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Catalytic, asymmetric aza-Baylis–Hillman reaction of *N*-sulfonated imines with 2-cyclohexen-1-one and 2-cyclopenten-1-one in the presence of a chiral phosphine Lewis base

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Abstract—In the aza-Baylis–Hillman reaction of *N*-sulfonated imines with 2-cyclohexen-1-one or 2-cyclopenten-1-one, we found that by using (*R*)-2′-dimethylphosphanyl-[1,1′]binaphthalenyl-2-ol **LB1** as a chiral phosphine Lewis base, the corresponding Baylis–Hillman adducts **2** or **3** can be obtained in good yields and moderate enantiomeric excess. The structure of this chiral phosphine Lewis base on chiral induction in this reaction has also been discussed.

1. Introduction

Great progress has been made in the execution of the Baylis–Hillman reaction,[1] for which several catalytic, asymmetric versions have been published[2,3] since Baylis and Hillman first reported the reaction of acetaldehyde with ethyl acrylate and acrylonitrile in the presence of catalytic amounts of strong Lewis base (LB) such as 1,4-diazabicyclo[2,2,2]octane (DABCO) in 1972.[4] However, the catalytic, asymmetric Baylis–Hillman reaction is still not fruitful, because it is limited to the specialized α,β-unsaturated ketones or acrylates, such as ethyl vinyl ketone (EVK) (71% ee),[2a] 2-cyclohexen-1-one (96% ee),[2b] or 1,1,1,3,3,3-hexafluoroisopropyl acrylate (99% ee)[2c–e] and naphthyl acrylate (91% ee).[2f,h] Recently, an aza-Baylis–Hillman reaction has attracted much attention.[5,6] A catalytic asymmetric aza-Baylis–Hillman reaction has also been disclosed in the presence of a chiral nitrogen Lewis base[6c] or chiral phosphine Lewis base.[7] Herein, we report an unprecedented catalytic, asymmetric aza-Baylis–Hillman reaction of *N*-sulfonated imines with 2-cyclohexen-1-one and 2-cyclopenten-1-one in the presence of a chiral phosphine Lewis base under mild reaction conditions.

2. Results and discussion

Previously, we reported that when using a more nucleophilic phosphine Lewis base such as PBu_3 or $PPhMe_2$ as a promote in the aza-Baylis–Hillman reaction of *N*-sulfonated imines **1** with 2-cyclopenten-1-one, the corresponding aza-Baylis–Hillman adducts can be obtained in high yields within 5 h,[6a,b] whereas, nitrogen Lewis bases, such as DABCO, DBU, and DMAP, showed no catalytic activities for this reaction. Based on these results, we attempted the catalytic, asymmetric aza-Baylis–Hillman reaction of *N*-sulfonated imines **1** with 2-cyclopenten-1-one in the presence of a chiral phosphine Lewis base. The selection of the chiral phosphine compounds becomes a key point for success in this asymmetric version. In fact, we utilized a chiral nitrogen Lewis base of 4-(3-ethyl-4-oxa-1-azatricyclo[4,4,0,$0^{3,8}$]dec-5-yl)-quinolin-6-ol β-**ICD** and a chiral phosphine Lewis base of (*R*)-2′-diphenylphosphanyl-[1,1′]binaphthalenyl-2-ol **LB4** as promoters to the catalytic, asymmetric aza-Baylis–Hillman of *N*-sulfonated imines **1** with a variety of activated olefins to achieve good enantioselectivities.[6c,7] Since $PPhMe_2$ is a very effective promoter in the aza-Baylis–Hillman reaction of **1** with 2-cyclopenten-1-one, we decided to utilize (*R*)-2′-dimethylphosphanyl-[1,1′]binaphthalenyl-2-ol **LB1** as a chiral phosphine Lewis base for this reaction because it has a similar structure as the chiral nitrogen Lewis base β-**ICD** and the chiral phosphine Lewis base (*R*)-2′-diphenylphosphanyl-[1,1′]binaphthalenyl-2-ol **LB4** (a phenolic hydroxy group

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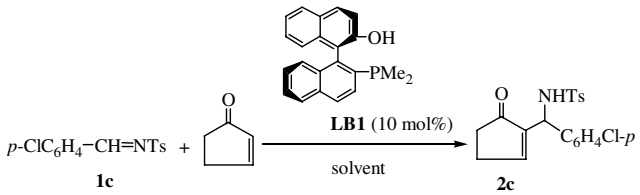
and a nucleophilic nitrogen atom or phoshine atom as a nucleophilic source to initiate the Baylis–Hillman reaction) and as the phosphine Lewis base $PPhMe_2$ (a naphthyl-PMe_2 group) (Fig. 1). In Scheme 1, we show how to prepare this more nucleophilic chiral phosphine Lewis base and another chiral phosphine Lewis base **LB3** (Scheme 1).[8,9]

The reaction conditions for the catalytic, asymmetric aza-Baylis–Hillman reaction of *N*-sulfonated imines **1** with 2-cyclopenten-1-one were systematically examined using *N*-(4-chlorobenzylidene)-4-methylbenzenesulfonamide **1c** as substrate in the presence of chiral phosphine Lewis base **LB1** (10 mol %) (Scheme 2) with the results summarized in Table 1. We found that the solvents, reaction temperatures and Lewis bases played very important roles for this reaction. For example, we have found that by using 10 mol % of **LB1** as a chiral Lewis base in THF at either 20 or 0 °C, the reaction proceeded smoothly to give the corresponding normal aza-Baylis–Hillman adduct **2c** in 84% and 86% yields with 33% ee within 1.0 and 0.5 h, respectively (Table 1, entries 1 and 2). In order to improve the enantioselectivity of this novel catalytic asymmetric reaction, we tried to carry out the reaction at lower temperatures. However, we found that at either −40 or −78 °C, the reaction was sluggish. Keeping the reaction temperature at −40 or −78 °C for 1 h and then increasing the temperature to room temperature (20 °C) naturally, the ee reached



Scheme 2.

Table 1. Aza-Baylis–Hillman reactions of *N*-(4-chlorobenzylidene)-4-methylbenzenesulfonamide (1.0 equiv) with 2-cyclopenten-l-one (1.0 equiv) in the presence of a chiral phosphine Lewis base **LB1** (10 mol %)

Entry	Solvent	Temperature (°C)	Time (h)	Compound **2c**	
				Yield[a] (%)	Ee[b] (%)
1	THF	20 (rt)	0.5	84	33
2	THF	0	1.0	86	33
3	THF	−40 to 20	48	77	47
4	THF	−78 to 20	12	93	64
5	CH_2Cl_2	−30 to 0	12	70	30
6	CH_2Cl_2	−78 to 20	12	81	34
7	DMF	−10	24	82	37
8	MeCN	−10	24	70	51
9	Et_2O	20	24	—	—

[a] Isolated yields.
[b] Determined by chiral HPLC.

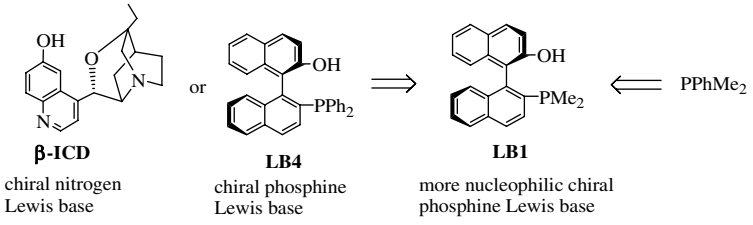
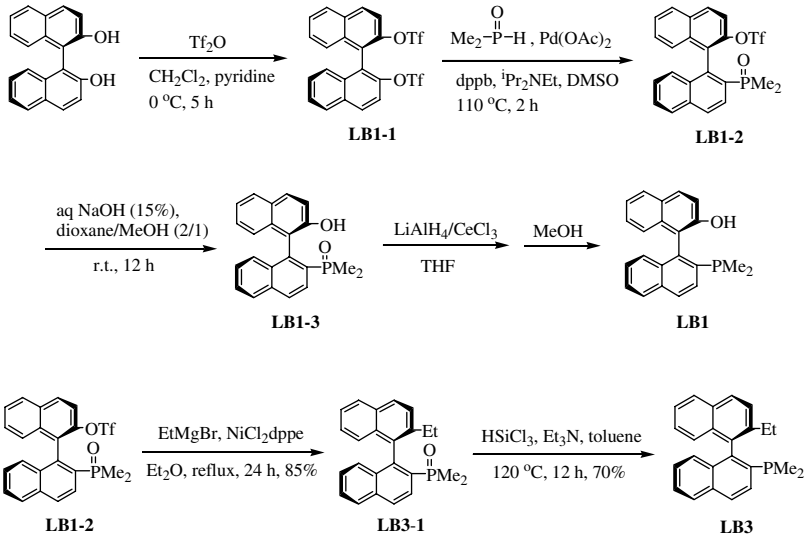


Figure 1. The structure of chiral phosphine Lewis base on the catalytic, asymmetric aza-Baylis–Hillman reaction.



Scheme 1.

47% and 64%, respectively (Table 1, entries 3 and 4). In other solvents, such as dichloromethane (CH_2Cl_2), *N*,*N*-dimethylformamide (DMF), or acetonitrile (MeCN), similar moderate ees were achieved (Table 1, entries 5–8). Whereas, since diethyl ether (Et_2O) cannot dissolve the starting materials **1**, no reaction occurred in Et_2O (Table 1, entry 9).

Upon further investigation, we realized that the structure of chiral phosphine Lewis base plays a significant role in this reaction. Using either (*R*)-[1,1′]binaphthalenyl-2-yl-dimethylphosphine **LB2** or (*R*)-2′-ethyl-[1,1′]binaphthalenyl-2-yl)dimethylphosphane **LB3**, which does not have a phenolic hydroxy group as **LB1**, as a chiral phosphine Lewis base, we found that the reaction rate decreased drastically while the achieved ee was also lower under the same conditions (Fig. 2). Furthermore by using (*R*)-2′-diphenylphosphanyl-[1,1′]binaphthalenyl-2-ol **LB4** as a chiral phosphine Lewis base, no reaction occurred due to its weak nucleophilicity in this reaction (Fig. 2). These ligands can easily be prepared according to the literature (Scheme 1).[8,9]

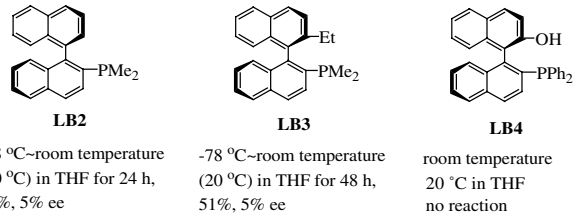
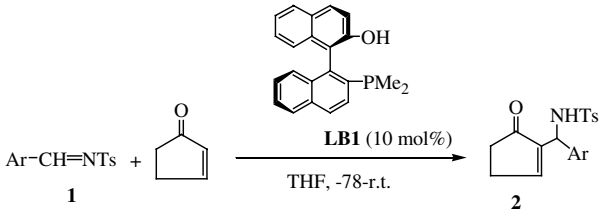


Figure 2. The structures of chiral phosphine Lewis bases on chiral induction of this aza-Baylis–Hillman reaction.

We found that the substituents on the benzene ring of starting materials **1** can affect the enantioselectivity in this catalytic, asymmetric reaction under the same conditions. The results are summarized in Table 2. For *N*-sulfonated imines **1** having electron-donating group on the benzene ring, the corresponding adducts were obtained in high yields, but in slightly lower enantioselectivities under the same conditions (Table 2, entries 1 and 2). For *N*-(*m*-chlorobenzylidene)-*p*-toluenesulfonamide **1d**, the similar result was obtained in 80% yield with 44% ee (Table 2, entry 3). For *N*-(*p*-bromobenzylidene)-*p*-toluenesulfonamide **1e**, *N*-(*p*-nitrobenzylidene)-*p*-toluenesulfonamide **1f** or *N*-(*m*-nitrobenzylidene)-*p*-toluenesulfonamide **1g**, similar moderate ees can be realized in good yields as *N*-(4-chlorobenzylidene)-4-methylbenzenesulfonamide **1c** (Table 1, entries 4–6). However, in all these cases, when using either β-**ICD** or **LB4** as a chiral Lewis base promoter resulted in no reaction.

By using 2-cyclohexen-1-one as a substrate for this catalytic, asymmetric aza-Baylis–Hillman reaction with **LB1** as a chiral phosphine Lewis base, the corresponding adducts **3** can be achieved in good yields with 14–23% ee. The results are summarized in Table 3. In addition to sulfonated imines **1**, we also examined the catalytic, asymmetric Baylis–Hillman reaction of aldehydes with 2-cyclopenten-1-one under the same conditions (Scheme 3). By using 2-phenylpropionaldehyde as the substrate, 13% ee of **4** can be achieved in excellent yield (96%).[2k] However, for other arylaldehydes, the reactions only gave trace amounts of the corresponding Baylis–Hillman adducts along with many unidentified products (Scheme 3). Furthermore, it should be noted that when 4-(3-ethyl-4-oxa-1-azatricyclo[4,4,0,$0^{3,8}$]dec-5-yl)-quinolin-6-ol β-**ICD**[2c] was used as a chiral nitrogen Lewis base for the above catalytic, asymmetric aza-Baylis–Hillman reaction or Baylis–Hillman reaction, no reaction occurred as well. Based on these results, it is clear that the catalytic, asymmetric aza-Baylis–Hillman reaction of imines with β-substituted Michael acceptor is more difficult and is highly dependent on the structures of the substrates including the employed Michael acceptors as well as the chiral Lewis bases. Further exploration of chiral Lewis base for this reaction is required.

Table 2. Aza-Baylis–Hillman reactions of *N*-sulfonated imines **1** (1.0 equiv) with 2-cyclopenten-1-one (1.0 equiv) in the presence of a chiral phosphine Lewis base **LB1** (20 mol %)

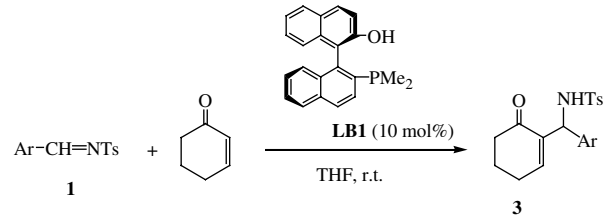


2a: Ar = *p*-EtC_6H_4, **2b**: Ar = *p*-$MeOC_6H_4$, **2d**: Ar = *m*-ClC_6H_4, **2e**: Ar = *p*-BrC_6H_4, **2f**: Ar = *p*-$NO_2C_6H_4$, **2g**: Ar = *m*-$NO_2C_6H_4$.

Entry	Ar	Time (h)	Compound **2**	
			Yield[a] (%)	Ee[b] (%)
1	*p*-EtC_6H_4	12	**2a**, 89	**2a**, 32
2	*p*-$MeOC_6H_4$	12	**2b**, 90	**2b**, 30
3	*m*-ClC_6H_4	12	**2d**, 80	**2d**, 44
4	*p*-BrC_6H_4	12	**2e**, 93	**2e**, 50
5	*p*-$NO_2C_6H_4$	12	**2f**, 70	**2f**, 54
6	*m*-$NO_2C_6H_4$	12	**2g**, 83	**2g**, 55

[a] Isolated yields.
[b] Determined by chiral HPLC.

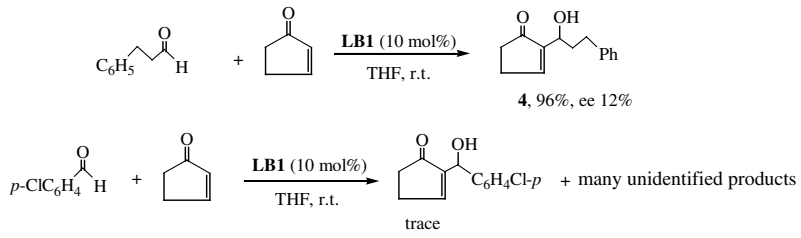
Table 3. Aza-Baylis–Hillman reactions of *N*-sulfonated imines **1** (1.0 equiv) with 2-cyclohexen-l-one in the presence of a chiral phosphine Lewis base **LB1** (10 mol %)



3a: Ar= *p*-EtC_6H_4, **3b**: Ar= *p*-FC_6H_4.

Entry	Ar	Time (h)	Compound **3**	
			Yield[a] (%)	Ee[a] (%)
1	*p*-EtC_6H_4	24	**3a**, 66	**3a**, 23
2	*p*-FC_6H_4	24	**3b**, 90	**3b**, 14

[a] Isolated yields.



Scheme 3.

3. Conclusion

In conclusion, we have found a very simple chiral phosphine Lewis base catalyst system to achieve the catalytic enantioselective aza-Baylis–Hillman reaction using 2-cyclopenten-1-one or 2-cyclohexen-1-one as a Michael acceptor. The is the first example of catalytic, asymmetric aza-Baylis–Hillman reaction using α,β-unsaturated cyclic ketones as Michael acceptors, although the achieved ee was not very high. We believe that the chiral phosphine Lewis base of **LB1** acted as a bifunctional chiral ligand in this reaction:[10] The phosphine atom acted as a Lewis base and the phenolic OH group (Brønsted acid) acted as a Lewis acid through hydrogen bonding to stabilize the in situ formed reaction intermediate. The key factor is the intramolecular hydrogen bonding between the phenolic OH and nitrogen anion stabilized by sulfonyl group to give a relatively rigid transition state for achieving enantioselectivity. Efforts are currently underway to elucidate the mechanistic details of this reaction and the key factors of Lewis bases and to disclose the scope and limitations of this reaction. Work along this line is currently in progress.

4. Experimental

4.1. General

Unless otherwise stated, all reactions were carried out under an argon atmosphere. All solvents were purified by distillation. 2-Cyclopenten-1-one and 2-cyclohexen-1-one were obtained from the Tokyo Chemical Industry (Tokyo Kasei Co. Ltd.) and used without purification. All *N*-tosyl imines were prepared according to the literature. Infrared spectra were measured on a Perkin–Elmer 983 spectrometer. ^{1}H NMR spectra were recorded on a 300 MHz spectrometer in $CDCl_3$ using tetramethylsilane as the internal standard. Mass spectra were recorded with a HP-5989 instrument and HRMS was measured by a Finnigan MA$^+$ mass spectrometer. Satisfactory CHN microanalyses were obtained with a Carlo–Erba 1106 analyzer. Melting points were obtained by means of a micro melting point apparatus and are uncorrected. The optical yield was determined by chiral HPLC. For aza-Baylis–Hillman adducts **2a**–**f**, the reversed phase chiral HPLC column (TBB KR 100 5CHI-TBB (250 mm × 4.6 mm and Chiralcel OJ-R) was employed because they are insoluble in petroleum ether/isopropyl alcohol. For aza-Baylis–Hillman adducts **3a**,**b**, chiral HPLC column AS was employed.

Chiral phosphine Lewis bases **LB1**–**LB4** were prepared by the known synthetic methods as elucidated in Scheme 1. **LB1-1**,[8] **LB1-2**,[8] **LB1-3**,[8] **LB2**,[8] and **LB4**[9] are known compounds. For new phosphine ligands **LB1** and **LB3**, the experimental details and their spectral data are shown as follows.

The specific rotation and the spectroscopic data of the key intermediate **LB1-2** (a known compound): $[\alpha]_D^{20} = -53.4$ (*c* 1.0, CH_3OH). ^{1}H NMR ($CDCl_3$, TMS, 300 MHz): δ 1.17 (3H, d, J = 13.2 Hz, Me), 1.50 (3H, d, J = 13.2 Hz, Me), 7.10–7.20 (2H, m, Ar), 7.30–7.40 (2H, m, Ar), 7.56–7.62 (3H, m, Ar), 7.96–8.04 (2H, m, Ar), 8.12 (3H, m, Ar). ^{31}P NMR ($CDCl_3$, 85% H_3PO_4, 300 MHz): δ 36.2.

Chiral phosphine Lewis base (*R*)-2′-dimethylphosphanyl-[1,1′]binaphthalenyl-2-ol **LB1**: To a solution of **LB1-3** (346 mg, 1.0 mmol) in THF (5.0 mL) was added $LiAlH_4$ (114 mg, 3.0 mmol) and anhydrous $CeCl_3$ (384 mg, 1.5 mmol) and the reaction mixture refluxed for 5 h under an argon atmosphere. The reaction was then quenched by the addition of methanol (10 mL) and the precipitates filtered off. The solvent was removed under reduced pressure from the filtration and the residue purified by a silica gel column chromatography to give **LB1** as a viscous oily compound (259 mg, 79%). $[\alpha]_D^{20} = -147.2$ (*c* 0.79, $CHCl_3$). IR ($CHCl_3$): ν 3197, 3044, 1619, 1510, 1429, 1337, 1268, 810 cm^{-1} (C=C); ^{1}H NMR ($CDCl_3$, TMS, 300 MHz): δ 0.97 (3H, d, J = 3.3 Hz, Me), 1.25 (3H, d, J = 3.3 Hz, Me), 4.80 (1H, s, OH), 6.89 (1H, d, J = 8.4 Hz, Ar), 7.20–7.38 (4H, m, Ar), 7.50 (1H, t, J = 6.9 Hz, Ar), 7.75–7.96 (4H, m, Ar), 8.04 (2H, d, J = 8.4 Hz, Ar). ^{13}C NMR ($CD_3C(O)CD_3$, TMS, 75 MHz): δ 13.90 (d, J = 13.6 Hz), 14.27 (d, J = 13.6 Hz), 117.45, 123.21, 123.26, 124.76, 125.82, 125.84, 126.40, 126.44, 126.73, 127.0, 128.0, 128.08, 128.76, 129.10, 130.12, 132.86, 132.94, 133.64, 133.96, 133.98, 150.86. ^{31}P NMR ($CDCl_3$, 85% H_3PO_4, 300 MHz): δ −51.8. MS (EI): *m*/*e* 330 (M$^+$, 26.87), 313 (M$^+$−17, 100), 268 (M$^+$−62, 17.60). HRMS (EI) Calcd for $C_{22}H_{19}OP$ requires M, 330.1174. Found: 330.1187 (M$^+$).

4.2. Synthesis of phosphine oxide LB3-1

To a solution of **LB1-2** (478 mg, 1.0 mmol) in Et_2O (20 mL) was added $NiCl_2$dppe (53 mg, 0.1 mmol) and EtMgBr (2.0 mmol) in Et_2O (5.0 mL) dropwise and the reaction solution refluxed for 24 h under an argon atmosphere. The reaction was quenched by the addition of 3%

HCl aqueous solution. The organic compounds were then extracted by Et_2O (2×20 mL) and the combined organic layers dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue purified by silica gel chromatography (eluent: EtOAc/petroleum ether, 1/2) to give the phosphine oxide **LB3-1** as a colorless solid (304 mg, 85%); mp 103–104 °C. $[\alpha]_D^{20} = -12.3$ (*c* 0.55, $CHCl_3$). IR ($CHCl_3$): *v* 3391, 3051, 2966, 1618, 1554, 1501, 1414, 1289, 1154, 1030, 930, 904, 821, 747 cm^{-1} (C=C). ^1H NMR ($CDCl_3$, TMS, 300 MHz): δ 0.87 (3H, d, $J = 13.4$ Hz, Me), 1.0 (3H, t, $J = 7.6$ Hz, Me), 1.13 (d, $J = 13.4$ Hz, Me), 2.10–2.20 (1H, m, CH_2), 2.40–2.54 (1H, m, CH_2), 6.93 (1H, d, $J = 8.4$ Hz, Ar), 7.10–7.30 (3H, m, Ar), 7.38–7.78 (3H, m, Ar), 7.90 (1H, d, $J = 8.4$ Hz, Ar), 7.92–8.10 (2H, m, Ar), 8.12–8.20 (1H, m, Ar), 8.40–8.51 (1H, m, Ar). ^{31}P NMR ($CDCl_3$, 85% H_3PO_4, 300 MHz): δ 37.5. MS (EI): *m/e* 358 (M^+, 26.57), 330 (M^+-28, 26.77), 281 (M^+-77, 100). Found: HRMS (EI) *m/e* 358.1467 (M^+), $C_{24}H_{23}OP$ requires M, 358.1487.

Chiral phosphine Lewis base (*R*)-2′-ethyl-[1,1′]binaphthalenyl-2-yl)dimethylphosphane **LB3**: At 0 °C, $HSiCl_3$ (10 mmol, 1.0 mL) was carefully added to a mixture of phosphine oxide **LB3-1** (716 mg, 2.0 mmol) and triethylamine (48 mmol, 2.1 mL) in toluene (50 mL) in a three-necked round-bottom flask under an argon atmosphere. The mixture was then heated to reflux for 16–24 h. To the cooled mixture was added ether and sodium bicarbonate. Solids were removed by filtration and the solvent removed under reduced pressure. The residue was purified by flash column chromatography (SiO_2, EtOAc/petroleum ether = 1/8) to give **LB3** as a viscous oily compound (479 mg, 70%); $[\alpha]_D^{20} = -19.6$ (*c* 1.09, $CHCl_3$). IR ($CHCl_3$): *v* 3391, 3048, 2962, 2896, 1501, 1424, 1261, 1096, 817 cm^{-1} (C=C). ^1H NMR ($CDCl_3$, TMS, 300 MHz): δ 0.84 (3H, d, $J = 3.7$ Hz, Me), 0.94 (3H, t, $J = 8.2$ Hz, Me), 1.13 (d, $J = 3.7$ Hz, Me), 2.12–2.40 (2H, m, CH_2), 6.86 (1H, d, $J = 8.4$ Hz, Ar), 7.0–7.20 (4H, m, Ar), 7.36 (1H, t, $J = 5.6$ Hz, Ar), 7.49 (1H, d, $J = 8.4$ Hz, Ar), 7.72 (1H, dd, $J = 8.4$, 2.9 Hz, Ar), 7.75–7.96 (4H, m, Ar). ^{31}P NMR ($CDCl_3$, 85% H_3PO_4, 300 MHz): δ −55.0. MS (EI): *m/e* 342 (M^+, 6.18), 313 (M^+-30, 100), 281 (M^+-61, 15.16). Found: HRMS (EI) *m/e* 342.1549 (M^+), $C_{24}H_{23}P$ requires M, 342.1537.

Typical reaction procedure for the aza-Baylis–Hillman reaction of *N*-sulfonated imines **1** with cyclopent-2-en-1-one in the presence of chiral phosphine Lewis base **LB1** (10 mol %).

To *N*-(*p*-chlorobenzylidene)-*p*-toluenesulfinamide (147 mg, 0.5 mmol) and **LB1** (17.0 mg, 0.05 mmol) in 1.0 mL of THF was added 2-cyclopenten-1-one (42 μL, 41.0 mg, 0.5 mmol) at −78 °C. The reaction mixture was stirred at −78 °C for 1 h and then the temperature allowed to rise to room temperature (20 °C) naturally with stirring for 24 h. The solvent was removed under reduced pressure and residue purified by flash chromatography (eluent: EtOAc/petroleum ether = 1/2) to give the corresponding aza-Baylis–Hillman adduct **2c** (158 mg, 84%).

4.3. *N*-[(4-Ethylphenyl)-(5-oxocyclopent-1-enyl)methyl]-4-methylbenzenesulfonamide 2a

Colorless solid. $[\alpha]_D^{20} = -3.2$ (*c* 1.15, $CHCl_3$). Mp 130–133 °C, 162 mg, 89%. This is a known compound and the IR, ^1H NMR and MS spectroscopic data of this racemic compound can be found in Ref. 6b. ^{13}C NMR ($CDCl_3$, TMS, 75 MHz): δ 15.49, 21.45, 26.71, 28.38, 34.95, 55.14, 126.67, 127.34, 128.04, 129.26, 135.79, 137.29, 143.10, 143.52, 143.88, 160.48, 208.45. Chiral HPLC: TBB column (reversed phase column); $\lambda = 254$ nm; eluent: hexane/isopropanol = 80/20 (0.1% HOAc); Flow rate: 1.0 mL/min, ee = 32%.

4.4. *N*-[(4-Methoxyphenyl)-(5-oxocyclopent-1-enyl)-methyl]-4-methylbenzenesulfonamide 2b

Colorless solid; $[\alpha]_D^{20} = -2.3$ (*c* 1.01, $CHCl_3$). Mp 126–128 °C, 165 mg, 90%. This is a known compound and the IR, ^1H NMR, and MS spectroscopic data of this racemic compound can be found in Ref. 6b. ^{13}C NMR ($CDCl_3$, TMS, 75 MHz): δ 21.45, 26.70, 34.99, 54.86, 55.23, 113.92, 127.36, 127.97, 129.30, 130.68, 137.32, 143.16, 143.61, 159.14, 160.37, 208.45. Chiral HPLC: Chiralcel OJ-R (reversed phase column); $\lambda = 254$ nm; eluent: ethanol/0.5 M $NaClO_2$ (pH = 7.0) = 70/30; Flow rate: 0.5 mL/min, ee = 30%.

4.5. *N*-[(4-Chlorophenyl)-(5-oxocyclopent-1-enyl)methyl]-4-methylbenzenesulfonamide 2c

Colorless solid. $[\alpha]_D^{20} = -6.5$ (*c* 1.23, $CHCl_3$). Mp 184–186 °C, 178 mg, 93%. This is a known compound and the IR, ^1H NMR, and MS spectroscopic data of this racemic compound can be found in Ref. 6b. ^{13}C NMR ($CDCl_3$, TMS, 75 MHz): δ 21.46, 26.80, 34.88, 54.64, 127.25, 127.71, 128.12, 128.63, 129.35, 133.63, 137.09, 142.94, 143.42, 160.90, 208.35. Chiral HPLC: TBB column (reversed phase column); $\lambda = 254$ nm; eluent: hexane/isopropanol = 80/20 (0.1% HOAc); Flow rate: 1.0 mL/min, ee = 63%.

4.6. *N*-[(3-Chlorophenyl)-(5-oxocyclopent-1-enyl)methyl]-4-methylbenzenesulfonamide 2d

Colorless solid. $[\alpha]_D^{20} = -2.0$ (*c* 0.85, $CHCl_3$). Mp 134–136 °C, 151 mg, 80%. IR ($CHCl_3$): *v* 3412, 1678 (C=O), 1610, 1390, 1102, 1010, 690 cm^{-1}. ^1H NMR ($CDCl_3$, TMS, 300 MHz): δ 2.13–2.54 (4H, m, CH_2), 2.37 (3H, s, Me), 5.24 (1H, d, $J = 8.4$ Hz, NH), 6.07 (1H, d, $J = 8.4$ Hz, CH), 7.08 (1H, dd, $J = 7.5$, 2.7 Hz, Ar), 7.15 (1H, d, $J = 7.5$ Hz, Ar), 7.17 (1H, d, $J = 7.5$ Hz, Ar), 7.19 (2H, d, $J = 8.4$ Hz, Ar), 7.20 (1H, s, Ar), 7.35 (1H, t, $J = 2.4$ Hz, =CH), 7.58 (2H, d, $J = 8.4$ Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz): δ 21.47, 26.84, 34.91, 54.92, 124.90, 126.90, 127.27, 127.94, 129.38, 129.85, 134.45, 137.18, 140.46, 142.75, 143.45, 161.02, 208.35. MS (EI): *m/e* 264 (M^+-111, 1.87), 220 (M^+-155, 100). Anal. Calcd for $C_{19}H_{18}ClNO_3S$: requires C, 60.71; H, 4.83; N, 3.73. Found: C, 60.79; H, 4.98; N, 3.49. Chiral HPLC: Chiralcel OJ-R (reversed phase column); $\lambda = 254$ nm; eluent:

ethanol/0.5 M $NaClO_2$ (pH = 7.0) = 70/30; Flow rate: 0.5 mL/min, ee = 44%.

4.7. *N*-[(4-Bromophenyl)-(5-oxocyclopent-1-enyl)methyl]-4-methylbenzenesulfonamide 2e

Colorless solid. $[\alpha]_D^{20} = -5.7$ (*c* 0.65, $CHCl_3$). Mp 181–183 °C, 180 mg, 93%. This is a known compound and IR, ^1H NMR, and MS spectroscopic data of this racemic compound can be found in Ref. 6b. ^{13}C NMR ($CDCl_3$, TMS, 75 MHz): δ 21.47, 26.80, 34.89, 54.79, 121.80, 127.25, 128.45, 129.35, 131.60, 137.09, 137.51, 142.85, 143.42, 160.92, 208.38. Chiral HPLC: TBB column (reversed phase column); λ = 254 nm; eluent: hexane/isopropanol = 90/10 (0.1% HOAc); Flow rate: 1.0 mL/min, ee = 50%.

4.8. *N*-[(4-Nitrophenyl)-(5-oxocyclopent-1-enyl)methyl]-4-methylbenzenesulfonamide 2f

A pale yellow solid. $[\alpha]_D^{20} = -2.4$ (*c* 0.97, $CHCl_3$). Mp 189–191 °C, 136 mg, 70%. This is a known compound and IR, ^1H NMR, and MS spectroscopic data of this racemic compound can be found in Ref. 6b. ^{13}C NMR ($CDCl_3$, TMS, 75 MHz): δ 21.47, 26.98, 34.83, 54.80, 123.75, 127.26, 127.68, 129.48, 137.06, 142.14, 143.76, 145.65, 147.23, 161.52, 208.24. Chiral HPLC: Chiralcel OJ-R (reversed phase column); λ = 254 nm; eluent: acetonitrile/0.5 M $NaClO_2$ (pH = 7.0) = 40/60; Flow rate: 0.5 mL/min, ee = 54%.

4.9. *N*-[(3-Nitrophenyl)-(5-oxocyclopent-1-enyl)methyl]-4-methylbenzenesulfonamide 2g

A pale yellow solid. $[\alpha]_D^{20} = -4.4$ (*c* 0.87, $CHCl_3$). Mp 155–157 °C, 160 mg, 83%. IR (KBr): ν 3423, 1681 (C=O), 1610, 1390, 1102, 1010, 690 cm^{-1}. ^1H NMR ($CDCl_3$, TMS, 300 MHz): δ 2.13–2.60 (4H, m, CH_2), 2.40 (3H, s, Me), 5.39 (1H, d, *J* = 8.4 Hz, NH), 6.25 (1H, d, *J* = 8.4 Hz, CH), 7.20 (2H, d, *J* = 8.4 Hz, Ar), 7.41 (1H, t, *J* = 2.7 Hz, =CH), 7.42 (1H, d, *J* = 8.4 Hz, Ar), 7.61 (2H, d, *J* = 8.4 Hz, Ar), 7.62 (1H, d, *J* = 8.4 Hz, Ar), 7.97 (1H, s), 8.06 (1H, dd, *J* = 8.4, 1.8 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz): δ 21.44, 26.98, 34.85, 54.58, 121.70, 122.75, 127.22, 129.49, 129.60, 133.02, 136.97, 140.58, 142.21, 143.71, 148.13, 161.66, 208.32. MS (EI): *m/e* 264 (M^+-122, 2.86), 231 (M^+-155, 100). Anal. Calcd for $C_{19}H_{18}N_2O_5S$: requires C, 59.06; H, 4.70; N, 7.25. Found: C, 59.02; H, 4.76; N, 7.13. Chiral HPLC: TBB column (reversed phase column); λ = 254 nm; eluent: hexane/isopropanol = 90/10 (0.1% HOAc); Flow rate: 1.0 mL/min, ee = 55%.

4.10. *N*-[(4-Ethylphenyl)-(6-oxocyclohex-1-enyl)methyl]-4-methylbenzenesulfonamide 3a

A colorless solid; $[\alpha]_D^{20} = +2.5$ (*c* 1.30, $CHCl_3$). Mp 106–108 °C, 120 mg, 66%. This is a known compound and IR, ^1H NMR, and MS spectroscopic data of this racemic compound can be found in Ref. 6b. ^{13}C NMR ($CDCl_3$, TMS, 75 MHz): δ 15.45, 21.46, 21.95, 25.75, 28.31, 37.91, 59.20, 126.17, 127.30, 127.82, 129.30, 136.49, 136.78, 137.78, 143.03, 143.38, 148.81, 199.0. Chiral HPLC: AS column; λ = 254 nm; eluent: hexane/isopropanol = 80/20; Flow rate: 0.7 mL/min., ee = 23%.

4.11. *N*-[(4-Fluorophenyl)-(6-oxocyclohex-1-enyl)methyl]-4-methylbenzenesulfonamide 3b

A colorless solid; $[\alpha]_D^{20} = +4.2$ (*c* 0.71, $CHCl_3$). Mp 126–128 °C, 168 mg, 90%. This is a known compound and IR, ^1H NMR, and MS spectroscopic data of this racemic compound can be found in Ref. 6b. ^{13}C NMR ($CDCl_3$, TMS, 75 MHz): δ 21.47, 21.90, 25.75, 38.32, 58.94, 115.17 (d, *J* = 21.5 Hz), 126.38, 127.25, 127.90 (d, *J* = 8.6 Hz), 129.54 (d, *J* = 20.5 Hz), 134.23, 135.46, 136.49, 143.25, 149.23, 167.03 (d, *J* = 253.5 Hz), 199.12. Chiral HPLC: AS column; λ = 254 nm; eluent: hexane/isopropanol = 80/20; Flow rate: 0.7 mL/min, ee = 14%.

4.12. *N*-[(4-Fluorophenyl)-(6-oxocyclohex-1-enyl)methyl]-4-methylbenzenesulfonamide 4

This is a known compound.[2k] A colorless oil; $[\alpha]_D$ = −3.4 (*c* 2.4, $CHCl_3$); 207 mg, 96%; ^1H NMR ($CDCl_3$, TMS, 300 MHz): δ 2.03 (1H, q, *J* = 7.2 Hz, CH_2), 2.04 (1H, d, *J* = 7.2 Hz, CH_2), 2.43–2.50 (2H, m, CH_2), 2.60–2.65 (2H, m, CH_2), 2.65 (1H, m, CH), 2.74–2.90 (1H, m, CH), 3.04 (1H, br s, OH), 4.50 (1H, s, CH), 7.18–7.38 (5H, m, Ar), 7.48 (1H, m, =CH). Chiral HPLC: AS column; λ = 254 nm; eluent: hexane/isopropanol = 80/20; Flow rate: 0.7 mL/min.

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