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Conformational lock in a Brønsted acid–Lewis base organocatalyst for the aza-Morita–Baylis–Hillman reaction

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Abstract—(*S*)-3-(*N*-Isopropyl-*N*-3-pyridinylaminomethyl)BINOL has been established as an efficient asymmetric bifunctional organocatalyst for the aza-MBH reaction. The acid–base functionalities cooperate in substrate activation and fixing of the organocatalyst conformation to promote the reaction with high enantiocontrol.

1. Introduction

Asymmetric catalysis is one of the most powerful approaches for synthesizing enantiomerically pure and useful compounds. In particular, the design and development of asymmetric catalysts possessing two or more reaction-promoting functionalities are of ongoing interest in asymmetric synthesis.[1–4] The functionalities activate the substrates by synergistic cooperation, affording the products in high yield and high enantioselectivity. Bifunctional organometallic catalysts are representative examples of this type.[1,2] Immobilized bifunctional catalysts, which can be recovered and reused have also been investigated.[3] However, the practical use of immobilized organometallic catalysts is generally difficult due to leaching of the metal, which results in deactivation of the catalyst and/or contamination of the product of the catalytic reaction. For this reason, the development of asymmetric systems that do not contain a metal has been of great importance in organic chemistry.[4,5] Herein, we report a new class of bifunctional metal-free catalysts for the enantioselective aza-Morita–Baylis–Hillman (aza-MBH) reaction of α,β-unsaturated carbonyl compounds with *N*-tosylimines. The combination of Brønsted acid and Lewis base units for the activation of substrates in a single chiral environment results in high enantioselectivity in the adduct.

The aza-MBH reaction is a C–C bond-forming reaction of activated alkenes with imines, catalyzed by Lewis bases such as amines or phosphines, resulting in highly functionalized allylic amines, which are valuable building blocks in medicinal chemistry.[6,7] Excellent organocatalytic systems using quinidine-derived catalysts have been independently reported by Shi,[7b,e] Adolfsson,[7c] Hatakeyama,[7d] and Jacobsen[7i] for this asymmetric process. Shi has also reported the use of chiral phosphinyl BINOL to promote the aza-MBH reaction.[7f–h] The development of efficient catalysts for the aza-MBH reaction has been a considerable challenge in organic synthesis.

2. Results and discussion

We designed an organic molecule, in which chiral Brønsted acid units are connected with a Lewis base unit via a spacer, as shown in Figure 1. Our aim was to create a chiral molecule in which both Brønsted acid and Lewis base units were optimally positioned for the activation

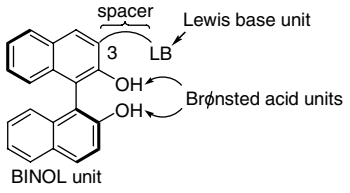

Figure 1. Concept of chiral bifunctional organocatalyst for aza-MBH reaction.

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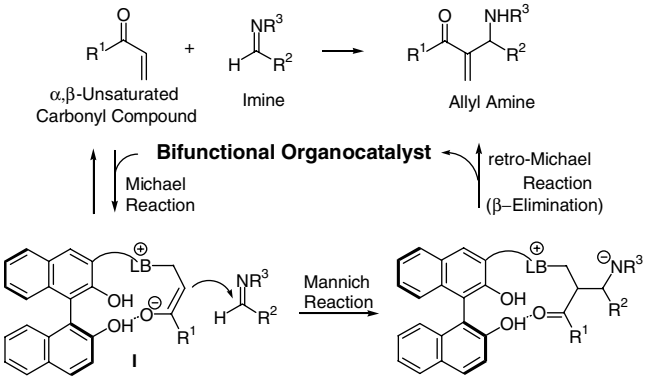
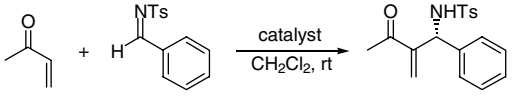
of α,β-unsaturated carbonyl compounds. The acid unit would activate the carbonyl group and the Lewis base unit would subsequently react with the β-position of the substrate in a Michael addition reaction (Scheme 1). The chiral Michael intermediate **I**, generated by cooperative interaction between each component of the organocatalyst, could furnish the product with high enantioselectivity via the Mannich and retro-Michael reactions.



Scheme 1. Proposed catalytic cycle for the bifunctional organocatalyst-mediated aza-MBH reaction.

With the aim of developing such organocatalysts, the reaction of the prototypical substrates methyl vinyl ketone **3a** and phenyl *N*-tosylimine **4a** was initially attempted in the presence of 4-, 3-, and 2-dimethylaminopyridine (4-, 3-, and 2-DMAP). As 4-DMAP can act efficiently as a Lewis base in this reaction[6d,f] (Table 1, entries 3–5), (*S*)-BINOLs bearing 4-dimethylaminopyridine were designed first (Fig. 2, compounds **1a**–**b**). Although a mixed reagent consisting of (*S*)-BINOL

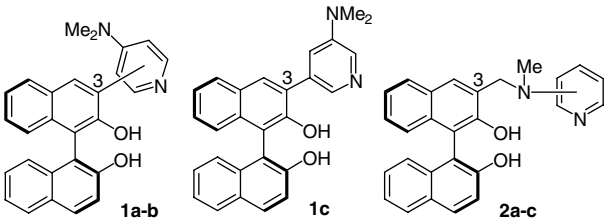
Table 1. Enantioselective aza-MBH reaction of **3a** with **4a** using organocatalysts



3a **4a** **5a**

Entry	Organocatalyst	Time (h)	Yield[a] (%)	ee[b] (%)
1	None	48	NR	—
2	(*S*)-BINOL	48	NR	—
3	2-DMAP	48	NR	—
4[d]	3-DMAP	48	27	—
5[d]	4-DMAP	7.5	55	—
6[c,d]	(*S*)-BINOL + 3-DMAP	168	48	3
7[c,d]	(*S*)-BINOL + 4-DMAP	8	60	2
8	**1a**	168	Trace	33
9	**1b**	168	21	2
10	**1c**	168	56	2
11	**2a**	168	41	73
12	**2b**	168	NR	—
13	**2c**	168	NR	—

[a] Isolated yield.
[b] Determined by HPLC (Daicel Chiralpak AD-H).
[c] 10 mol % of (*S*)-BINOL and 10 mol % of 3- or 4-DMAP were used.
[d] Decomposition of **4a** was observed.



1a: (*S*)-3-[4-(dimethylamino)pyridin-2-yl]BINOL
1b: (*S*)-3-[4-(dimethylamino)pyridin-3-yl]BINOL
1c: (*S*)-3-[3-(dimethylamino)pyridin-5-yl]BINOL
2a: (*S*)-3-(*N*-methyl-*N*-3-pyridinylaminomethyl)BINOL
2b: (*S*)-3-(*N*-methyl-*N*-2-pyridinylaminomethyl)BINOL
2c: (*S*)-3-(*N*-methyl-*N*-4-pyridinylaminomethyl)BINOL

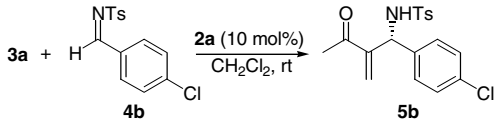
Figure 2. Novel chiral bifunctional organocatalysts for aza-MBH reaction.

(10 mol %) and 4-DMAP (10 mol %) promoted the reaction of **3a** with **4a** to give product **5a** (entry 7), the organocatalysts **1a** and **1b**, in which the pyridine ring is attached directly to the 3-position of BINOL, resulted in either low activity or none at all (entries 8–9). The organocatalyst **1c**, bearing 3-dimethylaminopyridine, was also synthesized and used in the reaction, resulting in a slight improvement in chemical yield (entry 10). The catalytic deficiency of **1** may be due to the inappropriate position of the Lewis base on the catalyst. Next, we synthesized organocatalysts **2a**–**c**, in which 3-, 2-, or 4-aminopyridine derivatives are attached via a methylene spacer. Although organocatalyst **2b**, which contains a 2-aminopyridine unit, was found to be ineffective (entry 12), catalyst **2a**, containing a 3-aminopyridine unit, afforded **5a** in 41% yield with 73% ee (entry 11). In contrast, the same reaction mediated by a mixed reagent, (*S*)-BINOL (10 mol %) and 3-DMAP (10 mol %), produced **5a** in 48% yield with low enantioselectivity (entry 6). The organocatalyst **2c** contains a 4-aminopyridine unit, for which intramolecular Michael addition would be impossible, and this catalyst was found not to promote the reaction (entry 13). These results indicate that the exact positioning of the active units on the catalyst can dramatically improve the efficiency of bifunctional asymmetric organocatalysis.

Encouraged by these results, we went on to study the effects of solvent and temperature on the reaction of **3a** with *p*-chlorophenyl *N*-tosylimine **4b** (Table 2). Ethereal solvents such as diethyl ether, *t*-BuOMe, cyclopentyl methyl ether (CPME), and dimethyl ether (DME) (entries 1–4), along with toluene (entry 6) gave relatively good results in comparison with THF (entry 5) and other polar, less polar, aprotic, and protic solvents, including halogenated solvents, DMF, acetonitrile, and methanol (entries 7–12). A mixed solvent system consisting of CPME–toluene (9/1) at −15 °C afforded the best outcome (entry 14). It was established that the most efficient organocatalyst for the reaction was **6a**, which bears an *i*-Pr substituent on the amino group (Table 3, entry 2).

Next, we investigated the substrate scope of this bifunctional asymmetric catalyst system under optimal conditions (Table 4). Whether the aromatic substituent R^2 of

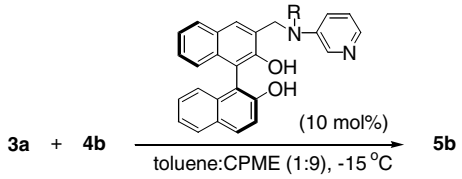
Table 2. Effect of solvent on aza-MBH reaction



Entry	Solvent	Time (h)	Yield[a] (%)	ee[b] (%)
1	Et_2O	108	74	72
2	*t*-BuOMe	72	92	73
3	CPME	72	97	78
4	DME	60	73	68
5	THF	48	71	59
6	Toluene	24	81	72
7	CH_2Cl_2	24	Quant.	59
8	$CHCl_3$	24	97	54
9	$ClCH_2CH_2Cl$	24	87	57
10	DMF	48	7	63
11	MeCN	48	60	67
12	MeOH	60	46	18
13	CPME–toluene (9/1)	72	93	83
14[c]	CPME–toluene (9/1)	144	97	90

[a] Isolated yield.
[b] Determined by HPLC (Daicel Chiralpak AD-H).
[c] Performed at −15 °C.

Table 3. Effect of *N*-substituent R on bifunctional organocatalysts



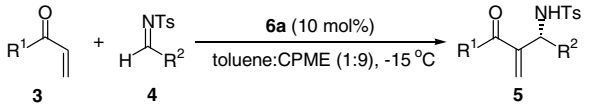
Entry	R		Time (h)	Yield[a] (%)	ee[b] (%)
1	Me	**2a**	144	97	90
2	*i*-Pr	**6a**	60	96	95
3	H	**6b**	240	62	87
4	Et	**6c**	132	90	91
5	*t*-Bu	**6d**	240	72	83
6	Bn	**6e**	72	Quant.	93

[a] Isolated yield.
[b] Determined by HPLC (Daicel Chiralpak AD-H).

4 was electron-withdrawing or electron-donating, organocatalyst **6a** efficiently promoted the reaction with high enantioselectivity (entries 1–10, and 15). 2-Furyl and 2-naphthyl tosylimines were also found to be suitable substrates (entries 11 and 12). The use of 1-naphthyl and *o*-chlorophenyl tosylimines resulted in moderate enantioselectivity (entries 13 and 14). Although the reactions of methyl or ethyl vinyl ketone and acrolein afforded the corresponding adducts with high enantioselectivity (entries 15–17), the enantioselectivity was only moderate when phenyl vinyl ketone was used (entry 18).

Catalysts **2a** and **6a** possess two phenolic hydroxy groups and two nitrogen atoms. In order to clarify the role of each unit in the reaction, we examined the following derivatives of the parent catalysts: two monoprotected catalysts **7a** (2′-OMe group) and **7b** (2-OMe group), an aniline derivative **8**, and pyridine derivatives **9a** and **9b**, with different spacer chain lengths, and **9c**, which contains an oxygen atom linkage (Fig. 3). Although catalyst **7a** was found to be ineffective in promoting the reaction (**5a**, 5% yield, 24% ee), **7b** showed a slightly decreased activity (**5a**, 85% yield, 79% ee) compared to the parent catalyst **2a**. Interestingly, it was found that **8** and **9** did not promote the reaction. These results and the significant enantioselectivity of **6a** are consistent with the idea that our designed organic molecules can act as bifunctional catalysts, utilizing both the phenolic 2′-hydroxy group and the pyridine moiety to activate the substrate. Since one acid–base pair fixes the conformation of organocatalyst **6a**, the other acid–base unit appears able to activate substrate **3** with high enantiocontrol, although the nucleophilicity of the pyridinyl nitrogen of **2a** (or **6a**) is low compared to that of **2b** or **2c**.[8] A molecular orbital calculation for **6a** also supported the suggested conformation (Fig. 4).

Table 4. Enantioselective aza-MBH reaction of **3** with **4** catalyzed by **6a**



Entry	**3**: R^1	**4**: R^2	Time (h)	Yield (%)[a]	ee[b] (%)
1	Me **3a**	Ph **4a**	168	**5a**, 93	87
2	Me **3a**	*p*-Cl–C_6H_4 **4b**	60	**5b**, 96	95
3	Me **3a**	*p*-F–C_6H_4 **4c**	72	**5c**, 95	93
4	Me **3a**	*p*-Br–C_6H_4 **4d**	36	**5d**, 93	94
5	Me **3a**	*p*-CN–C_6H_4 **4e**	60	**5e**, quant.	91
6	Me **3a**	*p*-Me–C_6H_4 **4f**	192	**5f**, 90	90
7	Me **3a**	*p*-Et–C_6H_4 **4g**	120	**5g**, 97	93
8	Me **3a**	*p*-MeO–C_6H_4 **4h**	132	**5h**, 93	94
9	Me **3a**	*m*-NO_2–C_6H_4 **4i**	24	**5i**, 94	86
10	Me **3a**	*m*-Cl–C_6H_4 **4j**	72	**5j**, 93	93
11	Me **3a**	2-Furyl **4k**	48	**5k**, quant.	93
12	Me **3a**	2-Naphthyl **4l**	108	**5l**, 94	91
13	Me **3a**	1-Naphthyl **4m**	288	**5m**, 88	70
14	Me **3a**	*o*-Cl–C_6H_4 **4n**	84	**5n**, 92	62
15	Me **3a**	*p*-NO_2–C_6H_4 **4o**	12	**5o**, 91	91
16	Et **3b**	*p*-NO_2–C_6H_4 **4o**	96	**5p**, 88	88
17	H **3c**	*p*-NO_2–C_6H_4 **4o**	36	**5q**, 95	94
18	Ph **3d**	*p*-NO_2–C_6H_4 **4o**	192	**5r**, 91	58

[a] Isolated yield.
[b] Determined by HPLC (Daicel Chiralpak AD-H or OD-H).

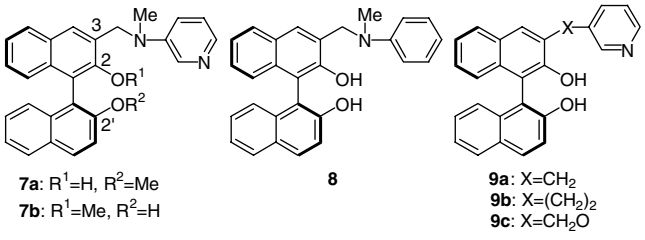


Figure 3.

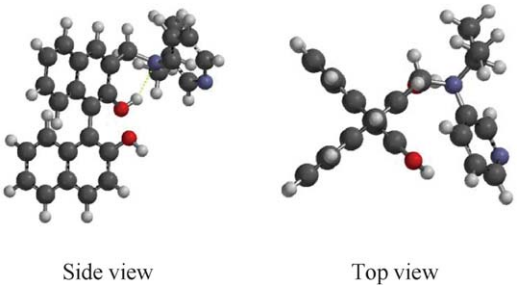


Figure 4. Molecular orbital calculation for **6a**: Spartan '04, job type: geometry optimization, method: Hartee–Fock, basis set: 6-31G**. N–H atomic distance: 2.004 Å; angle between N–H–O bonds: 144.72°.

3. Conclusion

We have discovered an efficient and novel bifunctional organocatalyst for the enantioselective aza-MBH reaction, (*S*)-3-(*N*-isopropyl-*N*-3-pyridinylaminomethyl)-BINOL.

The reaction was shown to be significantly influenced by the position of the Lewis base attached to BINOL. The acid–base functionalities harmoniously cooperate to activate the substrate and fix the conformation of the organocatalyst, resulting in promotion of the reaction with high enantioselectivity.

4. Experimental

4.1. General

Commercially available organic and inorganic compounds were used without further purification, except for the solvent, which was distilled from sodium/benzophenone or CaH_2. Column chromatography on SiO_2 was performed with Kanto Silica Gel 60 (40–100 μm).

^1H and ^{13}C NMR spectra were recorded with JEOL JNM-EX270 FT NMR (^1H NMR 270 MHz, ^{13}C NMR 67.7 MHz). All signals are expressed as ppm downfield from tetramethylsilane used as an internal standard. FT-IR spectra were recorded on a SHIMADZU FTIR-8300. Optical rotations were measured with JASCO P-1030 polarimeter. HPLC analyses were performed on a JASCO HPLC system (JASCO PU 980 pump and UV-975 UV/vis detector) using a mixture of hexane and *i*-PrOH as the eluent. Mass spectra were obtained on JEOL JMS-DX300 (for EI-MS), JEOL JMS-700 (for FAB-MS), and JMS-T100LC (for ESI-MS). Elemental analysis was performed on Perkin–Elmer 2400.

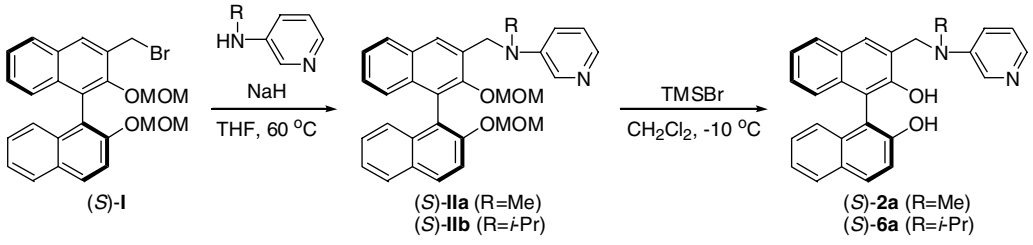
Adducts **5a–d**, **5f–l**, **5o–q** are known compounds.[6,7] For organocatalysts **2a** and **6a** and adducts **5e**, **5m**, **5n**, and **5r** as new compounds, their spectral data are shown as follows.

4.2. General procedure for synthesis of (*S*)-3-(*N*-methyl-*N*-3-pyridinylaminomethyl)-BINOL 2a and (*S*)-3-(*N*-isopropyl-*N*-3-pyridinylaminomethyl)-BINOL 6a

Compound (*S*)-**II**: A solution of the corresponding 3-*N*-methylaminopyridine[9a] (26.0 mg, 0.24 mmol) or 3-*N*-isopropylaminopyridine[9b,c] (32.7 mg, 0.24 mmol) in THF (0.7 mL) was added to a heterogeneous solution of NaH (16 mg, 0.24 mmol) in THF (0.3 mL) at 0 °C. After stirring for 2 h at 60 °C, a solution of (*S*)-**I**[10] (0.20 mmol) in THF (1.0 mL) was combined with the reaction mixture. The mixture was stirred for 15 min at room temperature and then quenched with saturated NH_4Cl aq at 0 °C. The organic phase was extracted with CH_2Cl_2, dried over Na_2SO_4, filtered, and concentrated. The residue obtained was purified by flash chromatography (SiO_2, CH_2Cl_2/MeOH = 19/1) to afford the title compound (*S*)-**II** (**IIa**, R = Me, quant.; **IIb**, R = *i*-Pr, 60% yield).

Compound (*S*)-**IIa**: Colorless oil; IR (neat): *ν* 3083, 2912, 2812, 1581, 1494, 1444, 1346, 1222 cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 8.25 (1H, d, *J* = 3.0 Hz), 7.99 (2H, d, *J* = 9.2 Hz), 7.89 (1H, d, *J* = 8.6 Hz), 7.75 (1H, d, *J* = 8.1 Hz), 7.61 (1H, s), 7.60 (1H, d, *J* = 8.4 Hz), 7.41–7.11 (6H, m), 7.19 (2H, d, *J* = 7.0 Hz), 5.16 (1H, d, *J* = 7.3 Hz), 5.06 (1H, d, *J* = 7.3 Hz), 4.91 (2H, s), 4.67 (1H, d, *J* = 5.9 Hz), 4.50 (1H, d, *J* = 5.9 Hz), 3.28 (3H, s), 3.18 (3H, s), 3.10 (3H, s); ^{13}C NMR ($CDCl_3$): *δ* 152.6, 152.4, 145.1, 137.6, 134.5, 133.7, 133.1, 130.7, 130.5, 129.9, 129.6, 127.8, 127.7, 126.8, 125.9, 125.8, 125.5, 125.4, 125.3, 125.0, 124.1, 123.5, 120.4, 118.2, 116.4, 99.3, 94.8, 57.0, 56.1, 52.7, 38.7; HRMS (ESI) calcd for $C_{31}H_{32}N_2NaO_4$, *m*/*z* = 517.2103 [(M+Na)$^+$]; found, *m*/*z* = 517.2093. $[\alpha]_D^{20} = -40.8$ (*c* 1.0, $CHCl_3$).

Compound (*S*)-**IIb**: Brown oil; IR (neat): *ν* 3095, 2945, 2829, 1596, 1514, 1444, 1375, 1221 cm^{-1}; ^1H NMR ($CDCl_3$): *δ* 8.27 (1H, br s), 7.99 (2H, d, *J* = 8.9 Hz), 7.89 (1H, d, *J* = 8.1 Hz), 7.75 (1H, d, *J* = 5.7 Hz), 7.74 (1H, s), 7.60 (1H, d, *J* = 8.4 Hz), 7.41–7.05 (8H, m), 5.15 (1H, d, *J* = 7.0 Hz), 5.07 (1H, d, *J* = 7.0 Hz), 4.74 (2H, s), 4.70 (1H, d, *J* = 5.7 Hz), 4.53 (1H, d, *J* = 5.7 Hz), 4.48–4.36 (1H, m), 3.18 (3H, s), 3.12 (3H,



s), 1.33 (3H, d, $J = 6.7$ Hz), 1.32 (3H, d, $J = 6.7$ Hz); ^{13}C NMR ($CDCl_3$): δ 152.7, 152.0, 145.2, 145.1, 137.4, 133.8, 132.0, 130.9, 129.9, 129.6, 127.8, 127.7, 126.8, 126.5, 125.7, 125.5, 125.4, 125.4, 125.1, 124.9, 124.1, 123.6, 120.6, 119.3, 116.6, 99.3, 95.0, 55.9, 56.0, 48.1, 44.7, 19.8, 19.7; HRMS (ESI) calcd for $C_{33}H_{35}N_2O_4$, $m/z = 523.2597$ [$(M+H)^+$]; found, $m/z = 523.2585$. $[\alpha]_D^{20} = -43.2$ (c 1.0, $CHCl_3$).

Compound (*S*)-**2a**: Trimethylsilyl bromide (53 μL, 0.4 mmol) was added to the mixture of (*S*)-**IIa** (0.2 mmol) and MS 4 Å (10 mg) in CH_2Cl_2 (1 mL) at 0 °C. After stirring for 30 min, the reaction mixture was quenched with water. The organic phase was extracted with CH_2Cl_2. The combined organic extracts were then dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by flash chromatography (SiO_2, CH_2Cl_2/MeOH = 9/1) to give the title compound (*S*)-**2a** (92% yield).

Compound (*S*)-**2a**: White solid. Mp 119–120 °C (hexane–CH_2Cl_2). IR (neat): ν 3389, 3012, 2933, 1284, 1612, 1588, 1510, 1424, 1412, 1367, 1220, 1012 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 8.28–8.18 (1H, br), 7.96 (2H, d, $J = 9.2$ Hz), 7.89 (2H, d, $J = 8.4$ Hz), 7.79 (1H, d, $J = 8.1$ Hz), 7.70 (1H, s), 7.39 (1H, d, $J = 8.9$ Hz), 7.34–7.13 (7H, m), 4.76 (2H, s), 3.18 (3H, s). ^{13}C NMR (67.7 MHz, $CDCl_3$): δ 153.3, 151.4, 145.2, 136.6, 133.8, 133.0, 129.0, 128.8, 128.1, 127.8, 127.1, 126.9, 126.5, 125.6, 124.4, 124.3, 123.7, 123.3, 119.5, 118.3, 113.3, 112.0, 53.0, 38.6. HRMS (ESI): m/z calcd for $C_{27}H_{23}N_2O_2$: 407.1760 [M^++H]; found: 407.1740. $[\alpha]_D^{20} = -17.8$ (c 0.7, $CHCl_3$).

Compound (*S*)-**6a**: Similar to the synthetic procedure for (*S*)-**2a**, (*S*)-**6a** was prepared from (S)-**IIb** (0.2 mmol) in 90% yield. Green solid. Mp 122–123 °C (hexane–CH_2Cl_2). IR (neat): ν 3440, 3055, 2966, 2823, 1705, 1620, 1585, 1566, 1497, 1431, 1342, 1272, 1184, 1134, 1061 cm^{-1}. ^{1}H NMR (270 MHz, $CDCl_3$): δ 8.18 (1H, d, $J = 2.7$ Hz), 7.94 (1H, dd, $J = 4.0$ and 0.8 Hz), 7.85 (1H, d, $J = 8.9$ Hz), 7.79 (1H, d, $J = 7.8$ Hz), 7.79–7.65 (2H, m), 7.28 (1H, d, $J = 8.9$ Hz), 7.28–7.00 (7H, m), 6.96 (1H, d, $J = 8.1$ Hz), 4.55 (2H, s), 4.04–3.93 (1H, m), 1.21 (3H, d, $J = 6.7$ Hz), 1.18 (3H, d, $J = 6.7$ Hz). ^{13}C NMR (67.7 MHz, $CDCl_3$): δ 152.4, 151.8, 143.8, 140.0, 133.5, 132.9, 130.6, 129.2, 128.8, 128.3, 128.2, 128.1, 127.9, 126.9, 126.7, 126.2, 124.3, 124.3, 124.2, 123.8, 123.5, 123.4, 117.8, 112.4, 112.3, 50.8, 47.0, 19.6, 19.4. HRMS (ESI): m/z calcd for $C_{29}H_{27}N_2O_2$: 435.2073 [M^++H]; found, 435.2062. $[\alpha]_D^{20} = -28.5$ (c 0.4, $CHCl_3$).

4.3. Procedure for enantioselective aza-MBH reaction catalyzed by (*S*)-6a (Table 4)

To a solution of organocatalyst **6a** (2.2 mg, 0.005 mmol) in a mixed solvent CPME and toluene (9/1, 0.1 mL) were added **3** (0.15 mmol) and imine **4** (0.05 mmol) at −15 °C. The mixture was stirred until the reaction had reached completion with monitoring with TLC analysis. The mixture was directly purified by flash column chromatography (SiO_2, hexane–EtOAc = 2/1) to give the corresponding adduct **5** as a white solid. All products were characterized by ^{1}H and ^{13}C NMR, MS, and IR spectroscopy. The absolute configurations of **5** were determined by comparing the specific rotation assignments with those in the literature.[6,7]

4.4. *N*-[1-(4-Cyanophenyl)-2-methylene-3-oxobutyl]-4-methylbenzenesulfonamide 5e

White solid. Mp 104–105 °C (hexane–EtOAc). IR (neat): ν 2210, 1655 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.56 (2H, d, $J = 8.4$ Hz), 7.45 (2H, d, $J = 8.4$ Hz), 7.21 (2H, d, $J = 8.4$ Hz), 7.18 (2H, d, $J = 8.4$ Hz), 6.05 (1H, s), 5.97 (1H, s), 5.20 (1H, d, $J = 9.2$ Hz), 2.36 (3H, s), 2.10 (3H, s). ^{13}C NMR ($CDCl_3$): δ 198.3, 145.4, 144.2, 143.5, 137.2, 132.0, 129.4, 129.2, 127.1, 118.3, 111.2, 58.5, 26.2, 21.5. HRMS (ESI) m/z calcd for $C_{19}H_{18}N_2O_3NaS$: 377.0936 [M^++Na]; found, 377.0922. $[\alpha]_D^{20} = +2.0$ (c 0.6, $CHCl_3$). Daicel Chiralpak AD-H column, detection at 254 nm, *i*-PrOH–hexane = 1/4, flow rate 0.5 mL/min, 33.2 min (minor isomer, *S*) and 39.6 min (major isomer, *R*).

4.5. 4-Methyl-*N*-(2-methylene-1-naphthalen-1-yl-3-oxobutyl)benzenesulfonamide 5m

White solid. Mp 119–120 °C (hexane–EtOAc). IR (neat): ν 1655 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.79 (2H, d, $J = 7.8$ Hz), 7.73 (2H, d, $J = 8.1$ Hz), 7.64 (2H, d, $J = 7.8$ Hz), 7.44 (1H, dd, $J = 7.9$ and 6.7 Hz), 7.36–7.24 (3H, m), 7.20 (2H, d, $J = 7.8$ Hz), 6.27 (1H, s), 6.22 (1H, s), 6.20 (1H, d, $J = 7.0$ Hz), 5.12 (1H, d, $J = 7.0$ Hz), 2.42 (3H, s), 2.23 (3H, s). ^{13}C NMR ($CDCl_3$): δ 198.2, 147.3, 143.3, 136.9, 134.5, 133.8, 130.3, 129.4, 128.7, 128.5, 127.6, 127.3, 126.4, 125.7, 124.9, 124.8, 122.9, 53.2, 26.4, 21.6. HRMS (ESI) m/z calcd for $C_{22}H_{21}NNaO_3S$: 402.1140 [M^++Na]; found, 402.1152. $[\alpha]_D^{20} = +18.3$ (c 0.6, $CHCl_3$). Daicel Chiralpak AD-H column, detection at 254 nm, *i*-PrOH–hexane = 1/4, flow rate 0.5 mL/min, 49.5 min (minor isomer, *S*) and 58.8 min (major isomer, *R*).

4.6. *N*-[1-(2-Chlorophenyl)-2-methylene-3-oxobutyl]-4-methylbenzenesulfonamide 5n

White solid. Mp 83–84 °C (hexane–EtOAc). IR (neat): ν 1670 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.63 (2H, d, $J = 8.4$ Hz), 7.33–7.06 (6H, m), 6.16, (2H, s), 5.77 (1H, d, $J = 8.4$ Hz), 5.69 (1H, d, $J = 8.4$ Hz), 2.37 (3H, s), 2.21 (3H, s). ^{13}C NMR ($CDCl_3$): δ 198.5, 145.4, 143.2, 143.1, 137.0, 135.9, 132.6, 129.5, 129.0, 128.7, 127.1, 126.7, 126.2, 55.4, 26.4, 21.5. HRMS (ESI) m/z calcd for $C_{18}H_{18}ClNNaO_3S$, 386.0594 [M^++Na]; found, 386.0604. $[\alpha]_D^{20} = +13.0$ (c 0.6, $CHCl_3$). Daicel Chiralpak AD-H column, detection at 254 nm, *i*-PrOH–hexane = 1/4, flow rate 0.3 mL/min, 48.6 min (minor isomer, *S*) and 55.7 min (major isomer, *R*).

4.7. *N*-[2-Benzoyl-1-(4-nitrophenyl)allyl]-4-methylbenzenesulfonamide 5r

White solid. Mp 143–144 °C (hexane–EtOAc). IR (neat): ν 1653, 1508, 1340 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ

7.87 (2H, d, $J = 8.6$ Hz), 7.48 (2H, d, $J = 8.1$ Hz), 7.33–7.13 (6H, m), 7.03 (1H, dd, $J = 9.4$ and 0.8 Hz), 7.00 (2H, d, $J = 7.8$ Hz), 6.10 (1H, d, $J = 8.9$ Hz), 5.87 (1H, s), 5.59 (1H, s), 5.31 (1H, d, $J = 9.2$ Hz), 2.17 (3H, s). ^{13}C NMR ($CDCl_3$): δ 196.3, 147.2, 146.0, 143.9, 143.7, 137.3, 136.4, 133.0, 130.3, 129.3, 128.3, 128.3, 127.4, 127.0, 123.7, 59.6, 21.6. HRMS (ESI) m/z calcd for $C_{23}H_{20}N_2NaO_5S$: 459.0991 [M^++Na]; found, 459.0990. $[\alpha]_D^{20} = -3.3$ (c 0.6, $CHCl_3$). Daicel Chiralpak OD-H column, detection at 254 nm, i-PrOH–hexane = 1/4, flow rate 0.5 mL/min, 42.4 min (major isomer, R) and 53.9 min (minor isomer, S).

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