Supporting Information-I

Asymmetric Synthesis of Tetrahydroquinolines through Supramolecular Organocatalysis

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General Methods: The ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz, respectively. The chemical shifts are reported in ppm downfield to TMS ($\delta = 0$) for ^{1}H NMR and relative to the central $CDCl_3$ resonance ($\delta = 77.0$) for ^{13}C NMR. *In the ^{13}C NMR spectra, the nature of the carbons (C, CH, CH_2 or CH_3) was determined by recording the DEPT-135 experiment, and is given in parentheses.* The coupling constants *J* are given in Hz. Column chromatography was performed using Acme's silica gel (particle size 0.063-0.200 mm). High-resolution mass spectra (HRMS) were recorded on ESI-TOF maXis. GCMS mass spectrometry was performed on Shimadzu GCMS-QP2010 mass spectrometer. IR spectra were recorded on JASCO FT/IR-5300. Mass spectra were recorded on either VG7070H mass spectrometer using EI technique or Shimadzu-LCMS-2010 A mass spectrometer. The X-ray diffraction measurements were carried out at 298 K on an automated Enraf-Nonious MACH 3 diffractometer using graphite monochromated, Mo-Kα (λ = 0.71073 Å) radiation with CAD4 software or the X-ray intensity data were measured at 298 K on a Bruker SMART APEX CCD area detector system equipped with a graphite monochromator and a Mo-Kα fine-focus sealed tube (λ = 0.71073 Å). For thin-layer chromatography (TLC), silica gel plates Merck 60 F254 were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. H_2SO_4 (35 mL), acetic acid (10 mL), and ethanol (900 mL) followed by heating.

Materials: All solvents and commercially available chemicals were used as received. Functionalized (*E*)-1-azido-2-(2-nitrovinyl) benzene **1a-h** was prepared according to the literature procedure.[1]

General Experimental Procedures

Procedure A: **General procedure for asymmetric Michael reaction of acetone 2 with 1-azido-2-(2-nitrovinyl)benzene 1 or (*E*)-β-nitrostyrene 7 through supramolecular-organocatalysis:** In an ordinary glass vial equipped with a magnetic stirring bar was taken a mixture of quinidine-N*H*-thiourea **3c** (8.9 mg, 0.015 mmol) and L-phenylalanine **4i** (2.5 mg, 0.015 mmol) in DCM (1.0 mL, 0.3 M) and was added 1-azido-2-(2-nitrovinyl)benzene **1** or (*E*)-β-nitrostyrene **7** (0.3 mmol). After stirring for a minute, acetone **2** (4.2 mmol) was added and the reaction mixture was stirred at 25 °C for 3 days. To the crude reaction mixture, aqueous NH_4Cl solution was added and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure products **5** or **8** were obtained through column chromatography (silica gel, mixture of hexane/ethyl acetate).

Procedure B: General procedure for the reductive cyclization of Michael products 5: In an oven dried round bottom flask, containing $InCl_3$ (2.2 mmol) and triethylsilane (0.07 mL, 0.4 mmol) in MeOH (2 mL, 0.05 M) at 0 °C was added the Michael product **5** (0.2 mmol) dissolved in MeOH. The mixture was stirred at the same temperature for 2 h and then brought to room temperature and stirred for another 10 h. To the crude reaction mixture was added water and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure tetrahydroquinolines **6** were purified by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Procedure C: General procedure for the preparation of *N*-methyl-tetrahydroquinoline 9aa from 6aa: Pure tetrahydroquinoline **6aa** (20 mg, 0.1 mmol) was taken in a 1:1 ratio of H_2O and EtOAc (1.0 mL, 0.1 M). To this solution was added sodium bicarbonate (10 mg, 0.12 mmol), and then dimethyl sulfate (0.01 mL, 0.12 mmol) was added drop wise. The mixture was stirred at 25 °C for 13 h. To the crude reaction mixture was added saturated $NaHCO_3$ solution and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure product **9aa** was purified by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Procedure D: General procedure for the preparation of chiral triazole 10ba-d_7 from the Michael product 5ba-d_7: To the pure Michael product **5ba-d_7** (20 mg, 0.07 mmol) in H_2O (1.0 mL, 0.07 M), were added phenyl acetylene (0.02 mL, 0.15 mmol), $CuSO_4.5H_2O$ (6.7 mg, 60 mol-%) and Na-(+)-ascorbate (5.5 mg, 40 mol-%) and stirred at 25 °C for 24 h. To the crude reaction mixture was added aqueous NH_4Cl solution and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure

chiral triazole product **10ba-d$_7$** was purified by column chromatography (silica gel, mixture of hexane/ethyl acetate).

Procedure E: General procedure for the preparation of 2-methylquinoline 12 from the Michael product (±)-5aa: In an oven dried round bottom flask, containing pure Michael product (±)-**5aa** (0.15 mmol) in MeOH (1 mL, 0.15 M) at 25 °C were added Et_3N (2.5 equiv.) and 1, 3- propanedithiol (2.5 equiv.) and the mixture was stirred at the same temperature for 2 h. To the crude reaction mixture was added aqueous NH_4Cl solution and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried (Na_2SO_4), filtered and concentrated. Pure product **12** was purified by column chromatography (silica gel, mixture of hexane/ethyl acetate).

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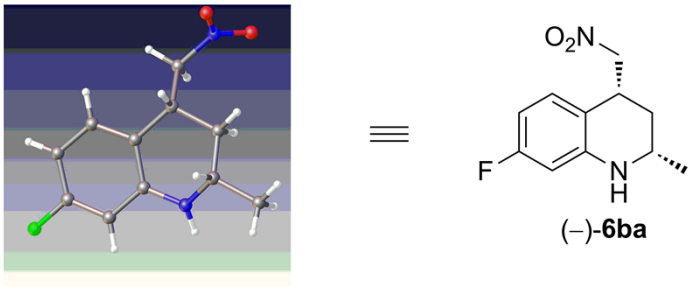
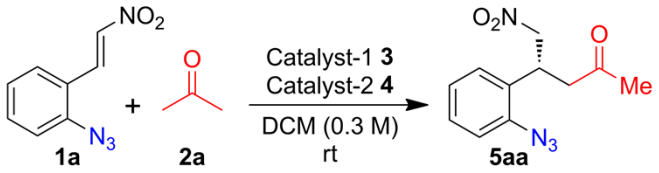


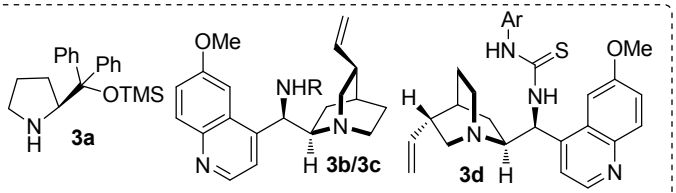
Figure S1: X-Ray crystal stucture of chiral (2*S*,4*R*)-7-fluoro-2-methyl-4-(nitromethyl)-1,2,3,4-tetrahydroquinoline (**6ba**) [*Flack parameter = –0.1*].

Table S1: Advanced Optimization through Supramolecular Catalysis[a]



Entry	Catalyst **3**/**4** (each 5 mol%)	Time (h)	Yield[b] (%) of **5aa**	ee[c] (%) of **5aa**
1	**3c**/**4b**	48	96	16
2	**3d**/**4b**	28	85	24
3	**3c**/**4c**	108	<5	–
4	**3c**/**4d**	72	<5	–
5	**3c**/**4e**	60	30	86
6	**3c**/**4f**	72	<10	–
7	**3c**/**4g**	108	45	92
8	**3c**/**4h**	72	<10	–
9	**3c**/**4i**	72	90	92
10[d]	**3c**/**4i**	72	46	92
11	**3d**/**4i**	96	30	9
12[e]	**3c**/**4j**	144	27	94
13	**3c**/**4j**	72	17	95
14	**3c**/**4k**	60	<10	–
15	**3c**/**4l**	60	<10	–
16	**3c**/**4m**	48	96	80
17	**3c**/**4n**	72	22	87
18	**3c**/**4o**	60	<10	–
19	**3c**/**4p**	108	20	92

[a] Unless otherwise mentioned, all reactions were carried out with (*E*)-1-azido-2-(2-nitrovinyl)benzene **1a** (0.3 mmol), acetone **2a** (4.2 mmol, 14 equiv.), catalysts **3** and **4** (5 mol% each) in DCM at rt. [b] Yield refers to the column purified product. [c] Ee was determined by CSP HPLC analysis. [d] Toluene (0.3 M) was used. [e] Benzene (0.3 M) was used.



3b: R = H and **3c:** R = CSNHAr; Ar = 3,5-$(CF_3)_2C_6H_3$

L-Proline **4a**, D-Proline **4b**, *trans*-4-Hydroxy-L-proline **4c**, L-Alanine **4d**, L-Cysteine **4e**, L-Histidine **4f**, L-Isoleucine **4g**, L-Leucine **4h**, L-Phenylalanine **4i**, L-Phenylglycine **4j**, L-Serine **4k**, L-Threonine **4l**, O-*tert*-Butyl-L-threonine **4m**, L-Tryptophan **4n**, L-Tyrosine **4o**, L-Valine **4p** and Methyl L-phenylalaninate **4q**

Library of catalysts used in this study

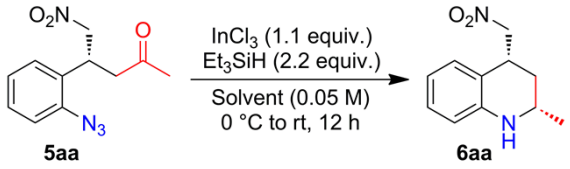
Advanced Optimization through Supramolecular Organocatalysis (Table S1): Results and Discussion:

Recently, asymmetric supramolecular-organocatalysis is becoming a novel tool for achieving high asymmetric induction and faster reaction rates from the reactions involving highly functionalized starting materials when compared to organocatalysis.[2] *Disappointingly, when we first performed the Michael reaction of* ***1a*** *and* ***2a*** *with known supramolecular assembly catalysts of Ramachary's* ***3d/4b***[2e] *or* Zhao's ***3c/4j***,[2b] *we ended up with either less yield or less ee (Table S1, entries 2, 12 and 13).* To overcome this problem, we thought of screening different supramolecular catalysts, assembled *in situ* from the standard organocatalysts **3** and **4** as shown in the Table S1. To verify this approach, we examined the Michael reaction of **1a** and 14 equiv of **2a** in the presence of each 5 mol % of quinidine-*N*H-thiourea **3c** or quinine-*N*H-thiourea **3d** with commercially available amino acids **4a-p** in DCM at 25 °C. After thorough investigation of the asymmetric Michael reaction of **1a** and **2a** under the catalysis of supramolecular assembly, *in situ* generated from **3c** or **3d** with sixteen amino acids **4a-p**; we got interesting results that the amino acids L-cysteine **4e**, L-isoleucine **4g**, L-phenylglycine **4j**, L-tryptophan **4n** or L-valine **4p** on combination with **3c** furnished the keto azide (–)-**5aa** in moderate to poor yields with high enantioselectivity (Table S1, entries 5, 7, 12, 13, 17 and 19). The same reaction under the combination of **3c** with amino acids L-phenylalanine **4i** or O-*tert*-butyl-L-threonine **4m** gave the keto azide (–)-**5aa** in 90-96% yield with high enantioselectivity within 2-3 days (Table S1, entries 9 and 16).

To investigate the topology of pre-transition state supramolecular assembly, we performed the Michael reaction with opposite catalysts combination of L-phenylalanine **4i** and quinine-*N*H-thiourea **3d**. The reaction furnished the opposite enantiomer of **5aa** in 30% yield with only 9% *ee* (Table S1, entry 11). When the combination of the catalysts was changed to **3d** and **4i**, there were no cooperative weak interactions observed between the catalysts and the product **5aa** was delivered in poor *ee* (9%) and low yield (30%) even after prolonged reaction time (Table S1, entry 11). These results clearly support the hypothesis that highly organized supramolecular assembly is involving in the pre-transition state of the Michael reaction to achieve high enantioselectivity.[2]

Finally, the best optimized condition for the asymmetric Michael reaction of **1a** and **2a** seems to be through **3c/4i**-catalysis in DCM at 25 °C for 72 h, which furnished the chiral keto-azide (–)-**5aa** in 90% yield with 92% *ee* (Table S1, entry 9).

***Table S2*: Optimization for the Reductive Amination of 5aa**



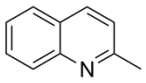
5aa **6aa**

Entry	Solvent	Yield[a]	dr[b]
1	CH_3CN	41	1:2
2	EtOH	45	1:5
3	MeOH	60	1:6

[a] Yield refers to the column-purified product. [b] dr was determined based on ^{1}H NMR or HPLC analysis.

***Table S3*: Optimization for aza-Wittig Reaction**

(±)-**5aa** **11**

Entry	Reagents and Conditions	Yield[a]
1	PBu_3 (1.1 equiv.) toluene (0.1 M), rt, 48 h 50 °C, 12 h	No reaction
2	*P*-TSA (20 mol%) DCM (0.1 M) rt, 24 h	No reaction
3	$Sc(OTf)_3$ (20 mol%) DCM (0.12 M) 0 °C to rt, 24 h	No reaction
4	$BF_3.Et_2O$ (1.1 equiv.) DCM (0.06 M), 0 °C to rt, 24 h	Starting material decomposed
5	$HSCH_2CH_2CH_2SH$ (2.5 equiv.) Et_3N (2.5 equiv.) MeOH (0.15 M), rt, 2 h	 **12** 50% yield

[a] Yield refers to the column-purified product.

Results and discussion for Table S3:

With the synthetic and medicinal applications in mind, we explored the utilization of the compound (±)-**5aa** in the synthesis of functionalized imine **11** through aza-Wittig reaction (Table S3). Reaction of the compound (±)-**5aa** with standard aza-Wittig conditions (1.1 equiv of PBu_3 in dry toluene at 25-50 °C for 48 h) did not furnish the expected imine (±)-**11** and

only starting material was recovered (entry 1, Table S3). In a similar manner, few more conditions were tried, which were also unsuccessful (entries 2-4, Table S3). Interestingly, treatment of the azide ketone (±)-**5aa** with each 2.5 equiv of propanedithiol and triethylamine in dry MeOH at 25 °C for 2 h furnished the unexpected 2-methylquinoline **12** in 50% yield through domino aza-Wittig/aromatization reactions (entry 5, Table S3).

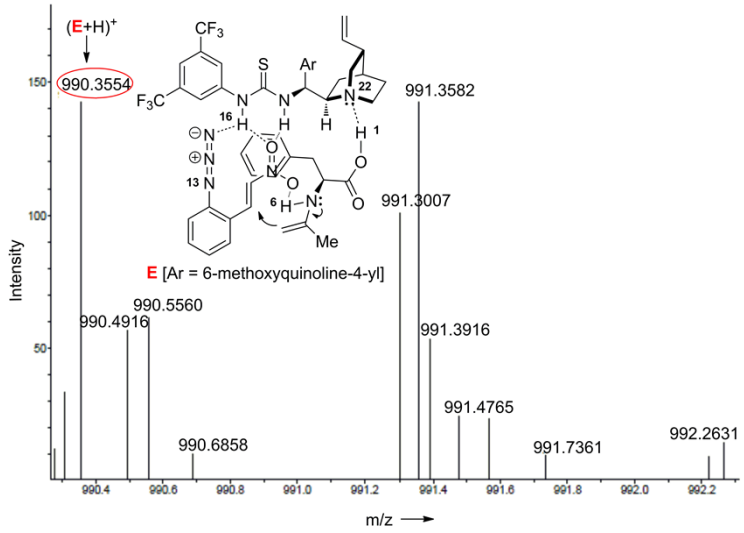


Figure S2-(i): ESI-HRMS (positive mode) spectrum of the reaction after 60 minutes of **1a** and **2a** catalyzed by **3c/4i** in DCM at 25 °C.

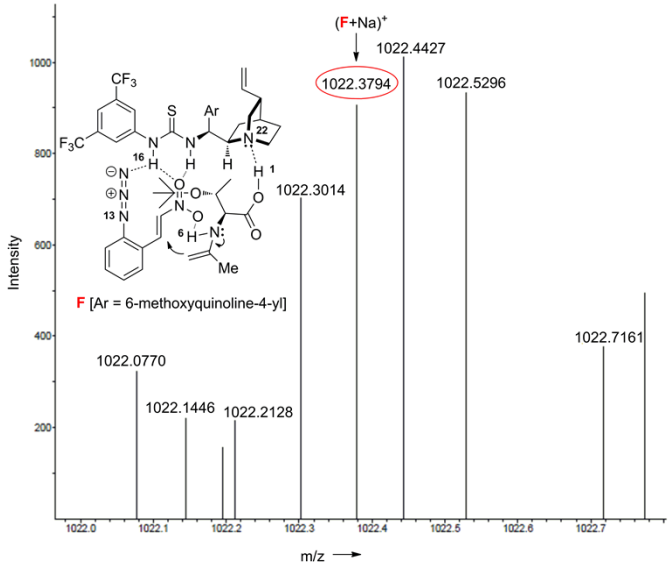
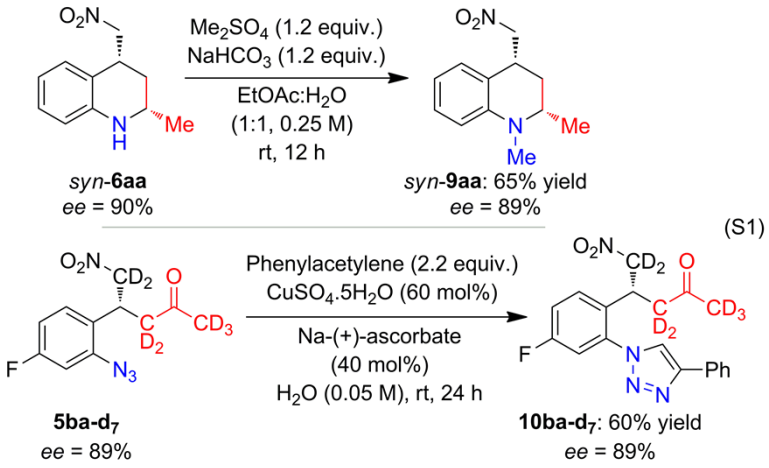


Figure S2-(ii): ESI-HRMS (positive mode) spectrum of the reaction after 60 minutes of **1a** and **2a** catalyzed by **3c/4m** in DCM at 25 °C.

Procedure for the Observation of pre-Transition State Intermediates of Supramolecular Assemblies of E and F through ESI-HRMS Analysis:[3]

The ESI-HRMS spectrum of an on-going reaction of **1a** (0.2 mmol) and **2a** (2.8 mmol, 14 equiv) in the presence of **3c/4i** (each 5 mol %) in the DCM at 25 °C after 60 minutes, reveals the formation of the pre-transition state supramolecular assembly intermediate **E**·H^+ (*m/z* 990.3560) [Figure S2-(i)]. In a similar manner, ESI-HRMS spectrum of an on-going reaction of **1a** (0.2 mmol) and **2a** (2.8 mmol, 14 equiv) in the presence of another catalytic system **3c/4m** (each 5 mol %) in the DCM at 25 °C after 60 minutes also revealed the formation of the key catalytic pre-transition state supramolecular assembly intermediate **F**·Na^+ (*m/z* 1022.3798) [Figure S2-(ii)]. Catalytic supramolecular assemblies of **E**·H^+ (*m/z* 990.3554) and **F**·Na^+ (*m/z* 1022.3794) were obtained in very low intensities in ESI-HRMS spectrum, due to this reason we are not able to see the isotopic pattern of both **E**·H^+ (*m/z* 990.3554) and **F**·Na^+ (*m/z* 1022.3794) in the ESI-HRMS spectrums.

Synthetic Applications: With applications in mind, we explored the utilization of (−)-*syn*-**6aa** and (−)-**5ba-d$_7$** in the synthesis of functionalized drug-like compounds (+)-*syn*-**9aa** and (+)-**10ba-d$_7$** *via* simple *N*-methylation and a click reaction, respectively (eq. S1). Compounds of the type (+)-*syn*-**9aa** and (+)-**10ba-d$_7$** are important molecules in medicinal chemistry,[4] which is emphasizing the value of the present catalytic approach to the chiral pharmaceuticals.



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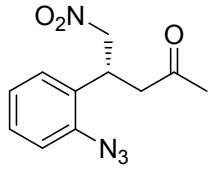
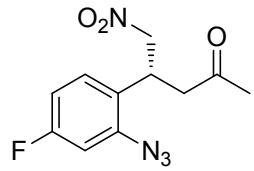
(*R*)-4-(2-azidophenyl)-5-nitropentan-2-one (**5aa**): Prepared following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Lux 5u amylose-2 column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 34.10 min (major), t_R = 43.43 min (minor); **$[\alpha]_D^{25}$ = −12.4 (*c* = 0.98 g/100 mL, $CHCl_3$, 92% *ee*);** IR (Neat): ν_{max} 2952, 2124 (N_3), 1713 (C=O), 1550 (NO_2), 1490, 1376, 1285, 1163 and 752 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.33 (1H, dt, *J* =



5aa

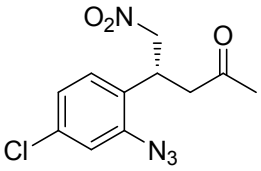
8.0, 1.6 Hz), 7.20-7.16 (2H, m), 7.10 (1H, dt, *J* = 7.6, 0.8 Hz), 4.74 (1H, dd, *J* = 12.4, 7.2 Hz), 4.71 (1H, dd, *J* = 12.4, 6.8 Hz), 4.22 (1H, quintet, *J* = 6.8 Hz), 3.03 (1H, dd, *J* = 18.4, 8.0 Hz), 2.95 (1H, dd, *J* = 18.0, 6.4 Hz), 2.15 (3H, s, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 205.5 (C, *C*=O), 137.8 (C), 129.4 (CH), 129.1 (CH), 125.2 (C, CH), 118.7 (CH), 77.7 (CH_2), 44.5 (CH_2), 34.9 (CH), 30.2 (CH_3); HRMS m/z 271.0807 (M + Na), calcd for $C_{11}H_{12}N_4O_3Na$ 271.0802.

(*R*)-4-(2-azido-4-fluorophenyl)-5-nitropentan-2-one (**5ba**): Prepared following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Lux 5u amylose-2 column (hexane/2-propanol = 90:10, flow rate 1.0 mL/min, λ = 254 nm), t_R = 15.04 min (major), t_R = 18.84 min (minor); **$[\alpha]_D^{25}$ = –11.2 (*c* = 0.35 g/100 mL, $CHCl_3$, 91% *ee*);** IR (Neat): ν_{max} 2933, 2115 (N_3), 1714 (C=O), 1594, 1546 (NO_2), 1500, 1359, 1294, 1211, 1163, 957 and 844 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.09 (1H, dd, *J* = 8.8, 6.0 Hz), 6.81 (1H, dd, *J* = 8.8, 2.4 Hz), 6.73 (1H, dt, *J* = 8.4, 2.4 Hz), 4.64 (1H, dd, *J* = 12.4, 7.2 Hz), 4.61 (1H, dd, *J* = 12.4, 6.4 Hz), 4.09 (1H, quintet, *J* = 6.8 Hz), 2.94 (1H, dd, *J* = 18.0, 7.2 Hz), 2.85 (1H, dd, *J* = 18.0, 6.4 Hz), 2.07 (3H, s, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 205.3 (C, *C*=O), 162.5 (C, d, *J* = 248.0 Hz, *C*-F), 139.4 (C, d, *J* = 8.0 Hz), 130.9 (CH, d, *J* = 10.0 Hz), 125.3 (C, d, *J* = 4.0 Hz), 112.1 (CH, d, *J* = 21.0 Hz), 106.1 (CH, d, *J* = 25.0 Hz), 77.6 (CH_2), 44.4 (CH_2), 34.4 (CH), 30.1 (CH_3); HRMS m/z 289.0707 (M + Na), calcd for $C_{11}H_{11}FN_4O_3Na$ 289.0707.



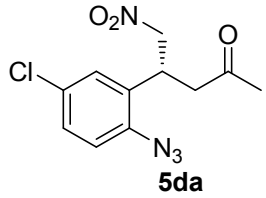
5ba

(*R*)-4-(2-azido-4-chlorophenyl)-5-nitropentan-2-one (**5ca**): Prepared following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Lux 5u amylose-2 column (hexane/2-propanol = 85:15, flow rate 1.0 mL/min, λ = 254 nm), t_R = 37.33 min (major), t_R = 44.84 min (minor); **$[\alpha]_D^{25}$ = –29.6 (*c* = 0.15 g/100 mL, $CHCl_3$, 92% *ee*);** IR (Neat): ν_{max} 2923, 2113 (N_3), 1715 (C=O), 1575, 1548 (NO_2), 1499, 1375, 1312, 1259, 1162 and 837 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.18 (1H, d, *J* = 8.5 Hz), 6.79 (1H, dd, *J* = 8.5, 2.5 Hz), 6.76 (1H, d, *J* = 2.0 Hz), 4.72 (1H, dd, *J* = 12.0, 7.0 Hz), 4.68 (1H, dd, *J* = 12.5, 6.5 Hz), 4.17 (1H, quintet, *J* = 7.0 Hz), 3.02 (1H, dd, *J* = 18.0, 7.5 Hz), 2.93 (1H, dd, *J* = 18.0, 6.5 Hz), 2.15 (3H, s, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 205.2 (C, *C*=O), 141.1 (C), 139.4 (C), 130.8 (CH), 126.1 (C), 115.6 (CH), 109.3 (CH), 77.6 (CH_2), 44.5 (CH_2), 34.7 (CH), 30.2 (CH_3); HRMS m/z 305.0417 (M + Na), calcd for $C_{11}H_{11}ClN_4O_3Na$ 305.0412.



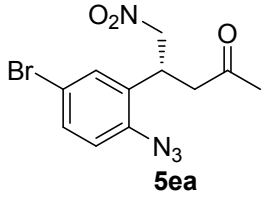
5ca

(*R*)-4-(2-azido-5-chlorophenyl)-5-nitropentan-2-one (**5da**): Prepared following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Lux 5u amylose-2 column (hexane/2-propanol = 85:15, flow rate 1.0 mL/min, λ = 254 nm), t_R = 28.57 min (major), t_R = 42.43 min (minor); **$[\alpha]_D^{25}$ = –15.1 (*c* = 0.28 g/100 mL, $CHCl_3$, 91% *ee*);** IR (Neat): ν_{max} 2922, 2117 (N_3), 1715 (C=O), 1548 (NO_2), 1486, 1375, 1291, 1153, 1117 and 812 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21 (1H, dd, *J* = 8.4, 2.4 Hz), 7.10 (1H, d, *J* = 2.4 Hz), 7.02 (1H, d, *J* = 8.4 Hz), 4.63 (2H, m), 4.10 (1H, quintet, *J* = 6.8 Hz), 2.95 (1H, dd, *J* = 18.4, 7.6 Hz), 2.85 (1H, dd, *J* = 18.0, 6.4 Hz), 2.09 (3H, s, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 205.0 (C, *C*=O), 136.4 (C), 131.2 (C), 130.4 (C), 129.4 (CH), 129.0 (CH), 119.8 (CH), 77.2 (CH_2), 44.2 (CH_2), 34.6 (CH), 30.1 (CH_3); HRMS m/z 305.0416 (M + Na), calcd for $C_{11}H_{11}ClN_4O_3Na$ 305.0412.



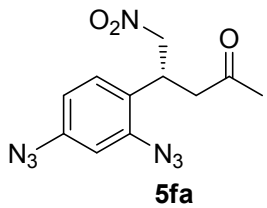
5da

(*R*)-4-(2-azido-5-bromophenyl)-5-nitropentan 2-one (**5ea**): Prepared following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Lux 5u amylose-2 column (hexane/2-propanol = 90:10, flow rate 1.0 mL/min, λ = 254 nm), t_R = 20.43 min (major), t_R = 29.10 min (minor); **$[\alpha]_D^{25}$ = –2.0 (*c* = 0.25 g/100 mL, $CHCl_3$, 91% *ee*);** IR (Neat): ν_{max} 2918, 2115 (N_3), 1714 (C=O), 1547 (NO_2), 1482, 1357, 1291, 1163, 1111 and 810 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.36 (1H, dd, *J* = 8.8, 2.4 Hz), 7.24 (1H, d, *J* = 2.4 Hz), 6.97 (1H, d, *J* = 8.4 Hz), 4.63 (2H, d, *J* = 6.8 Hz), 4.09 (1H, quintet, *J* = 6.8 Hz), 2.95 (1H, dd, *J* = 18.4, 7.6 Hz), 2.86 (1H, dd, *J* = 18.4, 6.4 Hz), 2.09 (3H, s, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 205.0 (C, *C*=O), 137.1 (C), 132.3 (CH), 132.0 (CH), 131.5 (C), 120.2 (CH), 118.0 (C), 77.2 (CH_2), 44.2 (CH_2), 34.6 (CH), 30.2 (CH_3); HRMS m/z 348.9913 (M + Na), calcd for $C_{11}H_{11}BrN_4O_3Na$ 348.9907.



5ea

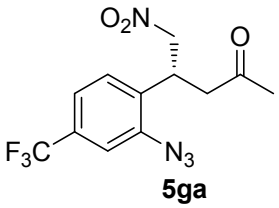
(*R*)-4-(2,4-diazidophenyl)-5-nitropentan-2-one (**5fa**): Prepared following the procedure **A** and purified b y column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Lux 5u amylose-2 column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 57.57 min (major), t_R = 68.51 min (minor); **$[\alpha]_D^{25}$ = –24.0 (*c* = 0.07 g/100 mL, $CHCl_3$, 90% *ee*);** IR (Neat): ν_{max} 2919, 2111 (2 x N_3), 1714 (C=O), 1547 (NO_2), 1499, 1375, 1312, 1286, 1259, 1162 and 837 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.17 (1H, d, *J* = 8.4 Hz), 6.79 (1H, dd, *J* = 8.0, 2.0 Hz), 6.76 (1H, d, *J* = 1.6 Hz), 4.72 (1H, dd, *J* = 12.4, 7.6 Hz), 4.68 (1H, dd, *J* = 12.4, 6.4 Hz), 4.16 (1H, quintet, *J* = 6.8 Hz), 3.02 (1H, dd, *J* = 18.4, 7.6 Hz), 2.93 (1H, dd, *J* = 18.0, 6.4 Hz), 2.15 (3H, s, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 205.3 (C, *C*=O), 141.1 (C), 139.4 (C), 130.8 (CH), 125.9 (C), 115.5 (CH), 109.3 (CH), 77.6



5fa

(CH_2), 44.4 (CH_2), 34.6 (CH), 30.2 (CH_3); HRMS m/z 312.0818 (M + Na), calcd for $C_{11}H_{11}N_7O_3Na$ 312.0816.

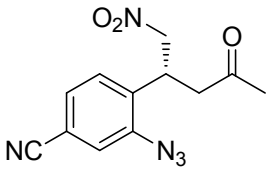
(*R*)-4-(2-azido-4-(trifluoromethyl)phenyl)-5-nitropentan-2-one (**5ga**): Prepared following the proc



5ga

edure **A** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Lux 5u amylose-2 column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 20.33 min (major), t_R = 23.78 min (minor); **$[\alpha]_D^{25}$ = –17.3 (*c* = 0.69 g/100 mL, $CHCl_3$, 92% *ee*);** IR (Neat): ν_{max} 2923, 2853, 2116 (N_3), 1718 (C=O), 1551 (NO_2), 1421, 1376, 1329, 1276, 1153, 1123, 1086 and 896 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38-7.37 (1H, m), 7.35-7.32 (2H, m), 4.77 (1H, dd, *J* = 12.8, 7.2 Hz), 4.73 (1H, dd, *J* = 12.8, 6.4 Hz), 4.26 (1H, quintet, *J* = 6.4 Hz), 3.06 (1H, dd, *J* = 18.4, 7.6 Hz), 2.97 (1H, dd, *J* = 18.4, 6.4 Hz), 2.17 (3H, s, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 204.9 (C, *C*=O), 138.9 (C), 133.3 (C), 131.5 (C, q, *J* = 33.0 Hz), 130.2 (CH), 123.2 (C, q, *J* = 271.0 Hz, *C*F_3), 121.8 (CH, q, *J* = 4.0 Hz), 115.5 (CH, q, *J* = 3.0 Hz), 77.1 (CH_2), 44.2 (CH_2), 34.8 (CH), 30.1 (CH_3); HRMS m/z 339.0680 (M + Na), calcd for $C_{12}H_{11}F_3N_4O_3Na$ 339.0675.

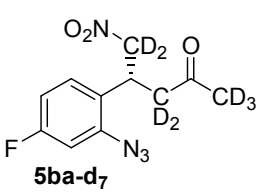
(*R*)-3-azido-4-(1-nitro-4-oxopentan-2-yl)benzonitrile (**5ha**): Prepared following the procedure **A**



5ha

and purified b y column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Lux 5u amylose-2 column (hexane/2-propanol = 85:15, flow rate 1.0 mL/min, λ = 254 nm), t_R = 36.63 min (major), t_R = 51.43 min (minor); **$[\alpha]_D^{25}$ = –19.7 (*c* = 0.25 g/100 mL, $CHCl_3$, 89% *ee*);** IR (Neat): ν_{max} 2924, 2232, 2114 (N_3), 1715 (C=O), 1548 (NO_2), 1501, 1408, 1374, 1294, 1220, 1164, 867 and 771 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (1H, s), 7.33 (1H, d, *J* = 8.0 Hz), 7.26 (1H, d, *J* = 8.0 Hz), 4.70 (1H, dd, *J* = 12.8, 7.6 Hz), 4.65 (1H, dd, *J* = 12.8, 6.4 Hz), 4.17 (1H, quintet, *J* = 6.4 Hz), 2.98 (1H, dd, *J* = 18.4, 7.2 Hz), 2.90 (1H, dd, *J* = 18.4, 6.4 Hz), 2.10 (3H, s, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 204.8 (C, *C*=O), 139.3 (C), 134.8 (C), 130.6 (CH), 128.5 (CH), 121.7 (CH), 117.4 (C), 113.1 (C, *C*≡N), 76.9 (CH_2), 43.9 (CH_2), 34.9 (CH), 30.2 (CH_3); HRMS m/z 296.0760 (M + Na), calcd for $C_{12}H_{11}N_5O_3Na$ 296.0754.

(*R*)-4-(2-azido-4-fluorophenyl)-5-nitropentan-2-one (5ba-d_7): Prepared following the procedure **A**

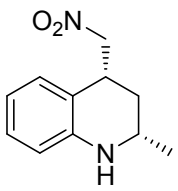


5ba-d_7

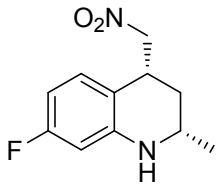
and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Lux 5u amylose-2 column (hexane/2-propanol = 90:10, flow rate 1.0 mL/min, λ = 254 nm), t_R = 31.29 min (major), t_R = 41.41 min (minor); **$[\alpha]_D^{25}$ = –10.2 (*c* = 0.31 g/100 mL, $CHCl_3$, 89% *ee*);** IR (Neat): ν_{max} 2920, 2117 (N_3), 1710 (C=O), 1594, 1536 (NO_2), 1501, 1296, 1211 and 958 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.16 (1H, dd, *J* = 9.0, 6.0 Hz), 6.89 (1H, dd, *J* = 9.0, 2.5 Hz), 6.81 (1H, dt, *J* = 8.0, 2.5 Hz), 4.70 (2H, 70% D-atom, m), 4.15

(1H, m); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 205.6 (C, *C*=O), 162.6 (C, d, *J* = 247.5 Hz, *C*-F), 139.5 (C, d, *J* = 8.7 Hz), 130.9 (CH, d, *J* = 8.7 Hz), 125.2 (C), 112.2 (CH, d, *J* = 21.2 Hz), 106.1 (CH, d, *J* = 25.0 Hz), 34.2 (CH); HRMS m/z 296.1144 (M + Na), calcd for $C_{11}H_4D_7FN_4O_3Na$ 296.1147.

(2*S*,4*R*)-2-methyl-4-(nitromethyl)-1,2,3,4-tetrahydroquinoline (*syn*-**6aa**): Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as solid. Mp 50 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 95:5, flow rate 0.5 mL/min, λ = 254 nm), t_R = 16.81 min (minor), t_R = 21.37 min (major) [for minor *anti*-isomer], t_R = 23.79 min (minor), t_R = 34.64 min (major) [for major *syn*-isomer]; **$[\alpha]_D^{25}$ = −21.1** (***c* = 0.28 g/100 mL, $CHCl_3$, 90% *ee*** for major *syn*-isomer; **89% *ee*** for minor *anti*-isomer and *dr* = 6:1); IR (neat): ν_{max} 3396 (NH), 2925, 2853, 1709, 1608, 1546 (NO_2), 1490, 1376, 1314, 1259, 1159 and 746 cm^{-1}; ^{1}H NMR ($CDCl_3$, major *syn*-isomer) δ 7.04 (1H, t, *J* = 7.5 Hz), 6.96 (1H, d, *J* = 7.5 Hz), 6.67 (1H, dt, *J* = 7.5, 0.8 Hz), 6.54 (1H, dd, *J* = 8.0, 0.8 Hz), 4.93 (1H, dd, *J* = 12.0, 5.0 Hz), 4.38 (1H, dd, *J* = 12.0, 10.5 Hz), 3.81-3.75 (2H, m), 3.46-3.40 (1H, m), 2.05 (1H, ddd, *J* = 12.5, 6.0, 2.5 Hz), 1.52 (1H, q, *J* = 11.5 Hz), 1.23 (3H, d, *J* = 6.5 Hz, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135, major *syn*-isomer) δ 145.4 (C), 128.1 (CH), 126.3 (CH), 118.6 (C), 117.8 (CH), 115.1 (CH), 80.5 (CH_2), 46.5 (CH), 35.5 (CH_2), 34.9 (CH), 22.3 (CH_3); HRMS m/z 207.1133 (M + H), calcd for $C_{11}H_{15}N_2O_2$ 207.1128.



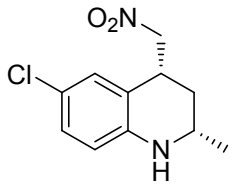
syn-**6aa**



syn-**6ba**

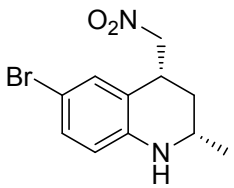
(2*S*,4*R*)-7-fluoro-2-methyl-4-(nitromethyl)-1,2,3,4-tetrahydroquinoline (*syn*-**6ba**): Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as solid. Mp 83 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 95:5, flow rate 0.5 mL/min, λ = 254 nm), t_R = 20.32 min (minor), t_R = 25.69 min (major) [for minor *anti*-isomer], t_R = 29.27 min (minor), t_R = 43.49 min (major) [for major *syn*-isomer]; **$[\alpha]_D^{25}$ = −11.4 [*c* = 0.07 g/100 mL, $CHCl_3$, 94% *ee*** (major *syn*-isomer), **97% *ee*** (minor *anti*-isomer) and *dr* = 5:1]; IR (neat): ν_{max} 3391 (NH), 2921, 2853, 1616, 1542 (NO_2), 1490, 1378, 1334, 1196, 1179, 1150 and 837 cm^{-1}; ^{1}H NMR ($CDCl_3$, major *syn*-isomer) δ 6.90-6.86 (1H, m), 6.35 (1H, dt, *J* = 8.4, 2.4 Hz), 6.22 (1H, dd, *J* = 10.4, 2.8 Hz), 4.89 (1H, dd, *J* = 12.0, 4.8 Hz), 4.38 (1H, dd, *J* = 12.0, 9.6 Hz), 3.87 (1H, br s, *N*H), 3.73-3.68 (1H, m), 3.49-3.41 (1H, m), 2.04 (1H, ddd, *J* = 12.8, 6.0, 2.8 Hz), 1.50 (1H, q, *J* = 11.2 Hz), 1.23 (3H, d, *J* = 6.0 Hz, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135, major *syn*-isomer) δ 162.6 (C, d, *J* = 242.0 Hz, *C*-F), 146.8 (C, d, *J* = 11.0 Hz), 127.5 (CH, d, *J* = 10.0 Hz), 114.3 (C), 104.3 (CH, d, *J* = 22.0 Hz), 101.1 (CH, d, *J* = 24.0 Hz), 80.3 (CH_2), 46.5 (CH), 35.2 (CH_2), 34.4 (CH), 22.2 (CH_3); HRMS m/z 225.1036 (M + H), calcd for $C_{11}H_{14}FN_2O_2$ 225.1034.

(2*S*,4*R*)-6-chloro-2-methyl-4-(nitromethyl)-1,2,3,4-tetrahydroquinoline (*syn*-**6da**): Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as solid. Mp 64 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 95:5, flow rate 0.5 mL/min, λ = 254 nm), t_R = 19.56 min (minor), t_R = 23.63 min (major) [for minor *anti*-isomer], t_R = 25.45 min (minor), t_R = 36.45 min (major) [for major *syn*-isomer]; **$[\alpha]_D^{25}$ = −34.1 [*c* = 0.20 g/100 mL, $CHCl_3$, 93% *ee*** (major *syn*-isomer), **90% *ee*** (minor *anti*-isomer) and *dr* = 5:1]; IR (neat): ν_{max} 3405 (NH), 2965, 2925, 1718, 1546 (NO_2), 1491, 1376, 1298, 1252, 1192, 1104 and 811 cm^{-1}; ^1H NMR ($CDCl_3$, major *syn*-isomer) δ 7.01-6.97 (1H, m), 6.94-6.93 (1H, m), 6.47 (1H, d, *J* = 8.4 Hz), 4.89 (1H, dd, *J* = 12.4, 4.8 Hz), 4.38 (1H, dd, *J* = 12.0, 10.0 Hz), 3.78-3.70 (1H, m), 3.46-3.39 (1H, m), 2.05 (1H, ddd, *J* = 12.8, 5.6, 2.4 Hz), 1.50 (1H, q, *J* = 11.2 Hz), 1.23 (3H, d, *J* = 6.4 Hz, CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135, major *syn*-isomer) δ 144.0 (C), 128.0 (CH), 126.2 (CH), 122.1 (C), 120.0 (C), 116.1 (CH), 80.1 (CH_2), 46.5 (CH), 35.0 (CH_2), 34.8 (CH), 22.2 (CH_3); HRMS m/z 241.0737 (M + H), calcd for $C_{11}H_{14}ClN_2O_2$ 241.0738.



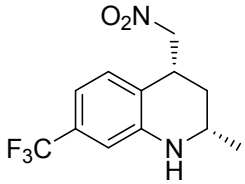
syn-**6da**

(2*S*,4*R*)-6-bromo-2-methyl-4-(nitromethyl)-1,2,3,4-tetrahydroquinoline (*syn*-**6ea**): Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as solid. Mp 54 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 95:5, flow rate 0.5 mL/min, λ = 254 nm), t_R = 22.07 min (minor), t_R = 26.18 min (major) [for minor *anti*-isomer], t_R = 28.77 min (minor), t_R = 42.55 min (major) [for major *syn*-isomer]; **$[\alpha]_D^{25}$ = −22.8 [*c* = 0.18 g/100 mL, $CHCl_3$, 90% *ee*** (major *syn*- isomer), **89% *ee*** (minor *anti*-isomer) and *dr* = 5:1]; IR (neat): ν_{max} 3400 (NH), 2923, 1598, 1547 (NO_2), 1488, 1376, 1299, 1190, 877 and 809 cm^{-1}; ^1H NMR ($CDCl_3$, major *syn*-isomer) δ 7.11 (1H, dd, *J* = 8.5, 1.5 Hz), 7.06 (1H, br s), 6.42 (1H, d, *J* = 9.0 Hz), 4.89 (1H, dd, *J* = 12.0, 4.5 Hz), 4.38 (1H, dd, *J* = 12.0, 10.0 Hz), 3.79 (1H, br s, *N*H), 3.77-3.71 (1H, m), 3.43-3.39 (1H, m), 2.04 (1H, ddd, *J* = 13.0, 6.0, 2.5 Hz), 1.49 (1H, q, *J* = 11.5 Hz), 1.23 (3H, d, *J* = 6.5 Hz, CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135, major *syn*-isomer) δ 144.4 (C), 130.9 (CH), 129.0 (CH), 120.6 (C), 116.5 (CH), 109.1 (C), 80.1 (CH_2), 46.5 (CH), 35.0 (CH_2), 34.8 (CH), 22.2 (CH_3); HRMS m/z 285.0235 (M + H), calcd for $C_{11}H_{14}BrN_2O_2$ 285.0233.



syn-**6ea**

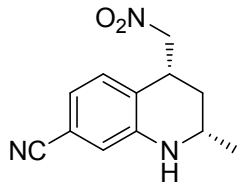
(2*S*,4*R*)-2-methyl-4-(nitromethyl)-7-(trifluoromethyl)-1,2,3,4-tetrahydroquinoline (*syn*-**6ga**): Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as solid. Mp 91 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 80:20, flow rate 1.0 mL/min, λ = 254 nm), t_R = 4.47 min (minor), t_R = 5.08 min (major) [for minor *anti*-



syn-**6ga**

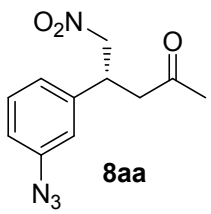
isomer], t_R = 5.61 min (minor), t_R = 6.30 min (major) [for major *syn*-isomer]; **$[\alpha]_D^{25}$ = −15.7 [*c* = 0.12 g/100 mL, $CHCl_3$, 91% *ee*** (major *syn*-isomer), **90% *ee*** (minor *anti*-isomer) and *dr* = 5:1]; IR (neat): ν_{max} 3419 (NH), 2927, 2856, 1724, 1622, 1550 (NO_2), 1494, 1376, 1328, 1138, 1076, 978 and 856 cm^{-1}; ^1H NMR ($CDCl_3$, major *syn*-isomer) δ 7.04 (1H, d, *J* = 8.0 Hz), 6.87 (1H, d, *J* = 8.5 Hz), 6.75 (1H, br s), 4.92 (1H, dd, *J* = 12.0, 5.0 Hz), 4.43 (1H, dd, *J* = 12.0, 9.5 Hz), 3.97 (1H, br s, *N*H), 3.81-3.75 (1H, m), 3.52-3.46 (1H, m), 2.08 (1H, ddd, *J* = 13.0, 6.0, 2.5 Hz), 1.55 (1H, q, *J* = 11.0 Hz), 1.26 (3H, d, *J* = 6.0 Hz, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135, major *syn*-isomer) δ 145.5 (C), 130.2 (C, q, *J* = 32.5 Hz), 126.4 (CH), 123.9 (C, *C*F_3, q, *J* = 271.2 Hz), 121.9 (C), 113.8 (CH, q, *J* = 3.7 Hz), 111.3 (CH, q, *J* = 3.7 Hz), 79.8 (CH_2), 46.5 (CH), 34.82 (CH), 34.80 (CH_2), 22.2 (CH_3); HRMS m/z 275.1002 (M + H), calcd for $C_{12}H_{14}F_3N_2O_2$ 275.1002.

(2*S*,4*R*)-2-methyl-4-(nitromethyl)-1,2,3,4-tetrahydroquinoline-7-carbonitrile (*syn*-**6ha**): Prepared following the procedure **B** and purified by column chromatography using EtOAc/hexane and isolated as solid. Mp 138 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 85:15, flow rate 0.8 mL/min, λ = 254 nm), t_R = 11.28 min (minor), t_R = 14.94 min (major) [for minor *anti*-isomer], t_R = 16.28 min (minor), t_R = 21.90 min (major) [for major *syn*-isomer]; **$[\alpha]_D^{25}$ = −11.8 [*c* = 0.08 g/100 mL, $CHCl_3$, 96% *ee*** (major *syn*-isomer), **91% *ee*** (minor *anti*-isomer) and *dr* = 4:1]; IR (neat): ν_{max} 3371 (NH), 2921, 2852, 2227, 1544 (NO_2), 1493, 1379, 1320, 1186, 1154, 1084, 1015, 854 and 804 cm^{-1}; ^1H NMR ($CDCl_3$, major *syn*-isomer) δ 7.02 (1H, dd, *J* = 8.0, 1.0 Hz), 6.90 (1H, dd, *J* = 8.0, 1.5 Hz), 6.75 (1H, d, *J* = 1.5 Hz), 4.90 (1H, dd, *J* = 12.5, 5.0 Hz), 4.45 (1H, dd, *J* = 12.5, 9.0 Hz), 4.01 (1H, br s, *N*H), 3.79-3.73 (1H, m), 3.53-3.46 (1H, m), 2.08 (1H, ddd, *J* = 13.0, 6.0, 3.0 Hz), 1.53 (1H, q, *J* = 12.0 Hz), 1.26 (3H, d, *J* = 6.5 Hz, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135, major *syn*-isomer) δ 145.6 (C), 126.9 (CH), 123.4 (C), 120.5 (CH), 118.8 (C), 117.4 (CH), 111.7 (C,*C*≡N), 79.4 (CH_2), 46.5 (CH), 34.9 (CH), 34.4 (CH_2), 22.1 (CH_3); HRMS m/z 232.1082 (M + H), calcd for $C_{12}H_{14}N_3O_2$ 232.1081.



syn-**6ha**

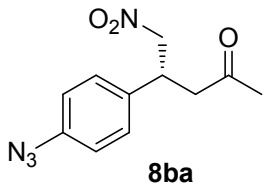
(*R*)-4-(3-azidophenyl)-5-nitropentan-2-one (**8aa**):♣ Prepared following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Lux 5u amylase-2 column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 44.02 min (major), t_R = 51.99 min (minor); **$[\alpha]_D^{25}$ = −3.8 (*c* = 0.10 g/100 mL, $CHCl_3$, 78% *ee*);** IR (Neat): ν_{max} 2922, 2853, 2106 (N_3), 1714 (C=O), 1547 (NO_2), 1376, 1287, 1163 and 786 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.32 (1H, t, *J* = 8.0 Hz), 7.00 (1H, br d, *J* = 8.0 Hz), 6.96 (1H, br ddd, *J* = 8.0, 2.4, 0.8 Hz), 6.85 (1H, t, *J* = 1.6 Hz), 4.69 (1H, dd, *J* = 12.8, 6.8 Hz), 4.59 (1H, dd, *J* = 12.4, 8.0 Hz), 4.00 (1H, quin, *J* = 7.2 Hz), 2.91 (2H, d, *J* = 7.2 Hz) 2.14 (3H, s, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 205.0 (C, *C*=O), 140.9 (C), 140.8



8aa

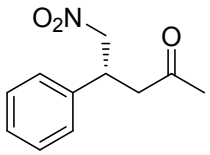
(C), 130.4 (CH), 123.8 (CH), 118.4 (CH), 118.2 (CH), 79.1 (CH_2), 45.9 (CH_2), 38.7 (CH), 30.3 (CH_3); HRMS m/z 271.0808 (M + Na), calcd for $C_{11}H_{12}N_4O_3Na$ 271.0802.

(*R*)-4-(4-azidophenyl)-5-nitropentan-2-one (8ba):♣ Prepared following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 254 nm), t_R = 22.60 min (minor), t_R = 27.25 min (major); **$[\alpha]_D^{25}$ = –1.5 (*c* = 0.26 g/100 mL, $CHCl_3$, 81% *ee*);** IR (Neat): ν_{max} 2922, 2097 (N_3), 1714 (C=O), 1550 (NO_2), 1508, 1376, 1285, 1163,1130, 1117 and 832 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21 (2H, d, *J* = 8.4 Hz), 6.99 (2H, d, *J* = 8.4 Hz), 4.68 (1H, dd, *J* = 12.4, 6.8 Hz), 4.57 (1H, dd, *J* = 12.4, 8.0 Hz), 3.99 (1H, quin, *J* = 6.8 Hz), 2.90 (2H, d, *J* = 7.2 Hz) 2.13 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 205.1 (C, *C*=O), 139.6 (C), 135.4 (C), 128.8 (2 x CH), 119.6 (2 x CH), 79.3 (CH_2), 46.0 (CH_2), 38.4 (CH), 30.3 (CH_3); HRMS m/z 271.0805 (M + Na), calcd for $C_{11}H_{12}N_4O_3Na$ 271.0802.



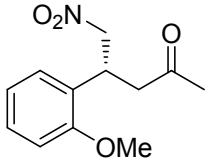
8ba

(*R*)-5-nitro-4-phenylpentan-2-one (8ca):♣ Prepared following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as solid. Mp 110 °C; The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralpak AD-H column (hexane/2-propanol = 90:10, flow rate 0.5 mL/min, λ = 220 nm), t_R = 16.44 min (minor), t_R = 17.54 min (major); **$[\alpha]_D^{25}$ = –1.5 (*c* = 0.20 g/100 mL, $CHCl_3$, 90% *ee*) ;** IR (Neat): ν_{max} 3044, 2968, 2917, 1710 (C=O), 1547 (NO_2), 1536, 1360, 1324,1184, 1161 and 751 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35-7.31 (2H, m), 7.29-7.25 (1H, m), 7.23-7.21 (2H, m) 4.69 (1H, dd, *J* = 12.4, 6.8 Hz), 4.60 (1H, dd, *J* = 12.4, 7.6 Hz), 4.01 (1H, quin, *J* = 7.2 Hz), 2.92 (2H, d, *J* = 7.2 Hz), 2.12 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 205.4 (C, *C*=O), 138.8 (C), 129.0 (2 x CH), 127.9 (CH), 127.3 (2 x CH), 79.4 (CH_2), 46.1 (CH_2), 39.0 (CH), 30.4 (CH_3); HRMS m/z 230.0788 (M + Na), calcd for $C_{11}H_{13}NO_3Na$ 230.0788.



8ca

♣ The absolute configuration of chiral products **8aa-fa** were established by comparison of (–)-**8ca** with the same chiral product synthesized from direct asymmetric Michael reaction (see Fei Xue et. al. *Adv. Synth. Catal.*, **2008**, *350*, 2194-2198; E. N. Jacobsen et. al. *J. Am. Chem. Soc*. **2006**, *128*, 7170 and W. Wang et. al. *Org. Lett*. **2009,** *11*, 2864).



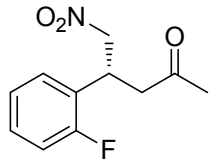
8da

(*R*)-4-(2-methoxyphenyl)-5-nitropentan-2-one (8da):♠ Prepared following the procedure **A** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel chiralpak AS-H column (hexane/2-propanol = 85:15, flow rate 1.0 mL/min, λ = 210 nm), t_R = 11.96 min (minor), t_R = 13.38 min (major).

$[\alpha]_D^{25}$ = –27.8 (*c* = 0.31 g/100 mL, $CHCl_3$, 92% *ee*); IR (Neat): ν_{max} 3003, 2970, 2942, 2915, 2844, 1709 (C=O), 1600, 1551 (NO_2), 1501, 1441, 1381, 1244, 1167, 1129, 1025 and 762 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.20-7.15 (1H, m), 7.06 (1H, dd, *J* = 7.6, 1.6 Hz), 6.85-6.80 (2H, m), 4.67 (1H, dd, *J* = 12.0, 7.2 Hz), 4.63 (1H, dd, *J* = 12.0, 6.8 Hz), 4.14 (1H, quin, *J* = 6.8 Hz), 3.78 (3H, s, O-CH_3), 2.95 (1H, dd, *J* = 17.6, 7.6 Hz), 2.88 (1H, dd, *J* = 17.6, 6.8 Hz), 2.05 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 206.1 (C, *C*=O), 157.0 (C), 129.2 (CH), 128.9 (CH), 126.4 (C), 120.9 (CH), 110.9 (CH), 77.8 (CH_2), 55.3 (CH_3, O-CH_3), 44.5 (CH_2), 35.3 (CH), 30.2 (CH_3); HRMS m/z 260.0894 (M + Na), calcd for $C_{12}H_{15}NO_4Na$ 260.0893.

♠ The absolute configuration of chiral products **5aa-ha,** and **8aa-fa** were established by comparison of (–)-**8da** with the same chiral product synthesized from direct asymmetric Michael reaction (see F. Xue et. al. *Adv. Synth. catal*. **2008**, *350*, 2194; and Ramachary et. al. *Org. Biomol. Chem.* **2010**, *8*, 4259).

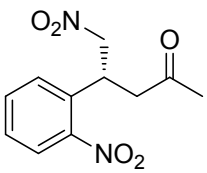
(*R*)-4-(2-fluorophenyl)-5-nitropentan-2-one (8ea): Prepared following the procedure **A** and purified



8ea

by column chromatography using EtOAc/hexane and isolated as solid Mp: 74 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel chiralpak AS-H column (hexane/2-propanol = 90:10, flow rate 1.0 mL/min, λ = 210 nm), t_R = 11.43 min (minor), t_R = 13.14 min (major). **$[\alpha]_D^{25}$ = –5.2 (*c* = 0.48 g/100 mL, $CHCl_3$, 93% *ee*);** IR (Neat): ν_{max} 2920, 2855, 1715 (C=O), 1556 (NO_2), 1501, 1436, 1386, 1233, 1156, 1112, 827 and 756 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.21-7.13 (2H, m), 7.03-6.95 (2H, m), 4.66 (1H, dd, *J* = 12.4, 6.8 Hz), 4.60 (1H, dd, *J* = 12.4, 7.6 Hz), 4.11 (1H, quin, *J* = 6.8 Hz), 2.93 (1H, dd, *J* = 18.4, 7.6 Hz), 2.87 (1H, dd, *J* = 18.4, 6.4 Hz), 2.05 (3H, s, CH_3). ^{13}C NMR ($CDCl_3$, DEPT-135) δ 205.2 (C, *C*=O), 160.8 (C, d, *J* = 244.0 Hz), 129.9 (CH, d, *J* = 4.0 Hz), 129.5 (CH, d, *J* = 9.0 Hz), 125.5 (C, d, *J* = 13.0 Hz), 124.5 (CH, d, *J* = 3.0 Hz), 116.0 (CH, d, *J* = 22.0 Hz), 77.7 (CH_2, d, *J* = 2.0 Hz), 44.5 (CH_2, d, *J* = 2.0 Hz), 34.4 (CH), 30.1 (CH_3); HRMS m/z 248.0693 (M + Na), calcd for $C_{11}H_{12}FNO_3Na$ 248.0693.

(*R*)-5-nitro-4-(2-nitrophenyl)pentan-2-one (8fa):♥ Prepared following the procedure **A** and purified



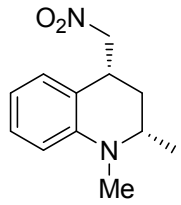
8fa

by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel chiralpak AD-H column (hexane/2-propanol = 90:10, flow rate 1.0 mL/min, λ = 254 nm), t_R = 18.22 min (minor), t_R = 20.31 min (major). **$[\alpha]_D^{25}$ = +28.6 (*c* = 0.41 g/100 mL, $CHCl_3$, 93% *ee*);** IR (Neat): ν_{max} 3019, 1720 (C=O), 1551 (NO_2), 1518, 1359, 1211 and 756 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.81 (1H, d, *J* = 8.4 Hz), 7.52 (1H, t, *J* = 7.6 Hz), 7.37 (1H, t, *J* = 8.0 Hz), 7.31 (1H, d, *J* = 8.0 Hz), 4.77 (1H, dd, *J* = 13.2, 6.4 Hz), 4.73 (1H, dd, *J* = 13.2, 7.2 Hz), 4.45 (1H, quin, *J* = 6.8 Hz), 2.97 (2H, d, *J* = 6.8 Hz), 2.08 (3H, s, CH_3);

^{13}C NMR ($CDCl_3$, DEPT-135) δ 204.8 (C, *C*=O), 149.8 (C), 133.5 (C), 133.2 (CH), 128.7 (CH), 128.5 (CH), 125.1 (CH), 77.9 (CH_2), 45.2 (CH_2), 33.8 (CH), 30.0 (CH_3); HRMS m/z 275.0638 (M + Na), calcd for $C_{11}H_{12}N_2O_5Na$ 275.0638.

♥ The absolute configuration of chiral products **5aa-ha** and **8aa-fa** were also established by comparison of (+)-**8fa** with the same chiral product synthesized from direct asymmetric Michael reaction (see W. Wang et. al. *Org. Lett*. **2009,** *11*, 2864 and L. –X. Wang et. al. *Eur. J. Org. Chem.* **2010**, 1849).

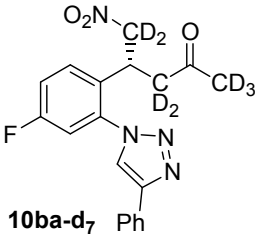
(2*S*,4*R*)-1,2-dimethyl-4-(nitromethyl)-1,2,3,4-tetrahydroquinoline (*syn*-**9aa**): Prepared following



syn-**9aa**

the procedure **C** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Daicel Chiralcel OD-H column (hexane/2-propanol = 95:5, flow rate 0.5 mL/min, λ = 254 nm), t_R = 20.56 min (minor), t_R = 34.60 min (major) [for minor *anti*-isomer], t_R = 22.75 min (major), t_R = 26.02 min (minor) [for major *syn*-isomer]; **$[\alpha]_D^{25}$ = +45.3 [*c* = 0.16 g/100 mL, $CHCl_3$, 89% *ee*** (major *syn*-isomer), **88% *ee*** (minor *anti*-isomer) and *dr* = 6:1]; IR (neat): ν_{max} 2959, 2926, 1605, 1545 (NO_2), 1501, 1375, 1326, 1047 and 751 cm^{-1}; ^{1}H NMR ($CDCl_3$, major *syn*-isomer) δ 7.18-7.15 (1H, m), 6.94 (1H, d, *J* = 7.5 Hz), 6.69-6.64 (2H, m), 4.84 (1H, dd, *J* = 12.0, 6.0 Hz), 4.53 (1H, dd, *J* = 12.0, 10.0 Hz), 3.71-3.65 (1H, m), 3.45-3.40 (1H, m), 2.88 (3H, s, NC*H*$_3$), 2.22-2.17 (1H, m), 1.73-1.67 (1H, m), 1.25 (3H, d, *J* = 6.5 Hz, C*H*$_3$); ^{13}C NMR ($CDCl_3$, DEPT-135, major *syn*-isomer) δ 146.3 (C), 128.5 (CH), 126.1 (CH), 121.3 (C), 116.7 (CH), 112.5 (CH), 80.2 (CH_2), 52.8 (CH), 36.4 (CH), 34.8 (CH_3), 33.9 (CH_2), 20.3 (CH_3); HRMS m/z 243.1102 (M + Na), calcd for $C_{12}H_{16}N_2O_2Na$ 243.1104.

(*R*)-4-(4-fluoro-2-(4-phenyl-1H-1,2,3-triazol-1-yl)phenyl)-5-nitropentan-2-one (**10ba-d$_7$**):

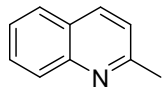


10ba-d$_7$

Prepared following the procedure **D** and purified by column chromatography using EtOAc/hexane and isolated as liquid. The enantiomeric excess (*ee*) was determined by chiral stationary phase HPLC using a Lux 5u cellulose 2 column (hexane/EtOH = 80:20, flow rate 1.0 mL/min, λ = 254 nm), t_R = 17.36 min (major), t_R = 21.37 min (minor); **$[\alpha]_D^{25}$ = +7.8 (*c* = 0.10 g/100 mL, $CHCl_3$, 89% *ee*);** IR (Neat): ν_{max} 3140, 2926, 2860, 1710 (C=O), 1605, 1545 (NO_2), 1507, 1381, 1249, 1178 and 773 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.19 (1H, s), 7.93 (2H, d, *J* = 7.6 Hz), 7.48 (2H, t, *J* = 7.6 Hz), 7.40 (2H, m) 7.28-7.24 (1H, m), 7.15 (1H, dd, *J* = 8.8, 3.6 Hz), 3.79 (1H, m); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 205.3 (C, *C*=O), 161.4 (C, d, *J* = 249.0 Hz, *C*-F), 148.3 (C), 137.2 (C, d, *J* = 9.0 Hz), 131.4 (C), 129.8 (C), 129.2 (CH, d, *J* = 9.0

Hz), 129.0 (2 x CH), 128.7 (CH), 125.9 (2 x CH), 121.9 (CH), 117.8 (CH, d, J = 20.0 Hz), 114.6 (CH, d, J = 24.0 Hz), 32.9 (CH); HRMS m/z 376.1798 (M + H), calcd for $C_{19}H_{11}D_7FN_4O_3$ 376.1797.

2-methylquinoline (12):[5] Prepared following the procedure **E** and purified by column chromatography using EtOAc/hexane and isolated as liquid. IR (Neat): ν_{max} 2920, 2855, 1600 , 1501, 1370, 1216, 816, 778 and 734 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.07 (1H, d, J = 8.4 Hz), 8.05 (1H, d, J = 8.4 Hz), 7.78 (1H, d, J = 8.0 Hz), 7.69 (1H, br t, J = 8.0 Hz), 7.49 (1H, t, J = 7.6 Hz), 7.30 (1H, d, J = 8.4 Hz), 2.76 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$, DEPT-135) δ 158.9 (C), 147.5 (C), 136.4 (CH), 129.6 (CH), 128.3 (CH), 127.5 (CH), 126.5 (C), 125.8 (CH), 122.0 (CH), 25.2 (CH_3); HRMS m/z 144.0808 (M + H), calcd for $C_{10}H_{10}N$ 144.0808.



12

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