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Asymmetric catalytic aza-Morita–Baylis–Hillman reaction using chiral bifunctional phosphine amides as catalysts

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Abstract

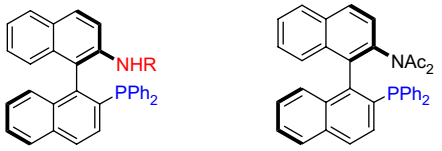
The asymmetric catalytic aza-Morita–Baylis–Hillman reaction of *N*-sulfonated imines with α,β-unsaturated ketones has been successfully conducted by using chiral bifunctional phosphine amides as catalysts. A series of new chiral bifunctional phosphine amides were designed, synthesized, and systematically studied for this asymmetric reaction. The corresponding aza-MBH adducts were obtained in good yields (75–99%) and up to very good enantiomeric excesses (51–95% ee) under mild conditions.

1. Introduction

The Morita–Baylis–Hillman (MBH) reaction has been an active topic in organic chemistry in the past decade because the resulting MBH adducts can find numerous applications in organic and medicinal chemistry.[1,2] Recently, the asymmetric version of aza-Morita–Baylis–Hillman has received much attention[3–7] in which *N*-sulfonated imines (ArCH=NTs) and *N*-phosphorated imines [ArCH=NP(O)R_2] were employed as electrophiles, and MVK and ethyl vinyl ketone (EVK) as various Michael acceptors. These processes took advantage of chiral nitrogen and phosphine Lewis bases as multifunctional organocatalysts to give moderate to high enantioselectivity and good yields. In order to further improve the outcomes of the asymmetric aza-Morita–Baylis–Hillman system, we envisioned that chiral phosphine-amide Lewis bases would serve as efficient catalysts because they can provide unique chiral environment, and their acidic protons on amide nitrogen can act as an efficient hydrogen-bonding donor to interact with substrates.[8] In this paper, we wish to report that chiral phosphine-amide derivatives can be utilized as catalysts for the asymmetric aza-MBH reaction of *N*-sulfonated imines (ArCH=NTs) with MVK and EVK to give up to excellent yields and enantioselectivity under mild conditions.

2. Results and discussion

These newly designed chiral phosphine-amide Lewis bases **L1**, **L3–L8** are shown in Figure 1. They were readily synthesized by treating (*R*)-(−)-2-(diphenylphosphino)-1,1′-binaphthyl-2′-amine[9] with the corresponding sulfonyl chloride, acyl chloride, or phosphoryl chloride in the presence of a base under mild conditions. The chiral phosphine-amide Lewis base **L2** was prepared by reacting (*R*)-(−)-2-(diphenylphosphoryl)-1,1′-binaphthyl-2′-amine[9] with trifluoromethanesulfonic



L1: R = SO_2CH_3
L2: R = SO_2CF_3
L3: R = $SO_2C_6H_4CH_3$-*p*
L4: R = COC_6H_5
L5: R = $COCH_3$
L6: R = CO_2CH_3
L7: R = $PO(C_6H_5)_2$

L8

Figure 1. Chiral phosphine-amide Lewis base catalysts **L1–L8**.

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anhydride at −78 °C in the presence of Et_3N and $SiHCl_3/PPh_3$ as reducing agents (see Supplementary data).

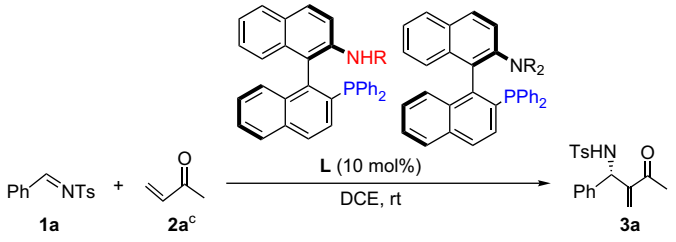
Initial studies were aimed at determining the most effective chiral phosphine-amide organocatalyst for this aza-MBH reaction. The reaction of *N*-benzylidene-4-methylbenzenesulfonamide **1a** with MVK **2a** was performed in 1,2-dichloroethane (DCE) solvent at room temperature in the presence of chiral phosphine-amide catalysts **L**s (10 mol %). The results are summarized in Table 1. As revealed in Table 1, catalysts **L1** (R=SO_2Me) and **L5** (R=COMe) resulted in the corresponding aza-MBH adduct **3a** in nearly quantitative yields, and 89% ee and 93% ee (Table 1, entries 1 and 5). Under the same condition, chiral phosphine-amide catalysts **L3** (R=$SO_2C_6H_4Me$-*p*), **L4** (R=COC_6H_5), **L6** (R=CO_2Me), and **L7** (R=$POPh_2$) showed lower catalytic activity in comparison to **L1** and **L5** counterparts (Table 1, entries 3, 4, 6, and 7). Furthermore, more sterically encumbered **L8** did not give any product while all starting materials remained unchanged in the reaction system. This observation indicates that an active amide proton of the catalyst is crucial for this asymmetric catalytic process (Table 1, entry 8).

Interestingly, chiral catalyst **L2** (R=SO_2CF_3) did not give any product. This observation indicates that a moderately acidic amide proton is necessary (Table 1, entry 2). Covalent N–H bonding connection is necessary to achieve the efficient catalytic transition state in which the catalyst can bring two reaction partners together. In this transition state, the phosphine site is added onto MVK **2a** to form Zwitterionic intermediate. Meanwhile, the amide hydrogen activates *N*-benzylidene-4-methylbenzenesulfonamide via hydrogen bonding and then brings it to react with Zwitterionic anion which is in the same chiral binding pocket.[10–12]

Based on the above results, **L1** and **L5** were next utilized as the catalysts for optimizing catalytic conditions in various solvents under different temperatures. The results are shown in Table 2. It was found that DCE, chloroform, and dichloromethane (DCM) are the solvents of choice (Table 2, entries 1–5 and 8–13). Unlike other asymmetric process,[4] adding benzoic acid as an extra proton source did not give any improvement on enantiomeric excess (Table 2, entries 6 and 14). Lowering the temperature to 0 °C and −10 °C resulted in higher enantioselectivity (90–96% ee) (Table 2, entries 7, 9, 15, and 16).

Under these optimized conditions, we subsequently examined the generality of this reaction using **L5** as the catalyst. A variety of sulfonated imines and α,β-unsaturated ketones were examined for this reaction. Since most of the aryl substituted sulfonated imines **1** cannot be dissolved well in DCE at 0 °C, the asymmetric reactions were thus performed at room temperature in this solvent; they were conducted at 0 °C in DCM in which there is no solubility problem. The results are summarized in Table 3. As can be seen in Table 3, the resulting adducts **3b–3l** were obtained in good yields (77–99%) and moderate to good enantiomeric excesses (46–85%) in DCE at room temperature. These same adducts were obtained in good yields (80%—quant) and higher enantioselectivity (61–91%) (Table 3, entries 1–11) in DCM at 0 °C. *o*-NO_2-benzaldehyde and *p*-MeO-benzaldehyde derived *N*-sulfonated imines **1d** and **1f** behaved poorly in DCE to give the lowest enantioselectivity of 46% ee (Table 3, entries

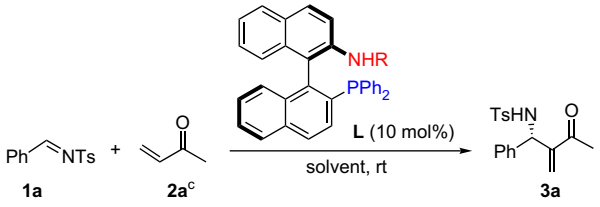
Table 1
Asymmetric aza-MBH reaction of *N*-sulfonated imine **1a** with methyl vinyl ketone catalyzed by **L1–L8** (10 mol %)



Entry	Catalyst	Time (h)	Yield[a] (%)	ee[b] (%)
1	**L1**	48	95	89
2	**L2**	48	0	—
3	**L3**	96	94	86
4	**L4**	48	89	78
5	**L5**	48	99	93
6	**L6**	60	91	59
7	**L7**	96	85	72
8	**L8**	96	0	—

[a] Isolated yields.
[b] Determined by HPLC.
[c] MVK of 2.0 equiv was used.

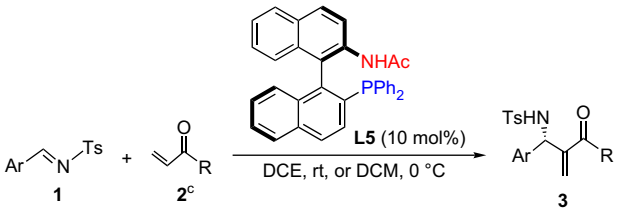
Table 2
Asymmetric aza-MBH reactions of *N*-sulfonated imine with methyl vinyl ketone using **L1** and **L5** catalysts



Entry	Catalyst	Solvent	Time (h)	Yield[a] (%)	ee[b] (%)
1	**L1**	DCM	72	99	75
2	**L1**	PhMe	72	99	51
3	**L1**	THF	120	49	45
4	**L1**	CH_3CN	74	99	75
5	**L1**	$CHCl_3$	72	99	82
6[d]	**L1**	DCM	48	99	61
7[e]	**L1**	DCM	90	96	90
8	**L5**	DCM	24	99	88
9[e]	**L5**	DCM	24	99	95
10	**L5**	PhMe	160	90	27
11	**L5**	THF	160	91	39
12	**L5**	DMSO	36	89	52
13	**L5**	CH_3CN	48	94	79
14[d]	**L5**	DCM	36	99	86
15[e]	**L5**	DCM	20	95	91
16[f]	**L5**	DCM	23	89	96

[a] Isolated yields.
[b] Determined by HPLC.
[c] MVK of 2.0 equiv was used.
[d] Benzoic acid of 0.1 equiv was added to this reaction.
[e] Reaction was carried out at 0 °C.
[f] Reaction was carried out at −10 °C.

Table 3
Asymmetric aza-MBH reactions of *N*-sulfonated imines **1** (0.25 mmol) with methyl vinyl ketone (0.50 mmol) and ethyl vinyl ketone (0.50 mmol) in the presence of catalyst **L5** (10 mol %)



Entry	Ar	R	DCE at rt			DCM at 0 °C		
			Time (h)	Yield[a] (%)	ee[b] (%)	Time (h)	Yield[a] (%)	ee[b] (%)
1	*p*-BrC_6H_4 **1b**	Me	48	**3b**, 98	82	24	**3b**, 86	90
2	*p*-$NO_2C_6H_4$ **1c**	Me	24	**3c**, 75	80	7	**3c**, 99	90
3	*o*-$NO_2C_6H_4$ **1d**	Me	12	**3d**, 78	46	28	**3d**, 85	61
4	*m*-$NO_2C_6H_4$ **1e**	Me	12	**3e**, 99	80	8	**3e**, 99	82
5	*o*-ClC_6H_4 **1f**	Me	12	**3f**, 76	65	48	**3f**, 80	65
6	*p*-ClC_6H_4 **1g**	Me	36	**3g**, 99	82	24	**3g**, 99	90
7	*m*-ClC_6H_4 **1h**	Me	12	**3h**, 89	84	24	**3h**, 90	89
8	*p*-FC_6H_4 **1i**	Me	36	**3i**, 99	85	24	**3i**, 90	91
9	*m*-FC_6H_4 **1j**	Me	20	**3j**, 77	75	24	**3j**, 91	80
10	*p*-$MeOC_6H_4$ **1k**	Me	48	**3k**, 99	46	48	**3k**, 98	82
11	*p*-MeC_6H_4 **1l**	Me	60	**3l**, 99	84	48	**3l**, 99	90
12	C_6H_5 **1a**	Et				60	**3m**, 95	74
13	*p*-BrC_6H_4 **1b**	Et				60	**3n**, 80	65
14	*p*-ClC_6H_4 **1g**	Et				60	**3o**, 86	51

[a] Isolated yields.
[b] Determined by chiral HPLC.
[c] MVK of 2 equiv was used.

3 and 10). However, the enantioselectivity of these two substrates was improved to 61% ee and 82% ee, respectively, under the same conditions in DCM. Most of the *N*-sulfonated imines performed well in DCM except for three cases, *o*-NO_2, *p*-Br, and *p*-Cl substituted *N*-sulfonated imines, that resulted in poor enantioselectivity of 51–65% ee (**3d**, **3n**, and **3o** in Table 3).

In conclusion, we have designed and synthesized new axially chiral phosphine-amide Lewis base catalysts for aza-MBH reaction. We found these catalysts behaved well under mild and concise conditions and resulted in the corresponding adducts in good to excellent yields and up to very good enantioselectivity. The adequate acidity of the amide proton of bifunctional chiral catalysts is found to be crucial to achieve the present asymmetric process. The new bifunctional chiral phosphine ligand showed the similar catalytic activity to our previously reported bifunctional chiral phosphine ligand [(*R*)-2′-diphenylphosphanyl-[1,1′]binaphthalenyl-2-ol].[4f] Efforts are in progress to elucidate the mechanistic details of this reaction and to study its scope and limitations.

3. Experimental

3.1. General

Melting points were determined on a digital melting point apparatus and temperatures were uncorrected. Optical rotations were determined at 589 nm (sodium D line) by using a Perkin–Elmer-341 MC digital polarimeter; $[\alpha]_D$-values are given in the unit of 10 deg^{-1} cm^2 g^{-1}. ^1H NMR spectra were recorded on a Bruker AM-300 spectrometer for solution in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard; coupling constants *J* are given in hertz. ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrophotometers (75 MHz) with complete proton decoupling-spectrophotometers ($CDCl_3$: 77.0 ppm). Infrared spectra were recorded on a Perkin–Elmer PE-983 spectrometer with absorption in cm^{-1}. Flash column chromatography was performed using 300–400 mesh silica gel. For thin-layer chromatography (TLC), silica gel plates (Huanghai GF254) were used. Chiral HPLC was performed on a SHIMADZU SPD-10A *vp* series with chiral columns (Chiralpak AD-H, AS-H, OD-H, and OJ-H columns 4.6×250 mm (Daicel Chemical Ind., Ltd.)). The purity of the products is determined by ^1H NMR spectroscopy and chiral HPLC traces (see Supplementary data). Elementary analysis was taken on a Carlo-Erba 1106 analyzer. Mass spectra were recorded by EI, and HRMS was measured on a HP-5989 instrument. The absolute configuration of aza-MBH adducts **3** has been determined by X-ray diffraction.[4a] As for the synthesis of ligands **L1**–**L8**, please see the previous literature.[9]

3.2. Representative procedure of MBH reaction *1a*

To a solution of **1a** (0.25 mmol, 61 mg) and **L5** (0.025 mmol, 13 mg) in 1.0 mL of DCE was added MVK (41 μL, 0.50 mmol) at 0 °C under argon (or 1.0 mL of DCE at room temperature). The reaction solution was monitored by TLC plates. After completion, the solvent was removed under reduced pressure and the residue was purified by a silica gel column chromatography (EtOAc/PE=1/4) to give the compound **3a** in 99% yield.

3.2.1. (*S*)-4-Methyl-N-(2-methylene-3-oxo-1-phenylbutyl)-benzenesulfonamide *3a*

This is a known compound.[4a,f] $[\alpha]_D^{20}$ +29 (*c* 1.0, $CHCl_3$); mp: 120–121 °C; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.16 (3H, s, Me), 2.42 (3H, s, Me), 5.26 (1H, d, *J*=8.6 Hz), 5.61 (1H, d, *J*=8.6 Hz), 6.10 (1H, s), 6.11 (1H, s), 7.11 (2H, m, Ar), 7.20–7.27 (5H, m, Ar), 7.66 (2H, d, *J*=8.1 Hz, Ar); HPLC: AD column; λ=254 nm; eluent: hexane/isopropanol=80/20; flow rate: 0.7 mL/min; t_{major}=19.44 min, t_{minor}=22.09 min; ee%=95% (93% in DCE).

3.2.2. (*S*)-N-(1-(4-Bromophenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide *3b*

This is a known compound.[4a,f] Yield: 86%; ee%: 82%; $[\alpha]_D^{20}$ +29 (*c* 0.3, $CHCl_3$); mp: 97–99 °C; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.15 (3H, s, Me), 2.41 (3H, s, Me), 5.19 (1H, d, *J*=9.1 Hz), 5.71 (1H, d, *J*=9.1 Hz), 6.06 (1H, s), 6.09 (1H, s), 6.98 (2H, d, *J*=7.8 Hz), 7.26 (2H, d, *J*=8.0 Hz), 7.31 (2H, dd, J_1=7.8 Hz, J_2=1.2 Hz), 7.62 (2H, *J*=8.0 Hz); HPLC: AD column; λ=254 nm; eluent: hexane/isopropanol=80/20; flow rate: 0.7 mL/min; t_{major}=18.96 min, t_{minor}=22.09 min; ee%=90% (82% in DCE).

3.2.3. (S)-4-Methyl-N-(2-methylene-1-(4-nitrophenyl)-3-oxobutyl)benzenesulfonamide ***3c***

This is a known compound.[4a,f] Yield: 99%; $[\alpha]_D^{20}$ −2.6 (*c* 0.5, $CHCl_3$); mp: 121–122 °C; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.15 (3H, s, Me), 2.44 (3H, s, Me), 5.32 (1H, d, *J*=9.4 Hz), 5.94 (1H, d, *J*=9.4 Hz), 6.08 (1H, s), 6.14 (1H, s), 7.25 (2H, d, *J*=8.3 Hz, Ar), 7.34 (2H, d, *J*=8.7 Hz, Ar), 7.65 (2H, d, *J*=8.3 Hz, Ar), 8.07 (2H, d, *J*=8.7 Hz); HPLC: AD column; *λ*=254 nm; eluent: hexane/isopropanol=80/20; flow rate: 0.7 mL/min; t_{major}=42.89 min, t_{minor}=55.79 min; ee%=90% (80% in DCE).

3.2.4. 4-Methyl-N-(2-methylene-1-(2-nitrophenyl)-3-oxobutyl)benzenesulfonamide ***3d***

This is a known compound.[4a,f] Yield: 85%; $[\alpha]_D^{20}$ +39 (*c* 1.0, $CHCl_3$); mp: 120–121 °C; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.17 (3H, s, Me), 2.40 (3H, s, Me), 5.91 (1H, d, *J*=9.0 Hz), 5.96 (1H, s), 5.97 (1H, d, *J*=9.0 Hz), 6.08 (1H, s), 7.23 (2H, d, *J*=8.1 Hz, Ar), 7.36 (1H, ddd, J_1=7.8 Hz, J_2=7.5 Hz, J_3=1.5 Hz, Ar), 7.50 (1H, ddd, J_1=7.8 Hz, J_2=7.5 Hz, J_3=1.2 Hz, Ar), 7.64 (1H, dd, J_1=7.8 Hz, J_2=1.2 Hz, Ar), 7.68 (2H, d, *J*=8.1 Hz, Ar), 7.75 (1H, dd, J_1=7.8 Hz, J_2=1.2 Hz, Ar); HPLC: OD column; *λ*=230 nm; eluent: hexane/isopropanol=60/40; flow rate: 0.5 mL/min; t_{major}=20.16 min, t_{minor}=16.72 min; ee%=61% (56% in DCE).

3.2.5. 4-Methyl-N-(2-methylene-1-(3-nitrophenyl)-3-oxobutyl)benzenesulfonamide ***3e***

This is a known compound.[4a,f] Yield: 99%; $[\alpha]_D^{20}$ +4.0 (*c* 1.0, $CHCl_3$); mp: 130–132 °C; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.18 (3H, s, Me), 2.41 (3H, s, Me), 5.32 (1H, d, *J*=9.4 Hz), 5.89 (1H, d, *J*=9.4 Hz), 6.12 (1H, s), 6.18 (1H, s), 7.25 (2H, d, *J*=8.6 Hz), 7.44 (1H, dd, J_1=8.2 Hz, J_2=7.8 Hz), 7.61 (1H, d, *J*=7.8 Hz), 7.65 (2H, d, *J*=8.6 Hz), 7.89 (1H, s), 8.05 (1H, d, *J*=8.2 Hz); HPLC: AD column; *λ*=254 nm; eluent: hexane/isopropanol=80/20; flow rate: 0.7 mL/min; t_{major}=25.61 min, t_{minor}=34.57 min; ee%=82% (80% in DCE).

3.2.6. N-(1-(2-Chlorophenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide ***3f***

This is a known compound.[4a,f] Yield: 80%; $[\alpha]_D^{20}$ +15 (*c* 1.0, $CHCl_3$); mp: 158–160 °C; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.21 (3H, s, Me), 2.37 (3H, s, Me), 5.68 (1H, d, *J*=8.6 Hz), 5.78 (1H, d, *J*=8.6 Hz), 6.16 (1H, s), 6.17 (1H, s), 7.06–7.15 (2H, m, Ar), 7.20 (2H, d, *J*=8.4 Hz, Ar), 7.21–7.24 (1H, m, Ar), 7.30–7.33 (1H, m, Ar), 7.63 (2H, d, *J*=8.4 Hz, Ar); HPLC: AD column; *λ*=254 nm; eluent: hexane/isopropanol=80/20; flow rate: 0.7 mL/min; t_{major}=18.39 min, t_{minor}=21.63 min; ee%=65% (65% in DCE).

3.2.7. N-(1-(4-Chlorophenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide ***3g***

This is a known compound.[4a,f] Yield: 99%; $[\alpha]_D^{20}$ +28 (*c* 0.8, $CHCl_3$); mp: 103–105 °C; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.11 (3H, s, Me), 2.38 (3H, s, Me), 5.24 (1H, d, *J*=9.1 Hz, NH), 5.99 (1H, d, *J*=9.1 Hz, CH), 6.03 (1H, s), 6.06 (1H, s), 7.01 (2H, d, *J*=8.6 Hz, Ar), 7.12 (2H, d, *J*=8.6 Hz, Ar), 7.19 (2H, d, *J*=8.1 Hz, Ar), 7.59 (2H, d, *J*=8.1 Hz, Ar); HPLC: AS column; *λ*=254 nm; eluent: hexane/isopropanol=65/35; flow rate: 0.7 mL/min; t_{major}=32.92 min, t_{minor}=43.85 min; ee%=90% (82% in DCE).

3.2.8. N-(1-(3-Chlorophenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide ***3h***

This is a known compound.[4a,f] Yield: 90%; $[\alpha]_D^{20}$ +18 (*c* 0.9, $CHCl_3$); mp: 85–86 °C; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.16 (3H, s, Me), 2.41 (3H, s, Me), 5.20 (1H, d, *J*=9.0 Hz), 5.69 (1H, d, *J*=9.0 Hz), 6.08 (1H, s), 6.12 (1H, s), 7.00–7.03 (2H, m), 7.13–7.15 (2H, m), 7.24 (2H, d, *J*=8.2 Hz), 7.63 (2H, *J*=8.2 Hz); HPLC: AD column; *λ*=254 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.7 mL/min; t_{major}=14.68 min, t_{minor}=18.65 min; ee%=89% (84% in DCE).

3.2.9. N-(1-(4-Fluorophenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide ***3i***

This is a known compound.[4a,f] Yield: 90%; $[\alpha]_D^{20}$ +24 (*c* 0.4, $CHCl_3$); mp: 106–108 °C; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.15 (3H, s, Me), 2.41 (3H, s, Me), 5.24 (1H, d, *J*=8.7 Hz), 5.75 (1H, d, *J*=8.7 Hz), 6.07 (1H, s), 6.09 (1H, s), 6.87 (2H, dd, J_1=9.0 Hz, J_2=8.6 Hz), 7.04–7.09 (2H, dd, J_1=8.6 Hz, $J_{2(H-F)}$=5.2 Hz), 7.23 (2H, d, *J*=8.1 Hz), 7.63 (2H, d, *J*=8.1 Hz); HPLC: AD column; *λ*=230 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.7 mL/min; t_{major}=10.75 min, t_{minor}=11.80 min; ee%=91% (85% in DCE).

3.2.10. N-(1-(3-Fluorophenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide ***3j***

This is a known compound.[4a,f] Yield: 91%; $[\alpha]_D^{20}$ +8.0 (*c* 0.3, $CHCl_3$); mp: 108–110 °C; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.16 (3H, s, Me), 2.41 (3H, s, Me), 5.24 (1H, d, *J*=9.2 Hz, NH), 5.78 (1H, d, *J*=9.2 Hz), 6.06 (1H, s), 6.11 (1H, s), 6.79–6.92 (3H, m, Ar), 7.14–7.23 (3H, m, Ar), 7.65 (2H, d, *J*=8.6 Hz, Ar); HPLC: AD column; *λ*=254 nm; eluent: hexane/isopropanol=80/20; flow rate: 0.7 mL/min; t_{major}=16.00 min, t_{minor}=19.10 min; ee%=80% (75% in DCE).

3.2.11. N-(1-(4-Methoxyphenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide ***3k***

This is a known compound.[4a,f] Yield: 98%; $[\alpha]_D^{20}$ +37 (*c* 0.5, $CHCl_3$); mp: 103–105 °C; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.17 (3H, s, Me), 2.41 (3H, s, Me), 3.74 (3H, s, Me), 5.21 (1H, d, *J*=8.3 Hz, NH), 5.49 (1H, d, *J*=8.3 Hz, CH), 6.10 (2H, s), 6.73 (2H, d, *J*=6.8 Hz, Ar), 6.99 (2H, d, *J*=6.8 Hz, Ar), 7.25 (2H, d, *J*=9.3 Hz, Ar), 7.65 (2H, d, *J*=9.3 Hz, Ar); HPLC: AS column; *λ*=230 nm; eluent: hexane/isopropanol=60/40; flow rate: 0.5 mL/min; t_{major}=46.17 min, t_{minor}=60.72 min; ee%=82% (46% in DCE).

3.2.12. N-(1-(4-Methyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide ***3l***

This is a known compound.[4a,f] Yield: 99%; $[\alpha]_D^{20}$ +53 (*c* 1.0, $CHCl_3$); mp: 112–114 °C; ^{1}H NMR ($CDCl_3$, TMS,

300 MHz) δ 2.16 (3H, s, Me), 2.27 (3H, s, Me), 2.42 (3H, s, Me), 5.23 (1H, d, J=8.4 Hz), 5.56 (1H, d, J=8.4 Hz), 6.10 (2H, s), 6.95 (2H, d, J=8.2 Hz, Ar), 7.00 (2H, d, J=8.2 Hz, Ar), 7.24 (2H, d, J=8.2 Hz, Ar), 7.65 (2H, d, J=8.2 Hz, Ar); HPLC: AD column; λ=254 nm; eluent: hexane/isopropanol=80/20; flow rate: 0.7 mL/min; t_{major}=16.34 min, t_{minor}=18.52 min; ee%=90% (84% in DCE).

3.2.13. 4-Methyl-N-(1-phenyl-2-methylene-3-oxo-pentyl)benzenesulfonamide **3m**

This is a known compound.[4a,f] Yield: 95%; $[\alpha]_D^{20}$ +12 (c 0.5, $CHCl_3$); mp: 90–92 °C; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.93 (3H, t, J=7.4 Hz, Me), 2.41 (3H, s, Me), 2.46–2.55 (2H, m, CH_2), 5.32 (1H, d, J=8.0 Hz), 5.89 (1H, d, J=8.0 Hz), 6.05 (1H, s), 6.09 (1H, s), 7.10–7.14 (2H, m, Ar), 7.18–7.20 (3H, m, Ar), 7.23 (2H, d, J=8.4 Hz, Ar), 7.66 (2H, d, J=8.4 Hz, Ar); HPLC: OJ column; λ=254 nm; eluent: hexane/isopropanol=80/20; flow rate: 0.7 mL/min; t_{major}=86.75 min, t_{minor}=13.35 min; ee%=74% in DCM.

3.2.14. 4-Methyl-N-[1-(4-bromophenyl)-2-methylene-3-oxo-pentyl]benzenesulfonamide **3n**

This is a known compound.[4a,f] Yield: 80%; $[\alpha]_D^{20}$ +9.0 (c 0.5, $CHCl_3$); mp: 133–135 °C; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.93 (3H, t, J=7.3 Hz, Me), 2.41 (3H, s, Me), 2.46–2.61 (2H, m, CH_2), 5.20 (1H, d, J=8.9 Hz), 5.73 (1H, d, J=8.9 Hz), 6.00 (1H, s), 6.08 (1H, s), 6.99 (2H, d, J=8.3 Hz, Ar), 7.22 (2H, d, J=8.0 Hz, Ar), 7.32 (2H, d, J=8.3 Hz, Ar), 7.63 (2H, d, J=8.0 Hz, Ar); HPLC: OD column; λ=230 nm; eluent: hexane/isopropanol=70/30; flow rate: 0.7 mL/min; t_{major}=10.55 min, t_{minor}=9.41 min; ee%=65% in DCM.

3.2.15. N-(1-(4-Chlorophenyl)-2-methylene-3-oxopentyl)-4-methylbenzenesulfonamide **3o**

This is a known compound.[4a,f] Yield: 86%; $[\alpha]_D^{20}$ +7.0 (c 0.75, $CHCl_3$); mp: 131–132 °C; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.95 (3H, t, J=7.2 Hz, Me), 2.41 (3H, s, Me), 2.43–2.61 (2H, m, CH_2), 5.23 (1H, d, J=9.0 Hz), 5.75 (1H, d, J=9.0 Hz), 6.03 (1H, s), 6.10 (1H, s), 7.07 (2H, d, J=8.4 Hz, Ar), 7.18 (2H, d, J=8.4 Hz, Ar), 7.26 (2H, d, J=8.1 Hz, Ar), 7.65 (2H, d, J=8.1 Hz, Ar); HPLC: OD column; λ=254 nm; eluent: hexane/isopropanol=90/10; flow rate: 0.7 mL/min; t_{major}=75.23 min, t_{minor}=24.78 min; ee%=51% in DCM.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.11.039.

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