Organic & Biomolecular Chemistry

PAPER

View Article Online
View Journal | View Issue

Cite this: *Org. Biomol. Chem.*, 2015, **13**, 7076

Organocatalytic asymmetric Michael addition of 1-acetylcyclohexene and 1-acetylcyclopentene to nitroolefins†

Utpal Nath, Ankush Banerjee, Bidhan Ghosh and Subhas Chandra Pan*

Received 1st May 2015,
Accepted 15th May 2015

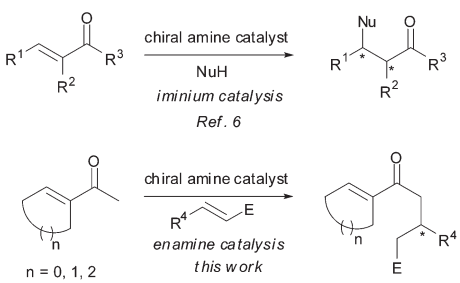
DOI: 10.1039/c5ob00878f

www.rsc.org/obc

Enantioselective organocatalytic Michael addition reactions of 1-acetylcyclohexene, 1-acetylcyclopentene and 1-acetylcyclobutene to nitroolefins have been developed. This is the first report where an α-branched enone has been activated by an amine catalyst for the asymmetric Michael addition reaction to an electrophile. The Michael products have also been cyclized to bicyclic compounds.

Enamine catalysis has been established as a powerful tool for making C–C and C–X bond formations in an asymmetric fashion.[1] After the rediscovery of proline catalyzed intermolecular aldol[2] and Mannich reactions,[3] enamine catalysis has been extensively utilized for the α-functionalization of enolizable aldehydes and ketones with a huge variety of electrophiles. Simple enones have also been activated by amine catalysts to generate dienamine[4] and have been utilized for a variety of enamine–iminium cascade reactions.[5] Despite these tremendous developments in recent years, α-branched enones have been rarely used in amine catalysis (Scheme 1).[6]

Melchiorre and co-workers pioneered using primary amine catalysts for the activation of acyclic enones and developed a highly enantioselective sulfa Michael addition to acyclic α-branched enones by iminium catalysis.[6a] Also, Luo, Cheng and co-workers reported iminium catalytic asymmetric Michael addition reactions of indoles, azoles and thiols to α-branched enones.[6b–d] However, the use of α-branched enones in enamine catalysis is almost not investigated.[7] Thus we embarked to employ α-branched enones in enamine catalysis, particularly in the Michael addition reactions to nitroolefins.[8]



Scheme 1 α-Branched enones in aminocatalysis.

We chose 1-acetylcyclohexene (**1a**) as the model substrate for our reaction. Compound **1a** has been previously utilized for tandem cyclization reactions with imines and nitroolefins[9] and recently in the synthesis of cyclopentenone derivatives.[10]

Surprisingly, however no chiral transformation has been reported using it.[11]

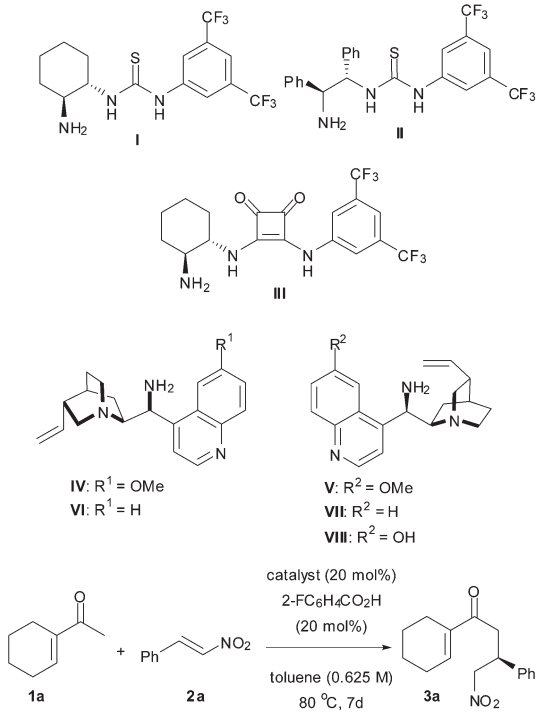
Initially we started screening catalysts with primary amine-thiourea **I** and **II** for the reaction of **1** with nitrostyrene (**2a**) using toluene as the solvent and 2-fluorobenzoic acid as the co-catalyst. After stirring at 80 °C for seven days the single Michael addition product **3** was formed in poor enantioselectivities and no cyclized product was formed (Table 1, entries 1 and 2). Primary amine-squaramide catalyst **III** was also not suitable for this reaction giving the product in poor yield. Recently, a variety of catalytic asymmetric transformations by carbonyl activation have been reported with 9-amino-9-deoxy-*epi*-cinchona alkaloid catalysts (**IV–VII**).[12] To our delight, these catalysts were found to be effective in our reaction and the *epi*-cinchonidine amine **VII** emerged as the best catalyst providing the product in 75% ee. Next, we prepared the 9-amino-6′-hydroxy-*epi*-cinchonidine catalyst **VIII**, however the enantioselectivity was modest. So, we decided to carry out further reactions with catalyst **VII**.

The next phase of the screening process involved different acid additives for our reaction. We thought that the acidity of the additive might play a role in the yield and enantioselectivity of the reaction and thus different acid co-catalysts were screened with catalyst **VII**. Highly acidic 2,4,5-trifluorobenzoic acid provided poor yield of the reaction with moderate

Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati 781039, India. E-mail: span@iitg.ernet.in; Fax: +91-361-2582349; Tel: +91-361-2583304

† Electronic supplementary information (ESI) available: Experimental procedures and ^{1}H, ^{13}C NMR and HPLC data of all products. CCDC 1033099. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c5ob00878f

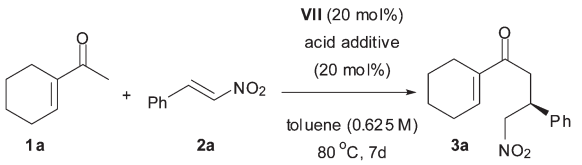
Table 1 Catalyst optimization



Entry[a]	Catalyst	Yield[b]	ee[c]
1	**I**	30	4
2	**II**	20	5
3	**III**	<10	nd
4	**IV**	35	−70
5	**V**	30	68
6	**VI**	40	−70
7	**VII**	55	75
8	**VIII**	52	71

[a] Reactions were carried out in 0.16 mL toluene (0.625 M) with 0.12 mmol of **1a** (1.2 equiv.) and 0.1 mmol of **2a** in the presence of 20 mol% catalyst and 20 mol% 2-fluorobenzoic acid. [b] Isolated yield after silica gel column chromatography. [c] Determined by chiral phase HPLC analysis. nd = not determined.

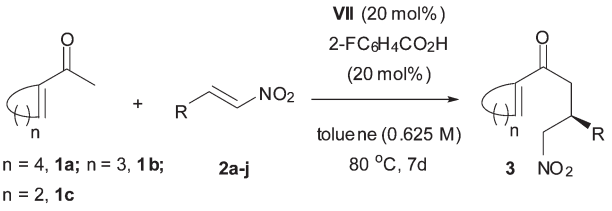
Table 2 Screening of acid-additive



Entry	Acid-additive	Yield[a]	ee[b]
1	2-Fluorobenzoic acid	55	75
2	2,4,5-Trifluorobenzoic acid	20	63
3	2-Nitrobenzoic acid	30	64
4	2-Bromobenzoic acid	35	64
5	2-Methoxybenzoic acid	20	77
6	Camphorsulfonic acid	<10	nd
7	Propionic acid	<10	nd

[a] Isolated yield after silica gel column chromatography. [b] Determined by chiral phase HPLC analysis. nd = not determined.

Table 3 Substrate scope



Entry[a]	Enone	R	3/yield[b]	ee[c]
1	**1a**	Ph	**3aa**/55	75
2	**1a**	4-FC_6H_4	**3ab**/47	54
3	**1a**	4-$OMeC_6H_4$	**3ac**/52	54
4	**1a**	2-MeC_6H_4	**3ad**/72	58
5	**1a**	2,5-$(OMe)_2C_6H_3$	**3ae**/53	60
6	**1a**	1-Naphthyl	**3af**/74	58
7	**1a**	2-Furyl	**3ag**/63	62
8	**1a**	Iso-butyl	**3ah**/35	86
9	**1a**	*tert*-Butyl	**3ai**/37	73
10	**1a**	*c*-Hexyl	**3aj**/37	72
11	**1b**	Ph	**3ba**/74	54
12	**1b**	4-$OMeC_6H_4$	**3bc**/53	77
13	**1b**	2-MeC_6H_4	**3bd**/71	70
14	**1b**	Iso-butyl	**3bh**/35	70
15	**1c**	Ph	**3ca**/71	58

[a] Reactions were carried out in 0.4 mL toluene (0.625 M) with 0.3 mmol of **1a** (1.2 equiv.) and 0.25 mmol of **2a** in the presence of 20 mol% **VII** and 20 mol% 2-fluorobenzoic acid. [b] Isolated yield after silica gel column chromatography. [c] Determined by chiral phase HPLC analysis.

enantioselectivity (entry 2, Table 2). A similar enantioselectivity was also achieved with 2-nitrobenzoic acid (entry 3). The yield and enantioselectivity did not increase much with 2-bromobenzoic acid (entry 4). Interestingly, 2-methoxybenzoic acid afforded a higher enantioselectivity of the product but with poor yield (entry 5). Camphorsulfonic acid and propionic acid are not suitable co-catalysts for our reaction (entries 6 and 7 respectively). Thus 2-fluorobenzoic acid was the acid additive of choice. Other solvents were also screened but toluene was the optimal solvent.

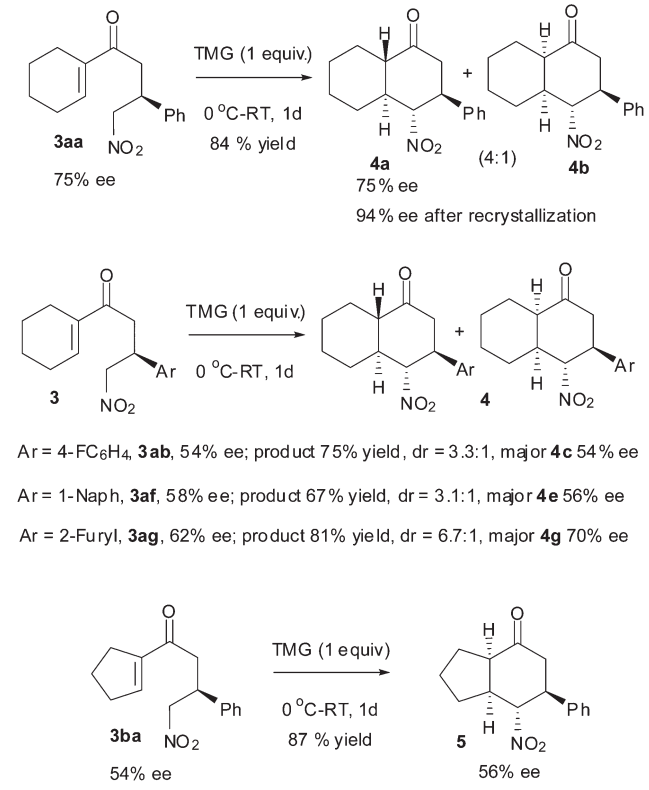
With the optimized conditions in hand we ventured in the substrate scope for this reaction. Initially, different aromatic nitroolefins were synthesized and then treated with **1a**. The products were obtained in good yields with varying enantioselectivities (Table 3, entries 1–6). Substituted benzaldehyde derived nitroolefins having electron-donating or electron-withdrawing substituents at the 4-position on the aromatic ring were employed and they demonstrated similar reactivity, and comparable enantioselectivities were attained (entries 2 and 3).

Surprisingly, 2-substitution on the phenyl group showed higher reactivity but the enantioselectivity remained the same (entry 4). A 2,5-disubstituted nitroolefin **2e** provided product **3ae** in similar enantioselectivity (entry 5). A higher yield was

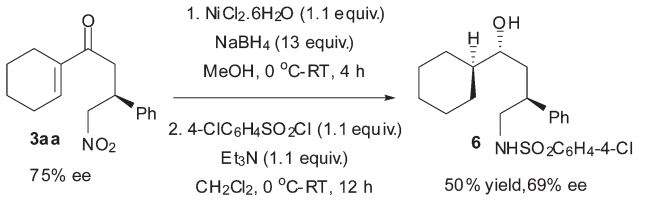
obtained with 1-naphthyl substituted nitroolefin (**2f**) and a moderate enantioselectivity was observed (entry 6). Heteroaromatic nitroolefin was also employed in our reaction and a similar enantioselectivity was obtained (entry 7). Interestingly, aliphatic nitroolefins were also found to be suitable substrates providing the products in higher enantioselectivities albeit in lower yields due to side products formation (entries 8–10). The highest enantioselectivity (86% ee) was achieved with isovaleraldehyde derived nitroolefin **2h** (entry 8). Aliphatic α-branched aldehyde derived nitroolefins **2i** and **2j** exhibited similar reactivity but slightly lower enantioselectivities were obtained (entries 9 and 10). To expand the scope on the enone side, we screened 1-acetylcyclopentene (**1b**) and 1-acetylcyclobutene (**1c**) with different nitroolefins (entries 11–15). The yields of the products with 1-acetylcyclopentene are found to be similar to 1-acetylcyclohexene (**1a**); and the enantioselectivities obtained are good (entries 11–14). 4-Methoxybenzaldehyde derived nitroolefin **2c** provided product **3bc** in 77% enantiomeric excess. Aliphatic nitroolefin **2h** was also employed and good enantioselectivity was attained (entry 14). Finally, 1-acetylcyclobutene (**1c**) was prepared and reacted with nitrostyrene (**2a**) to afford product **3ca** in 71% yield and 58% ee.

To illustrate the utility of our method, we have converted products **3** to cyclized products **4** and **5** by treatment with 1,1,3,3-tetramethylguanidine (TMG)[13] (Scheme 2). Initially, **3aa** was treated with TMG and to our delight two diastereomers **4a** and **4b** were formed in a 4 : 1 ratio. The relative structure of the major diastereomer **4a** was unambiguously determined by X-ray crystallography[14] and was obtained in 75% ee. Pleasingly, the enantioselectivity was enhanced to 94% ee after single recrystallization. Similarly, the relative structure of the minor isomer **4b** was determined by comparison of the ^{1}H NMR with a known compound.[9d] Then we converted **3ab**, **3af** and **3ag** to their cyclized products **4** under identical conditions and similar results were obtained. Cyclization of **3ag** affords major diastereomer **4g** in 81% overall yield with an improved enantioselectivity (70% ee). Interestingly, cyclization of **3ba** having a cyclopentene moiety provided only a single diastereomer **5** and the enantioselectivity was retained. The relative structure of **5** was solved by the 2D NMR method. However, a one-pot reaction of the amine catalyzed Michael reaction followed by TMG mediated cyclization did not work.

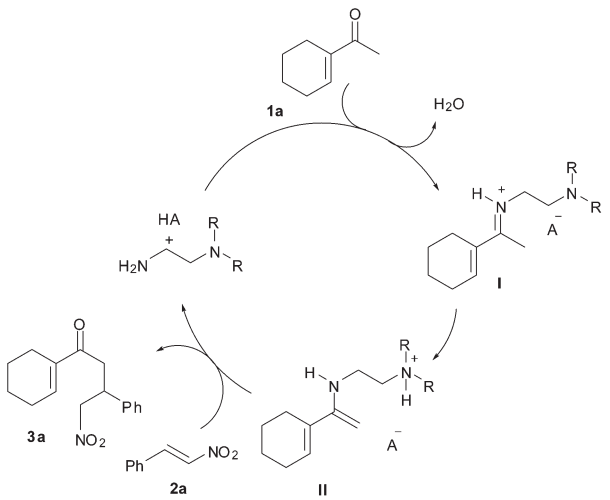
To demonstrate further application of our method we envisaged the reduction of the nitro group in **3aa** with an expectation of absolute stereochemistry determination. After attempting different methods we found that the combination of nickel chloride and sodium borohydride could reduce the nitro group with the simultaneous reduction of enone functionalities (Scheme 3). After derivatizing the amino group with 4-chlorophenylsulfonyl chloride compound **6** was obtained as the major diastereomer whose relative configuration was determined by the 2D NMR method (see the ESI† for details). Unfortunately compound **6** did not crystallize under various conditions.



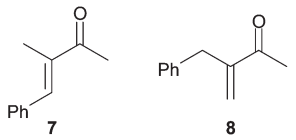
Scheme 2 TMG mediated cyclization of **3**.



Scheme 3 Reduction of compound **3aa**.



Scheme 4 The proposed mechanism.



Scheme 5 Enones **7** and **8**.

A plausible mechanism has been shown without the stereoinduction (Scheme 4). It seems that the catalyst plays a bifunctional role activating concomitantly both enone and nitroolefin.[5e] Initially, the iminium ion **I** is generated from the amine and acid catalyst (HA) and then it isomerizes to enamine **II**. In the enamine **II**, the tertiary amino group is protonated and could interact with the nitro functionality, and thus assists in stereocontrol.

After the development of the catalytic asymmetric Michael addition reaction of cyclic α-branched enones **1** with nitroolefins, we became interested to employ acyclic α-branched enones in the Michael reaction. Thus, we synthesized enones **7** and **8** (Scheme 5). Unfortunately, these enones remained unreacted under our reaction conditions.

Conclusion

In summary, this report describes the chiral amine catalyzed asymmetric Michael addition reaction between α-branched enones and nitroolefins. The enantioselectivity of the products is good to moderate and the nitroolefin scope is broad. The utility of our method has been shown by converting to bicyclized compounds and high enantioselectivity could be attained by recrystallization. α-Branched enones are challenging substrates in asymmetric organocatalysis and this is the first demonstration that α-branched enones could be activated by an amine catalyst for an asymmetric reaction with a Michael acceptor.

Experimental

General

All the reagents used are of commercial grade and used without purification. Reactions were monitored by silica gel 60 F254 (0.25 mm). NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard for ^1H NMR (400 MHz or 600 MHz) and $CDCl_3$ solvent as the internal standard for ^{13}C NMR (100 MHz or 150 MHz). IR spectra of the compounds were recorded in KBr or neat. HRMS spectra were recorded using the ESI mode. HPLC data were recorded using Waters and Dionex (Ultimate 3000) HPLC instruments. Catalysts **I**,[15] **II**,[16] **III**,[17] **IV–VII**[18] and **VIII**[19] were prepared according to the reported procedures.

Experimental procedures

General procedure for the asymmetric Michael reaction. A 10 mL round bottomed flask was charged with enone **1** (0.3 mmol, 1.2 equiv.), nitroolefin **2** (0.25 mmol, 1 equiv.), catalyst **VII** (0.05 mmol, 20 mol%) and 2-fluorobenzoic acid (0.05 mmol, 20 mol%) in toluene (0.4 mL). The reaction mixture was stirred at 80 °C for 7 days. The product **3** was purified by silica gel column chromatography (EtOAc : hexane = 1 : 50–1 : 40).

Preparation of racemic Michael adducts 3. 0.6 mmol (0.085 mL) of diisopropylamine was taken in a 10 mL R.B. flask and 1 mL dry THF was added to it (the reaction was carried out under an argon atmosphere). The whole container was cooled to −78 °C and then 0.345 mL of a 1.6 M solution of *n*-BuLi in hexane (0.55 mol) was added to it and the mixture was stirred for 1 min at −78 °C. Then a solution of **1** (0.5 mmol) in 0.5 mL dry THF was added and the mixture was stirred for 15 min at −78 °C. Next nitroolefin **2** (0.6 mmol) was added as a solution in 0.5 mL dry THF. The solution was stirred for 15 min at −78 °C and subsequently for 12 hour at 0 °C. The reaction mixture was diluted with 1 M aqueous NH_4Cl and EtOAc. The organic layer was extracted, washed with water, brine and then dried with Na_2SO_4, filtered and evaporated in *vacuo* to get the crude product **3** which was purified by silica gel column chromatography.

Procedure for the preparation of nitroolefins. Nitroolefins **2a–2g**,[20a] **2h**[20b] and **2i–2j**[20c] were synthesized by the reported procedures.

Characterization data of the compounds

1-Cyclohexenyl-4-nitro-3-phenylbutan-1-one (3aa). Yellow thick oil, 37.6 mg, 55% yield. **FT-IR** (KBr): 3444(s), 2925(s), 2853(w), 1713(s), 1551(s), 1377(w). **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.27–7.34 (m, 2H), 7.22–7.27 (m, 3H), 6.89 (s, 1H), 4.75 (dd, J = 12.4, 6.4 Hz, 1H), 4.62 (dd, J = 12.4, 8.4 Hz, 1H), 4.06–4.09 (m, 1H), 3.02–3.16 (m, 2H), 2.17–2.23 (broad doublet, 4H), 1.25–1.60 (m, 4H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.1, 141.2, 139.7, 139.3, 129.1, 127.8, 127.6, 79.8, 40.2, 39.8, 26.3, 23.2, 22.0, 21.6 ppm. HRMS calculated for $[C_{16}H_{19}NO_3 + H^+]$: 274.1438, found: 274.1434. **HPLC:** Chiralpak IA column. Flow rate 1 mL min^{-1}. UV detection at 214 nm. τ(major) = 12.859, τ(minor) = 15.019 using hexane : isopropanol = 96 : 4 as the eluent, ee 75%.

1-Cyclohexenyl-3-(4-fluorophenyl)-4-nitrobutan-1-one (3ab). Yellow thick oil, 34.4 mg, 47% yield. **FT-IR** (KBr): 3438(m), 2931(m), 2859(w), 1663(s), 1552(s), 1511(s), 1225(m), **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.19–7.21 (m, 2H), 6.88–7.18 (m, 2H), 6.87 (s, 1H), 4.72 (dd, J = 12.8, 6.4 Hz, 1H), 4.56 (dd, J = 12.8, 8.4 Hz, 1H), 4.06–4.14 (m, 1H), 3.04–3.08 (m, 2H), 2.15–2.23 (broad doublet, 4H), 1.23–1.59 (m, 4H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 197.7, 161.0, 141.1, 139.3, 135.3, 129.3, 116.1, 79.8, 40.2, 39.0, 26.3, 23.2, 21.9, 21.5 ppm, HRMS calculated for $[C_{16}H_{18}FNO_3 + H^+]$: 293.1343, found: 293.1347. **HPLC:** Chiralpak IA column. Flow rate 1 mL min^{-1}. UV detection at

214 nm. τ(major) = 16.7, τ(minor) = 20.3 using hexane : isopropanol = 96 : 4 as the eluent, ee 54%.

1-Cyclohexenyl-3-(4-methoxyphenyl)-4-nitrobutan-1-one (3ac). Yellow thick oil, 39.5 mg, 52% yield. **FT-IR** (KBr): 3441.61(s), 2921(m), 2852(w), 1713(m), 1550(s), **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.11–7.24 (m, 2H), 6.86 (s, 1H), 6.80–6.82 (m, 2H), 4.68 (dd, J = 12.4, 6.8 Hz, 1H), 4.53 (dd, J = 12.4, 8.4 Hz, 1H), 3.74–4.01 (m, 1H), 3.73 (s, 3H), 3.00–3.059 (m, 2H), 2.14–2.19 (broad doublet, 4H), 1.18–1.56 (m, 4H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.1, 159.1, 141.0, 139.3, 131.4, 128.6, 114.4, 80.1, 55.4, 40.3, 39.0, 26.2, 23.1, 21.9, 21.6 ppm. HRMS calculated for [$C_{17}H_{21}NO_4$ + H^+]: 304.1543, found: 304.1574. **HPLC:** Chiralpak IA column. Flow rate 1 mL min^{-1}. UV detection at 214 nm. τ(major) = 10.1, τ(minor) = 11.7 using hexane : isopropanol = 96 : 4 as the eluent, ee 54%.

1-Cyclohexenyl-4-nitro-3-*o*-tolylbutan-1-one (3ad). Light yellow thick oil, 51.8 mg, 72% yield. **FT-IR** (KBr): 3443(s), 2925(s), 2854(w), 1660(s), 1551(s), 1377(w). **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.1–7.22 (m, 4H), 6.87 (s, 1H), 4.73 (dd, J = 12.8, 7.2 Hz, 1H), 4.52 (dd, J = 12.8, 7.6 Hz, 1H), 4.35–4.41 (m, 1H), 3.0–3.15 (m, 2H), 2.44 (s, 3H), 2.14–2.23 (m, 4H), 1.2–1.5 (m, 4H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.7, 141.2, 139.4, 135.3, 129.2, 116.2, 116.0, 79.9, 40.2, 39.0, 29.9, 26.3, 22.8, 22.0, 21.6 ppm. HRMS calculated for [$C_{17}H_{21}NO_3$ + H^+]: 288.1594, found: 288.1613. **HPLC:** Chiralpak IA column. Flow rate 1 mL min^{-1}. UV detection at 214 nm. τ(major) = 11.0, τ(minor) = 11.9 using hexane : isopropanol = 96 : 4 as the eluent, ee 58%.

1-Cyclohexenyl-3-(2,5-dimethoxyphenyl)-4-nitrobutan-1-one (3ae). Brown thick oil, 44.0 mg, 53% yield. **FT-IR** (KBr): 3448(m), 2921(s), 2850(m), 1712(w), 1551(s), 1502(m), 1225(m), **^{1}H NMR** (600 MHz, $CDCl_3$) δ_H 6.89 (s, 1H), 6.71–6.80 (m, 3H), 4.76 (apparent d, J = 6.8, 2H), 4.21 (t, J = 6.4, 1H), 3.83 (s, 3H), 3.74 (s, 3H), 3.15 (d, J = 7.2, 2H), 2.13–2.18 (broad doublet, 4H), 1.58–1.65 (m, 4H) ppm. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 198.5, 153.6, 151.4, 140.4, 139.2, 128.2, 115.8, 112.8, 111.9, 77.9, 55.8, 55.7, 38.3, 36.2, 26.1, 23.0, 22.6, 21.8 ppm, HRMS calculated for [$C_{18}H_{25}NO_5$ + H^+]: 334.1649, found: 334.1693, **HPLC:** Chiralpak AS-H column. Flow rate 1.2 mL min^{-1}. UV detection at 214 nm. τ(major) = 21, τ(minor) = 32 using hexane : isopropanol = 96 : 4 as the eluent, ee 60%.

1-Cyclohexenyl-3-(naphthalen-1-yl)-4-nitrobutan-1-one (3af). Light brown thick oil, 60.0 mg, 74% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 8.19 (d, J = 12, 1H), 7.88 (d, J = 12, 1H), 7.78 (d, J = 6, 1H), 7.59 (t, J = 18, 1H), 7.52 (t, J = 12, 1H), 7.42 (t, J = 18, 1H), 7.35 (d, J = 6, 1H), 6.88 (s, 1H), 4.81–4.88 (m, 2H), 3.48 (q, J = 7.2, 1H), 3.25 (d, J = 6.6, 2H), 2.19–2.21 (br s, 2H), 2.15–2.18 (br s, 2H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.0, 141.1, 139.3, 135.6, 134.3, 131.2, 129.3, 128.4, 127.0, 126.2, 125.4, 122.7, 79.0, 40.2, 32.1, 29.9, 26.3, 23.2, 22.0, 21.6 ppm. HRMS calculated for [$C_{20}H_{21}NO_3$ + H^+]: 324.1594, found: 324.1597. **HPLC:** Chiralpak AS-H column. Flow rate 1 mL min^{-1}. UV detection at 214 nm. τ(major) = 21.9, τ(minor) = 42.7 using hexane : isopropanol = 96 : 4 as the eluent, ee 58%.

1-Cyclohexenyl-3-(furan-2-yl)-4-nitrobutan-1-one (3ag). Yellow thick oil, 51.0 mg, 63% yield. **FT-IR** (KBr): 3441(s), 2921(s), 2852(w), 1713(s), 1551(s), 1020(m). **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.33 (s, 1H), 6.93 (s, 1H), 6.28 (s, 1H), 6.14 (s, 1H), 4.62–4.76 (m, 1H), 4.07–4.23 (m, 1H), 3.03–3.20 (m, 2H), 2.17–2.27 (br d, 4H) ppm. **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.6, 152.5, 142.3, 141.4, 139.3, 110.6, 107.2, 68.1, 37.7, 33.6, 26.3, 23.2, 22.0, 21.6 ppm. HRMS calculated for [$C_{14}H_{17}NO_4$ + H^+]: 264.1230, found: 264.1241. **HPLC:** Chiralpak AS-H column. Flow rate 1 mL min^{-1}. UV detection at 214 nm. τ(major) = 20, τ(minor) = 32 using hexane : isopropanol = 96 : 4 as the eluent, ee 62%.

1-Cyclohexenyl-5-methyl-3-(nitromethyl)hexan-1-one (3ah). Light yellow thick oil, 22.2 mg, 35% yield. **FT-IR** (KBr): 3443(m), 2923(m), 2852(w), 1728(s), 1613(s), 1457(m), 1289(m), **^{1}H NMR** (600 MHz, $CDCl_3$) δ_H 6.87 (s, 1H), 4.78 (dd, J = 12.6, 10.2 Hz, 2H), 4.61 (dd, J = 12.6, 4.2 Hz, 2H), 2.72–2.81 (m, 1H), 2.59–2.62 (d, 1H), 2.44–2.50 (m, 2H), 1.90–2.05 (m, 2H), 1.82–1.86 (t, 1H), 1.63–1.67 (q, 4H), 1.19–1.24 (t, 2H), 0.87–0.89 (d, 6H) ppm. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 200.8, 141.6, 139.6, 87.5, 43.3, 42.7, 26.1, 25.8, 23.3, 22.9, 22.7, 22.5, 22.0 ppm. HRMS calculated for [$C_{14}H_{23}NO_3$ + H^+]: 254.1751, found: 254.1789. **HPLC:** Chiralpak IA column. Flow rate 0.7 mL min^{-1}. UV detection at 254 nm. τ(major) = 34.4, τ(minor) = 37.9 using hexane : isopropanol = 95 : 5 as the eluent, ee 86%.

1-Cyclohexenyl-4,4-dimethyl-3-(nitromethyl)pentan-1-one (3ai). Light yellow thick oil, 23.5 mg, 37% yield. **FT-IR** (KBr): 3442(m), 2925(s), 2856(w), 1715(m), 1552(w), 1374(w), **^{1}H NMR** (600 MHz, $CDCl_3$) δ_H 6.91 (s, 1H), 4.50 (dd, J = 12.6, 4.8 Hz, 1H), 4.29 (dd, J = 12.6, 7.2 Hz, 1H), 2.77–2.83 (m, 1H), 2.62–2.70 (m, 2H), 2.29–2.21 (m, 2H), 1.62 (m, 4H), 0.94 (s, 9H) ppm.**^{13}C NMR** (151 MHz, $CDCl_3$) δ 199.2, 140.1, 139.4, 88.8, 42.5, 35.9, 27.6, 27.3, 27.1, 26.3, 23.5, 22.1 ppm. HRMS calculated for [$C_{14}H_{23}NO_3$ + H^+]: 254.1751, found: 254.1756. **HPLC:** Chiralpak IA column. Flow rate 0.7 mL min^{-1}. UV detection at 254 nm. τ(major) = 24.2, τ(minor) = 38.7 using hexane : isopropanol = 95 : 5 as the eluent, ee 73%.

1-Cyclohexenyl-3-cyclohexyl-4-nitrobutan-1-one (3aj). Light yellow thick oil, 26.0 mg, 37% yield. **FT-IR** (KBr): 3437(m), 2925(m), 2853(m), 1716(w), 1551(s), 1449(w), 1376(s), **^{1}H NMR** (600 MHz, $CDCl_3$) δ_H 6.96 (s, 1H), 4.67 (dd, J = 14.4, 2.4 Hz, 1H), 4.43 (dd, J = 14.4, 9 Hz, 1H), 2.66–2.68 (m, 1H), 2.20–2.27 (m, 4H), 2.00–2.04 (m, 4H), 1.62–1.65 (m, 4H), 0.94–1.23 (m, 11H) ppm. **^{13}C NMR** (151 MHz, $CDCl_3$) δ 203.8, 142.1, 141.7, 75.5, 41.2, 38.6, 32.1, 29.9, 26.7, 26.5, 25.1, 23.6, 22.9, 22.1, 21.6 ppm. HRMS calculated for [$C_{16}H_{25}NO_3$ + H^+]: 280.1907, found: 280.2012. **HPLC:** Chiralpak IA column. Flow rate 1 mL min^{-1}. UV detection at 254 nm. τ(major) = 7.2, τ(minor) = 13.0 using hexane : isopropanol = 96 : 4 as the eluent, ee 72%.

1-Cyclopentenyl-4-nitro-3-phenylbutan-1-one (3ba). White thick oil, 48 mg, 74% yield. **FT-IR** (KBr): 3439(s), 2955(w), 2923(m), 2853(w), 1710(w), 1548(s), 1377(w), **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.05–7.39 (m, 5H), 6.7 (s, 1H), 4.79 (dd, J = 12.4, 6.4 Hz, 1H), 4.61 (dd, J = 12.4, 8.4 Hz, 1H), 4.02–4.12 (m, 1H), 3.03–3.2 (m, 3H), 2.48–2.58 (m, 4H), 1.84–1.95 (m, 4H) ppm. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 195.6, 145.6, 144.7, 139.4, 129.2, 127.6, 127.2, 79.7, 42.0, 39.6, 34.2, 30.7,

22.8 ppm, HRMS calculated for $[C_{15}H_{17}NO_3 + H^+]$: 260.1281, found: 260.1259. **HPLC:** Chiralpak IA column. Flow rate 1 mL min^{-1}. UV detection at 214 nm. τ(major) = 15.4, τ(minor) = 19.9 using hexane : isopropanol = 96 : 4 as the eluent, ee 54%.

1-Cyclopentenyl-3-(4-methoxyphenyl)-4-nitrobutan-1-one (3bc). Yellow thick oil, 38 mg, 53% yield. **FT-IR** (KBr): 3437(m), 2922(s), 2852(w), 1737(s), 1458(m), 1275(m), 1260(m), **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.14 (d, 2H), 6.85 (d, 2H), 6.73 (s, 1H), 4.72 (dd, J = 16, 6.4 Hz, 1H), 4.56 (dd, J = 16, 8 Hz, 1H), 4.00–4.05 (m, 1H), 3.77 (s, 3H), 3.03–3.15 (m, 2H), 2.49–2.55 (m, 4H), 1.89–1.92 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 195.6, 159.2, 144.6, 142.9, 128.7, 114.9, 144.6, 80.0, 55.5, 42.2, 39.0, 34.2, 30.8, 22.9 ppm. HRMS calculated for $[C_{16}H_{19}NO_4 + H^+]$: 290.1387, found: 290.1368. HPLC: Chiralpak IA column. Flow rate 1 mL min^{-1}. UV detection at 214 nm. τ(major) = 20, τ(minor) = 32 using hexane : isopropanol = 96 : 4 as the eluent, ee 77%.

1-Cyclopentenyl-4-nitro-3-*o*-tolylbutan-1-one (3bd). White thick oil, 48.4 mg, 71% yield. **FT-IR** (KBr): 3443(s), 2955(w), 2923(s), 2853(w), 1662(w), 1551(s), 1376(w), **^{1}H NMR** (600 MHz, $CDCl_3$) δ_H 7.10–7.25 (m, 4H), 6.75 (s, 1H), 4.72 (dd, J = 12.6, 7.2 Hz, 1H), 4.61 (dd, J = 12.6, 7.8 Hz, 1H), 4.39–4.42 (m, 1H), 3.9 (m, 1H), 3.15–3.22 (m, 1H), 2.5–2.62 (m, 4H), 1.9–2.0 (m, 3H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$) δ = 195.6, 145.6, 144.6, 137.7, 136.7, 131.4, 127.6, 126.1, 125.6, 79.3, 42.0, 34.2, 29.9, 22.9, 19.8 ppm. HRMS calculated for $[C_{16}H_{19}NO_3 + H^+]$: 274.1438, found: 274.1411 **HPLC:** Chiralpak AS-H column. Flow rate 1 mL min^{-1}. UV detection at 214 nm. τ(major) = 17.3, τ(minor) = 26.3 using hexane : isopropanol = 96 : 4 as the eluent, ee 70%.

1-Cyclopentenyl-5-methyl-3-(nitromethyl)hexan-1-one (3bh). Light yellow thick oil, 21 mg, 35% yield. **FT-IR** (KBr): 3448(m), 2924(m), 2854(w), 1660(s), 1551(s), 1377(w), **^{1}H NMR** (600 MHz, $CDCl_3$) δ_H 6.70 (s, 1H), 4.85 (dd, J = 13.8, 2.4 Hz, 1H), 4.50 (dd, J = 13.8, 5.4 Hz, 1H), 2.79–2.84 (m, 1H), 2.69–2.66 (m, 2H), 2.59–2.61 (m, 2H), 2.54–2.57 (m, 2H), 2.26–2.31 (m, 1H), 1.94–1.98 (m, 2H), 1.20 (t, J = 6.6 Hz, 2H), 0.91 (d, J = 6.6 Hz, 6H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$) δ 192.7, 155.5, 145.5, 142.4, 78.6, 43.9, 40.8, 34.5, 30.7, 25.4, 25.3, 23.3, 23.1, 22.9 ppm. HRMS calculated for $[C_{13}H_{21}NO_3 + H^+]$: 240.1594, found: 240.1623. HPLC: Chiralpak IA column. Flow rate 0.7 mL min^{-1}. UV detection at 254 nm. τ(major) = 19.6, τ(minor) = 27.5 using hexane : isopropanol = 95 : 5 as the eluent, ee 70%.

1-Cyclobutenyl-4-nitro-3-phenylbutan-1-one (3ca). Yellow thick oil. 59% yield (36 mg, 0.15 mmol). **FT-IR** (KBr): 2925(s), 2854(w), 1729(s), 1557(s), 1456(m), 1378(m). **^{1}H NMR** (600 MHz, $CDCl_3$) δ_H 7.32–7.27 (m, 5H), 7.17 (s, 1H), 4.91 (dd, J = 8, 4.8, 1H), 4.76 (dd, J = 8.0, 2.0, 1H), 3.40–3.35 (m, 1H), 3.30–3.25 (m, 1H), 2.40 (br d, J = 17.2, 1H), 1.43–1.35 (m, 4H), ^{13}C NMR (151 MHz, $CDCl_3$) δ 201.5, 129.6, 129.5, 129.2, 129.0, 127.9, 127.3, 80.6, 43.1, 32.1, 31.9, 29.6, 22.9, 19.5. HRMS calculated for $[C_{14}H_{15}NO_3 + H^+]$: 246.1125, found: 246.1147. **HPLC:** Chiralpak IA column. Flow rate 1 mL min^{-1}. UV detection at 214 nm. τ(major) = 30.7, τ(minor) = 35.3 using hexane : isopropanol = 99 : 1 as the eluent, ee 58%.

Procedure for base mediated cyclization of compound 3

1,1,3,3-Tetramethylguanidine (0.095 mmol, 1 eq.) is added to a solution of **3** (0.095 mmol, 1 eq.) in dichloromethane at 0 °C. The solution is then allowed to stir for 24 h at room temperature. The crude is subjected to column chromatographic separation (3% ethyl acetate in petroleum ether) to obtain a pure cyclized product.

4-Nitro-3-phenyloctahydronaphthalen-1(2*H*)-one (4a + 4b = 4 : 1). Colorless crystalline solid. 84% overall yield (22 mg, 0.8 mmol). Melting point 166–167 °C. **FT-IR** (KBr): 2933(s), 2854(m), 1721(s), 1547(s), 1456(w), 1445(w), 1364(w), **^{1}H NMR** (600 MHz, $CDCl_3$) δ_H 7.18–7.37 (m, 5H), 5.33 (dd, J = 10.8, 3.6, 0.25H, C*H*NO_2), 4.84 (apparent t, J = 10.8, 1H), 3.84 (dt, J = 12.4, 5.6, 0.25H, C*H*Ph), 3.60 (dt, J = 12.4, 5.6, 1H), 2.84–2.87 (m, 0.5H, H10), 2.65–2.75 (m, 2H), 2.49–2.54 (m, 0.25H, H9), 2.07–2.25 (m, 3H), 1.71–1.93 (m, 3H), 1.18–1.41 (m, 5H) ppm. **^{1}H NMR** (400 MHz, C_6D_6) δ_H 6.89–7.07 (m, 7H), 4.8 (dd, J = 10.8, 3.6, 0.25H, C*H*NO_2), 4.30 (apparent t, J = 10.8, 1H), 3.52 (dt, J = 12.4, 5.6, 0.25H, C*H*Ph), 3.20 (dt, J = 12.4, 5.6, 1H), 2.33 (two pseudo AB quartet, 14.8, 2H), 2.21, 1.84 (two pseudo AB quartet, 13.6, 0.5H), 1.95–1.98 (d, J = 12.4, 1H), 1.73 (q, J = 10.8, 1H) ppm.**^{13}C NMR** (150 MHz, $CDCl_3$) 206.5, 137.9, 129.4, 128.5, 127.1, 95.0, 51.3, 48.1, 46.3, 45.9, 30.3, 25.1, 24.9, 24.7 ppm. HRMS calculated for $[C_{16}H_{19}NO_3 + H^+]$: 274.1438, found: 274.1434. **HPLC:** Chiralpak IA column. Flow rate 1 mL min^{-1}. UV detection at 254 nm. τ(major) = 18.6, τ(minor) = 23.1 using hexane : isopropanol = 96 : 4 as the eluent, ee 75%. Recrystallized using chloroform–hexane as the solvent in 73% yield (from **3aa**). After recrystallization ee was 94%.

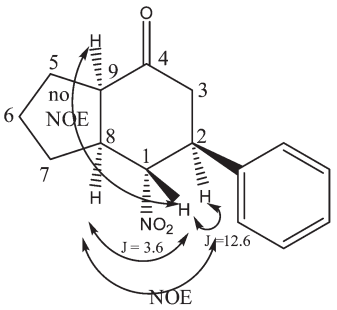
3-(4-Fluorophenyl)-4-nitrooctahydronaphthalen-1(2H)-one (4c). Colourless crystalline solid. 81% overall yield (22 mg, 0.077 mmol). **FT-IR** (KBr): 2927(s), 2852(w), 1719(s), 1561(s). **^{1}H NMR** (600 MHz, $CDCl_3$) δ_H 7.25–7.22 (m, 0.5H), 7.20–7.17 (m, 2H), 7.04–7.01 (t, J = 9, 2H), 5.27 (dd, J = 12.4, 4.2, 0.3H), 4.78 (t, J = 10.6, 1H), 3.86–3.81 (m, 0.3H), 3.61–3.56 (m, 1H), 2.70–2.64 (m, 2H), 2.48 (apparent t, J = 14.4, 0.3H), 2.34 (br d, J = 12.6, 0.3H), 2.22 (dt, J = 10.8, 3.6, 1H), 2.16–2.08 (m, 2H), 1.89–1.86 (m, 1H), 1.83–1.80 (m, 1H), 1.73 (br d, J = 6.6, 4H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 206.2, 133.7, 128.8, 128.8, 116.5, 116.3, 95.1, 51.3, 47.3, 46.3, 45.9, 30.28, 25.1, 24.9, 24.7 ppm. HRMS calculated for $[C_{16}H_{18}FNO_3 + H^+]$: 292.1343, found: 292.1347. **HPLC:** Chiralpak IA column. Flow rate 0.8 mL min^{-1}. UV detection at 214 nm. τ(major) = 30.7, τ(minor) = 35.3 using hexane : isopropanol = 95 : 5 as the eluent, ee 54%.

1′-Nitro-2′,3′,4′a,5′,6′,7′,8′,8′a-octahydro-1,2′-binaphthyl-4′(1′*H*)-one (4e). White crystalline solid. 75% overall yield (23 mg, 0.07125 mmol). **FT-IR** (KBr): 2926(s), 2856(w), 1708(s), 1552(s). **^{1}H NMR** (600 MHz, $CDCl_3$) δ_H 8.15 (d, J = 8.4, 0.25H), 8.05 (d, J = 8.4, 1H), 7.86 (t, J = 8.4, 1H), 7.78 (d, J = 8.4, 1H), 7.58–7.52 (m, 2H), 7.52–7.48 (m, 2H), 7.45 (d, J = 2.4, 0.24H), 7.43 (s, 0.25H), 5.67 (dd, J = 12, 4.8, 0.25H), 5.21 (t, J = 10.2, 1H), 4.81 (dt, J = 12.4, 4.8, 0.25H), 4.63 (dt, J = 13.8, 4.8, 1H), 2.87 (d, J = 5.4, 0.24H), 2.83 (dd, J = 15.0, 4.8, 1H), 2.66 (t, J = 13.8, 1H), 2.46 (t, J = 14.4, 0.25H), 2.32–2.25 (m, 2H), 2.15 (br d, J = 13.2,

1H), 1.93–1.89 (m, 1H), 1.86–1.83 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 206.5, 134.4, 130.0, 129.3, 128.8, 128.5, 127.1, 126.3, 125.6, 123.0, 122.9 ppm. HRMS calculated for [$C_{20}H_{21}NO_3$ + H^+]: 324.1594, found: 324.1589. **HPLC:** Chiralpak IA column. Flow rate 1 mL min^{-1}. UV detection at 214 nm. τ(minor) = 22.7, τ(major) = 31.0 using hexane : isopropanol = 96 : 4 as the eluent, ee 56%.

3-(Furan-2-yl)-4-nitrooctahydronaphthalen-1(2*H*)-one (4g). Colourless crystalline solid. 73% overall yield (18 mg, 0.069 mmol). **FT-IR** (KBr): 2922(s), 2855(w), 1722(s), 1551(s). **^{1}H NMR** (600 MHz, $CDCl_3$) δ_H 7.36 (d, J = 1.8, 1H), 7.32 (d, J = 1.8, 0.16H), 6.28 (d, J = 1.8, 1H), 6.16 (d, J = 3, 0.16H), 6.12 (d, J = 3.0, 1H), 5.28 (dd, J = 12, 4.2, 0.16H), 4.83 (t, J = 10.8, 1H), 4.01 (dt, J = 12, 7.2, 0.16H), 3.73–3.79 (m, 1H), 2.85 (dt, J = 16.8, 1.2, 1H), 2.74–2.68 (m, 1.5H), 2.21–2.16 (m, 1H), 2.12–2.05 (m, 2H), 1.87–1.84 (m, 1H), 1.81–1.78 (m, 1H), 1.73 (br d, 1H), 1.36–1.27 (m, 2H), 1.23–1.19 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 206.1, 150.8, 143.0, 110.7, 107.7, 93.3, 51.0, 45.3, 43.3, 41.3, 30.3, 25.0, 24.8, 24.7 ppm. HRMS calculated for [$C_{14}H_{16}NO_4$ + H^+]: 263.1158, found: 263.1154. **HPLC:** Chiralpak IA column. Flow rate 0.8 mL min^{-1}. UV detection at 214 nm. τ(minor) = 24.8, τ(major) = 33.4 using hexane : isopropanol = 95 : 5 as the eluent, ee 70% after crystallisation.

7-Nitro-6-phenylhexahydro-1*H*-inden-4(2*H*)-one (5). Colorless solid. 87% yield (21 mg, 0.83 mmol). **FT-IR** (KBr): 2923 (s), 2852(m), 1712(m), 1629(m), 1548(m), 1454(w), 1384(w), 1265(w), 1019(m). **^{1}H NMR** (600 MHz, $CDCl_3$) δ_H 7.18–7.37 (m, 5H, Ph), 5.00 (t, J = 3.6, 1H, C*H*NO_2), 3.66–3.71 (td, J = 12.8, 4.8, 1H, C*H*Ph), 3.41 (dd, J = 2.4, 12.6, 1H), 3.22–3.24 (m, 1H, H9), 2.93 (m, 1H, H8), 2.65 (dd, J = 10.6, 4.8, 1H), 2.36–2.39 (m, 1H),1.99–2.02 (m, 1H), 1.75–1.82 (m, 2H), 1.39–1.46 (m, 1H) ppm. **^{13}C NMR** (150 MHz, $CDCl_3$): 206.8, 129.3, 128.5, 127.3, 100.2, 89.43, 49.8, 45.0, 42.7, 40.6, 30.2, 29.9, 25.9, 22.6 ppm. HRMS calculated for [$C_{15}H_{17}NO_3$ + H^+]: 260.1281, found: 260.1259 **HPLC:** Chiralpak IA column. Flow rate 1 mL min^{-1}. UV detection at 214 nm. τ(major) = 13.7, τ(minor) = 18.1 using hexane : isopropanol = 96 : 5 as the eluent, ee 56%.



4-Chloro-*N*-(4-cyclohexyl-4-hydroxy-2 phenylbutyl)benzenesulfonamide (6). White crystalline solid. 50% overall yield (13 mg, 0.07125 mmol). **FT-IR** (KBr): 2925(s), 2853(w), 1350(s), 1164(s), 1092(s), 1013(s). **^{1}H NMR** (600 MHz, $CDCl_3$) δ_H 7.83 (d, J = 7.8, 2H), 7.52 (d, J = 7.8, 2H), 7.28 (t, J = 7.8, 2H), 7.23 (d, J = 3.2, 1H), 7.06 (m, J = 7.2, 2H), 3.89 (dd, J = 12, 6.6, 2H), 3.76 (dd, J = 14.4, 7.2, 1H), 3.16 (t, J = 12, 1H), 2.57–2.50 (m, 1H), 2.17 (dd, J = 7.8, 3.6, 1H), 1.82 (dd, J = 11.4, 3.6, 1H), 1.64–1.60 (m, 1H), 1.16–1.14 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.6, 139.4, 137.8, 129.7, 129.0, 128.9, 127.3, 127.2, 65.6, 55.7, 43.6, 42.6, 35.1, 31.8, 30.3, 26.8, 26.6, 26.4, 26.2 ppm. HRMS calculated for [$C_{22}H_{28}ClNO_3S$ + H^+]: 422.1551, found: 422.1579. **HPLC:** Chiralpak OJ column. Flow rate 1 mL min^{-1}. UV detection at 254 nm. τ(major) = 18.3, τ(minor) = 27.6 using hexane : isopropanol = 97 : 3 as the eluent, ee 69%.

Acknowledgements

We thank the Board of Research in Nuclear Sciences, India for the DAE Young Scientist Research Award to S. C. P. We also thank the Central Instruments Facility, IIT Guwahati for instrumental facility.

Notes and references

1 For selected reviews, see: (*a*) B. List, *Chem. Commun.*, 2006, 819; (*b*) S. Mukherjee, J. W. Yang, S. Hoffmann and B. List, *Chem. Rev.*, 2007, **107**, 5471; (*c*) P. M. Pikho, I. Majander and A. Erkkilä, in *Asymmetric Organocatalysis*, ed. B. List, Springer-Verlag, Heidelberg, 2010, vol. 291, pp. 29–75.

2 B. List, R. A. Lerner and C. F. Barbas III, *J. Am. Chem. Soc.*, 2000, **122**, 2395.

3 B. List, *J. Am. Chem. Soc.*, 2000, **122**, 9336.

4 For a timely review, see: D. B. Ramachary and Y. V. Reddy, *Eur. J. Org. Chem.*, 2012, 865.

5 For selected examples, see: (*a*) X. Wu, M.-L. Li, D.-F. Chen and S.-S. Chen, *J. Org. Chem.*, 2014, **79**, 4743; (*b*) E. Masalo, M. Benaglia, R. Annunziata, A. Palmieri, G. Celentano and A. Forni, *Adv. Synth. Catal.*, 2014, **356**, 495; (*c*) M. P. Lalonde, M. A. McGowan, N. S. Rajapaksa and E. N. Jacobsen, *J. Am. Chem. Soc.*, 2013, **135**, 1891; (*d*) Y. Liu, T.-R. Kang, Q.-Z. Liu, L.-M. Chen, Y.-C. Wang, J. Liu, Y.-M. Xie, J.-L. Yang and L. He, *Org. Lett.*, 2013, **15**, 6090; (*e*) G. Bencinenni, L.-Y. Wu, A. Mazzanti, B. Giannichi, F. Pesciaioli, M.-P. Song, G. Bartoli and P. Melchiorre, *Angew. Chem., Int. Ed.*, 2009, **121**, 7336; (*f*) D.-Q. Xu, A.-B. Xia, S.-P. Luo, J. Tang, S. Zhang, J.-R. Jiang and Z.-Y. Xu, *Angew. Chem., Int. Ed.*, 2009, **48**, 3821; (*g*) H. Yang and R. G. Carter, *J. Org. Chem.*, 2009, **74**, 5151; (*h*) T. Itoh, M. Yokoya, K. Miyauchi, K. Nagata and A. Ohsawa, *Org. Lett.*, 2006, **8**, 1533; (*i*) H. Sundén, I. Ibrahem, L. Eriksson and A. Córdova, *Angew. Chem., Int. Ed.*, 2005, **44**, 4877; (*j*) Y. Yamamoto, N. Momiyama and H. Yamamoto, *J. Am. Chem. Soc.*, 2004, **126**, 5962; (*k*) D. B. Ramachary, N. S. Chowdhari and C. F. Barbas III, *Angew. Chem., Int. Ed.*, 2003, **42**, 4233.

6 (*a*) X. Tian, C. Cassani, Y. Liu, A. Moran, A. Urakawa, P. Galzerano, E. Arceo and P. Melchiorre, *J. Am. Chem. Soc.*, 2011, **133**, 17934; (*b*) N. Fu, L. Zhang, S. Luo and J.-P. Cheng, *Org. Lett.*, 2014, **16**, 4626; (*c*) N. Fu, L. Zhang, S. Luo and J.-P. Cheng, *Org. Chem. Front.*, 2014, **1**, 68;

(*d*) N. Fu, L. Zhang, S. Luo and J.-P. Cheng, *Chem. – Eur. J.*, 2013, **19**, 15669.

7 For a single example of catalytic asymmetric addition of α-branched enones to imines, see ref. 5*c*.

8 For reviews on organocatalytic asymmetric Michael additions, see: (*a*) Y. Zhang and W. Wang, *Catal. Sci. Technol.*, 2012, **2**, 42; (*b*) M. Thirumalaikumar, *Org. Prep. Proced. Int.*, 2011, **43**, 67; (*c*) J. L. Vicario, D. Badia and L. Carrillo, *Synthesis*, 2007, 2065; (*d*) D. Almasi, D. A. Alonso and C. Najera, *Tetrahedron: Asymmetry*, 2007, **18**, 299; (*e*) S. B. Tsogoeva, *Eur. J. Org. Chem.*, 2007, 1701.

9 (*a*) C. Lin, H. Fang, Z. Tu, J.-T. Liu and C.-F. Yao, *J. Org. Chem.*, 2006, **71**, 6588; (*b*) F. Richter and H.-H. Otto, *Tetrahedron Lett.*, 1987, **28**, 2945; (*c*) C. Veyrat, L. Wartski and J. Seyden-Penne, *Tetrahedron Lett.*, 1986, **27**, 2981; (*d*) G. Pitaco, A. Risaliti, M. L. Trevisan and E. Valentin, *Tetrahedron*, 1977, **33**, 3145.

10 M. Moger, A. K. Pradhan, R. M. Hindupur and H. N. Pati, *Tetrahedron Lett.*, 2014, **55**, 2675.

11 For a different method producing related structures, see: (*a*) P. He, X. Liu, J. Shi, L. Lin and X. Feng, *Org. Lett.*, 2011, **13**, 936–939. For a recent report on ε-selective asymmetric bisvinylogous Michael addition with 2,5-cyclic dienones, see: (*b*) Z. Zhou, X. Feng, X. Yin and Y.-C. Chen, *Org. Lett.*, 2014, **16**, 2370. For a recent report on δ-regioselective Michael addition with cyclohexenylidene malonitriles, see: (*c*) L. Dell'Amico, G. Rassu, V. Zambrano, A. Sartori, C. Curti, L. Battistini, G. Pelosi, G. Casiraghi and F. Zanardi, *J. Am. Chem. Soc.*, 2014, **136**, 11107.

12 For recent reviews, see: (*a*) P. Melchiorre, *Angew. Chem., Int. Ed.*, 2012, **51**, 9748; (*b*) L. Jiang and Y.-C. Chen, *Catal. Sci. Technol.*, 2011, **1**, 354; (*c*) L.-W. Xu, J. Luo and Y. Lu, *Chem. Commun.*, 2009, 1807; (*d*) Y.-C. Chen, *Synlett*, 2008, 1919; (*e*) G. Bartoli and P. Melchiorre, *Synlett*, 2008, 1759.

13 Y. Hoashi, T. Yabuta and Y. Takemoto, *Tetrahedron Lett.*, 2004, **45**, 9185.

14 CCDC 1033099 contains the crystallographic data for **4a** (available also in the ESI†).

15 A. R. Brown, W.-H. Kuo and E. N. Jacobsen, *J. Am. Chem. Soc.*, 2010, **132**, 9286.

16 T. He, J.-Y. Qian, H.-L. Song and X.-Y. Wu, *Synlett*, 2009, 3195.

17 W. Yang and D.-M. Du, *Adv. Synth. Catal.*, 2011, **353**, 1241.

18 B. Vakulya, S. Varga, A. Csámpai and T. Soós, *Org. Lett.*, 2005, **7**, 1967.

19 W. Chen, W. Du, Y.-Z. Duan, Y. Wu, S.-Y. Yang and Y.-C. Chen, *Angew. Chem., Int. Ed.*, 2007, **46**, 7667.

20 (*a*) D. M. Mampreian and A. H. Hoveyda, *Org. Lett.*, 2004, **6**, 2829; (*b*) O. Bassas, J. Huuskonen, K. Rissanen and A. M. P. Koskinen, *Eur. J. Org. Chem.*, 2009, 1340; (*c*) B. M. Trost and C. Mueller, *J. Am. Chem. Soc.*, 2008, **130**, 2438.