the catalyst enhances the hydrophobicity of the catalysts and its interaction with the organic substrates in water, while the tertiary amine protonated with acid additive, activates and favourably orients the carbonyl group of the acceptor aldehyde through hydrogen bond formation.

Results and discussion

Catalyst screening

A number of chiral primary amino acid based diamines were synthesized (Fig. 1) and their effectiveness for catalyzing the aldol reaction of TBS-protected hydroxyacetone **2b** with 4-nitrobenzaldehyde (**3a**) in water in the presence of trifluoroacetic

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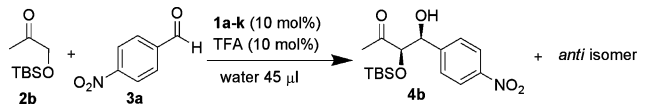
Table 1 Screening of organocatalysts **1a–1k**[a]



Entry	Catalyst	Time (h)	Yield[b] (%)	dr[c] (*syn*:*anti*)	ee[d] (*syn*) (%)
1	**1a**	70	53	70 : 30	55
2	**1b**	60	65	58 : 42	54
3	**1c**	20	90	74 : 26	20
4	**1d**	20	88	85 : 15	86
5	**1e**	18	90	85 : 15	90
6	**1f**	16	90	85 : 15	92
7	**1g**	16	92	86 : 14	94
8	**1h**	16	90	84 : 16	92
9	**1i**	18	90	85 : 15	93
10	**1j**	20	89	84 : 16	91
11	**1k**	60	66	64 : 36	45

[a] Reaction condition: 0.75 mmol of TBS-protected hydroxyacetone, 0.25 mmol of 4-nitrobenzaldehyde, 10 eq. of water, 10 mol% of catalyst loading **1a–1k**, 10 mol% acid additive TFA, temperature 25 °C. [b] Isolated yield determined after chromatographic purification. [c] Diastereoselectivity determined from HPLC spectra of crude reaction mixture. [d] Enantiomeric excess determined from HPLC using chiralpak columns.

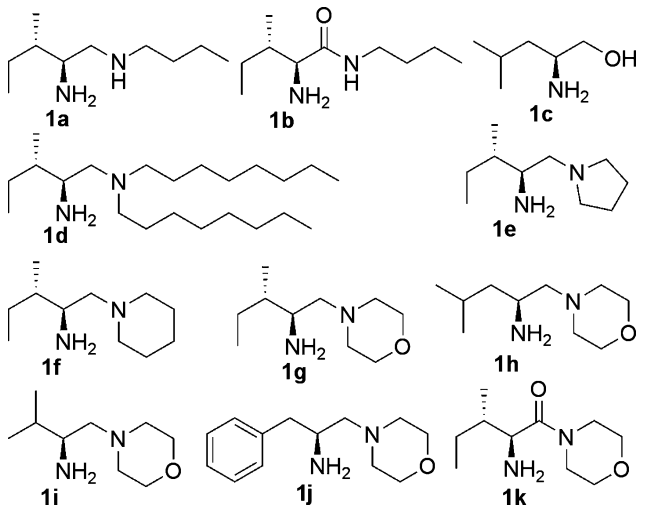
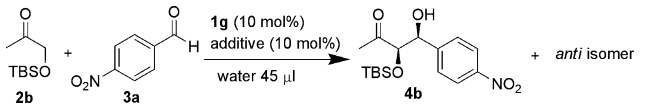


Fig. 1 Structure of different organocatalysts.

acid (TFA) as the acid additive was studied. It has been observed by us and others that the acid additive helps in enhancing the stereoselectivity of the reaction by increasing the iminium-enamine catalysis and suppressing the general base catalysis.[13]

Initially, the direct aldol reaction of TBS-protected hydroxyacetone **2b** and 4- nitrobenzaldehyde (**3a**) catalyzed by chiral diamine **1a** using 10 mol% of TFA as acid additive in water produced aldol product **4b** in 53% yield, dr of 70 : 30 (*syn*:*anti*) and ee of 55% (Table 1, entry 1). A similar reaction with chiral amide catalyst **1b** affords the product in 65% yield, dr of 58 : 42 (*syn*:*anti*) and ee of 54% (Table 1, entry 2), while reaction with the amino alcohol catalyst **1c** gave **4b** in very low enantioselectivity. Further, screening with primary-tertiary diamine catalysts having *N*,*N*-dioctyl **1d**, pyrrolidinyl **1e**, piperidinyl **1f** and morphinyl **1g** groups gave the aldol product in moderate to high enantioselectivity and nearly similar diastereoselectivity (Table 1, entries 4–7). The catalyst **1g** having a morphinyl group gave the highest level of

Table 2 Effect of different acid additives on the yield and stereoselectivity of **4b**[a]



Entry	Additive	Time (h)	Yield[b] (%)	dr[c] (*syn*:*anti*)	ee[d] (*syn*) (%)
1	Formic acid	14	89	84 : 16	87
2	Acetic acid	14	91	84 : 16	88
3	Chloroacetic acid	14	93	83 : 17	93
4	Trichloroacetic acid	12	94	86 : 14	96
5	Trifluoroacetic acid	16	92	86 : 14	94
6	Benzoic acid	14	94	80 : 20	84
7	*p*-Nitrobenzoic acid	14	90	85 : 15	86
8	Dinitrobenzoic acid	14	91	82 : 14	89
9	*p*-Nitrophenol	14	94	84 : 16	92
10	2,4-Dinitrophenol	14	95	86 : 14	93
11	Camphorsulfonicacid	24	90	78 : 22	83
12	*p*-Tolunesulfonicacid	24	88	83 : 17	91
13	TfOH	30	90	85 : 15	90
14	—	60	74	80 : 20	76

[a] Reaction condition: 0.75 mmol of TBS-protected hydroxyacetone, 0.25 mmol of 4-nitrobenzaldehyde, 10 eq. of water, 10 mol% of catalyst loading **1g**, 10 mol% acid additives, temperature 25 °C. [b] Isolated yield determined after chromatographic purification. [c] Diastereoselectivity determined from HPLC spectra of crude reaction mixture. [d] Enantiomeric excess determined from HPLC using chiralpak columns.

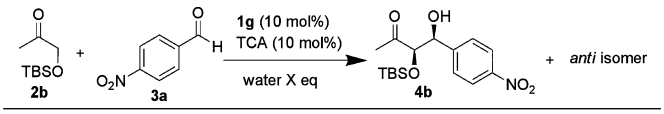
enantioselectivity (94%) of the aldol product. Therefore, further optimization of the catalyst structure was performed by varying the hydrophobic group and keeping the tertiary amine component (morphinyl) constant.

Thus, catalysts **1h**, **1i** and **1j** were synthesized and used as catalysts of the model aldol reaction (Table 1, entries 8–10). The results indicate that these catalysts afford the aldol product **4b** with comparable diastereoselectivity and enantioselectivity, however on repeating the reaction catalyzed by these catalysts, we showed that the catalyst **1g** produces the aldol product **4b** with the highest enantioselectivity. Therefore it was selected for performing all further optimization of the reaction conditions.

Additive screening

It has been observed by different research groups[14] including ours[10] that addition of acid affects the enantioselectivity of the product. In order to find the best acid additive for the aldol reaction, we performed various reactions in the presence of different acid additives (Table 2). The direct aldol reactions performed in the presence of acids such as formic acid, acetic acid, chloroacetic acid and trichloroacetic acid (TCA) show that with increase in the acidity of the acid the enantioselectivity increases (Table 2, entries 1–4). The highest ee of 96% was obtained with tricholoroacetic acid (TCA). The aromatic acids in general result in moderate enantioselectivity (Table 2, entries 6–8). The aldol reactions performed in the presence of 4-nitrophenol and 2,4-dinitrophenol gave aldol addition product with 92% and 91% ee, respectively (Table 2, entries 9 and 10). Sulfonic acids such as camphorsulfonic acid, *p*-toluenesulfonic acid and trifluoromethanesulfonic acid (TfOH) gave **4b** with upto 91% ee. All the acid additives show a similar level of diastereoselectivity but camphorsulfonic acid and

Table 3 Variation in the amount of water using catalyst **1g**[a]



Entry	Amount of water (eq)	Time (h)	Yield[b] (%)	dr[c] (*syn*:*anti*)	ee[d] (*syn*) (%)
1	2.5	12	94	85 : 15	95
2	5	12	92	84 : 14	95
3	10	12	94	86 : 14	96
4	15	30	83	85 : 15	94
5	22	30	80	86 : 14	94
6	33	36	74	86 : 14	96
7	55	48	70	86 : 14	95
8	—	18	93	82 : 16	85

[a] Reaction condition: 0.75 mmol of TBS-protected hydroxyacetone, 0.25 mmol of 4-nitrobenzaldehyde, x eq. of water, 10 mol% of catalyst loading **1g**, 10 mol% acid additive TCA, temperature 25 °C. [b] Isolated yield determined after chromatographic purification. [c] Diastereoselectivity determined from HPLC spectra of crude reaction mixture. [d] Enantiomeric excess determined from HPLC using chiralpak columns.

benzoic acid afford the product with the lowest diastereoselectivity. Further, the aldol reaction in the absence of acid additives produces the aldol product in low enantioselectivity (Table 2, entry 14). This study shows that tricholoroacetic acid (TCA) is the best acid additive, which affords **4b** with 96% ee, diastereoselectivity of 86 : 14 (*syn*:*anti*) and yield of 92%. Thus all further optimizations of the direct aldol reaction catalyzed by **1g** were performed using tricholoroacetic acid (TCA) as the additive.

Effect of water

The optimization of the reaction conditions by varying the amount of water shows little effect on the enantioselectivity of **4b**, but an increase in the amount of water lowers the yield of **4b** and slows down the reaction (Table 3). The reaction performed in the absence of water results in lower enantioselectivity of the aldol addition product **4b** (Table 3, entry 8). The addition of 10 equivalents of water was found to be optimum in terms of reaction time and enantioselectivity and thus was used for all further aldol reactions (Table 3, entry 3).

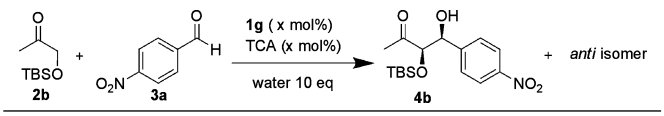
Effect of substrate ratio and catalyst loading

Further, optimizing the amount of ketone shows that decreasing the amount of ketone slows down the reaction rate and results in the formation of **4b** in low yield and slightly low enantioselectivity. The use of 3 eq. of ketone was found to be optimum for high enantiomeric excess (96%), and diastereoisomeric ratio of 86 : 14 (*syn*:*anti*). Decreasing the catalyst loading to 5 mol% led to an increase in the reaction time with no change in the stereoselectivity of **4b** (Table 4, entries 4–5). The catalyst loading of 2 mol% of catalyst **1g** results in slight lowering in enantioselectivity (Table 4, entry 8).

Effect of protecting group

The aldol reaction of hydroxyacetone (**2a**) with 4-nitrobenzaldehyde (**3a**) using catalyst **1g** in aqueous medium produced aldol adduct **4a** in very low yield and enantioselectivity

Table 4 Effect of variation in the amount of ketone and catalyst loading on the yield and stereoselectivity of **4b**[a]



Entry	Amount of ketone (eq)	Catalyst loading (mmol%)	Time (h)	Yield[b] (%)	dr[c] (*syn*:*anti*)	ee[d] (*syn*) (%)
1	4	10	10	93	86 : 14	96
2	3	10	12	94	86 : 14	96
3	2.5	10	18	88	85 : 15	95
4	2	10	30	85	83 : 17	94
5	1.5	10	36	80	84 : 16	93
6	3	15	12	92	85 : 15	95
7	3	5	30	90	85 : 15	95
8	3	2	60	81	80 : 20	89
9	2	5	40	87	85 : 15	92

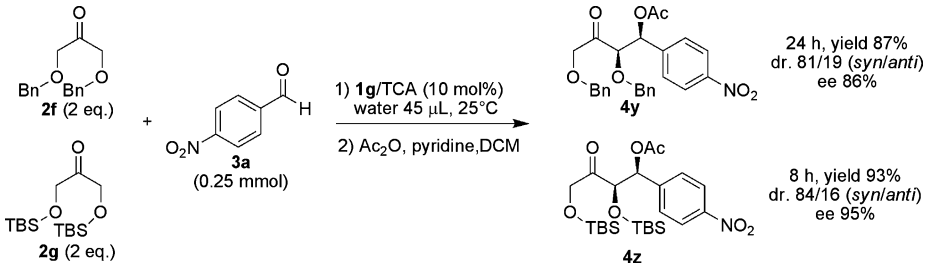
[a] Reaction condition: x mmol of TBS-protected hydroxyacetone, 0.25 mmol of 4-nitrobenzaldehyde, 10 eq. of water, x mol% of catalyst loading, x mol% acid additive, temperature 25 °C. [b] Isolated yield determined after chromatographic purification. [c] Diastereoselectivity determined from HPLC spectra of crude reaction mixture. [d] Enantiomeric excess determined from HPLC using chiralpak columns.

(Table 5, entry 1). In order to see the effect of different protecting groups on hydroxyacetone, it was protected with other groups like *tert*-butyldiphenylsilane (TBDPS), tri-*iso*propylsilane (TIPS) and benzyl (Bn) and were used for aldol reactions. The aldol reactions of ketones **2b–2d** with 4-nitrobenzaldehyde (**3a**) under standard reaction conditions was performed (Table 5). Moderate level of enantioselectivity and yield was observed with ketone **2c** (Table 5, entry 3). Whereas excellent level of enantioselectivity was observed with benzyl protected ketone **2e** but the product was obtained in poor yield (Table 5, entry 5). Unfortunately, aldol product formed by the reaction of ketone **2d** and 4-nitrobenzaldehyde (**3a**) could not be resolved on HPLC under various conditions tried (Table 5, entry 4).

Scope of reaction

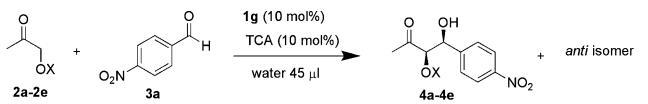
In order to study the scope and limitation of the catalyst **1g**, the aldol reaction of **2b** was performed with different aromatic aldehydes **3a–3r**. All the aldol products were obtained with high stereoselectivities and yield, reflecting the catalytic versatility of **1g** (Table 6). Excellent level of enantioselectivities were observed with 2-nitro (97% ee), 3-nitro (96% ee), 4-nitro (96% ee), 3-trifluoromethyl (96% ee) and 4-trifluoromethyl (95% ee) substituted benzaldehydes (Table 6, entries 1–5). The aldol products **4k–4q**, **4s** and **4v** were obtained in enantiomeric excess range of 90% to 93% (Table 6, entries 7–13, 15 and 18). The electron rich aldehydes **3p** and **3q** are slow to react with **2b**, however they produce aldol adducts **4t** (ee 91%) and **4u** (ee 84%) in yield of 75% (70 h) and 74% (96h), respectively (Table 6, entries 16–17). Moderate enantioselectivity and diastereoselectivity was observed with 2-naphthaldehyde (Table 6, entry 19). Unfortunately, aldol product formed from 2-trifluoromethyl- and 3,4-dichloro-benzaldehydes could not be resolved on HPLC under any condition despite our best efforts (Table 6, entries 6 and 14).

Further, study of the scope of the aldol reaction was extended to include different dihydroxyacetone derivatives (Scheme 1). Using the optimized conditions, the 1,3-dibenzyloxyacetone **2f** produced



Scheme 1 Direct aldol reactions of protected-dihydroxyacetone derivatives.

Table 5 Effect of protecting groups[a]



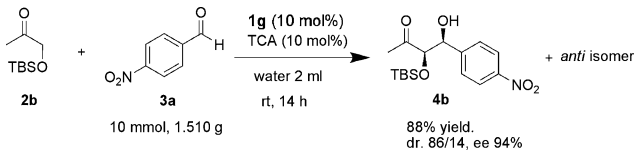
Entry	Donor	Product	Time (h)	Yield[b] (%)	dr[c] (*syn*:*anti*)	ee[d] (*syn*) (%)
1	**2a**	**4a**	60	20	74 : 26	31
2	**2b**	**4b**	12	94	86 : 14	96
3	**2c**	**4c**	36	81	92 : 08	83
4	**2d**	**4d**	60	72	—	—
5	**2e**	**4e**	60	70	70 : 30	94

[a] Reaction condition: 0.75 mmol of ketone, 0.25 mmol of 4-nitro benzaldehyde, 10 eq. of water, 10 mol% of catalyst loading **1g**, 10 mol% acid additive TCA, temperature 25 °C. [b] Isolated yield determined after chromatographic purification. [c] Diastereoselectivity determined from HPLC spectra of crude reaction mixture. [d] Enantiomeric excess determined from HPLC using chiralpak columns.

the aldol addition product **4y** with 86% ee and dr of 81 : 19 (*syn*:*anti*). The TBS-protected dihydroxyacetone **2g**, under similar conditions, produced the aldol adduct **4z** in high yield (93%) and with excellent enantioselectivity (95%).

To demonstrate the practical utility, the aldol reaction of 4-nitrobenzaldehyde (**3a**) and TBS-protected hydroxyacetone **2b** was performed at 10 mmol scale (Scheme 2). The aldol addition product **4b** was obtained in high yield (88%) and high enantioselectivity (94% of *syn* isomer). The optically pure catalyst could be recovered in 90% yield after workup.[15]

The absolute configuration of *syn* aldol product **4b** has been assigned as (3*R*,4*S*) in comparison to the direction of optical rotation



Scheme 2 Gram scale preparation of aldol adduct **4b**.

and HPLC analysis data of free diol, obtained after deprotection of **4b**, with that reported in literature.[12f] The remaining aldol products are assigned analogously. The absolute stereochemistry of aldol addition product **4y** and **4z** has been assigned as (3*R*,4*S*) by comparison of the HPLC data with that reported in the literature.[8a]

The catalyst **1g**, on reaction with hydroxyacetone derivatives, form an enamine intermediate, which reacts with aldehyde resulting in the formation of the aldol products. The acid additives protonate the tertiary amine of the catalyst **1g**, which helps in activation and orientation of the aldehyde through H-bonding.[12] The *syn* diastereoselectivity could be explained by the preferential formation of *Z*-enamine (**TS-1b**), which is stabilized over the *E*-enamine (**TS-1a**) *via* intramolecular hydrogen bonding (Fig. 2).[6,16]

Conclusions

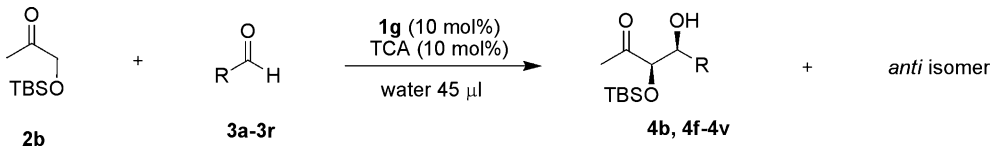
In conclusion, we have successfully performed direct asymmetric *syn*-selective aldol reactions between a variety of aromatic aldehydes with protected hydroxyacetone and protected dihydroxyacetone derivatives in the presence of water catalyzed by L-isoleucine derived primary-tertiary diamine organocatalysts. The methodology developed is very simple, environmentally benign, and highly enantioselective. Further, exploration of primary-tertiary diamine catalysts for other asymmetric reactions is ongoing in our laboratory and the results will be reported in due course.

Experimental Section

General remarks

NMR spectra were obtained at 300 MHz (Jeol AL-300) and 500 MHz (Bruker Avance 500 MHz) using $CDCl_3$ as solvent with Me_4Si in $CDCl_3$ as the internal standard. Chemical shifts (δ) are expressed in ppm and Hz downfield from internal TMS. Spectral patterns are designated as s = singlet; d = doublet; dd = doublet of doublets; t = triplet; br = broad; m = multiplet. Infrared spectra were recorded on a FT-IR Bruker (270–30) spectrophotometer. MS were recorded on Bruker Esquire 3000 LC Mass spectrometer. Optical rotation was determined with JASCO DIP-360

Table 6 Screening of various aromatic aldehydes using catalyst **1g**[a]



2b **3a-3r** **4b, 4f-4v**

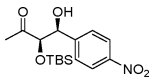
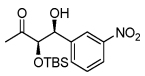
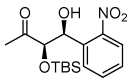
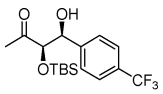
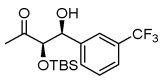
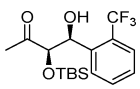
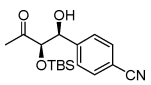
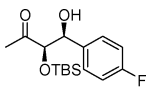
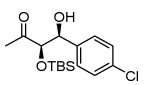
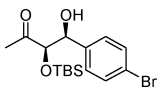
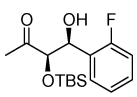
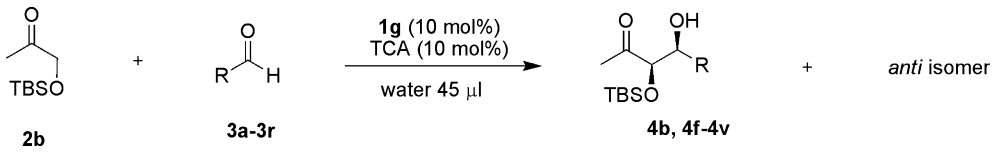
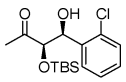
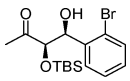
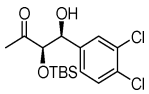
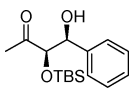
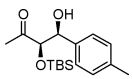
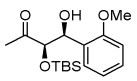
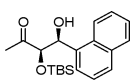
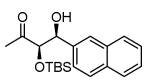
Entry	R = **3a–3r**	Product (**4b**, **4f–4v**)	Time (h)	Yield[b] (%)	dr[c] (*syn*:*anti*)	ee[d] (*syn*) (%)
1	4-$NO_2C_6H_4$ **3a**	 **4b**	12	94	86 : 14	96
2	3-$NO_2C_6H_4$ **3b**	 **4f**	18	91	90 : 10	96
3	2-$NO_2C_6H_4$ **3c**	 **4g**	20	89	93 : 7	97
4	4-$CF_3C_6H_4$ **3d**	 **4h**	24	89	86 : 14	95
5	3-$CF_3C_6H_4$ **3e**	 **4i**	30	84	84 : 16	96
6[e]	2-$CF_3C_6H_4$ **3f**	 **4j**	30	82	86 : 14	*NR*
7	4-CNC_6H_4 **3g**	 **4k**	18	91	83 : 17	91
8	4-FC_6H_4 **3h**	 **4l**	30	83	77 : 23	91
9	4-ClC_6H_4 **3i**	 **4m**	30	84	83 : 17	90
10	4-BrC_6H_4 **3j**	 **4n**	30	82	82 : 18	92
11	2-FC_6H_4 **3k**	 **4o**	30	81	85 : 15	93

Table 6 *(Contd.)*



Entry	R = **3a–3r**	Product (**4b**, **4f–4v**)	Time (h)	Yield[b] (%)	dr[c] (*syn*:*anti*)	ee[d] (*syn*) (%)
12	2-ClC_6H_4 **3l**	 **4p**	30	82	84 : 16	90
13	2-BrC_6H_4 **3m**	 **4q**	30	85	82 : 18	91
14[e]	3, 4-$Cl_2C_6H_4$ **3n**	 **4r**	30	78	78 : 22	*NR*
15	C_6H_4 **3o**	 **4s**	48	74	81 : 19	93
16	4-$CH_3C_6H_4$ **3p**	 **4t**	70	75	73 : 27	91
17	2-$OMeC_6H_4$ **3q**	 **4u**	96	74	68 : 32	84
18	1-Naph **3r**	 **4v**	70	65	82 : 18	92
19	2-Naph **3s**	 **4x**	70	70	68 : 32	83

[a] Reaction condition: 0.75 mmol of TBS-protected hydroxyacetone, 0.25 mmol of 4-nitrobenzaldehyde, 10 eq. of water, 10 mol% of catalyst loading **1g**, 10 mol% acid additive TCA, temperature 25 °C. [b] Isolated yield determined after chromatographic purification. [c] Diastereoselectivity determined from ^1H NMR of crude reaction mixture. [d] Enantiomeric excess determined from HPLC using chiralpak columns. [e] NR = Not resolved on HPLC using chiralpak columns.

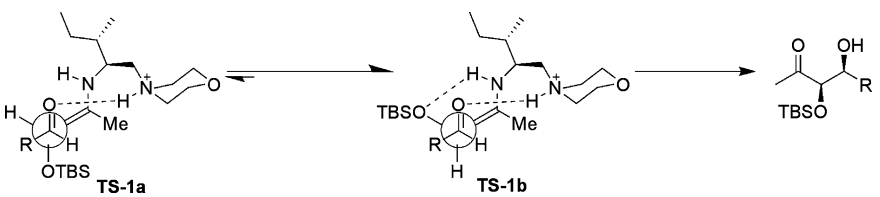


Fig. 2 Proposed transition state of *syn* selective aldol reaction of protected hydroxyacetone with aldehyde.

polarimeter at 25 °C. Enantiomeric excess was determined by using Shimadzu LC-20AD using Daicel Chiralpak AD-H, OD-H, AS-H and IB column. Analytical thin-layer chromatography(TLC) was performed on either (i) aluminium sheets pre-coated with silica gel 60F254 (Merck, India) or (ii) glass plates (7.5 × 2.5 cm) coated with silica gel GF-254 (Spectrochem, India) containing 13% calcium sulfate as binder, using various combinations of ethyl acetate and hexane as eluents. Visualization of the spots was accomplished by exposing to UV light or iodine vapours. Column chromatography was performed on 60–120 and 100–200 mesh silica (Spectrochem, India) using mixtures of hexane and ethyl acetate or chloroform and methanol as an eluents.

Materials

Different amino acids and aldehydes, dicyclohexylcarbodiimide and di-*tert*-butylpyrocarbonate were purchased from Aldrich, Spectrochem India and S.d. fine-chem. Ltd., India and were used as received. Lithium aluminium hydride (reagent grade, 95%, pellets) and hydroxyacetone were purchased from Aldrich and Merck, respectively. TBS-protected hydroxyacetone **2b** was prepared according to the reported procedure.[17] TIPS-protected hydroxyacetone **2c** and TBDPS-protected hydroxyacetone **2d** was prepared following the same procedure as for TBS-protected hydroxyacetone **2b**. Protected dihydroxyacetone derivatives **2g** and **2f** were prepared according to the literature method.[18]

General procedure for synthesis of organocatalyst 1a, 1d–1j

To an ice cold stirred solution of *N*-Boc protected amino acids (4.3 mmol) and morpholine (0.453 mL, 5.1 mmol) in dichloromethane (15 mL), a solution of dicyclohexylcarbodiimide (0.98 g, 4.75 mmol) in dichloromethane was added dropwise. The resulting mixture was stirred and the temperature of the reaction mixture was allowed to rise to room temperature. The progress of the reaction was monitored by TLC (ethyl acetate–hexane). After completion of the reaction, the reaction mixture was filtered and concentrated under reduced pressure to obtain the crude product, which was purified on column chromatography to obtain a thick liquid in 75–85% yield. The thick liquid was redissolved in CH_2Cl_2 and cooled to 0 °C, then TFA in CH_2Cl_2 (TFA/CH_2Cl_2) was added dropwise. The resulting mixture was stirred for 8 to 12 h until the reaction was complete (TLC) and then concentrated under reduced pressure. The resulting residue was redissolved in CH_2Cl_2 and neutralized with saturated solution of sodium carbonate and extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude product was purified by column chromatography using $CHCl_3$–MeOH as an eluent to obtain a light yellow/orange liquid in 80–85% yield. The liquid was dissolved in dry THF and cooled to 0 °C followed by slow addition of $LiAlH_4$. The solution was refluxed for 5–8 h until the reaction was complete (TLC). After cooling to 0 °C ethyl acetate was added followed by water. The solid was filtered and washed with THF (4–5 times). The combined organic solvent was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography using $CHCl_3$–MeOH as eluent to afford product as a oil in 48–62% yield.

(2*S*,3*S*)-*N*′-butyl-3-methylpentane-1,2-diamine (1a)

Yield, 48%; brown oil; $[\alpha]_D^{25}$ +15 (*c* 0.1 in MeOH); δ_H(300 MHz; $CDCl_3$; Me_4Si) 0.87–0.94 (9H, m, 3 × C*H*$_3$), 1.14–1.21 (1H, m, C*H*), 1.31–1.38 (3H, m, C*H*$_2$), 1.44–1.52 (3H, m, C*H*$_2$), 2.01 (2H, br s, N*H*$_2$), 2.37 (1H, dd, *J* 12.1 Hz and *J* 10.3 Hz, C*H*) and 2.56–2.73 (4H, m, C*H* and C*H*$_2$); δ_C(100 MHz; $CDCl_3$; Me_4Si) 11.6, 14.4, 15.1, 20.5, 25.2, 32.1, 39.8, 49.7, 53.4, 55.2 and 57.8; HRMS (TOF MS) calcd for $C_{10}H_{24}N_2$ (M^++H): 173.2018, found: 173.2002.

(2*S*,3*S*)-3-methyl-*N*′, *N*′-dioctylpentane-1,2-diamine (1d)

Yield, 52%; brown oil; $[\alpha]_D^{25}$ +18 (*c* 0.1, MeOH); δ_H(300 MHz; $CDCl_3$; Me_4Si) 0.58–0.92 (12H, m, 4 × C*H*$_3$), 1.12–158 (27H, br m, 13 × C*H*$_2$ and C*H*), 2.05 (2H, br s, N*H*$_2$), 2.14–2.51 (6H, m, 3 × C*H*$_2$), 2.64–2.71(1H, m, C*H*); δ_C(75 MHz; $CDCl_3$; Me_4Si) 11.5, 14.1, 15.1, 22.6, 25.3, 27.1, 27.5, 28.4, 29.2, 29.3, 29.6, 31.7, 31.8, 38.7, 49.1, 54.6 and 58.7; HRMS (TOF MS) calcd for $C_9H_{20}N_2O$ (M^++H): 341.3896, found: 341.3721.

(2*S*,3*S*)-2-amino-3-methyl-1-(pyrrolidin-1-yl)pentane (1e)

Yield, 51%; brown oil; $[\alpha]_D^{25}$ +10 (*c* 0.1 in MeOH); δ_H(300 MHz; $CDCl_3$; Me_4Si) 0.88–0.93 (6H, m, 2 × C*H*$_3$), 1.14–1.26 (1H, m, C*H*), 1.34–1.53 (2H, m, C*H*$_2$), 1.78 (2H, br s, N*H*$_2$), 2.23–2.28 (5H, m, 2 × C*H*$_2$), 2.33–2.63 (5H, m, 2 × C*H*$_2$) and 2.64–2.83 (1H, m, C*H*); δ_C(75 MHz; $CDCl_3$; Me_4Si) 11.6, 14.9, 23.5, 25.2, 38.8, 53.6, 54.2 and 59.8; HRMS (TOF MS) calcd for $C_{10}H_{22}N_2$ (M^++H): 171.1861, found: 171.1863.

(2*S*,3*S*)-2-amino-3-methyl-1-(piperidin-1-yl)pentane (1f)

Yield, 58%; yellow oil; $[\alpha]_D^{25}$ +13 (*c* 0.1 in MeOH); δ_H(300 MHz; $CDCl_3$; Me_4Si) 0.83–0.92 (6H, m, 2 × C*H*$_3$), 1.15–1.22 (1H, m, C*H*), 1.29–1.61 (8H, m, 4 × C*H*$_2$) 1.97 (2H, br s, N*H*$_2$), 2.09–2.25 (4H, m, 2 × C*H*$_2$), 2.50 (2H, br s, C*H*$_2$) and 2.75–2.82 (1H, m, C*H*); δ_C(75 MHz; $CDCl_3$; Me_4Si) 11.4, 14.8, 24.3, 25.3, 26.0, 29.6, 38.5, 51.7, 54.9 and 62.3; HRMS (TOF MS) calcd for $C_{11}H_{24}N_2$ (M^++H): 185.2018, found: 185.2027.

(2*S*,3*S*)-2-amino-3-methyl-1-morpholinopentane[19] (1g)

Yield, 57%; yellow oil; $[\alpha]_D^{25}$ +17 (*c* 0.1, MeOH); δ_H(300 MHz; $CDCl_3$; Me_4Si) 0.88–0.93 (6H, m, 2 × C*H*$_3$), 1.17–1.24 (1H, m, C*H*), 1.35–1.39 (1H, m, C*H*$_2$), 1.45–1.52 (1H, m, C*H*$_2$), 2.09 (2H, br s, N*H*$_2$), 2.15–2.35 (4H, m, 2 × C*H*$_2$) 2.54–2.60 (2H, m, 2 × C*H*$_2$) 2.79–2.86 (1H, m, C*H*) and 3.65–3.75 (4H, m, 2 × C*H*$_2$); δ_C(75 MHz; $CDCl_3$; Me_4Si) 11.5, 14.9, 25.2, 38.7, 51.2, 54.0, 62.6 and 67.1; HRMS (TOF MS) calcd for $C_{10}H_{22}N_2O$ (M^++H): 187.1810, found: 187.1808.

(*S*)-2-amino-4-methyl-1-morpholinopentane (1h)

Yield, 56%; brown oil; $[\alpha]_D^{25}$ +25 (*c* 0.1 in MeOH); δ_H(300 MHz; $CDCl_3$; Me_4Si) 0.88–0.93 (6H, m, 2 × C*H*$_3$), 1.13–1.25 (2H, m, C*H*$_2$), 1.71–1.78 (1H, m, C*H*), 2.00 (2H, br s, N*H*$_2$), 2.10–2.26 (2H, m, C*H*$_2$), 2.32–2.37 (2H, m, C*H*$_2$), 2.53–2.59 (2H, m, C*H*$_2$), 2.97–3.02 (1H, m, C*H*) and 3.64–3.75 (4H, m, 2 × C*H*$_2$); δ_C(100 MHz; $CDCl_3$; Me_4Si) 22.1, 23.5, 24.7, 44.9, 45.1, 54.1, 66.2 and 67.1;

HRMS (TOF MS) calcd for $C_{10}H_{22}N_2O$ (M^++H): 187.1810, found: 187.1806.

(*S*)-2-amino-3-methyl-1-morpholinobutane (1i)

Yield, 54%; brown oil; $[\alpha]_D^{25}$ +28 (*c* 0.1 in MeOH); δ_H(300 MHz; $CDCl_3$; Me_4Si) 0.93–0.99 (6H, m, 2 × CH_3), 1.65–1.76 (1H, m, C*H*), 2.24–2.39 (4H, m, 2 × CH_2), 2.55–2.61 (2H, m, CH_2), 2.77–2.84 (1H, m, C*H*), 3.07 (2H, br s, NH_2) and 3.60–3.75 (4H, m, 2 × CH_2); δ_C(75 MHz; $CDCl_3$; Me_4Si) 18.5, 18.9, 30.9, 53.1, 53.8, 61.3 and 66.9; HRMS (TOF MS) calcd for $C_9H_{20}N_2O$ (M^++H): 173.1654, found: 173.1650.

(*S*)-2-amino-1-morpholino-3-phenylpropane (1j)

Yield, 62%; brown oil; $[\alpha]_D^{25}$ +21 (*c* 0.1 in MeOH); δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.94 (2H, br s, NH_2), 2.23–2.40 (4H, m, 2 × CH_2), 2.49–2.56 (3H, m, C*H* and CH_2) 2.74 (1H, dd, *J* 4.4 and *J* 4.6, CH_2), 3.17–3.26 (1H, m, C*H*) 3.64–3.75 (4H, m, 2 × CH_2) and 7.19–7.32 (5H, m, Ar*H*); δ_C(125 MHz; $CDCl_3$; Me_4Si) 42.0, 48.9, 54.0, 65.1, 67.1, 126.3, 128.4, 129.1 and 139.0; HRMS (TOF MS) calcd for $C_{13}H_{20}N_2O$ (M^++H): 221.1654, found: 221.1653.

General procedure for enantioselective aldol reactions

To a stirring mixture of catalyst (0.025 mmol), TBS-protected hydroxyacetone **2b** (143 uL, 0.75 mmol) in water (45 uL, 2.5 mmol), the additive TCA (4.07 mg, 0.025 mmol) was added at 25 °C and the mixture was allowed to stir for 5 min followed by addition of aldehyde (0.25 mmol). The mixture was stirred for 9–70 h and the progress of the reaction was monitored at regular intervals by TLC. On the completion of reaction, saturated solution of NH_4Cl (5 mL) was added to it and resulting mixture was extracted with ethyl acetate (3 × 15 mL). The organic layer was separated, dried over anhydrous sodium sulfate, filtered, and evaporated to obtained crude aldol product. The ^{1}H NMR of the crude reaction mixture was recorded to determine the diastereoselectivity. The column chromatography on silica gel (mesh 60–120) using hexane–ethyl acetate (9/1) as an eluent gave the corresponding aldol adducts as a *syn*:*anti* mixture. The enantiomeric excess of aldol addition products **4a–4x** was derermined using various chiral columns. The enantiomeric excess of aldol addition product **4y** and **4z** was determined after their acetylation on chiral HPLC. Racemic standards were prepared using (±) 3-methyl-1-morpholinobutan-2-amine catalyst synthesized form (±) valine.

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(4′-nitrophenyl)butan-2-one[7,8b] (4b)

Yield: 94%; *syn*/*anti* = 86 : 14; enantiomeric excess: 96% of *syn* diastereomer determined by HPLC (Diacel Chiralpak IB; hexane/*i*-PrOH 92 : 8; flow rate 0.2 mL min^{-1}; λ = 211; t_R (*syn*, major) = 30.6 min, t_R (*syn*, minor) = 24.4 min; $[\alpha]_D^{25}$ +22 (*c* 0.1 in $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3508, 2929, 2856, 1706, 1600, 1516 and 1346; δ_H(300 MHz; $CDCl_3$; Me_4Si) –0.35 (3H, s, SiCCH_3 (*syn*)), –0.20 (3H, s, SiCCH_3 (*anti*)), –0.02 (3H, s, SiCCH_3 (*syn*)) 0.01 (3H, s, SiCCH_3 (*anti*)), 0.86 (9H, s, SiC(CH_3)$_3$), 2.14 (3H, s, COCH_3 (*anti*)), 2.21 (3H, s, COCH_3 (*syn*)), 3.17 (1H, d, *J* 9 Hz, O*H*), 4.10 (1H, d, *J* 6 Hz, C*H*OTBS (*anti*)), 4.18 (1H, dd, *J* 1.5 Hz and *J* 2.7 Hz, C*H*OTBS (*syn*)), 4.91 (1H, br s, C*H*OH (*anti*)), 5.02 (d, 1H, *J* 8.8 Hz, C*H*OH (*syn*)), 7.53 (2H, d, *J* 7.8 Hz, Ar*H*), 8.21–8.24 (1H, m, Ar*H*); δ_C(125 MHz; $CDCl_3$; Me_4Si) –5.6, –5.1, 18.0, 25.6, 27.3, 74.6, 81.8, 123.4, 127.0, 147.5, 148.2 and 210.8; *m*/*z* (ESI): 361.9 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(3′-nitrophenyl)butan-2-one[8b] (4f)

Yield: 91%; *syn*/*anti* = 90 : 10; enantiomeric excess: 96% of *syn* diastereomer determined by HPLC (Diacel Chiralpak OD-H; hexane/*i*-PrOH 92 : 8; flow rate 0.2 mL min^{-1}; λ = 211 nm; t_R (*syn*, major) = 48.9 min, t_R (*syn*, minor) = 36.4 min; $[\alpha]_D^{25}$ +28 (*c* 0.1 in $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3410, 2930, 2858, 1700, 1531 and 1349; δ_H(300 MHz; $CDCl_3$; Me_4Si) –0.35 (3H, s, SiCH_3 (*syn*)), –0.24 (3H, s, SiCH_3 (*anti*)), –0.03 (3H, s, SiCH_3 (*syn*)), –0.01 (3H, s, SiCH_3 (*anti*)), 0.86 (9H, s, SiC(CH_3)$_3$), 2.16 (3H, s, COCH_3 (*anti*)), 2.22 (3H, s, COCH_3 (*syn*)) 3.17 (1H, d, *J* 9 Hz, O*H*), 4.18 (1H, d, *J* 2.7 Hz C*H*OTBS (*syn*)), 5.01–5.05 (1H, m, C*H*OH (*syn*)) 7.54 (1H, t, *J* 7.8 Hz, Ar*H*), 7.68 (1H, d, *J* 7.8 Hz, Ar*H*), 8.14–8.18 (1H, m, Ar*H*) and 8.26 (1H, br s, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) –5.6, –5.1, 17.9, 25.6, 27.3, 74.4, 81.7, 121.3, 122.7, 129.2, 132.1, 143.1, 148.2 and 210.8; *m*/*z* (ESI): 361.9 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(2′-nitrophenyl)butan-2-one (4g)

Yield: 89%; *syn*/*anti* = 93 : 7; enantiomeric excess: 97% of *syn* diastereomer determined by HPLC (Diacel Chiralpak OD-H; hexane/*i*-PrOH 95 : 5; flow rate 0.5 mL min^{-1}; λ = 209 nm; t_R (*syn*, major) = 16.6 min, t_R (*syn*, minor) = 18.1 min; $[\alpha]_D^{25}$ +27 (*c* 0.1 in $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3423, 2928, 2856, 1722, 1556 and 1346; δ_H(300 MHz; $CDCl_3$; Me_4Si) –0.44 (3H, s, SiCH_3 (*syn*)), –0.09 (3H, s, SiCH_3 (*syn*)), 0.77 (9H, s, SiC(CH_3)$_3$ (*syn*)), 0.89 (9H, s, SiC(CH_3)$_3$ (*anti*)), 2.22 (3H, s, COCH_3 (*anti*)), 2.37 (3H, s, COCH_3 (*syn*)), 3.14 (1H, br s, O*H*), 4.49 (1H, d, *J* 1.8 Hz, C*H*OTBS (*syn*)), 5.78 (1H, br s, C*H*OH (*syn*)), 7.45–7.51 (1H, m, Ar*H*), 7.65–7.71 (1H, m, Ar*H*), 7.76–7.79 (1H, m, Ar*H*) and 8.07 (1H, dd, *J* 8.1 Hz and *J* 1.5 Hz, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) –6.0, –5.2, 18.2, 25.6, 26.5, 70.2, 80.2, 124.8, 128.6, 129.8, 133.3, 137.1, 147.1 and 207.0; *m*/*z* (ESI): 361.9 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(4′-trifluoromethylphenyl)butan-2-one (4h)

Yield: 89%; *syn*/*anti* = 86 : 14; enantiomeric excess: 95% of *syn* diastereomer determined by HPLC (Diacel chiralpak AS-H; hexane/*i*-PrOH 98 : 2; flow rate 1 mL min^{-1}; λ = 218 nm; t_R (*syn*, major) = 7.7 min, t_R (*syn*, minor) = 13.9 min; $[\alpha]_D^{25}$ +32 (*c* 0.1 in $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3525, 2929, 2858, 1709, 1618 and 1326; δ_H(300 MHz; $CDCl_3$; Me_4Si) –0.37 (3H, s, SiCH_3 (*syn*)), –0.23 (3H, s, SiCH_3 (*anti*)), –0.05 (3H, s, SiCH_3 (*syn*)), –0.02 (3H, s, SiCH_3 (*anti*)), 0.85 (9H, s, SiC(CH_3)$_3$), 2.12 (3H, s, COCH_3 (*anti*)), 2.21 (3H, s, COCH_3 (*syn*)), 3.07 (1H, d, *J* 8.4 Hz, O*H*), 4.08 (1H, d, *J* 6.3 Hz, C*H*OTBS (*anti*)), 4.14 (1H, d, *J* 2.7 Hz, C*H*OTBS (*syn*)), 4.84 (1H, d, *J* 6.6 Hz, C*H*OH (*anti*)), 4.97 (1H, d, *J* 6 Hz, C*H*OH (*syn*)), 7.44–7.49 (2H, m, Ar*H*) and 7.59–7.63 (2H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) –5.2, –3.6, 18.0, 25.6, 27.3, 74.8, 82.2, 125.1, 126.5, 127.5, 129.9, 144.8 and 211.1; *m*/*z* (ESI): 385.0 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(3′-trifluoromethylphenyl)butan-2-one (4i)

Yield: 84%; *syn*/*anti* = 84 : 16; enantiomeric excess: 96% of *syn* diastereomer determined by HPLC (Diacel Chiralpak AS-H; hexane/*i*-PrOH 95 : 5; flow rate 0.5 mL min^{-1}; λ = 217 nm; t_R (*syn*, major) = 9.0 min, t_R (*syn*, minor) = 15.2 min; $[\alpha]_D^{25}$ +39 (*c* 0.1 in $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3413, 2932, 2860, 1701 and 1331; δ_H(300 MHz; $CDCl_3$; Me_4Si) –0.41 (3H, s, SiCH_3 (*syn*)), –0.29 (3H, s, SiCH_3 (*anti*)), –0.06 (3H, s, SiCH_3 (*syn*)), –0.05 (3H, s, SiCH_3 (*anti*)), –0.84 (9H, s, SiC(CH_3)$_3$), 2.13 (3H, s, COCH_3 (*anti*)), 2.22 (3H, s, COCH_3 (*syn*)), 4.05 (1H, d, *J* 6.9 Hz, C*H*OTBS (*anti*)), 4.15 (1H, d, *J* 2.7 Hz, C*H*OTBS (*syn*)), 4.80 (1H, d, *J* 6.9 Hz, C*H*OH (*anti*)), 4.98 (1H, d, *J* 2.4 Hz, C*H*OH (*syn*)), 7.44–7.58 (3H, m, Ar*H*) and 7.63–7.65 (1H, m, Ar*H*); δ_C(125 MHz; $CDCl_3$; Me_4Si) –6.0, –5.2, 17.9, 25.5, 27.3, 74.7, 82.1, 122.9, 125.2, 126.4, 127.5, 129.9, 130.2, 144.7 and 211.2; *m*/*z* (ESI): 385.0 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(2′-trifluoromethylphenyl)butan-2-one (4j)

Yield: 82%; *syn*/*anti* = 86/14; $[\alpha]_D^{25}$ +35 (*c* 0.1 in $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3457, 2932, 2859, 1714 and 1312; δ_H(300 MHz; $CDCl_3$; Me_4Si) –0.45 (1H, s, SiCH_3 (*syn*)), –0.13 (1H, s, SiCH_3 (*syn*)), 0.81 (9H, s, SiC(CH_3)$_3$ (*anti*)), 0.82 (9H, s, SiC(CH_3)$_3$ (*syn*)), 2.21 (3H, s, COCH_3 (*anti*)), 2.28 (3H, s, COCH_3 (*syn*)), 2.96 (1H, br s, O*H*), 4.19 (1H, d, *J* 6 Hz, C*H*OTBS (*anti*)), 4.22 (1H, d, *J* 2.1 Hz, C*H*OTBS (*syn*)), 5.45 (1H, br s, C*H*OH (*syn*)), 7.41 (1H, t, *J* 7.5 Hz, Ar*H*), 7.58 (1H, t, *J* 7.5 Hz, Ar*H*), 7.65 (1H, d, *J* 8.1 Hz, Ar*H*) and 7.73 (1H, d, *J* 7.8 Hz, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) –6.1, –5.4, 18.1, 25.7, 27.4, 70.4, 81.8, 123.1, 125.7, 126.5, 127.9, 129.6, 131.6, 139.3 and 208.6. *m*/*z* (ESI): 385.0 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(2′-cyanophenyl)butan-2-one[8b] (4k)

Yield: 91%; *syn*/*anti* = 83 : 17; enantiomeric excess: 91% of *syn* diastereomer determined by HPLC (Diacel Chiralpak AS-H; hexane–ethanol 95 : 5; flow rate 0.5 mL min^{-1}; λ = 234 nm; t_R (*syn*, major) = 15.1 min, t_R (*syn*, minor) = 20.6 min; $[\alpha]_D^{25}$ (*c* 0.1 in $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3509, 2930, 2857, 2229, 1711 and 1353; δ_H(300 MHz; $CDCl_3$; Me_4Si) –0.37 (3H, s, SiCH_3 (*syn*)), –0.23 (3H, s, SiCH_3 (*anti*)), –0.04 (3H, s, SiCH_3 (*syn*)), –0.02 (3H, s, SiCH_3 (*anti*)), 0.87 (9H, s, SiC(CH_3)$_3$), 2.13 (3H, s, COCH_3 (*anti*)), 2.21 (3H, s, COCH_3 (*syn*)), 3.09 (1H, d, *J* 8.7 Hz, O*H*), 4.06 (1H, d, *J* 6.3 Hz, C*H*OTBS (*anti*)), 4.13 (1H, d, *J* 2.7 Hz, C*H*OTBS (*syn*)), 4.96 (1H, dd, *J* 8.7 Hz and *J* 2.4 Hz, C*H*OH (*syn*)), 7.46–7.48 (2H, m, Ar*H*) and 7.62–7.67 (2H, m, Ar*H*); δ_C(125 MHz; $CDCl_3$; Me_4Si) –5.7, –5.1, 18.0, 25.6, 27.3, 74.7, 81.8, 111.5, 118.6, 126.9, 127.9, 132.0, 146.3 and 210.9; *m*/*z* (ESI): 342.0 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(4′-fluorophenyl)butan-2-one (4l)

Yield: 83%; *syn*/*anti* = 77 : 23; enantiomeric excess: 91% of *syn* diastereomer determined by HPLC (Diacel Chiralpak AS-H; hexane–ethanol 95 : 5; flow rate 0.5 mL min^{-1}; λ = 205 nm; t_R (*syn*, major) = 9.9 min, t_R (*syn*, minor) = 11.7 min; $[\alpha]_D^{25}$ +35 (*c* 0.1 in $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3441, 2930, 2858, 1711 and 1509; δ_H(300 MHz; $CDCl_3$; Me_4Si) –0.31 (3H, s, SiCH_3 (*syn*)), –0.21 (3H, s, SiCH_3 (*anti*)), –0.05 (3H, s, SiCH_3 (*syn*)), –0.03 (3H, s, SiCH_3 (*anti*)), 0.86 (9H, s, SiC(CH_3)$_3$ (*anti*)), 0.87 (9H, s, SiC(CH_3)$_3$ (*syn*)), 2.03 (3H, s, COCH_3 (*anti*)), 2.12 (3H, s, COCH_3 (*syn*)), 4.01 (1H, d, *J* 6 Hz, C*H*OTBS (*anti*)), 4.03 (1H, d, *J* 3 Hz, C*H*OTBS (*syn*)), 4.70 (1H, d, *J* 6.3 Hz, C*H*OH (*anti*)), 4.81 (1H, br s, C*H*OH (*syn*)), 6.96–7.03 (2H, m, Ar*H*) and 7.24–7.32 (2H, m, Ar*H*); δ_C(125 MHz; $CDCl_3$; Me_4Si) –5.7, –5.2, 18.1, 25.6, 27.3, 74.7, 82.4, 115.0, 115.2, 127.7, 128.7, 136.2, 161.4, 163.3 and 211; *m*/*z* (ESI): 335.0 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(4′-chlorophenyl)butan-2-one[5a] (4m)

Yield: 84%; *syn*/*anti* = 83 : 17; enantiomeric excess: 90% of *syn* diastereomer determined by HPLC (Diacel Chiralpak AD-H; hexane–ethanol 98 : 2; flow rate 0.5 mL min^{-1}; λ = 223; t_R (*syn*, major) = 23.2 min, t_R (*syn*, minor) = 21.6 min; $[\alpha]_D^{25}$ +31 (*c* 0.1, $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3450, 2948, 2867, 1714, 1523 and 1346; δ_H(300 MHz; $CDCl_3$; Me_4Si) –0.31 (3H, s, SiCH_3 (*syn*)), –0.19 (3H, s, SiCH_3 (*anti*)), –0.05 (3H, s, SiCH_3 (*syn*)), –0.03 (3H, s, SiCH_3 (anti)), 0.87 (9H, s, SiC(CH_3)$_3$), 2.10 (3H, s, COCH_3 (*anti*)), 2.18 (3H, s, COCH_3 (*syn*)), 4.07 (1H, d, *J* 6.3 Hz, C*H*OTBS (*anti*)), 4.11 (1H, d, *J* 3.3 Hz, C*H*OTBS (*syn*)), 4.75 (1H, d, *J* 6.3 Hz, C*H*OH (*anti*)), 4.89 (1H, d, *J* 3.0 Hz, C*H*OH (*anti*)), 7.25–7.27 (2H, m, Ar*H*), 7.30–7.34 (2H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) –5.6, –5.1, 18.0, 25.6, 27.3, 74.7, 81.7, 123.3, 127.0, 147.5, 148.1 and 210.8; *m*/*z* (ESI): 350.9 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(4′-bromophenyl)butan-2-one (4n)

Yield: 82%; *syn*/*anti* = 82 : 18; enantiomeric excess: 92% of *syn* diastereomer determined by HPLC (Diacel Chiralpak AD-H; hexane–ethanol 95 : 5; flow rate 0.5 mL min^{-1}; λ = 224 nm; t_R (*syn*, major) = 14.0 min, t_R (*syn*, minor) = 13.3 min; $[\alpha]_D^{25}$ +34 (*c* 0.1, $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3440, 2929, 2857, 1711 and 1352; δ_H(300 MHz; $CDCl_3$; Me_4Si) –0.31 (3H, s, SiCH_3 (*syn*)), –0.19 (3H, s, SiCH_3 (*anti*)), –0.05 (3H, s, SiCH_3 (*syn*)), –0.03 (3H, s, SiCH_3 (*anti*)), 0.87 (9H, s, SiC(CH_3)$_3$), 2.09 (3H, s, COCH_3 (*anti*)), 2.18 (3H, s, COCH_3 (*syn*)), 4.06 (1H, d, *J* 6.3 Hz, C*H*OTBS (*anti*)), 4.09 (1H, d, *J* 0.9 Hz, C*H*OTBS (*syn*)), 4.74 (1H, d, *J* 6.3 Hz, C*H*OH (*anti*)), 5.10 (1H, d, *J* 5.7 Hz, C*H*OH (*syn*)), 7.21 (2H, d, *J* 8.7 Hz, Ar*H*), 7.46–7.49 (2H, d, *J* 8.1 Hz, Ar*H*); δ_C(125 MHz; $CDCl_3$; Me_4Si) –5.7, –5.2, 18.0, 25.6, 27.3, 74.7, 82.1, 121.6, 127.8, 131.3, 139.6 and 211.2; *m*/*z* (ESI): 394.9 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(2′-fluorophenyl)butan-2-one (4o)

Yield: 81%; *syn*/*anti* = 85 : 15; enantiomeric excess: 93% of *syn* diastereomer determined by HPLC (Diacel Chiralpak AS-H; hexane/*i*-PrOH 95 : 5; flow rate 0.5 mL min^{-1}; λ = 208 nm; t_R (*syn*, major) = 10.2 min, t_R (*syn*, minor) = 11.7 min; $[\alpha]_D^{25}$ +29 (*c* 0.1, $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3449, 2930, 2857, 1713, 1460 and 1355; δ_H(300 MHz; $CDCl_3$; Me_4Si) –0.40 (3H, s, SiCH_3 (*syn*)), –0.14 (3H, s, SiCH_3 (*anti*)), –0.08 (3H, s, SiCH_3 (*syn*)), 0.82 (9H, s, SiC(CH_3)$_3$ (*syn*)), 0.87 (9H, s, SiC(CH_3)$_3$ (*anti*)), 2.15 (3H, s, COCH_3 (*anti*)), 2.27 (3H, s, COCH_3 (*syn*)), 2.94 (1H, br s, O*H*), 4.21 (1H, d, *J* 6 Hz, C*H*OTBS (*anti*)), 4.25 (1H, d, *J* 2.7 Hz,

C*H*OTBS (*syn*)), 5.10 (1H, d, *J* 5.7 Hz, C*H*OH (*anti*)), 5.27 (1H, br s, C*H*OH (*syn*)), 6.99–7.05 (1H, m, Ar*H*), 7.12–7.18 (1H, m, Ar*H*), 7.24–7.31 (1H, m, Ar*H*) and 7.38–7.46 (1H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) −6.1, −5.2, 17.9, 25.7, 26.9, 69.7, 81.0, 115.0, 115.3, 124.1, 128.0, 129.3, 158.3, 160.7 and 209.4; *m*/*z* (ESI): 334.9 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(2′-chlorophenyl)butan-2-one (4p)

Yield: 82%; *syn*/*anti* = 84 : 16; enantiomeric excess: 90% of *syn* diastereomer determined by HPLC (Diacel Chiralpak OD-H; hexane/*i*-PrOH 95 : 5; flow rate 0.3 mL min^{-1}; λ = 206 nm; t_R (*syn*, major) = 21.5 min, t_R (*syn*, minor) = 20.6 min; $[\alpha]_D^{25}$ +32 (*c* 0.1 in $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3460, 2929, 2857, 1714 and 1410; δ_H(300 MHz; $CDCl_3$; Me_4Si) −0.50 (3H, s, SiCH_3 (*syn*)), −0.13 (3H, s, SiCH_3 (*syn*)), −0.03 (3H, s, SiCH_3 (*anti*)), 0.04 (3H, s, SiCH_3 (*anti*)), 0.80 (9H, s, SiC(CH_3)$_3$ (*syn*)), 0.90 (9H, s, SiC(CH_3)$_3$ (*anti*)), 2.17 (3H, s, COCH_3 (*anti*)), 2.33 (3H, s, COCH_3 (*syn*)), 2.93 (1H, d, *J* 9 Hz, O*H*), 4.34 (1H, d, *J* 5.4 Hz, C*H*OTBS (*anti*)), 4.41 (1H, d, *J* 1.8 Hz, C*H*OTBS (*syn*)), 5.37 (1H, d, *J* 8.7 Hz, C*H*OH (*syn*)), 7.21–7.36 (3H, m, Ar*H*) and 7.46–7.49 (m, 1H, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) −6.3, −5.4, 18.1, 25.6, 26.9, 71.8, 79.4, 126.6, 128.5, 128.9, 129.3, 131.2, 138.1 and 208.9; *m*/*z* (ESI): 350.9 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(2′-bromophenyl)butan-2-one (4q)

Yield: 85%; *syn*/*anti* = 82 : 18; enantiomeric excess: 92% of *syn* diastereomer determined by HPLC (Diacel Chiralpak OD-H; hexane/*i*-PrOH 96 : 4; flow rate 0.3 mL min^{-1}; λ = 254; t_R (*syn*, major) = 19.7 min, t_R (*syn*, minor) = 20.8 min; $[\alpha]_D^{25}$ +31 (*c* 0.1, $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3446, 2930, 2857, 1712, 1466 and 1353; δ_H(300 MHz; $CDCl_3$; Me_4Si) −0.51 (3H, s, SiCH_3 (*syn*)), −0.13 (3H, s, SiCH_3 (*syn*)), 0.05 (3H, s, SiCH_3 (*anti*)), 0.09 (3H, s, SiCH_3 (*anti*)), 0.79 (9H, s, SiC(CH_3)$_3$ (*syn*)), 0.91 (9H, s, SiC(CH_3)$_3$ (*anti*)), 2.13 (3H, s, COCH_3 (*anti*)), 2.34 (3H, s, COCH_3 (*syn*)), 2.95 (1H, d, *J* 9 Hz, O*H*), 4.36 (1H, d, *J* 5.1 Hz, C*H*OTBS (*anti*)), 4.45 (1H, d, *J* 1.5 Hz, C*H*OTBS (*syn*)), 5.33 (1H, d, *J* 8.7, C*H*OH (s*yn*)), 7.14–7.19 (1H, m, Ar*H*), 7.32–7.37 (1H, m, Ar*H*), 7.45–7.48 (1H, dd, *J* 7.8 Hz and *J* 1.5 Hz, Ar*H*) and 7.523–7.553 (1H, m, Ar*H*); δ_C(125 MHz; $CDCl_3$; Me_4Si) −6.3, −5.1, 18.1, 25.6, 26.9, 73.8, 79.3, 121.2, 127.2, 129.0, 129.2, 132.6, 139.5 and 208.8; *m*/*z* (ESI): 394.9 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(3′,4′-dichlorophenyl)butan-2-one (4r)

Yield: 78%; *syn*/*anti* = 78 : 22; $[\alpha]_D^{25}$ +19 (*c* 0.1 in $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3438, 2928, 2856, 1712 and 1470; δ_H(300 MHz; $CDCl_3$; Me_4Si) −0.29 (3H, s, SiCH_3 (*syn*)), −0.19 (3H, s, SiCH_3 (*anti*)), −0.03 (3H, s, SiCH_3 (*syn*)), −0.02 (3H, s, SiCH_3 (*anti*)), 0.88 (9H, s, SiC(CH_3)$_3$), 2.12 (3H, s, COCH_3 (*anti*)), 2.19 (3H, s, COCH_3 (*syn*)), 3.03 (1H, d, *J* 9 Hz, O*H*), 4.03 (1H, d, *J* 6.6 Hz, C*H*OTBS (*anti*)), 4.09 (1H, d, *J* 2.7 Hz, C*H*OTBS (*syn*)), 4.86 (1H, d, *J* 5.4 Hz, C*H*OH (*syn*)), 7.13–7.16 (1H, m, Ar*H*) and 7.39–7.46 (m, 2H, Ar*H*); δ_C(125 MHz; $CDCl_3$; Me_4Si) −5.6, −5.1, 18.1, 25.6, 27.4, 74.2, 81.8, 125.3, 128.3, 130.2, 131.7, 132.5, 141.0 and 211.1; *m*/*z* (ESI): 384.9 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(phenyl)butan-2-one[8b] (4s)

Yield: 74%; *syn*/*anti* = 81 : 19; enantiomeric excess: 93% of *syn* diastereomer determine by HPLC (Diacel Chiralpak OD-H, hexane/*i*-PrOH 98 : 2; flow rate 0.5 mL min^{-1}; λ = 210; t_R (*syn*, major) = 33.3 min, t_R (*syn*, minor) = 24.3 min; $[\alpha]_D^{25}$ +20 (*c* 0.1, $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3452, 2929, 2857, 1714, 1390 and 1255; δ_H(300 MHz; $CDCl_3$; Me_4Si) −0.36 (3H, s, SiCH_3 (*syn*)), −0.23 (3H, s, SiCH_3 (*anti*)), −0.08 (3H, s, SiCH_3 (*syn*)), −0.05 (3H, s, SiCH_3 (*anti*)), 0.85 (9H, s, SiC(CH_3)$_3$ (*anti*)), 0.86 (9H, s, SiC(CH_3)$_3$ (*syn*)), 2.08 (3H, s, COCH_3 (*anti*)), 2.18 (3H, s, COCH_3 (*syn*)), 4.10 (1H, d, *J* 6.6 Hz, C*H*OTBS (*anti*)), 4.14 (1H, d, *J* 2.7 Hz, C*H*OTBS (*syn*)), 4.76 (1H, d, *J* 6.6 Hz, C*H*OH (*anti*)), 4.91 (1H, d, *J* 3.0 Hz, C*H*OH (*syn*)), 7.27–7.37 (5H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) −6.0, −5.2, 17.9, 25.5, 27.3, 74.7, 82.0, 123.0, 124.5, 128.6, 129.3, 130.5, 141.7 and 211.2.

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(4′-methylphenyl)butan-2-one[8b] (4t)

Yield: 75%; *syn*/*anti* = 73 : 27; enantiomeric excess: 91% of *syn* diastereomer determine by HPLC (Diacel Chiralpak AS-H, hexane/*i*-PrOH 95.5; flow rate 0.5 mL min^{-1}; λ = 207 nm; t_R (*syn*, major) = 11.1 min, t_R (*syn*, minor) = 16.9 min; $[\alpha]_D^{25}$ +31 (*c* 0.1, $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3461, 2929, 2857, 1709, 1466 and 1255; δ_H(300 MHz; $CDCl_3$; Me_4Si) −0.32 (3H, s, SiCH_3 (*syn*)), −0.18 (3H, s, SiCH_3 (*anti*)), −0.07 (3H, s, SiCH_3 (*syn*)), −0.04 (3H, s, SiCH_3 (*anti*)), 0.86 (9H, s, SiC(CH_3)$_3$ (*anti*)), 0.87 (9H, s, SiC(CH_3)$_3$ (*syn*)), 2.06 (3H, s, COCH_3 (*anti*)), 2.16 (3H, s, COCH_3 (*syn*)), 2.33 (3H, s, PhCH_3), 4.11 (1H, d, *J* 3.3 Hz, C*H*OTBS (*syn*)), 4.73 (1H, d, *J* 6.3 Hz, C*H*OH (*anti*)), 4.85 (1H, br s, C*H*OH (*syn*)) and 7.12–7.23 (4H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) −5.5, −5.2, 18.0, 21.1, 25.6, 27.3, 75.2, 82.7, 126.0, 126.9, 128.9, 136.7, 137.4, 137.9 and 211.3.

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(2′-methoxyphenyl)butan-2-one (4u)

Yield: 74%; *syn*/*anti* = 68 : 32; enantiomeric excess: 84% of *syn* diastereomer determine by HPLC (Diacel Chiralpak OD-H, hexane/*i*-PrOH 95.5; flow rate 0.5 mL min^{-1}; λ = 206 nm; t_R (*syn*, major) = 25.9 min, t_R (*syn*, minor) = 13.4 min; $[\alpha]_D^{25}$ +21 (*c* 0.1, $CHCl_3$); δ_H(400 MHz; $CDCl_3$; Me_4Si) −0.47 (3H, s, SiCH_3 (*syn*)), −0.22 (3H, s, SiCH_3 (*anti*)), −0.15 (3H, s, SiCH_3 (*syn*)), −0.07 (3H, s, SiCH_3 (*anti*)), 0.80 (9H, s, SiC(CH_3)$_3$ (*syn*)), 0.83 (9H, s, SiC(CH_3)$_3$ (*anti*)), 2.2 (3H, s, COCH_3 (*anti*)), 2.27 (3H, s, COCH_3 (*syn*)), 3.85 (3H, s, OCH_3 (*syn*)), 3.86 (3H, s, OCH_3 (*anti*)), 4.29 (1H, d, *J* 6.6 Hz, C*H*OTBS (*anti*)), 4.31 (1H, d, *J* 2.4 Hz, C*H*OTBS (*syn*)), 4.87 (1H, d, *J* 6.4 Hz, C*H*OH (*anti*)), 5.27 (1H, br s, C*H*OH (*syn*)), 6.84–6.99 (2H, m, ArH) and 7.24–7.28 (2H, m, ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) −6.2, −5.3, 18.1, 25.6, 26.9, 55.2, 70.6, 80.6, 109.9, 120.4, 127.1, 128.8, 155.7, 156.6 and 209.9; MS (ESI-TOF) 347.0736 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(1′-naphthyl)butan-2-one (4v)

Yield: 65%; *syn*/*anti* = 83 : 17; enantiomeric excess: 93% of *syn* diastereomer determined by HPLC (Diacel Chiralpak

AD-H, hexane/*i*-PrOH 95 : 5; flow rate 0.5 mL min^{-1}; λ = 217; t_R (*syn*, major) = 21.8 min, t_R (*syn*, minor) = 15.5 min; $[\alpha]_D^{25}$ +32 (*c* 0.1, $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3455, 2929, 2857 and 1709; δ_H(300 MHz; $CDCl_3$; Me_4Si) –0.93 (3H, s, SiCH_3 (*syn*)), –0.50 (3H, s, SiCH_3 (*anti*)), –0.33 (3H, s, SiCH_3 (*syn*)), –0.14 (3H, s, SiCH_3 (*anti*)), 0.71 (9H, s, SiC(CH_3)$_3$ (*anti*)), 0.79 (9H, s, SiC(CH_3)$_3$ (*syn*)), 2.11 (3H, s, COCH_3 (*anti*)), 2.31 (3H, s, COCH_3 (*syn*)), 4.26 (1H, d, *J* 1.5 Hz, C*H*OTBS (*syn*)), 4.31 (1H, d, *J* 6.6 Hz, C*H*OTBS (*anti*)), 5.64 (1H, br s, C*H*OH (*syn*)), 7.41–7.49 (2H, m, Ar*H*), 7.53–7.88 (4H, m, Ar*H*) and 7.94–8.06 (2H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) –6.4, –5.7, 17.9, 25.5, 26.9, 72.5, 80.7, 122.2, 123.8, 124.9, 125.5, 126.5, 128.3, 129.1, 129.7, 133.7, 136.0 and 211.9; *m*/*z* (ESI): 367.0 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldimethylsilyloxy)-4-hydroxy-4-(2′-naphthyl)butan-2-one[8b] (4x)

Yield: 70%; *syn*/*anti* = 68 : 32; enantiomeric excess: 83% of *syn* diastereomer determine by HPLC (Diacel Chiralpak AS-H, hexane/*i*-PrOH 80 : 20; flow rate 1 mL min^{-1}; λ = 226 nm; t_R (*syn*, major) = 4.1 min., t_R (*syn*, minor) = 6.2 min; $[\alpha]_D^{25}$ +24 (*c* 0.1 in $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3450, 2928, 2856, 1713 and 1255; δ_H(300 MHz; $CDCl_3$; Me_4Si) –0.46 (3H, s, SiCH_3 (*syn*)), –0.27 (3H, s, SiCH_3 (*anti*)), –0.10 (3H, s, SiCH_3 (*syn*)), –0.05 (3H, s, SiCH_3 (*anti*)), 0.84 (9H, s, SiC(CH_3)$_3$), 2.08 (3H, s, COCH_3 (*anti*)), 2.20 (3H, s, COCH_3 (*syn*)), 2.75 (1H, br s, O*H* (*anti*)), 3.12 (1H, br s, O*H* (*syn*)), 4.21 (1H, d, *J* 3.3 Hz, C*H*OTBS (*anti*)), 4.23 (1H, d, *J* 2.7 Hz, C*H*OTBS (*syn*)), 4.94 (1H, d, *J* 6.6 Hz, C*H*OH (*anti*)), 5.06–5.08 (1H, m, C*H*OH (*syn*)), 7.40–7.51 (3H, m, Ar*H*) and 7.79–7.84 (4H, m, Ar*H*); δ_C(125 MHz; $CDCl_3$; Me_4Si) –5.7, –5.2, 18.0, 25.6, 27.4, 75.4, 82.2, 123.9, 125.1, 125.9, 126.1, 127.6, 128.9, 128.0, 133.0, 137.9 and 211.4; *m*/*z* (ESI): 367.0 (M^++Na).

(3*R*,4*S*)-4-acetoxy-1,3-bis(benzyloxy)-4-(4′-nitrophenyl)butan-2-one[8a] (4y)

Yield: 87%; *syn*/*anti* = 81 : 19; enantiomeric excess: of *syn* diastereomer determine by HPLC (Diacel Chiralpak AD-H, hexane/*i*-PrOH 80 : 20; flow rate 1.0 mL min^{-1}; λ = 254 nm; t_R (*syn*, major) = 18.8, t_R (*syn*, minor) = 30.3; $[\alpha]_D^{25}$ +11 (*c* 0.1 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$; Me_4Si) 2.06 (3H, s, OCOCH_3 (*anti*)), 2.07 (3H, s, OCOCH_3 (*syn*)), 4.05 (1H, d, *J* 18.5 Hz, CH_2Ph (*anti*)), 4.18 (1H, d, *J* 11.8 Hz, CH_2Ph (*syn*)), 4.24 (1H, d, *J* 18.1 Hz, CH_2Ph (*syn*)), 4.26–4.50 (3H, CH_2Ph and C*H*OBn) 4.44 (1H, d, *J* 11.6 Hz, CH_2Ph (*syn*)), 4.50 (1H, d, *J* 11.6 Hz, CH_2Ph (*anti*)), 4.51 (2H, s, CH_2OBn (*anti*)), 4.56 (2H, s, CH_2OBn (*syn*)), 6.11 (1H, d, *J* 5.4 Hz, C*H*OAc (*anti*)), 6.23 (1H, d, *J* 2.8 Hz, C*H*OAc (*syn*)), 6.94 (2H, d, *J* 7.2 Hz, ArH), 7.11–7.44 (10H, m, ArH) and 8.12 (2H, d, *J* 8.4 Hz, ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 20.7, 73.5, 74.0, 74.1, 74.3, 83.5, 123.5, 127.5, 128.1, 128.3, 128.4, 128.5, 128.6, 128.7, 135.7, 136.8, 143.9, 147.7, 169.5 and 205.8; MS (ESI-TOF) 486.0552 (M^++Na).

(3*R*,4*S*)-4-acetoxy-1,3-bis(*tert*-butyldimethylsiloxy)-4-(4′-nitrophenyl)butan-2-one[8a] (4z)

Yield: 92%; *syn*/*anti* = 84 : 16; enantiomeric excess: 95% of *syn* diastereomer determine by HPLC (Diacel Chiralpak OD-H, hexane/*i*-PrOH 99.5 : 0.5; flow rate 1.0 mL min^{-1}; λ = 254 nm; t_R (*syn*, major) = 19.9 min., t_R (*syn*, minor) = 37.1 min.; $[\alpha]_D^{25}$ +35 (*c* 0.1 in $CHCl_3$); δ_H(400 MHz; $CDCl_3$; Me_4Si) –0.42 (1H, s, SiCH_3 (*syn*)), –0.09 (1H, s, SiCH_3 (*syn*)), 0.01 (1H, s, SiCH_3 (*anti*)), 0.02 (1H, s, SiCH_3 (*anti*)), 0.03 (1H, s, SiCH_3 (*anti*)), 0.04 (1H, s, SiCH_3 (*anti*)), 0.09 (1H, s, SiCH_3 (*syn*)), 0.1 (1H, s, SiCH_3 (*syn*)), 0.85 (9H, s, SiC(CH_3)$_3$ (*syn*)), 0.87 (9H, s, SiC(CH_3)$_3$ (*anti*)), 0.89 (9H, s, SiC(CH_3)$_3$ (*anti*)), 0.93 (9H, s, SiC(CH_3)$_3$ (*syn*)), 2.12 (3H, s, OCOCH_3 (*anti*)), 2.13 (3H, s, OCOCH_3 (*syn*)), 4.11 (1H, d, *J* 19.3 Hz, CH_2OTBS (*anti*)), 4.46 (2H, d, *J* 6.1 Hz, CH_2OTBS (*syn*)), 4.51 (1H, d, *J* 2.5 Hz, CH_2OTBS (*anti*)), 4.57 (1H, d, *J* 3.3 Hz, C*H*OTBS (*syn*)), 4.62 (1H, d, *J* 4.6 Hz, C*H*OTBS (*anti*)), 6.07 (1H, d, *J* 4.6 Hz, C*H*OAc (*anti*)), 6.13 (1H, d, *J* 3.3 Hz, C*H*OAc (*syn*)), 7.47–7.53 (2H, m, ArH) and 8.18–8.23 (2H, m, ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) –5.8, –5.4, –5.3, –4.9, 18.0, 18.5, 20.9, 25.5, 25.8, 68.7, 75.5, 78.3, 123.5, 127.9, 144.1, 147.7, 169.5 and 207.2; MS (ESI-TOF): 534.1389 (M^++Na).

(3*R*,4*S*)-3-(*tert*-butyldiphenylsilyloxy)-4-hydroxy-4-(4′-nitrophenyl)butan-2-one (4c)

Yield: 81%; *syn*/*anti* = 92 : 08; enantiomeric excess: 83% of *syn* diastereomer determine by HPLC (Diacel Chiralpak IB, hexane/*i*-PrOH 99 : 1; flow rate 1.5 mL min^{-1}; λ = 210 nm; t_R (*syn*, major) = 46.6 min., t_R (*syn*, minor) = 51.8 min.; $[\alpha]_D^{25}$ –14.3 (*c* 0.1 in $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3443, 2931, 2858, 1715, 1522 and 1346; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.08 (9H, s, SiC(CH_3)$_3$ (*syn*)), 1.11 (9H, s, SiC(CH_3)$_3$ (*anti*)), 1.82 (3H, s, COCH_3 (*syn*)), 1.92 (3H, s, COCH_3 (*anti*)), 3.23 (1H, d, *J* 7.8 Hz, O*H* (*syn*), 3.47 (1H, d, *J* 5.1 Hz, O*H* (*anti*) 4.27 (1H, d, *J* 6 Hz, C*H*OTBDPS (*anti*)), 4.41 (d, 1H, *J* 3.6 Hz, C*H*OTBDPS (*syn*)), 4.87–4.89 (1H, m, C*H*OH (*syn*)), 7.22–7.57 (12H, m, Ar*H*) and 8.07–8.14 (2H, m, Ar*H*); δ_C(125 MHz; $CDCl_3$; Me_4Si) 19.2, 26.9, 27.4, 74.4, 81.7, 123.3, 127.2, 127.3, 127.8, 127.9, 128.0, 130.2, 130.3, 130.4, 131.8, 131.9, 135.6, 135.7, 135.8, 147.4, 147.6 and 210.1; *m*/*z* (ESI): 485.4 (M^++Na).

(3*R*,4*S*)-3-(benzyloxy)-4-hydroxy-4-(4′-nitrophenyl)butan-2-one.[12f] (4e)

Yield: 70%; *syn*/*anti* = 70 : 30; enantiomeric excess: 94% of *syn* diastereomer determine by HPLC (Diacel Chiralpack AS-H, hexane/*i*-PrOH 70 : 30; flow rate 0.5 mL min^{-1}; λ = 254 nm; t_R (*syn*, major) = 16.6 min., t_R (*syn*, minor) = 27.7 min.; $[\alpha]_D^{25}$ +52 (*c* 0.1 in $CHCl_3$); IR ($CHCl_3$): ν/cm^{-1} 3446, 2946, 2867, 1714, 1523 and 1346; δ_H(300 MHz; $CDCl_3$; Me_4Si) 2.21 (3H, s, COCH_3), 3.96 (1H, d, *J* 3.6 Hz, C*H*OBn), 4.34 (1H, d, *J* 11.7 Hz, CH_aH$_b$Ph), 4.59 (1H, d, *J* 11.7 Hz, CH$_a$$H_b$Ph), 5.08 (1H, d, *J* 3.3 Hz, C*H*OH), 7.08–7.11 (2H, m, Ar*H*), 7.25–7.35 (3H, m, Ar*H*), 7.48 (2H, d, *J* 9.0 Hz, Ar*H*) and 8.18 (2H, d, *J* 9.0 Hz, Ar*H*); δ_C(75 MHz; $CDCl_3$; Me_4Si) 27.8, 73.5, 73.8, 87.0, 123.4, 127.0, 127.7, 128.0, 128.2, 128.4, 128.5, 130.1, 135.9, 147.5 and 209.8; *m*/*z* (ESI): 338.0 (M^++Na).

Catalyst Recovery

After workup of the reaction, the aqueous portion was separated and neutralized with saturated solution of sodium carbonate. The neutralized aqueous solution was extracted with ethyl acetate (3 × 10 mL), dried over anhydrous Na_2SO_4, and distilled to obtain the desired catalyst in 90% yield.

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