Electronic Supplementary Information

Aqueous Chemoenzymatic One-Pot Enantioselective Synthesis of Tertiary α-Aryl Cycloketones via Pd-Catalyzed C-C Formation and Enzymatic C=C Asymmetric Hydrogenation

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Chemicals and materials

All chemicals and reagents were purchased from J & K, Acros, Aldrich and Aladdin, and chemicals were obtained from authentic suppliers at least of reagent grade and used without further purification. Glucose dehydrogenase, formate dehydrogenase, nicotinamide adenine dinucleotide (NADH) and nicotinamide adenine dinucleotide phosphate (NADPH) were purchased from Aladdin (Shanghai, China).

Materials and analytical methods

SEM image of DON@Pd was recorded on Nova Nano SEM450 field-emission microscope. TEM images of DON@Pd were recorded on Talos F200S. Inductively coupled plasma-optical emission spectroscopy (ICP-OES) was carried out on Optima 8300. XPS spectra were collected by a Thermo Scientific K-Alpha X-ray photoelectron spectrometer. X-Ray diffraction analysis were performed on Rigaku XtaLAB P200. Spots were visualized under UV light (Vil-ber Lourmat VL-6.LC, 254 nm) or after treatment with 5% ethanolic phosphomolybdic acid solution and heating of the dried plates. Shimadzu's GC2010 gas chromatograph with a flame ionization detector (FID) using nitrogen as carrier gas was used for gas phase detection. Enantiomeric excesses (ee) were determined by analytical high performance liquid chromatography (HPLC) analysis on an *Agilent Technologies* 1290 Infinity instrument with a chiral stationary phase using a *Daicel* Chiralcel OD-H column, *Daicel* Chiralcel OJ-H column, *Daicel* Chiralcel AS column or a *Daicel* Chiralcel AD column (*n*-heptane/isopropanol mixtures as solvent). Optical rotations were measured on a JASCO DIP-1000 digital polarimeter equipped with a sodium vapor lamp at 589 nm and the concentration of samples was denoted as *c*. For thin-layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF^{254}, 0.25 mm) were used. The products were purified by preparative column chromatography on silica gel E. Merck 9385. NMR spectra were recorded on a Bruker AV 400 spectrometer at 400 MHz (^{1}H NMR and ^{13}C NMR). Chemical shifts were reported in ppm relative to internal TMS for ^{1}H NMR data, respectively. Data are presented in the following space: chemical shift, multiplicity, coupling constant in hertz (Hz), and signal area integration in natural numbers.

Experimental section

Preparation of enzymes

Expression of YqjM-RBS-GDH

The encoding gene YqjM from *Bacillus subtilis* and glucose dehydrogenase from *Bacillus megaterium* IAM1030 were expressed in *E. coli* BL21 (DE3) by using a pET-28b expression vector. The recombinant strain (pET-YqjM-RBS-GDH) was cultured in 10 mL of Luria−Bertani (LB) medium containing kanamycin (50 μg/mL) overnight at 37 ºC in baffled shake flasks. Next, the activated bacterial solution was transferred to a 50 mL LB medium containing kanamycin (50 μg/mL) at 1% inoculation amount. When the culture's optical cell density of OD_{600} reached 0.6-0.8 after culture at 37 ºC, IPTG was added to induce the expression of the target gene. After induction at 20 ºC, 180 rpm for 20 h, sedimentation was collected by centrifugation (4°C, 8000 rpm, 30 min) and washed several times with precooling PBS buffer (50 mM, pH 7.0). The medium was discarded and cells were resuspended in sterile water. Then cells were snap-frozen in liquid nitrogen and lyophilized. The expression process of the other three old yellow enzymes was similar. The resuspended cells were disrupted by high-pressure homogenization, and the supernatant obtained after centrifugation (4°C, 12,000 rpm, 20 min). The sample was analyzed by SDS-PADE (Figure S1).

Expression of ADH-A

The encoding gene ADH-A from *Rhodococcus ruber* was expressed in *E. coli* BL21 (DE3) by using the pET-22b(+) expression vector. The recombinant strain (pET-22b(+)-ADH-A) was cultured in 10 mL of LB medium containing ampicillin (50 μg/mL) overnight at 37 ºC in baffled shake flasks. Next, the activated bacterial solution was transferred to a 50 mL LB medium containing ampicillin (50 μg/mL) at 1% inoculation amount. When the culture's optical cell density of OD_{600} reached 0.6-0.8 after culture at 37 ºC, IPTG was added to induce the expression of the target gene. After induction at 20 ºC, 140 rpm for 24 h, sedimentation was collected by centrifugation (4°C, 8000 rpm, 30 min) and washed several times with precooling PBS buffer (50 mM, pH 7.0). The medium was discarded and cells were re-suspended in sterile water. Then cells were snap-frozen in liquid nitrogen and lyophilized.

Synthesis of DON[1]

Dendritic organosilica nanoparticles (DON) were prepared based on a continuous phase microemulsion method. Firstly, 1.25 g cetyltrimethyammniumbromide (CTAB), 1.25 g *n*-butanol and 5 g cyclohexane were dissolved in 100 g urea solution (0.4 M) and then the mixture was ultrasonicated for 30 min; Secondly, the solution of tetraethyl orthosilicate (TEOS, 0.875 g) and bis(triethoxysilyl)ethane (BTSE, 0.375 g) was added dropwise to the above mixture and stirred at

25 °C for 30 min; Next, the mixture was stirred at 70 °C for 24 h. The products were washed with ethanol and water for three times. Finally, DON were redispersed in 250 mL of acetone and refluxed at 80 °C for 48 h to remove the templates and then washed with ethanol and dried at room temperature.

Synthesis of DON@Pd[1]

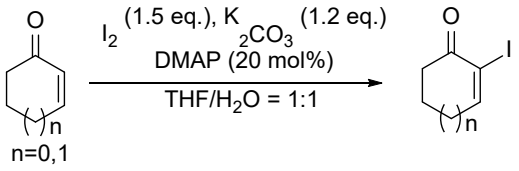
Post-modification method was employed to achieve the amino-functionalization of DON. Briefly, 1.0 g of the DON were added into 100 mL of *n*-hexane, and ultrasonicated for 30 min. Then, 1.0 mL of APTES was added, and the mixture was refluxed at 80 °C for 12 h. Finally, the solid products were washed with ethanol for three times and dried at 60 °C for 12 h prior to use.

Immobilization of Pd nanoparticles (Pd NPs) in the channels was achieved via a *in situ* growth approach. Typically, 56 mg of amino-functionalized DON were ultrasonically dispersed in 10 mL of ultrapure water and the mixture was stirred for 15 min at 30 °C. Next, a solution of sodium tetrachloropalladate (8.14 mg) for DON@Pd (5%) was added dropwise to the reaction mixture and further stirred for 4 h at 30 °C. Then, $NaBH_4$ (10 equiv.) were added to the above solutions with stirring for 2 h. The resulting solids were isolated by centrifugation, and washed with water and ethanol, dried under vacuum at 60 °C for 12 h, obtaining DON@Pd.

Synthesis of immobilized enzymes

The amino-functionalized DON were firstly activated with glutaraldehyde (0.4 wt%) at room temperature. Then, the glutaraldehyde-activated DON (100 mg) were redispersed in 5 mL Tris-HCl buffer (50 mM, pH 7.5) by sonication for 10 min. Subsequently, 5 mL of purified enzyme solution (5 mg/mL) was added, and the mixed solution was shaken at 170 rpm for 2 h. The final immobilized enzymes were washed with Tris-HCl buffer (50 mM, pH 7.5) for three times. Finally, the products were freeze-dried overnight.

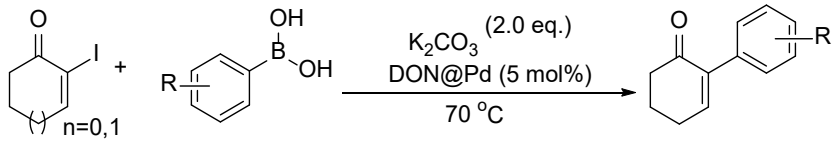
Synthesis of 2-iodocycloenones[2]



To a stirred solution of cycloenone (30 mmol) in a mixed solvent of THF (75 mL) and water (75 mL) was added potassium carbonate (5.0 g, 36 mmol), iodine (11.4 g, 45 mmol) and 4-dimethylamiopryidine (0.73 g, 6 mmol) at room temperature. The reaction mixture was stirred for 3 h to complete the reaction. The solution was diluted with 150 mL of

ethyl acetate, washed with 100 mL of saturated aqueous sodium thiosulfate and 100 mL of brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was chromatographied on silica gel column with ethyl acetate/petroleum ether (1:20 to 1:10) to give 2-iodocycloenone.

Suzuki-Miyaura coupling reaction



2-Iodocycloenones (0.25 mmol), arylboronic acids (0.25 mmol), K_2CO_3 (0.5 mmol) and DON@Pd (or Pd/C) (5 mol%) were added to a 25 mL reaction flask, and dissolved with 8 mL Tris-HCl buffer (50 mM, pH 7.5) and 2 mL [BMIm][NTf_2]. The mixture was heated to 70 °C and stirred for 6 hours. The reaction progress was monitored by TLC. After the reaction was completed, the catalyst was filtered and washed repeatedly with ultrapure water. Products were extracted with diethyl ether (20 mL), and the organic phase was dried using anhydrous Na_2SO_4. The solvent was concentrated in vacuo to obtain the crude products. The products were purified by column chromatography using petroleum ether/ethyl acetate (20:1) as eluent.

Enzymatic asymmetric hydrogenation of 2-phenylcyclohexenone

without cofactor regeneration system: 2-Phenylcyclohexenone (0.25 mmol), NADPH/NADH (0.15 mmol) and whole cells contain YqjM (0.2 g) were added to a 25 mL reaction flask, and dissolved with 8 mL Tris-HCl buffer (50 mM, pH 7.5) and 2 mL [BMIm][NTf_2]. The mixture was stirred for 12 hours at room temperature. After the reaction was completed, the catalyst was separated. Products were extracted with diethyl ether (20 mL), and the organic phase was dried using anhydrous Na_2SO_4. The solvent was concentrated in vacuo to obtain the crude products. The products were purified by column chromatography using petroleum ether/ethyl acetate (20:1) as eluent. The values of ee were determined by HPLC.

Using extra GDH for cofactor regeneration: 2-Phenylcyclohexenone (0.25 mmol), NADPH (0.002 mmol), glucose/ammonium formate (2 mmol), whole cells contain YqjM (0.2 g) and GDH/FDH (100 U) were added to a 25 mL reaction flask, and dissolved with 8 mL Tris-HCl buffer (50 mM, pH 7.5) and 2 mL [BMIm][NTf_2]. The mixture was stirred for 12 hours at room temperature.

Using co-expressed YqjM-RBS-GDH for cofactor regeneration: 2-Phenylcyclohexenone (0.25 mmol), NADPH (0.002 mmol), glucose (2 mmol) and whole cells contain YqjM-RBS-GDH (0.2 g) were added to a 25 mL reaction flask,

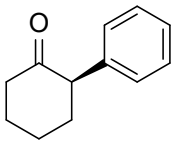
and dissolved with 8 mL Tris-HCl buffer (50 mM, pH 7.5) and 2 mL [BMIm][NTf_2]. The mixture was stirred for 12 hours at room temperature. After the reaction was completed, the catalyst was separated. Products were extracted with diethyl ether (20 mL), and the organic phase was dried using anhydrous Na_2SO_4. The solvent was concentrated in vacuo to obtain the crude products. The products were purified by column chromatography using petroleum ether/ethyl acetate (20:1) as eluent. The values of ee were determined by HPLC.

Chemoenzymatic asymmetric synthesis of tertiary α-aryl cycloanones

2-Iodocycloenones (0.25 mmol), arylboronic acids (0.25 mmol), K_2CO_3 (0.5 mmol) and DON@Pd (5 mol%) were added to a 25 mL reaction flask, and dissolved with 8 mL Tris-HCl buffer (50 mM, pH 7.5) and 2 mL [BMIm][NTf_2]. The mixture was heated to 70 °C and stirred for 6 hours. After the reaction was completed, the temperature was cooled to room temperature and then the pH was adjusted to 7.5. Then, NADPH (0.002 mmol), glucose (2 mmol) and whole cells (0.2 g) were added to the mixture and stirred for 12 h. After the reaction was completed, the catalyst was separated. Products were extracted with diethyl ether (20 mL), and the organic phase was dried using anhydrous Na_2SO_4. The solvent was concentrated in vacuo to obtain the crude products. The products were purified by column chromatography using petroleum ether/ethyl acetate (20:1) as eluent. The values of ee were determined by HPLC.

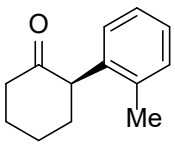
(*R*)-2-phenylcyclohexanone (**2a**)

The *R* configuration of **2a** was determined by optical rotation compared with the literature data. The optical rotation of the product **2a** is $[\alpha]_D^{22}$ = +108.9 (*c* 0.45, $CHCl_3$, 99% ee) [Lit. $[\alpha]_D^{22}$ = +102 (*c* 0.45, $CHCl_3$, 93% ee)]



White solid, 81% yield, 99% ee, $[\alpha]_D^{22}$ = +108.9 (*c* 0.45, $CHCl_3$), **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.5 Hz, 2H), 7.27 (s, 1H), 7.14 (d, *J* = 7.5 Hz, 2H), 3.61 (dd, *J* = 12.1, 5.4 Hz, 1H), 2.57 – 2.41 (m, 2H), 2.32 – 2.22 (m, 1H), 2.15 (q, *J* = 5.9 Hz, 1H), 2.02 (ddd, *J* = 14.1, 9.9, 3.9 Hz, 2H), 1.83 (t, *J* = 10.3 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 209.59, 138.05, 127.82, 127.81, 127.64, 127.64, 126.18, 56.68, 41.49, 34.39, 27.12, 24.62. HPLC analysis (Chiralpak OD-H column, hexane/2-propanol = 99:1, flow rate = 1.0 mL/min, wavelength = 210 nm): t_R = 17.6 (major) and 15.6 min (minor).

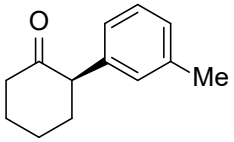
(*R*)-2-(2-tolyl)cyclohexanone (**2b**)



White solid, 54% yield, 97% ee, **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.16 (h, *J* = 7.3 Hz, 4H), 3.78 (dd, *J* = 12.9, 5.3 Hz, 1H), 2.62 – 2.46 (m, 2H), 2.31 – 2.24 (m, 1H), 2.20 (s, 4H), 2.04 (dd, *J* = 13.5, 9.6 Hz, 2H), 1.90 – 1.77 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 209.98, 137.37, 136.14, 130.26,

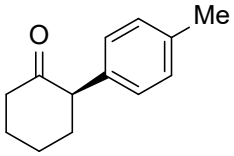
127.61, 126.82, 125.97, 53.83, 42.54, 34.18, 27.77, 25.88, 19.73. HPLC analysis (Chiralpak OD-H column, hexane/2-propanol = 95:5, flow rate = 1.0 mL/min, wavelength = 210 nm): t_R = 18.3 (major) and 16.6 min (minor).

(*R*)-2-(3-tolyl)cyclohexanone (**2c**)



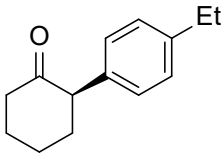
White solid, 70% yield, 93% ee, **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.24 (d, *J* = 10.2 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 8.2 Hz, 2H), 3.57 (dd, *J* = 12.2, 5.5 Hz, 1H), 2.58 – 2.42 (m, 2H), 2.34 (s, 3H), 2.29 – 2.22 (m, 1H), 2.20 – 2.11 (m, 1H), 2.02 (dt, *J* = 18.1, 6.4 Hz, 2H), 1.88 – 1.77 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 210.49, 138.68, 137.85, 129.30, 128.25, 127.71, 125.51, 57.36, 42.19, 35.01, 27.80, 25.32, 21.50. HPLC analysis (Chiralpak AS column, hexane/2-propanol = 98:2, flow rate = 1.0 mL/min, wavelength = 210 nm): t_R = 11.0 (major) and 12.4 min (minor).

(*R*)-2-(4-tolyl)cyclohexanone (**2d**)



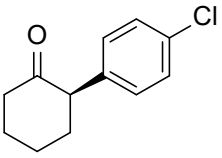
White solid, 74% yield, 95% ee, **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.14 (d, *J* = 7.8 Hz, 2H), 7.05 – 6.96 (m, 2H), 3.57 (dd, *J* = 12.1, 5.4 Hz, 1H), 2.50 (d, *J* = 1.6 Hz, 2H), 2.33 (s, 3H), 2.29 – 2.20 (m, 1H), 2.13 (dtdd, *J* = 8.3, 5.8, 4.5, 2.6 Hz, 1H), 2.06 – 1.92 (m, 2H), 1.86 – 1.76 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 210.62, 136.45, 135.71, 129.10, 129.09, 128.36, 128.35, 57.01, 42.17, 35.09, 27.82, 25.34, 21.09. HPLC analysis (Chiralpak OD-H column, hexane/2-propanol = 95:5, flow rate = 1.0 mL/min, wavelength = 210 nm): t_R = 14.1 (major) and 13.2 min (minor).

(*R*)-2-(4-ethylphenyl)cyclohexanone (**2e**)



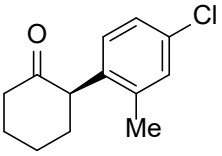
White solid, 90% yield, 95% ee, **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.17 (d, *J* = 7.6 Hz, 2H), 7.05 (d, *J* = 7.8 Hz, 2H), 3.58 (dd, *J* = 12.0, 5.5 Hz, 1H), 2.64 (q, *J* = 7.7 Hz, 2H), 2.57 – 2.40 (m, 2H), 2.33 – 2.20 (m, 1H), 2.19 – 2.09 (m, 1H), 2.06 – 1.93 (m, 2H), 1.82 (dq, *J* = 11.7, 8.5, 6.2 Hz, 2H), 1.23 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 210.70, 142.69, 135.92, 128.39, 128.39, 127.87, 127.87, 57.02, 42.18, 35.11, 28.46, 27.84, 25.33, 15.39. HPLC analysis (Chiralpak AS column, hexane/2-propanol = 99:1, flow rate = 1.0 mL/min, wavelength = 210 nm): t_R = 9.3 (major) and 10.7 min (minor).

(*R*)-2-(4-chlorophenyl)cyclohexanone (**2f**)



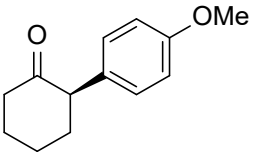
White solid, 93% yield, 96% ee, **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.38 – 7.27 (m, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 3.59 (dd, *J* = 12.3, 5.4 Hz, 1H), 2.60 – 2.39 (m, 2H), 2.26 (dt, *J* = 11.3, 4.5 Hz, 1H), 2.17 (s, 1H), 2.06 – 1.90 (m, 2H), 1.89 – 1.74 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 209.87, 137.24, 132.70, 131.63, 129.96, 128.51, 124.77, 56.84, 42.23, 35.29, 27.82, 25.40. HPLC analysis (Chiralpak AS column, hexane/2-propanol = 98:2, flow rate = 1.0 mL/min, wavelength = 210 nm): t_R = 10.2 (major) and 12.3 min (minor).

(*R*)-2-(4-chloro-2-methylphenyl)cyclohexanone (**2g**)



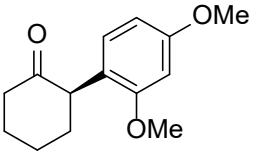
White solid, 48% yield, 91% ee, **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.17 (d, *J* = 7.0 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 1H), 3.73 (dd, *J* = 12.8, 5.1 Hz, 1H), 2.61 – 2.43 (m, 2H), 2.26 – 2.12 (m, 5H), 2.10 – 1.94 (m, 2H), 1.83 (tt, *J* = 12.2, 6.0 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 209.64, 138.14, 135.88, 132.33, 130.12, 129.01, 126.05, 53.35, 42.52, 34.25, 27.77, 25.84, 19.61. HPLC analysis (Chiralpak OD-H column, hexane/2-propanol = 99:1, flow rate = 1.0 mL/min, wavelength = 210 nm): t_R = 18.6 (major) and 17.8 min (minor).

(*R*)-2-(4-methoxyphenyl)cyclohexanone (**2h**)



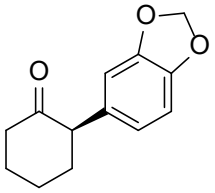
White solid, 71% yield, 96% ee, **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.06 (dd, *J* = 9.0, 2.4 Hz, 2H), 6.90 – 6.86 (m, 2H), 3.79 (d, *J* = 1.5 Hz, 3H), 3.56 (dd, *J* = 12.2, 5.5 Hz, 1H), 2.56 – 2.39 (m, 2H), 2.30 – 2.21 (m, 1H), 2.18 – 2.09 (m, 1H), 1.99 (dq, *J* = 12.7, 4.2 Hz, 2H), 1.87 – 1.77 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 210.74, 158.43, 130.86, 129.44, 129.09, 114.07, 113.82, 56.56, 55.21, 42.17, 35.28, 27.85, 25.38. HPLC analysis (Chiralpak OD-H column, hexane/2-propanol = 95:5, flow rate = 1.0 mL/min, wavelength = 210 nm): t_R = 15.5 (major) and 12.2 min (minor).

(*R*)-2-(2,4-dimethoxyphenyl)cyclohexanone (**2i**)



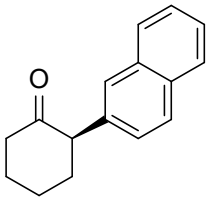
White solid, 40% yield, 98% ee, **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.01 (d, *J* = 8.2 Hz, 1H), 6.53 – 6.42 (m, 2H), 3.86 (dd, *J* = 12.9, 5.4 Hz, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 2.59 – 2.35 (m, 2H), 2.24 – 2.06 (m, 2H), 2.00 (d, *J* = 9.9 Hz, 2H), 1.89 – 1.69 (m, 1H), 1.57 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 210.32, 159.70, 157.86, 129.04, 120.32, 104.15, 98.67, 55.43, 55.32, 50.47, 42.32, 33.63, 27.64, 25.80. HPLC analysis (Chiralpak OJ-H column, hexane/2-propanol = 99:1, flow rate = 0.7 mL/min, wavelength = 210 nm): t_R = 18.3 (major) and 17.5 min (minor).

(*R*)-2-(benzo[*d*][1,3]dioxol-5-yl)cyclohexanone (**2g**)



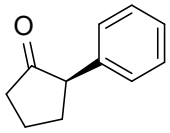
White solid, 61% yield, 98% ee, **^{1}H NMR** (400 MHz, Chloroform-d) δ 6.76 (d, *J* = 8.0 Hz, 1H), 6.64 (d, *J* = 1.7 Hz, 1H), 6.57 (dd, *J* = 8.0, 1.7 Hz, 1H), 5.93 (s, 2H), 3.56−3.50 (m, 1H), 2.55−2.49 (m, 1H), 2.48−2.39 (m, 1H), 2.28−2.21 (m, 1H), 2.19−2.10 (m, 1H), 2.04−1.91 (m, 2H), 1.87−1.73 (m, 2H). **^{13}C NMR** (101 MHz, CDCl3) δ 210.6, 147.7, 146.6, 132.7, 121.7, 109.1, 108.3, 101.1, 57.3, 42.3, 35.5, 27.9, 25.6. HPLC analysis (Chiralpak AS column, hexane/2-propanol = 99:1, flow rate = 1.0 mL/min, wavelength = 210 nm): t_R = 11.9 (major) and 13.8 min (minor).

(*R*)-2-(naphthalen-2-yl)cyclohexanone (**2k**)



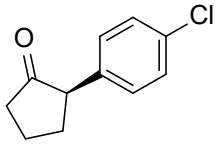
White solid, 60% yield, 91% ee, **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.94 – 7.75 (m, 3H), 7.60 (s, 1H), 7.55 – 7.39 (m, 2H), 7.29 (s, 1H), 3.79 (dd, *J* = 12.2, 5.5 Hz, 1H), 2.54 (ddd, *J* = 18.5, 12.3, 7.7 Hz, 2H), 2.35 (dt, *J* = 13.9, 4.1 Hz, 1H), 2.28 – 2.12 (m, 2H), 2.06 (dt, *J* = 9.1, 4.6 Hz, 1H), 1.94 – 1.82 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 210.49, 136.39, 133.47, 132.54, 127.82, 127.73, 127.63, 127.04, 126.99, 125.89, 125.61, 57.48, 42.25, 35.06, 27.83, 25.33. HPLC analysis (Chiralpak OD-H column, hexane/2-propanol = 95:5, flow rate = 1.0 mL/min, wavelength = 210 nm): t_R = 31.8 (major) and 25.8 min (minor).

(*R*)-2-phenylcyclopentanone (**2l**)



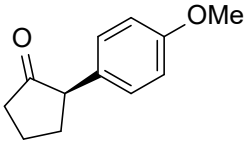
Yellow oil, 78% yield, >99% ee, **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.38-7.20 (m, 5 H), 3.36-3.30 (m, 1 H), 2.55-2.42 (m, 2 H), 2.36-1.89 (m, 4 H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 217.9, 138.4, 128.5, 128.1, 126.8, 55.4, 38.6, 31.9, 21.0. HPLC analysis (Chiralpak AD column, hexane/2-propanol = 99:1, flow rate = 1.0 mL/min, wavelength = 210 nm): t_R = 6.0 (major).

(*R*)-2-(4-chlorophenyl)cyclopentanone (**2m**)



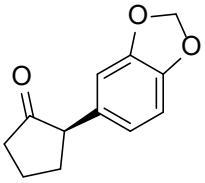
White solid, 76% yield, 97% ee, **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.31-7.29 (m, 2 H), 7.13 (d, J = 8.4 Hz, 2 H), 3.30-3.27 (m, 1 H), 2.53-2.44 (m, 2 H), 2.34-1.89 (m, 4 H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 217.3, 136.8, 132.8, 129.6, 128.8, 54.9, 38.5, 31.8, 21.0. HPLC analysis (Chiralpak AD column, hexane/2-propanol = 99:1, flow rate = 1.0 mL/min, wavelength = 210 nm): t_R = 5.9 (major) and 6.9 min (minor).

(*R*)-2-2-(4-methoxyphenyl)cyclopentanone (**2n**)



White solid, 73% yield, 98% ee, **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.26 (d, *J* = 2.0 Hz, 1H), 7.24 (d, *J* = 2.2 Hz, 1H), 7.02 (d, *J* = 2.1 Hz, 1H), 7.00 (d, *J* = 2.1 Hz, 1H), 3.93 (s, 2H), 3.44 – 3.36 (m, 1H), 2.66 – 2.54 (m, 3H), 2.41 (ddd, *J* = 18.8, 10.6, 8.6 Hz, 1H), 2.33 – 2.14 (m, 2H), 2.13 – 2.00 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 218.45, 158.53, 130.44, 129.09, 129.09, 114.08, 114.08, 55.28, 54.57, 38.29, 31.80, 20.79. HPLC analysis (Chiralpak AD column, hexane/2-propanol = 99:1, flow rate = 1.0 mL/min, wavelength = 210 nm): t_R = 21.8 (major) and 24.2 min (minor).

(*R*)-2-(benzo[*d*][1,3]dioxol-5-yl)cyclopentanone (**2o**)



White solid, 71% yield, 96% ee, **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 6.73 (d, *J* = 7.9 Hz, 1H), 6.66 – 6.57 (m, 2H), 5.87 (s, 2H), 3.26 – 3.14 (m, 1H), 2.50 – 2.33 (m, 2H), 2.21 (ddd, *J* = 18.8, 10.6, 8.6 Hz, 1H), 2.13 – 2.04 (m, 1H), 2.04 – 1.94 (m, 1H), 1.87 (dddd, *J* = 12.0, 10.8, 8.1, 6.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 218.08, 147.83, 146.50, 132.11, 121.31, 108.54, 108.34, 100.99, 55.07, 38.25, 31.89, 20.71. HPLC analysis (Chiralpak AD column, hexane/2-propanol = 95:5, flow rate = 1.0 mL/min, wavelength = 210 nm): t_R = 14.5 (major) and 15.9 min (minor).

Enzymatic asymmetric hydrogenation of α-alkyl enones

α-Substituted cycloenones (0.25 mmol), NADPH (0.002 mmol) and glucose (2 mmol) were added to a 25 mL reaction flask, and dissolved with 8 mL Tris-HCl buffer (50 mM, pH 7.5) and 2 mL [BMIm][NTf_2], then whole cells were added (0.2 g). The mixture was stirred at room temperature for 12 hours. The reaction progress was monitored by TLC. After the reaction was completed, the catalyst was filtered. Products were extracted with diethyl ether (20 mL), and the organic phase was dried using anhydrous Na_2SO_4. The solvent was concentrated in vacuo to obtain the crude products. The products were purified by column chromatography using petroleum ether/ethyl acetate (20:1) as eluent. The conversions and the values of ee were determined by GC.

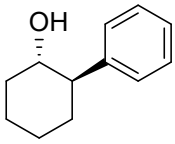
Three-step one-pot chemoenzymatic asymmetric synthesis of chiral α-aryl cycloalkanol

2-Iodocycloenones (0.25 mmol), arylboronic acids (0.25 mmol), K_2CO_3 (0.5 mmol) and DON@Pd (5 mol%) were added to a 25 mL reaction flask, and dissolved with 8 mL Tris-HCl buffer (50 mM, pH 7.5) and 2 mL [BMIm][NTf_2]. The mixture was heated to 70 °C and stirred for 6 hours. After the reaction was completed, the temperature was cooled to room temperature and the pH was adjusted to 7.5. Then, NADPH (0.002 mmol), glucose (2 mmol) and whole cells (0.2

g) were added to the mixture stirring for 12 h. After the reaction was completed, ADH-A (0.2 g) and fresh NADPH (0.002 mmol) were added to the mixture stirring for 12 h. After the reaction was completed, products were extracted with diethyl ether (20 mL), and the organic phase was dried using anhydrous Na_2SO_4. The solvent was concentrated in vacuo to obtain the crude product. The products were purified by column chromatography using petroleum ether/ethyl acetate (20:1) as eluent. The value of ee was determined by HPLC.

(1*S*,2*R*)-2-phenylcyclohexan-1-ol (**4**)[3]

The absolute configuration of **4** was determined by optical rotation compared with the literature data. The optical rotation of the product **4** is $[\alpha]_D^{23}$ = +58.9 (*c* 1.83, MeOH) [Lit. $[\alpha]_D^{23}$ = +59.3 (*c* 1.83, MeOH, 98% ee)].



White solid, 62% yield, 98% ee, **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.32 (t, *J* = 7.4 Hz, 2H), 7.24 (d, *J* = 7.5 Hz, 3H), 3.63 (td, *J* = 10.0, 4.2 Hz, 1H), 2.41 (ddd, *J* = 13.2, 9.9, 3.5 Hz, 1H), 2.10 (dt, *J* = 8.0, 3.3 Hz, 1H), 1.85 (d, *J* = 13.3 Hz, 2H), 1.79 – 1.71 (m, 1H), 1.65 (d, *J* = 4.4 Hz, 1H), 1.55 – 1.39 (m, 2H), 1.39 – 1.25 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.31, 128.79, 128.77, 127.95, 127.93, 126.85, 74.44, 53.24, 34.45, 33.34, 26.08, 25.09. HPLC analysis (Chiralpak OD-H column, hexane/2-propanol = 99:1, flow rate = 0.5 mL/min, wavelength = 210 nm): t_R = 6.8 (major) and 6.0 min (minor).

Reusability of the catalysts

2-Iodocycloenones (0.25 mmol), arylboronic acids (0.25 mmol), K_2CO_3 (0.5 mmol) and DON@Pd (5 mol%) were added to a 25 mL reaction flask, and dissolved with 8 mL Tris-HCl buffer (50 mM, pH 7.5) and 2 mL [BMIm][NTf_2]. The mixture was heated to 70 °C and stirred for 6 hours. After the reaction was completed, DON@Pd were separated from the reaction system by centrifuge; Then the temperature was kept to room temperature and the pH was adjusted to 7.5. Finally, NADPH (0.002 mmol), glucose (2 mmol) and whole cells (0.2 g) were added to the mixture stirring for 12 h. After the reaction was completed, cells (or the immobilized enzymes) were separated from the reaction system by centrifuge and then washed with Tris-HCl buffer (50 mM, pH 7.5) to remove the remaining substrate and product. The both catalysts were then used in a new cycle. The experimental results were shown in Figure S6 and S8.

Molecular docking

AutoDock 4 was used for the docking of ketones into the model structures. A grid box of 30 × 30 × 30 with spacing of 1.0 Å, which encompassed the active sites of YqjM, was set as the search space to explore suitable substrate-binding modes. The PDBQT format was employed for both the input and output of molecular structures.

Determination of enzyme loading

The enzyme loading on the enzyme@DON was determined through the Bradford method using bovine serum albumin (BSA) as a standard.

Construction of YqjM mutant

Site-directed YqjM mutant was generated by overlap extension PCR and sequenced to confirm the amplification product. Two partially overlapping PCR products were generated by using the upstream primer YqjM-F or downstream primer YqjM-R with the corresponding internal primer (Table S3), and then annealed to create a gene product containing two mutations 60G and 69G. The expression vector pET28a-YqjM-GDH containing wild-type YqjM gene was digested with Nde I and Pst I restriction enzymes. The YqjM mutant gene was inserted into the digested vector using GenBuilder DNA Assembly kit (Genscript), and then transformed into *E. coli* DH5a for amplification. Mutant was confirmed by sequencing and then transformed into *E. coli* BL21(DE3) cells (Novagen) for expression.

The effect of cosolvents on relative enzyme activity

For assaying the effect of co-solvents, activities of free YqjM were tested in the buffer solution containing 20 vol.% different cosolvents (DMF, DME, acetone, DMSO, THF, [BMIm][PF_6], and [BMIm][NTf_2]). As shown in Figure S1, the results were presented via relative activity, and the activity of the sample without adding cosolvent was regarded as 100%.

The activity of YqjM was assayed in 1mL of the reaction mixture consisting of 100 μL of 10 mM 2-methylcyclohenxenone, appropriate amounts of free YqjM in cell lysates, and 800 μL of Tris-HCl (100 mM, pH 7.5). Then, 100 μL of 1.5 mM NADPH was added, and the activity levels were measured by monitoring the consumption of NADPH by a spectrophotometric method. The absorbance at 340 nm and the concentration of NADPH was determined based on the standard calibration curve. One unit of YqjM activity was defined as the enzyme mass that consumed 1 μM of NADPH per minute under the above conditions.

Stability of the whole cell and enzyme@DON

To study the organic solvent tolerance, the yield of whole cell and enzyme@DON were measured by incubation in 10 mL of the different organic solvents at room temperature for 3 h. To study the pH stability, the yield of whole cell and enzyme@DON were measured by incubation in Tris-HCl buffer (50 mM, pH 4.0) or acetate buffer (50 mM, pH 10.0) at

room temperature for various times. To study the thermal stability, the yield of whole cell and enzyme@DON were measured by incubation in Tris-HCl (50 mM, pH 7.5) buffer at 50 and 60°C for various times. To study the storage stability, the yield of whole cell and enzyme@DON were measured at different time intervals during the storage period (0-12 days) at room temperature.

Results and discussion

The effect of cosolvents on relative enzyme activity

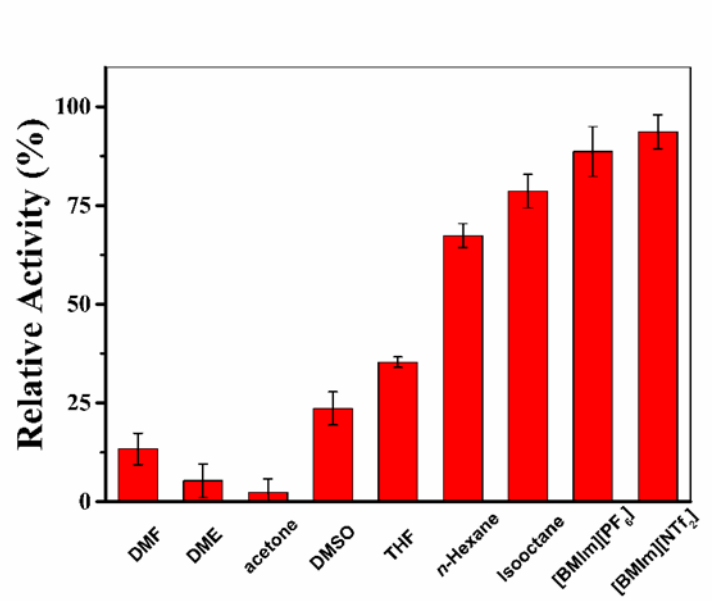


Figure S1. The effect of cosolvents on relative enzyme activity.
Free YqjM were incubated in the buffer solution (50 mM, pH 7.5) containing 20 vol.% different cosolvents for 3 h.

Characterization of catalysts

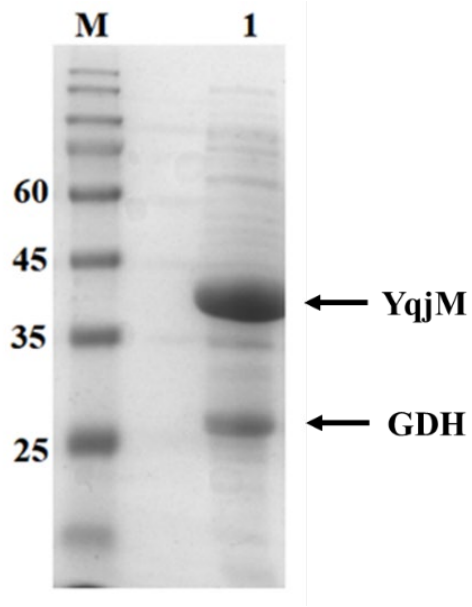


Figure S2. SDS-PAGE analysis of YqjM-RBS-GDH, whole cell sample of *E. coli* BL21(DE3) producing the YqjM and GDH; sample loading normalized to OD_{600} = 0.7.

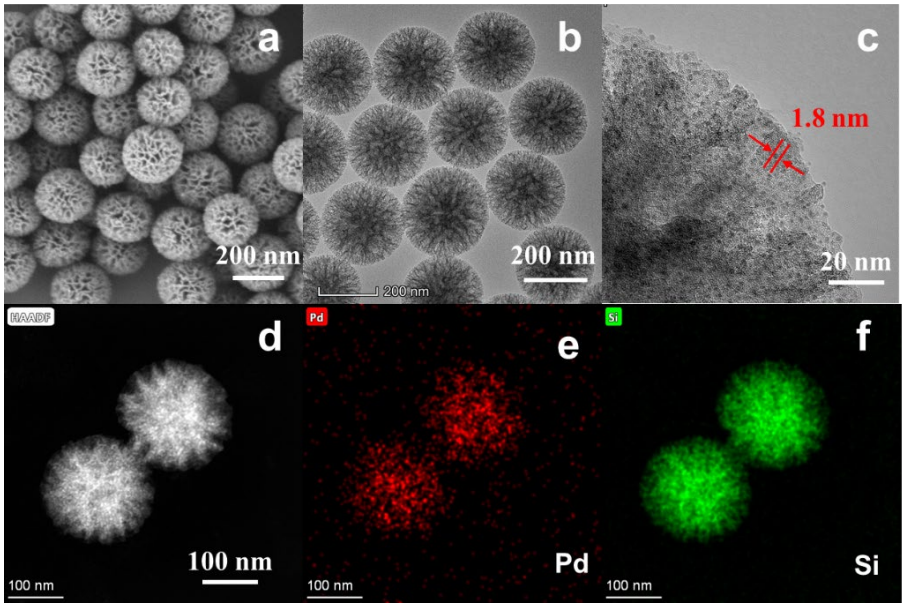


Figure S3. (a) SEM and (b,c) TEM images of DON@Pd. (d-f) Elemental mappings of DON@Pd.

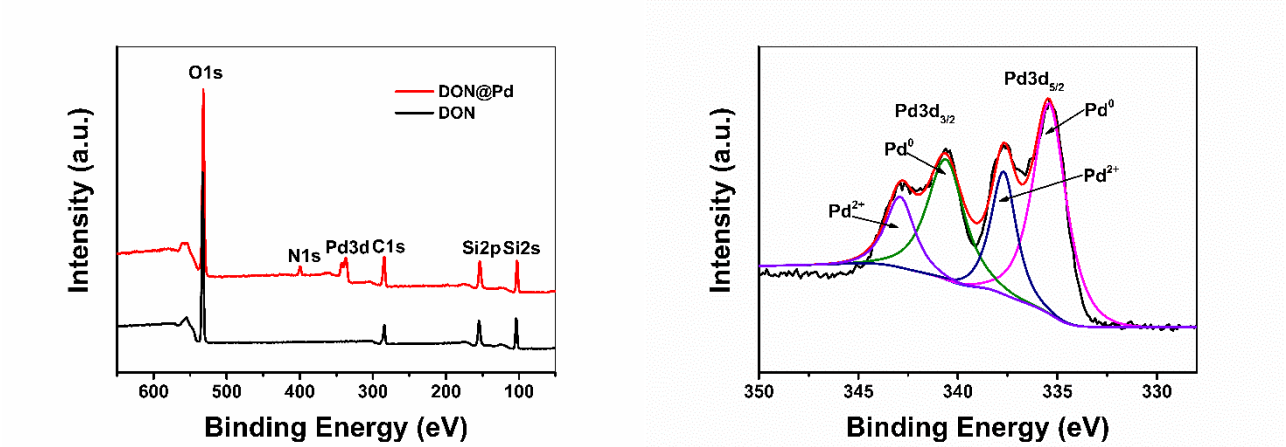


Figure S4. X-ray photoelectron spectroscopy (XPS) was conducted to estimate the elemental composition of DON and DON@Pd.

The survey XPS data verified the existence of Si, O, C, N, and Pd elements without any impurities. The high-resolution Pd3d spectrum can be curve-fit into two sets of spin-orbit doublets with peaks at 335.1, 340.6 eV and 336.3, 341.5 eV, corresponding to Pd^0 and Pd^{2+} states, respectively.

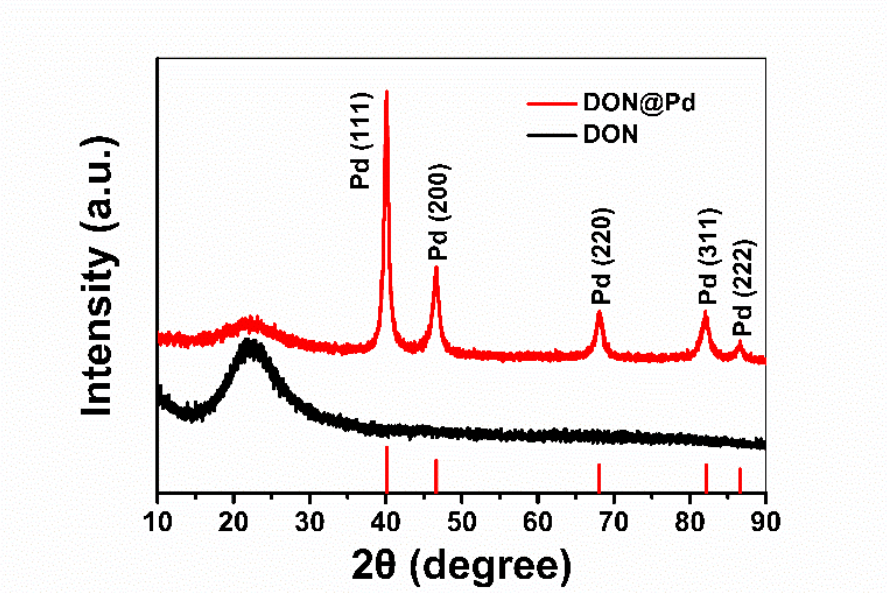


Figure S5. X-ray diffraction (XRD) patterns of the DON and DON@Pd.

The five distinct peaks centered at 2θ = 40.0°, 46.6°, 68.4°,82.4° and 86.0° were assigned to the (111), (200), (220), (311) and (222) crystalline planes of the face-centered cubic (fcc) structures of Pd (JCPDS01-1190), indicating that the Pd NPs were successfully synthesized.

Induced docking experiment

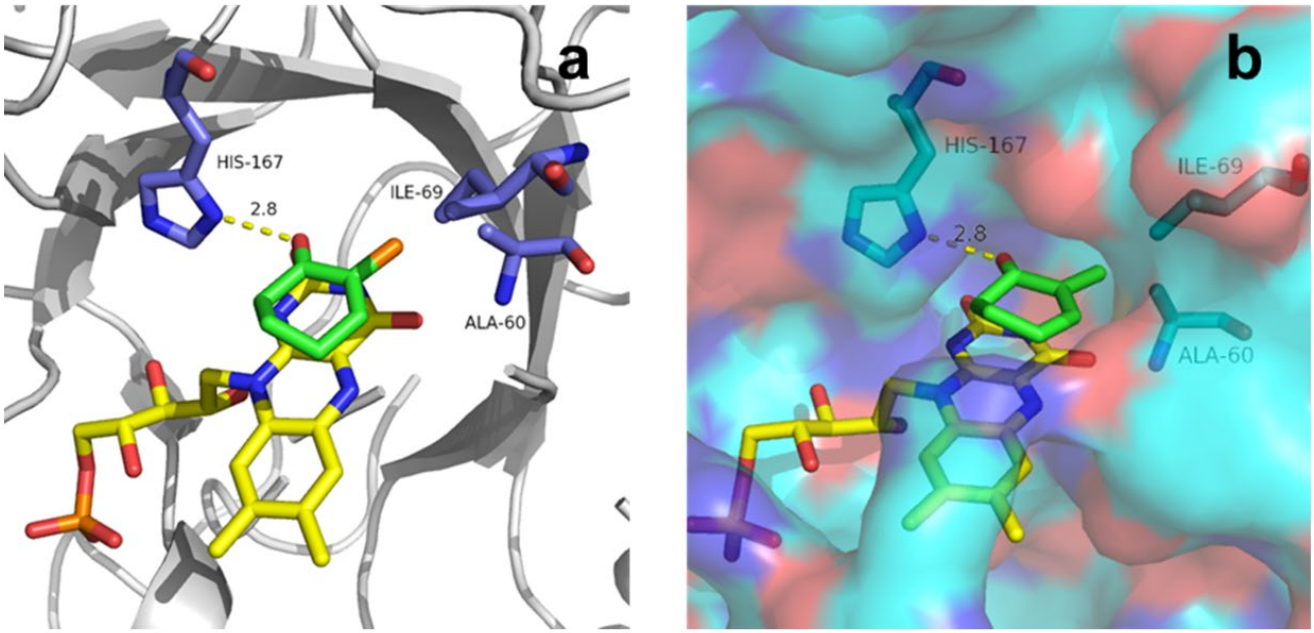


Figure S6. Docking of (a) **3a** within the active site of YqjM, and surface representation of the active site view of YqjM with (b) **3a**

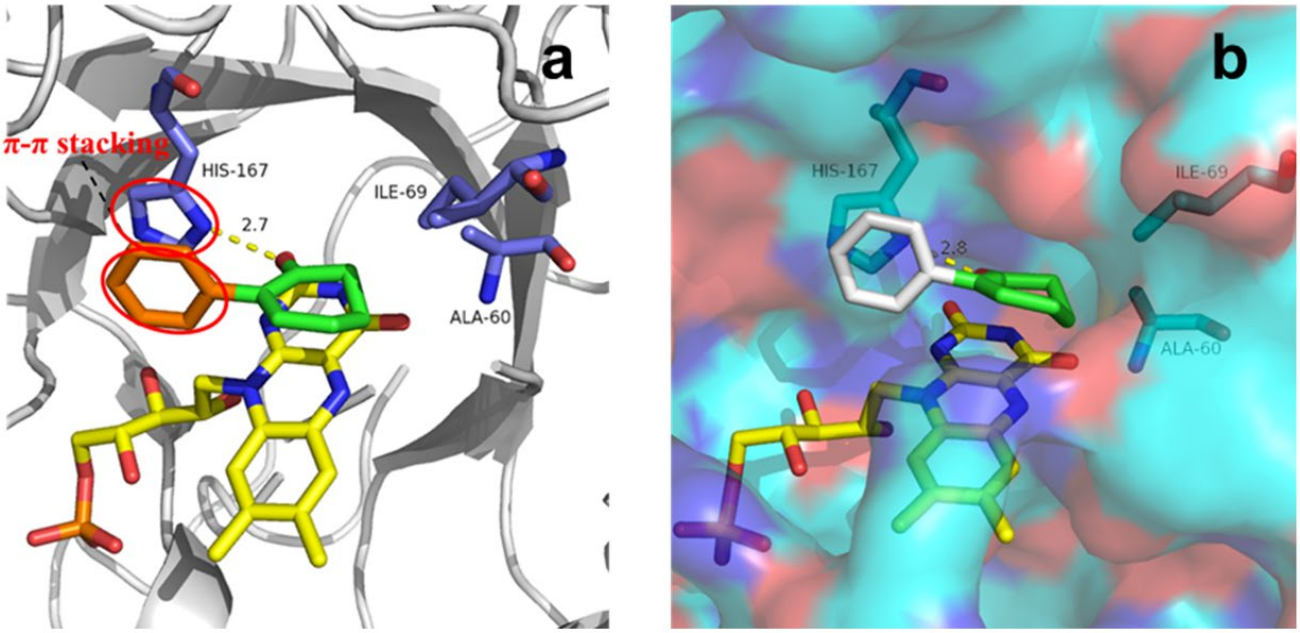


Figure S7. Docking of (a) **2a** within the active site of YqjM, and Surface representation of the active site view of YqjM with (b) **2a**

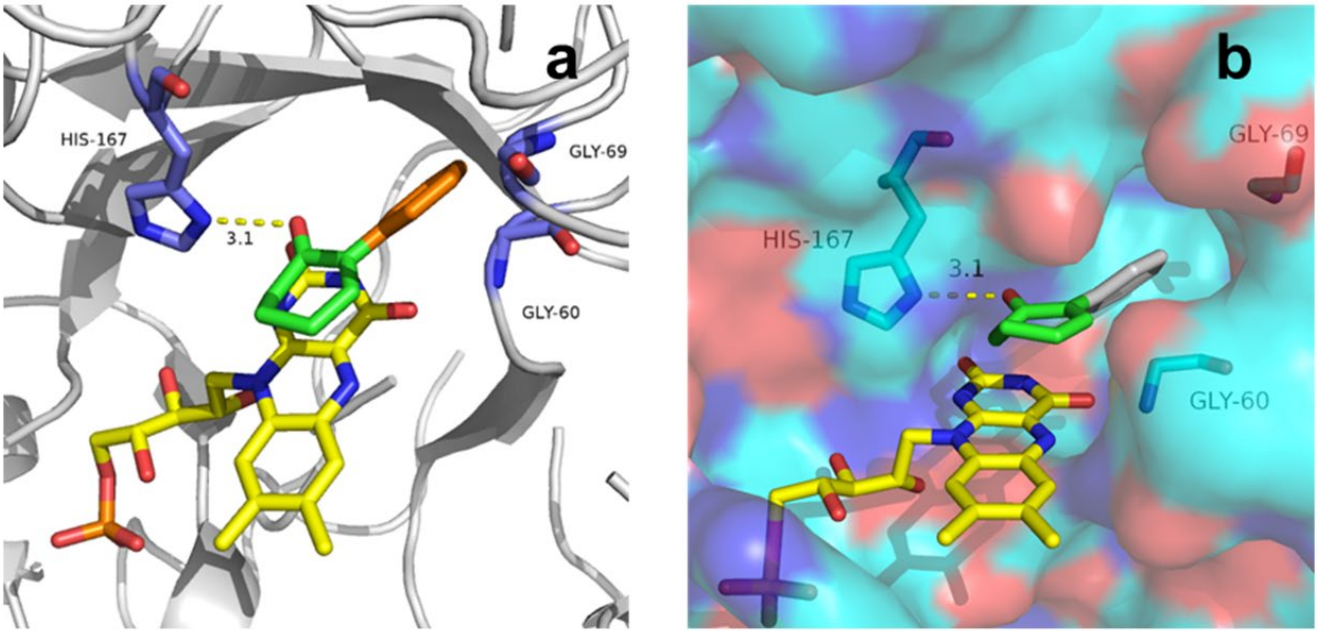


Figure S8. Docking of (a) **2a** within the active site of YqjM mutant, and Surface representation of the active site view of YqjM mutant with (b) **2a**

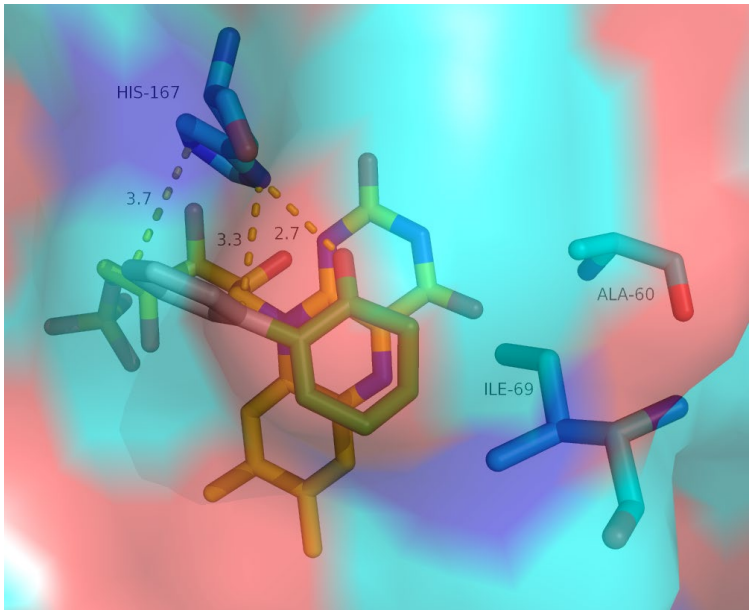


Figure S9. Surface representation of the active site view of YqjM with **2a** docked at active site.

Recyclability of the Pd-catalysts

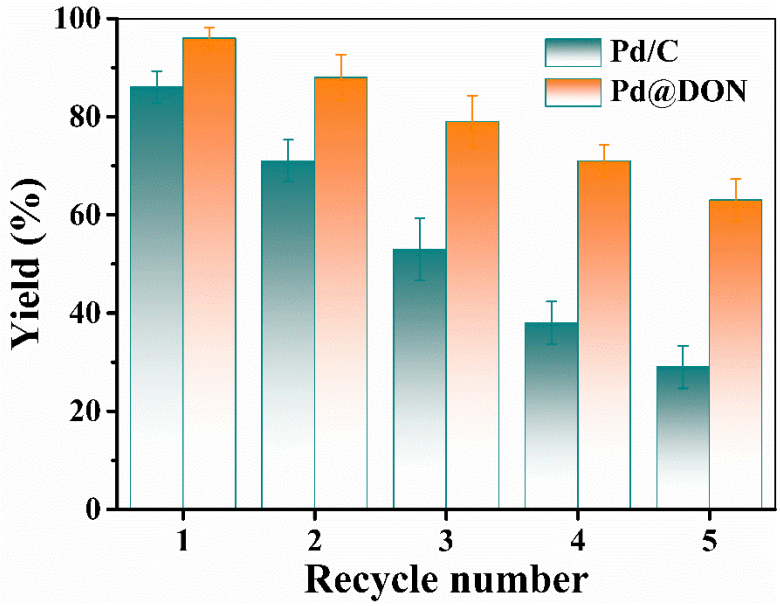


Figure S10. Recyclability of the Pd/C and DON@Pd.

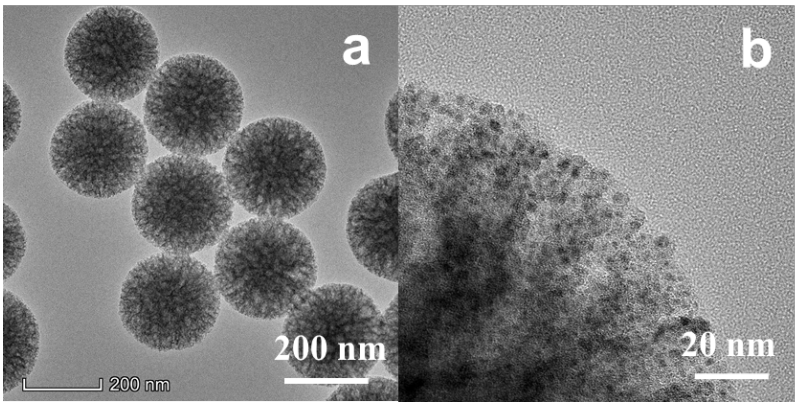


Figure S11. TEM images of DON@Pd with 4.4% Pd loading amount after 5 cycles of reaction.

Stability and recyclability of the immobilized enzymes

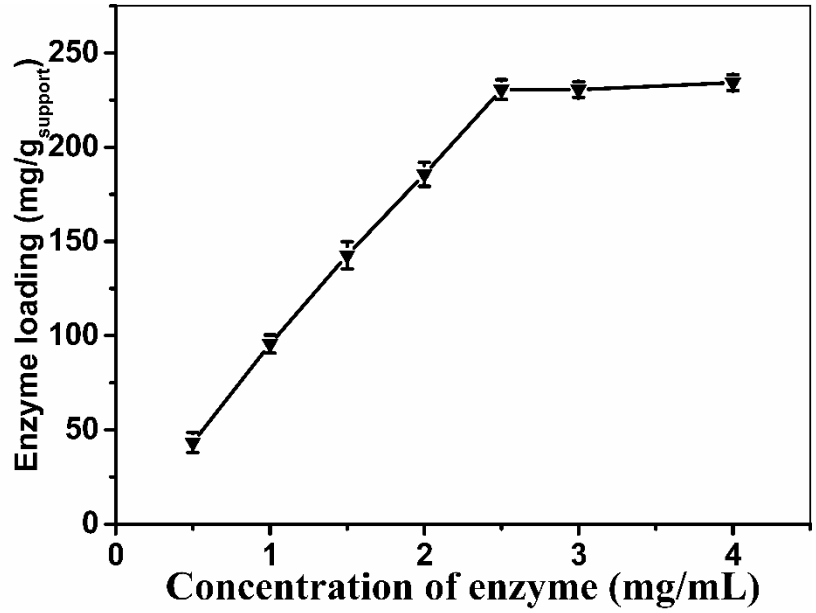


Figure S12. Effect of initial enzyme concentration on enzyme loading.

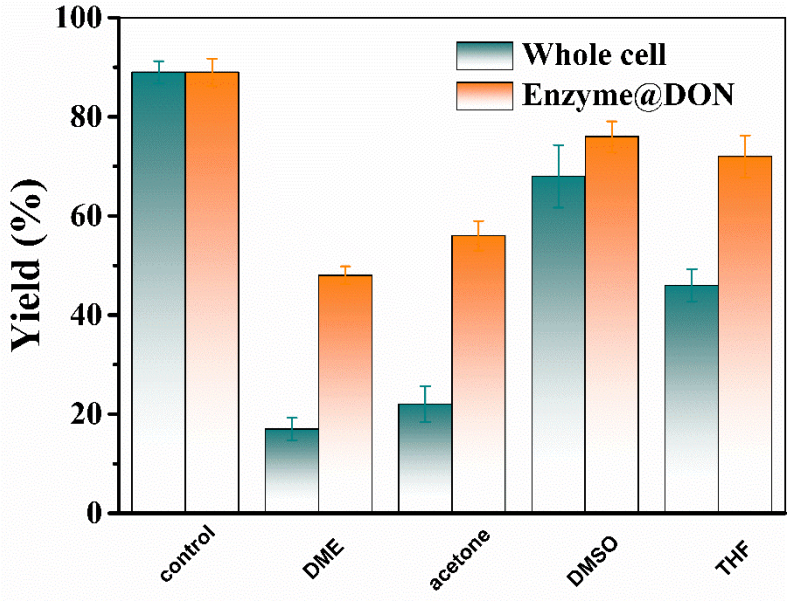


Figure S13. Effect of organic solvents on the yield of whole cell and enzyme@DON.

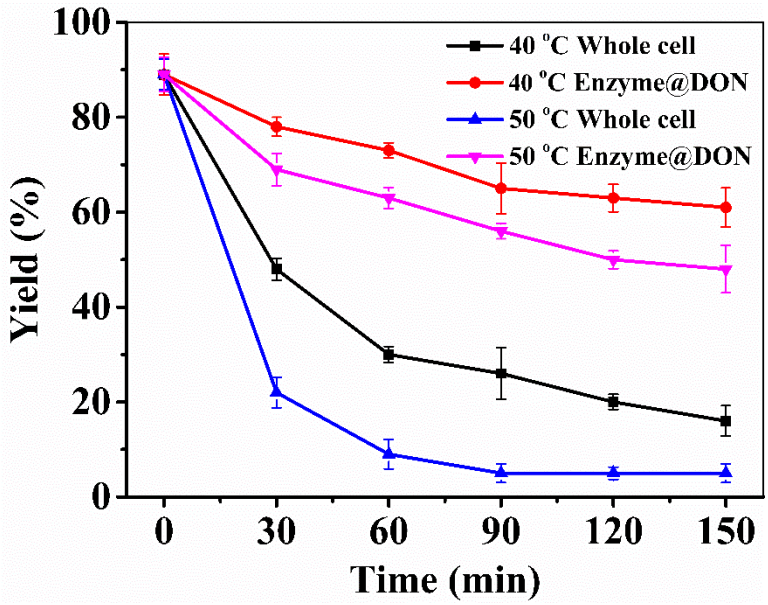


Figure S14. Thermal stabilities of whole cell and enzyme@DON at 40 ºC and 50 ºC..

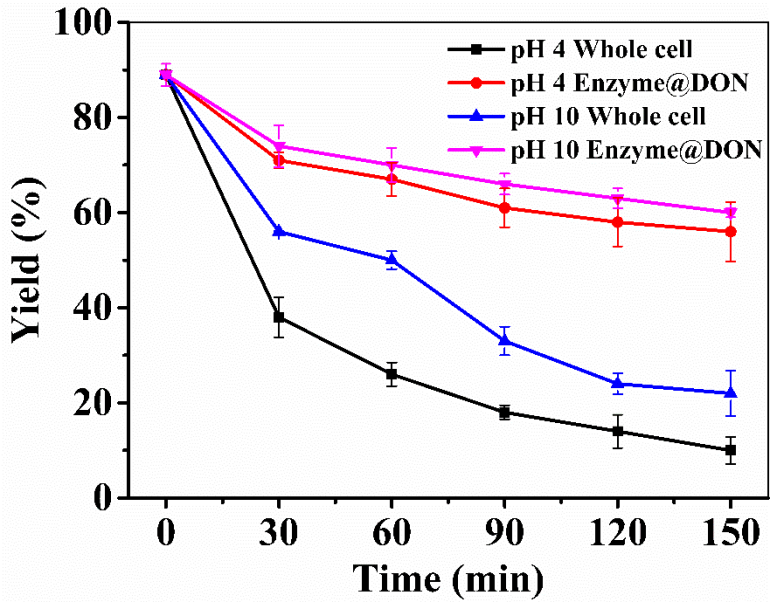


Figure S15. pH stabilities of whole cell and enzyme@DON at pH 4 and pH 10.

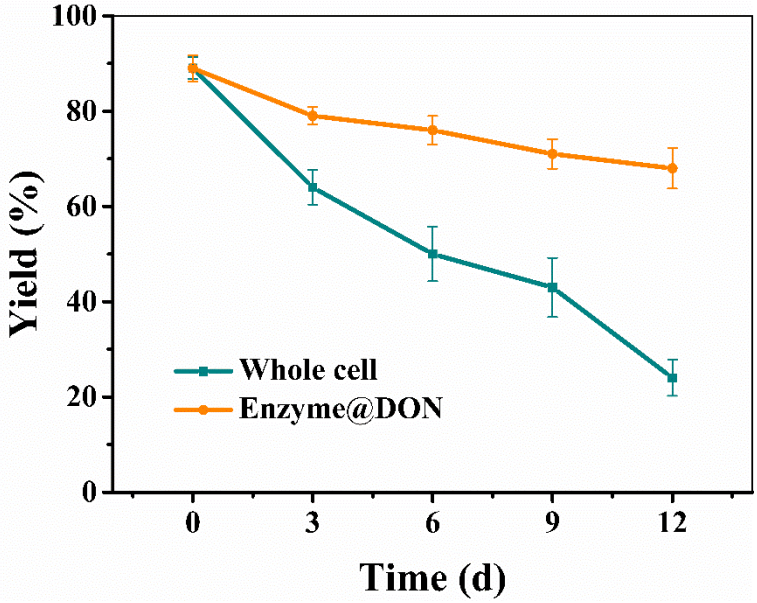


Figure S16. Storage stabilities of whole cell and enzyme@DON.

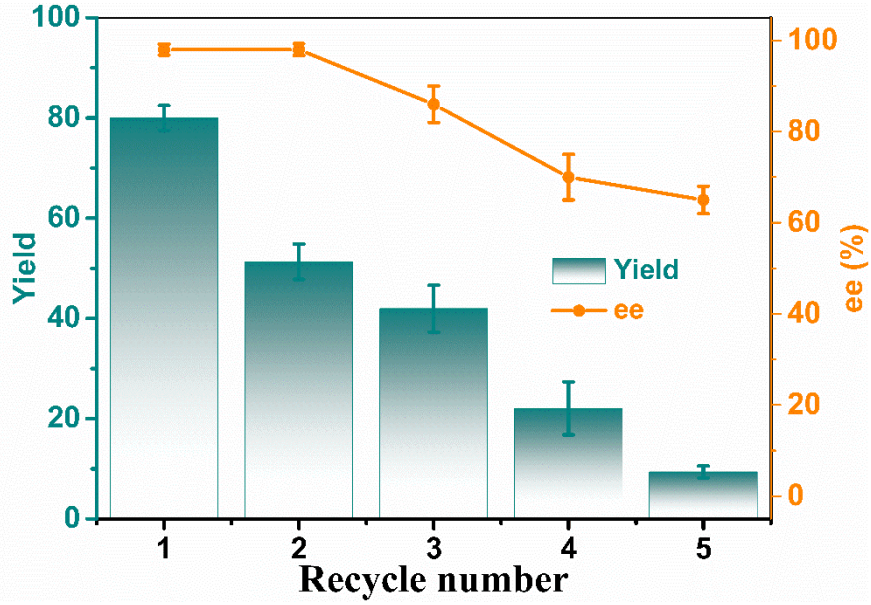


Figure S17. Recyclability of the whole cell

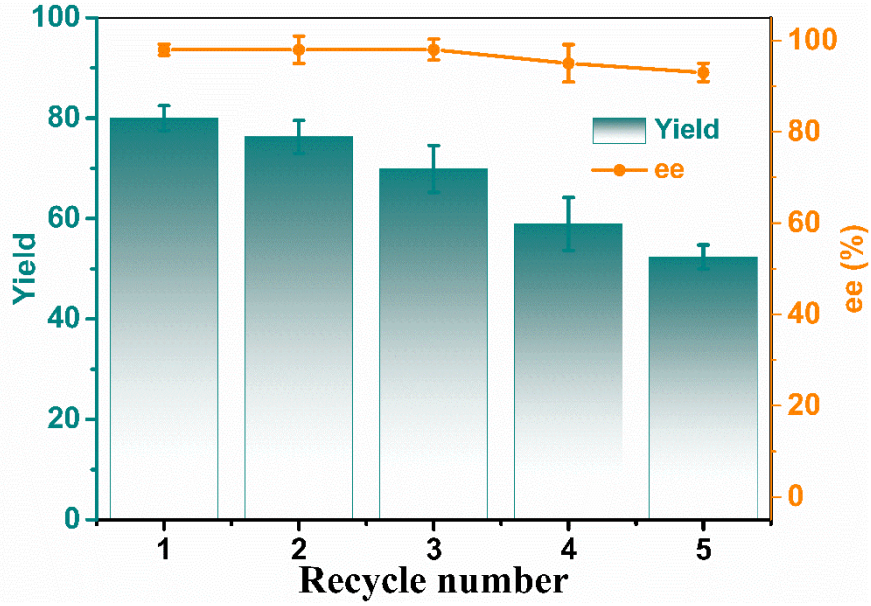


Figure S18. Recyclability of enzyme@DON.

Supporting Tables

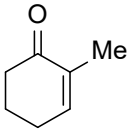
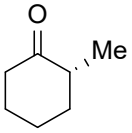
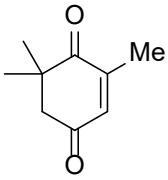
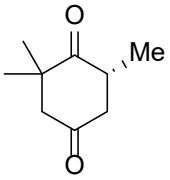
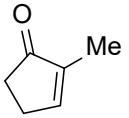
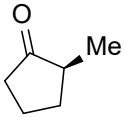
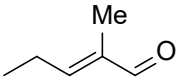
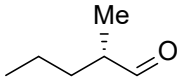
Table S1. Optimization of the Suzuki-Miyaura coupling reaction[a]

Entry	Catalysts	Pd [mol%]	Solvents	Temperature [°C]	Time [h]	Yield[b] [%]
1	Pd/C	5	Buffer	70	12	80
2	DON@Pd	5	Buffer	70	12	91
3	DON@Pd	5	Buffer/[BMIm][NTf_2][c]	70	6	98
4	DON@Pd	5	Buffer/[BMIm][NTf_2][c]	80	6	97
5	DON@Pd	5	Buffer/[BMIm][NTf_2][c]	60	6	81
6	DON@Pd	2.5	Buffer/[BMIm][NTf_2][c]	70	6	93

[a] All reactions were carried out using 2-iodocyclohexenone (0.25 mmol), phenylboronic (0.25 mmol), K_2CO_3 (0.5 mmol);

[b] Isolated yield; [c] 4 mL Tris-HCl buffer (50 mM, pH 7.5) and 1 mL [BMIm][NTf_2].

Table S2. Enzymatic asymmetric hydrogenation of α-alkyl enones

Entry	Substrates	Products	This work		Literature data[4]	
			Conversion (%)[a]	ee (%)[a]	Conversion (%)[b]	ee (%)[b]
1[c]			>99	91	95	93
2[d]			>99	98	91	99
3[e]			>99	>99	72	93
4[f]			90	34	78	10

[a] Reactions were carried out in [BMIm][NTf_2] (20%) using substrate (25 mM), the conversion and the values of ee were determined by GC. [b] Reactions were carried out in Tris-HCl buffer (50 mM, pH 7.5) using substrate (5 mM). GC conditions: CP-Chirasil Dex CB (df = 0.25 μm, 0.32 mm i.d. × 25 m); carrier gas, N_2 (flow 30 mL/min); injection temp, 250 °C. [c] Initial column temperature 100 °C hold 2 min, then progress rate, 15 °C/min to 210 °C, hold 2.5 min, t_R = 6.9 (major) and 6.8 min (minor). [d] Initial column temperature 110 °C hold 5 min, then progress rate, 30 °C/min to 200 °C, hold 2 min, t_R = 5.8 (major) and 6.1 min (minor). [e] Initial column temperature 80 °C hold 10 min, then progress rate, 30 °C/min to 200 °C, hold 2 min, t_R = 7.8 (major). [f] Initial column temperature 40 °C hold 2 min, then progress rate, 20 °C/min to 180 °C, hold 1.5 min, t_R = 5.1 (major) and 5.3 min (minor).

Table S3. Primer sequences used for construction of YqjM mutant

	Oligonucleotide sequence 5'-3'
YqjM-F	CAGCGGCCTGGTGCCGCGCGGCAGCCATATGGCCAGAAAATTATTTACACC
YqjM-R	GTCTGCGTGAACAAGGGCGCCTGAGCTGCAGTCAATTAAGTCAACAC
60G-R	CGTCCTTGAGGGTTAACCGCTGAGCCCTCTACAATAATCAGTC
69G-F	GGTTAACCCTCAAGGACGAGGCACTGACCAAGACTTAGGC

References:

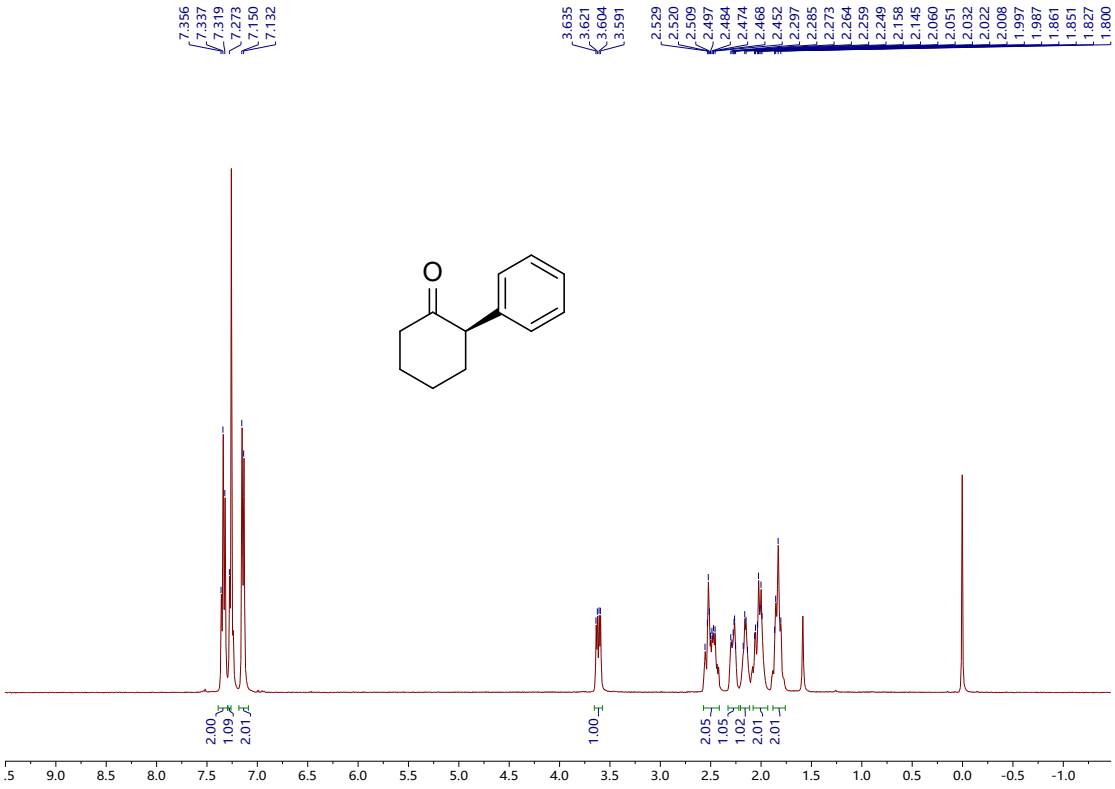
(1) (a) Gao, J.; Kong, W.; Zhou, L.; He, Y.; Ma, L.; Wang, Y.; Yin, L.; Jiang, Y. Monodisperse Core-Shell Magnetic Organosilica Nanoflowers with Radial Wrinkle for Lipase Immobilization. *Chem. Eng. J.* **2017,** *309*, 70–79. (b) Gao, L.; Wang, Z.; Liu, Y.; Liu, P.; Gao, S.; Gao, J.; Jiang, Y. Co-immobilization of metal and enzyme into hydrophobic nanopores for highly improved chemoenzymatic asymmetric synthesis. *Chem. Commun.* **2020,** *56,* 13547-13550.

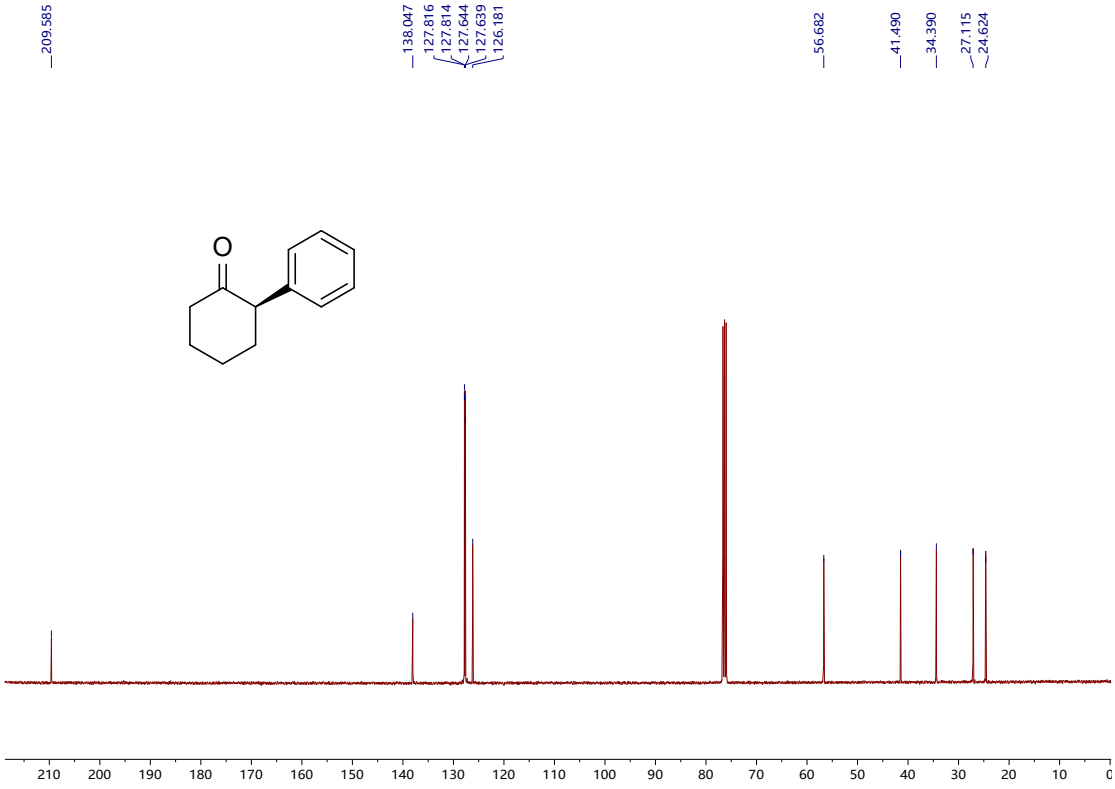
(2) Liu, C; Xie, J.; Li, Y.; Chen, J.; Zhou, Q. Asymmetric Hydrogenation of a,a'-Disubstituted Cycloketones through Dynamic Kinetic Resolution: An Efficient Construction of Chiral Diols with Three Contiguous Stereocenters. *Angew. Chem., Int. Ed.* **2013,** *52*, 593-596.

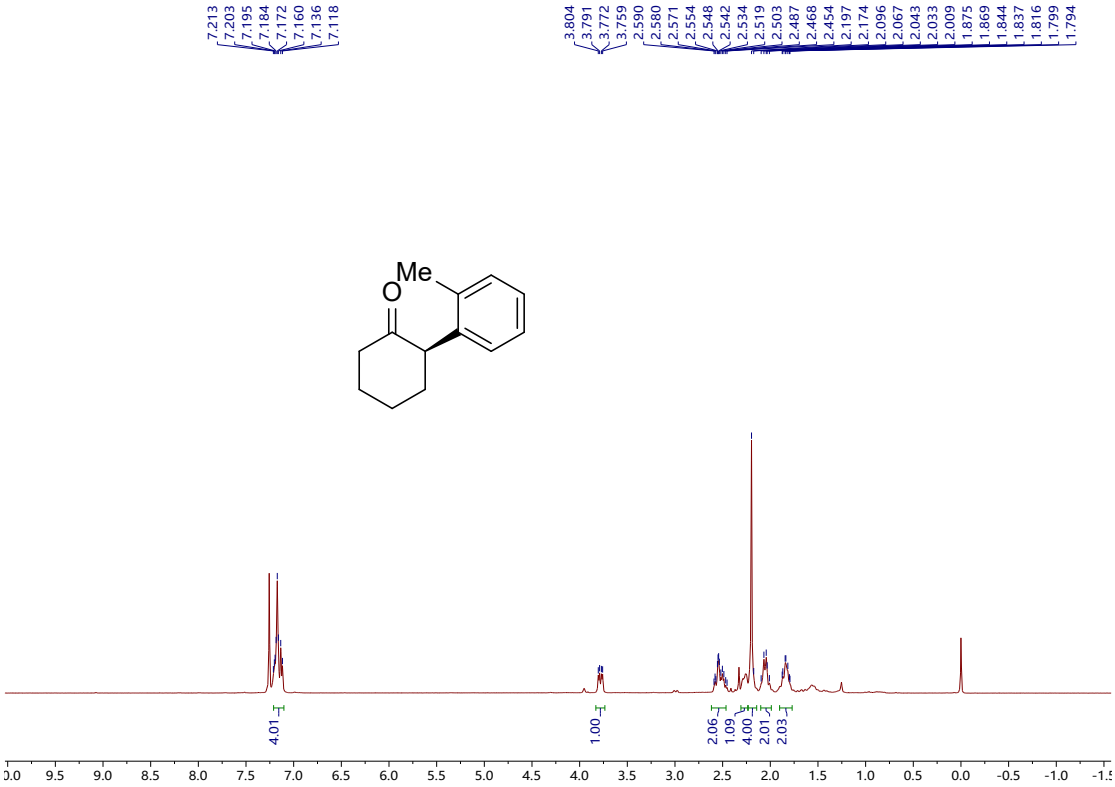
(3) Murakami, K.; Sasano, Y.; T omizawa, M.; Shibuya, M.; Kwon, E.; Iwabuchi, Y. Highly Enantioselective Organocatalytic Oxidative Kinetic Resolution of Secondary Alcohols Using Chiral Alkoxyamines as Precatalysts: Catalyst Structure, Active Species, and Substrate Scope, *J. Am. Chem. Soc.* **2014**, *136*, 17591–17600.

(4) Hall, M.; Stueckler, C.; Ehammer, H.; Pointner, E.; Oberdorfer, G.; Gruber, K.; Hauer, B.; Stuermer, R.; Kroutil, W.; Macheroux, P.; Faber, K. Asymmetric Bioreduction of C=C Bonds Using Enoate Reductases OPR1, OPR3 and YqjM: Enzyme-Based Stereocontrol. *Adv. Synth. Catal.* **2008,** *350*, 411–418.

NMR spectra of compounds



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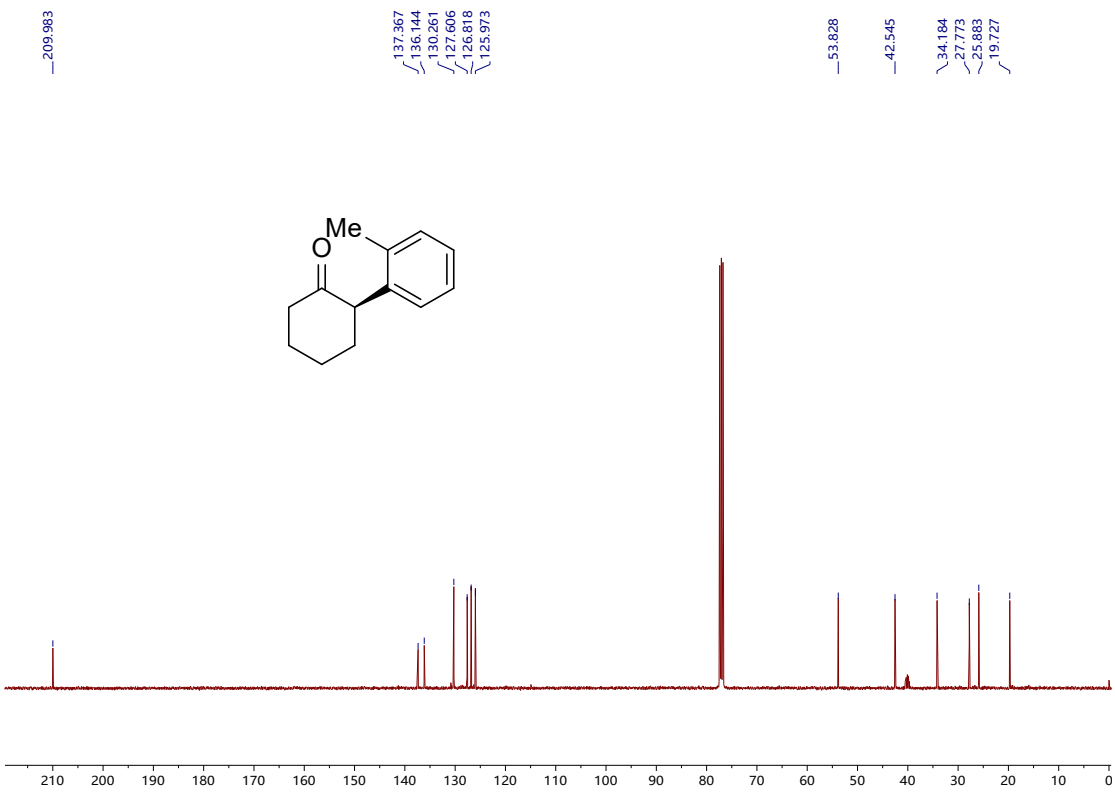
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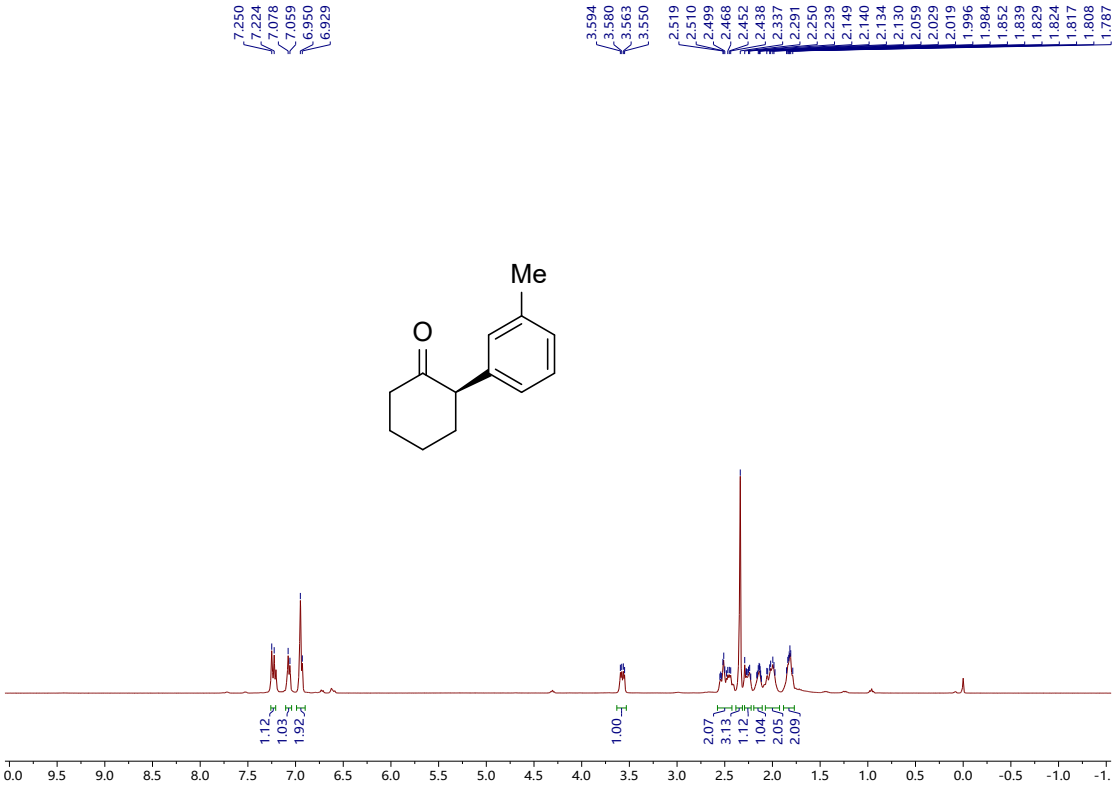
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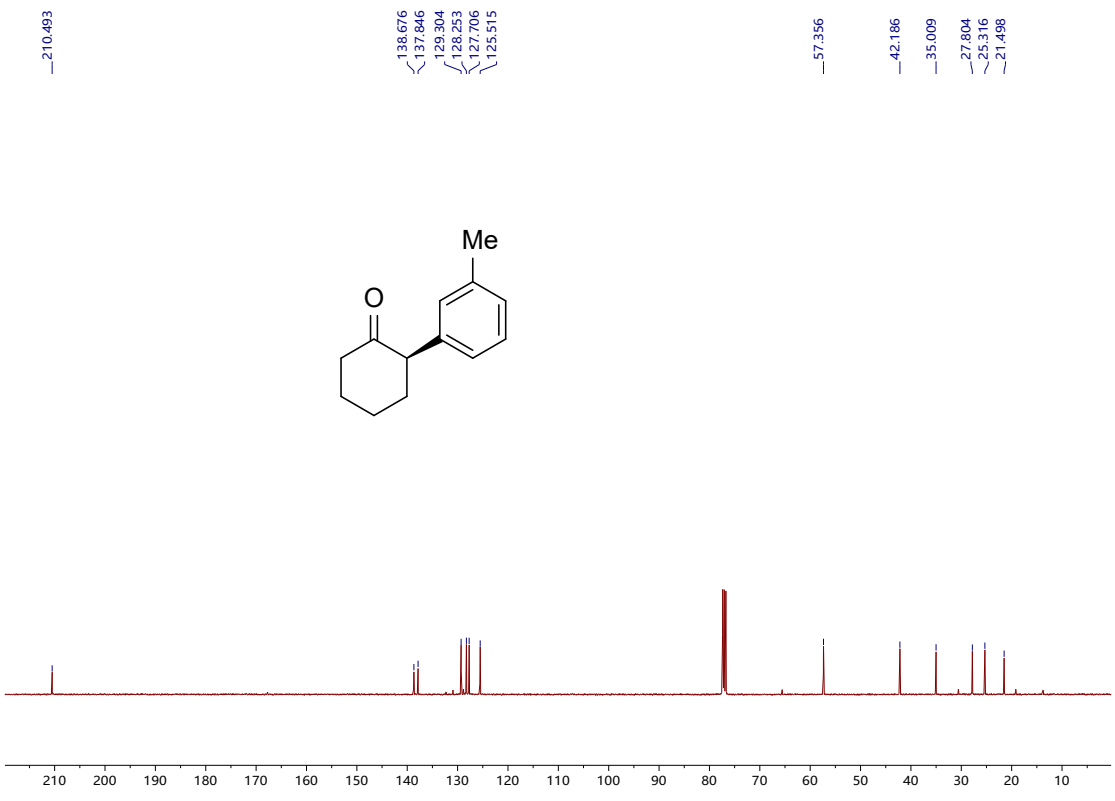
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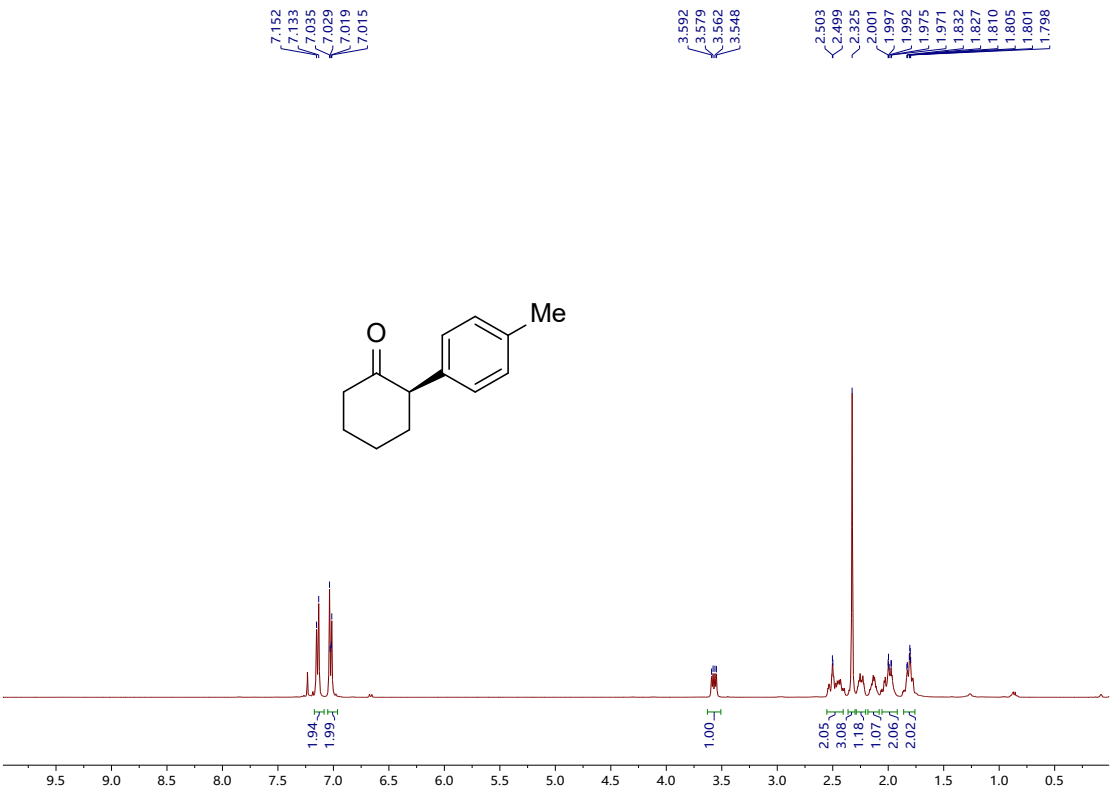
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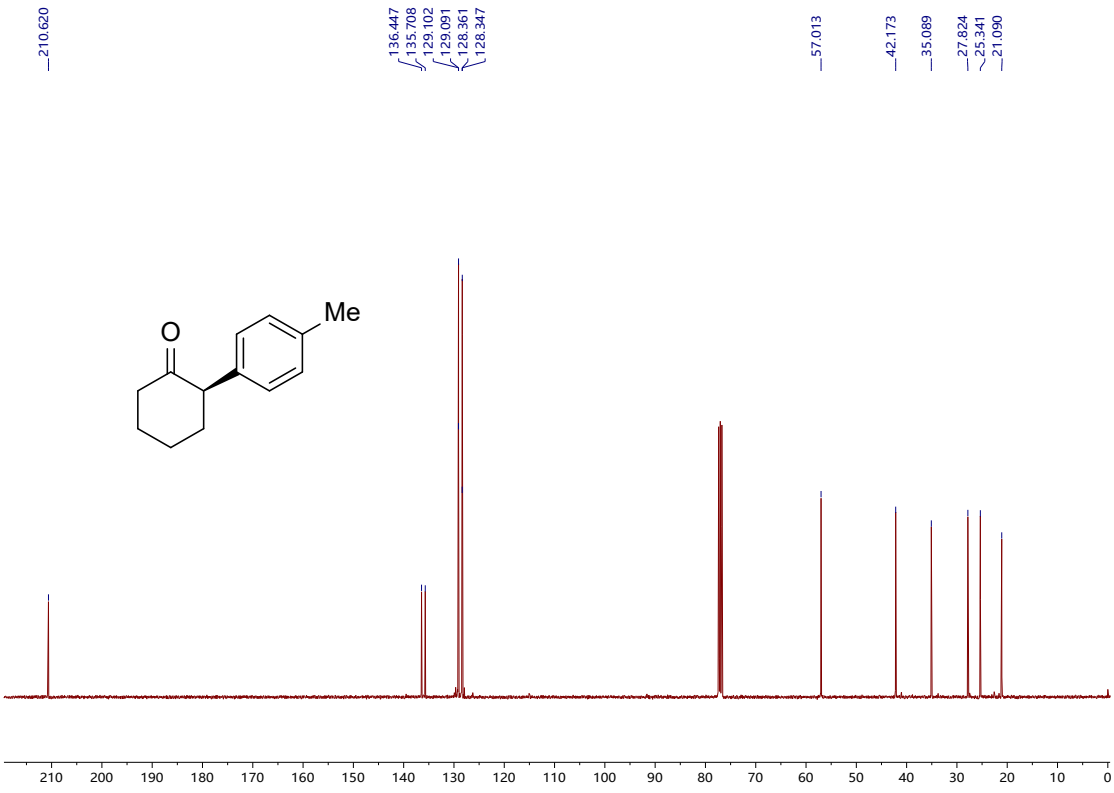
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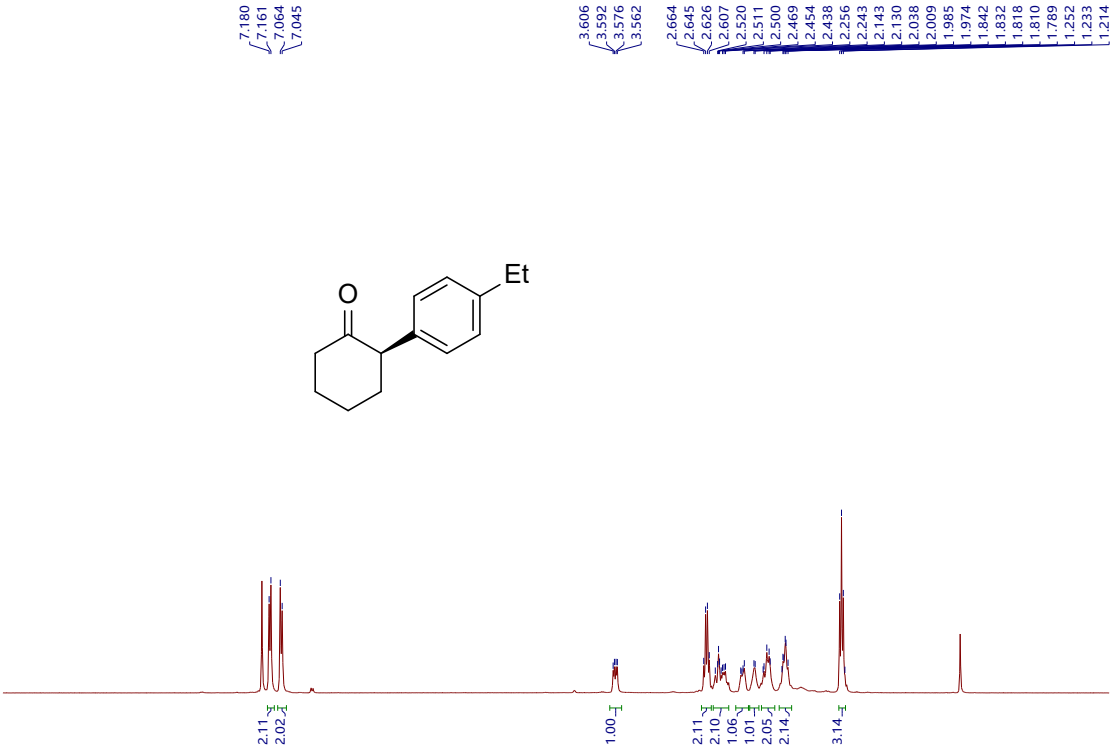
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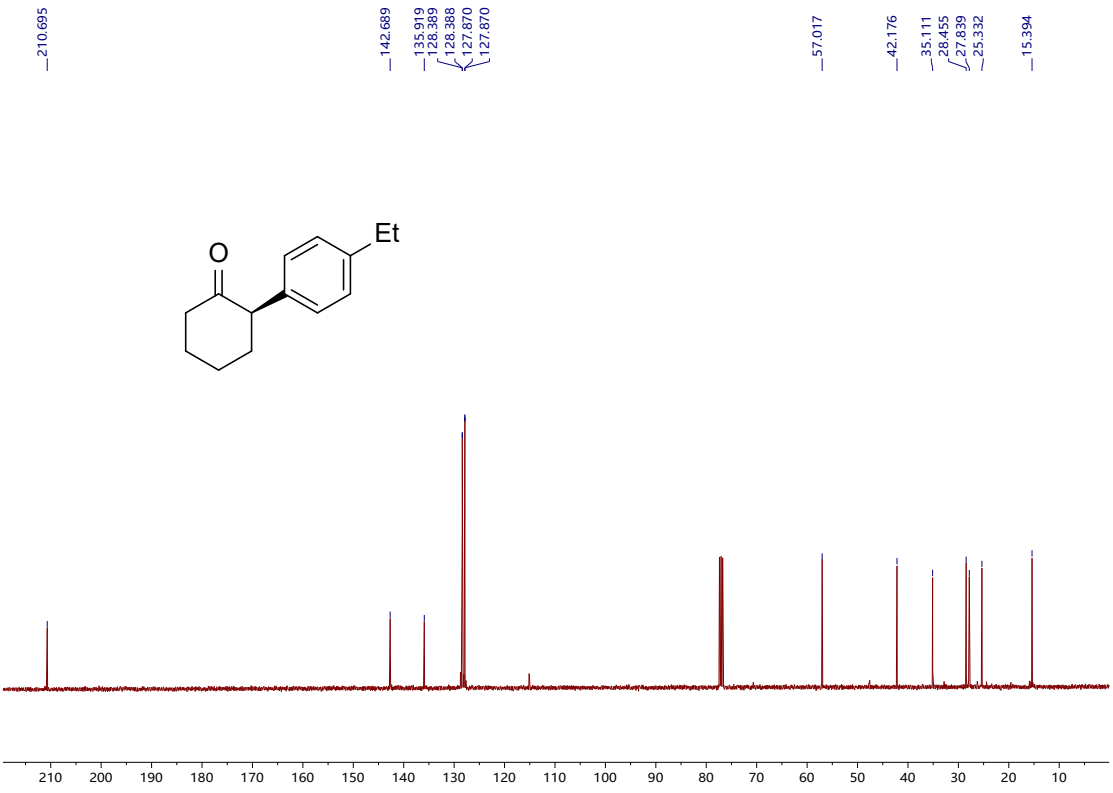
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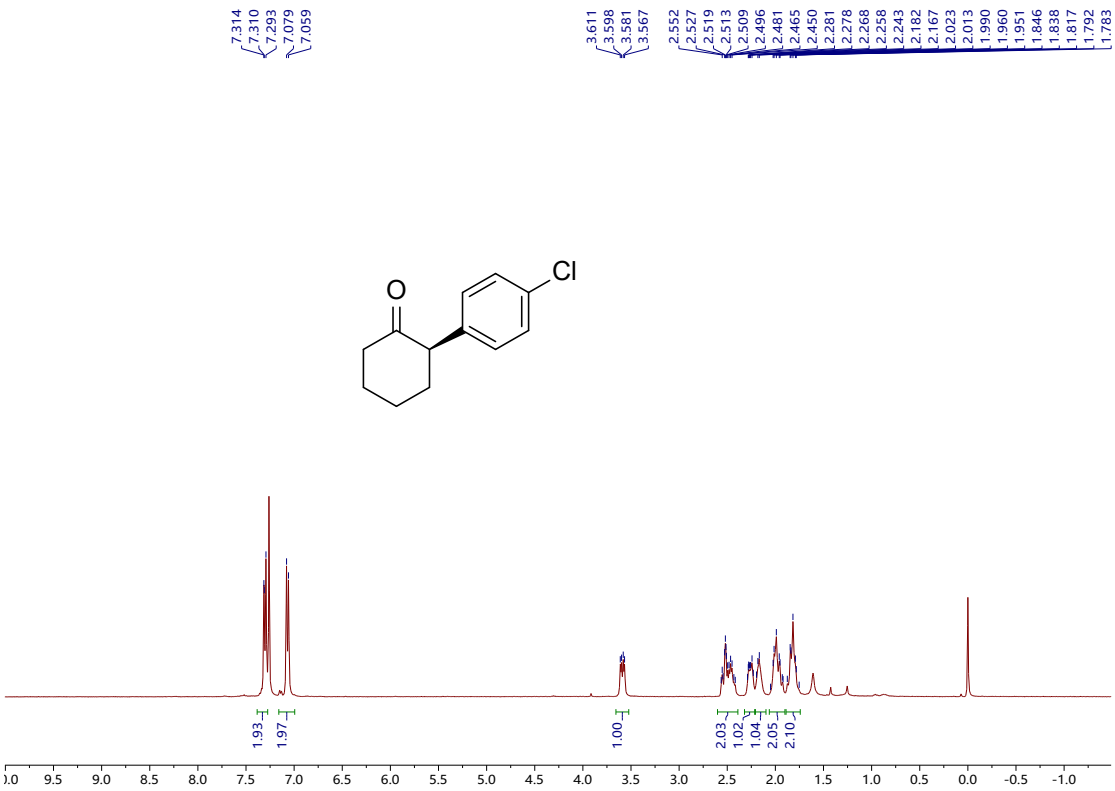
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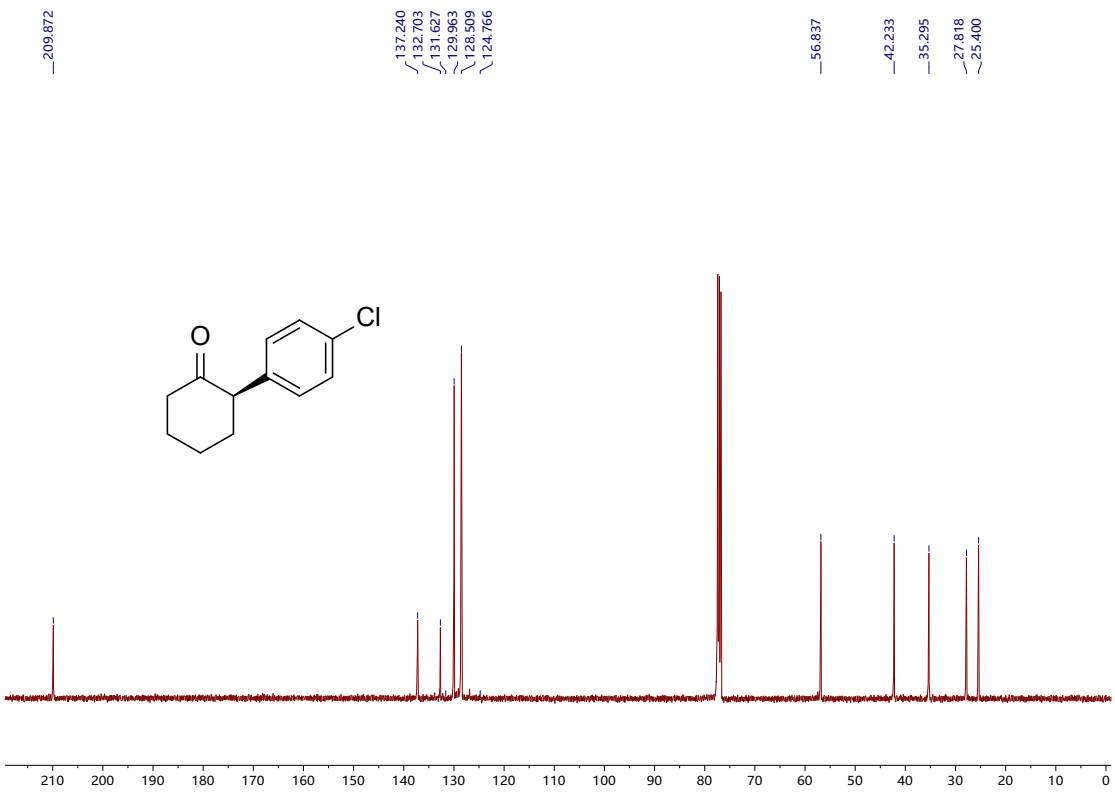
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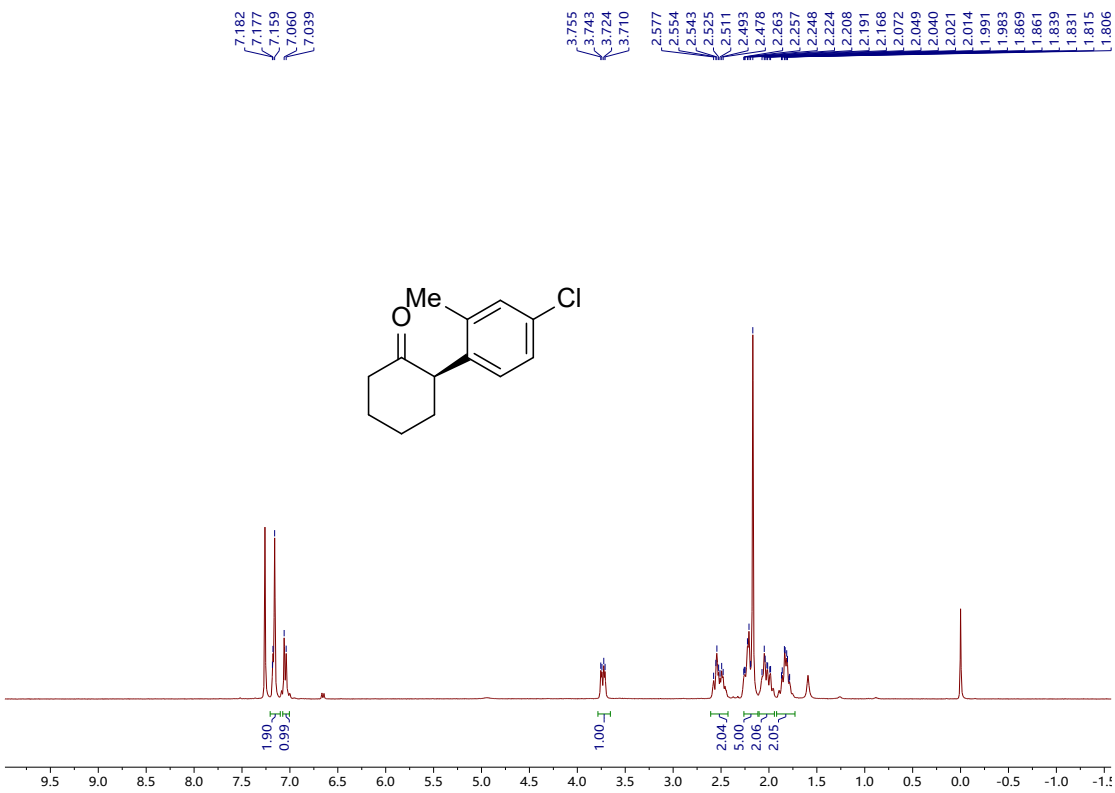
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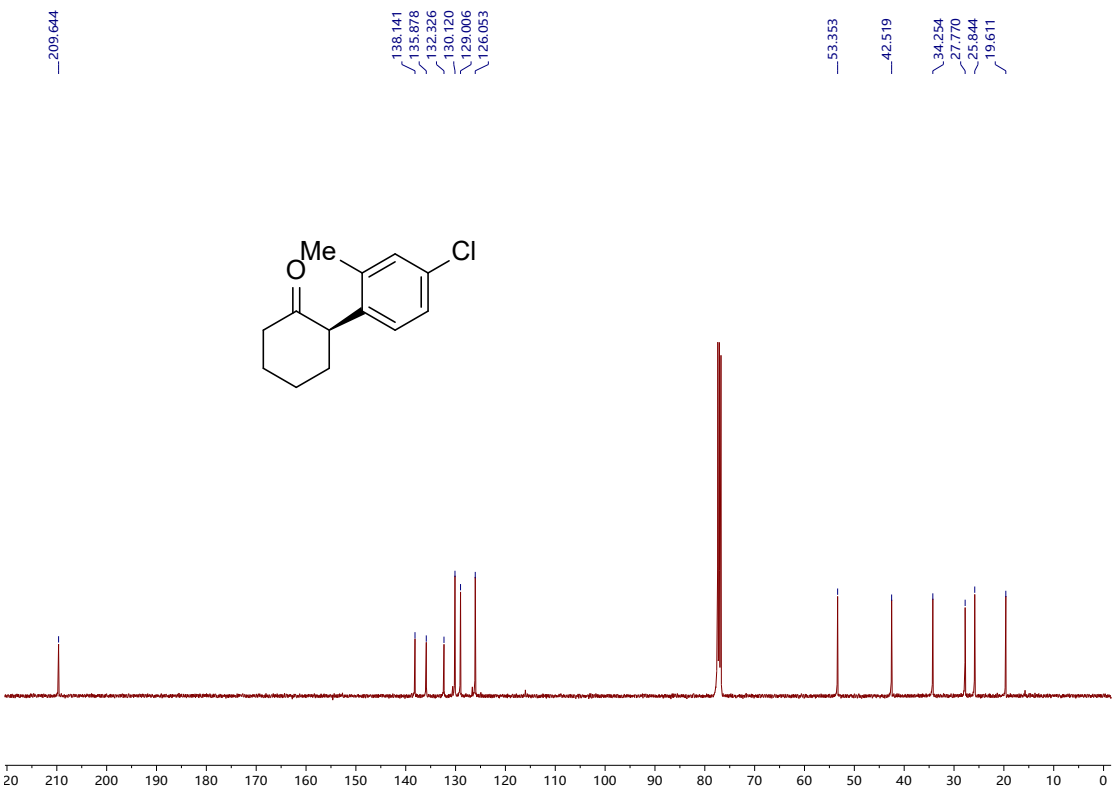
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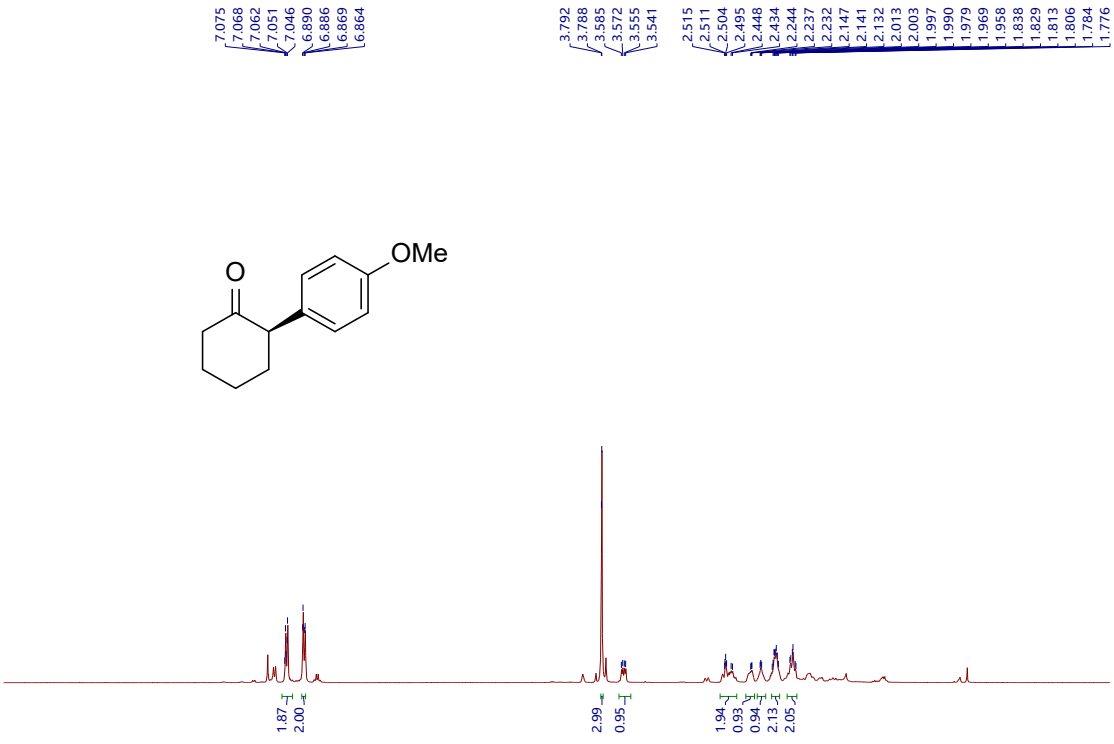
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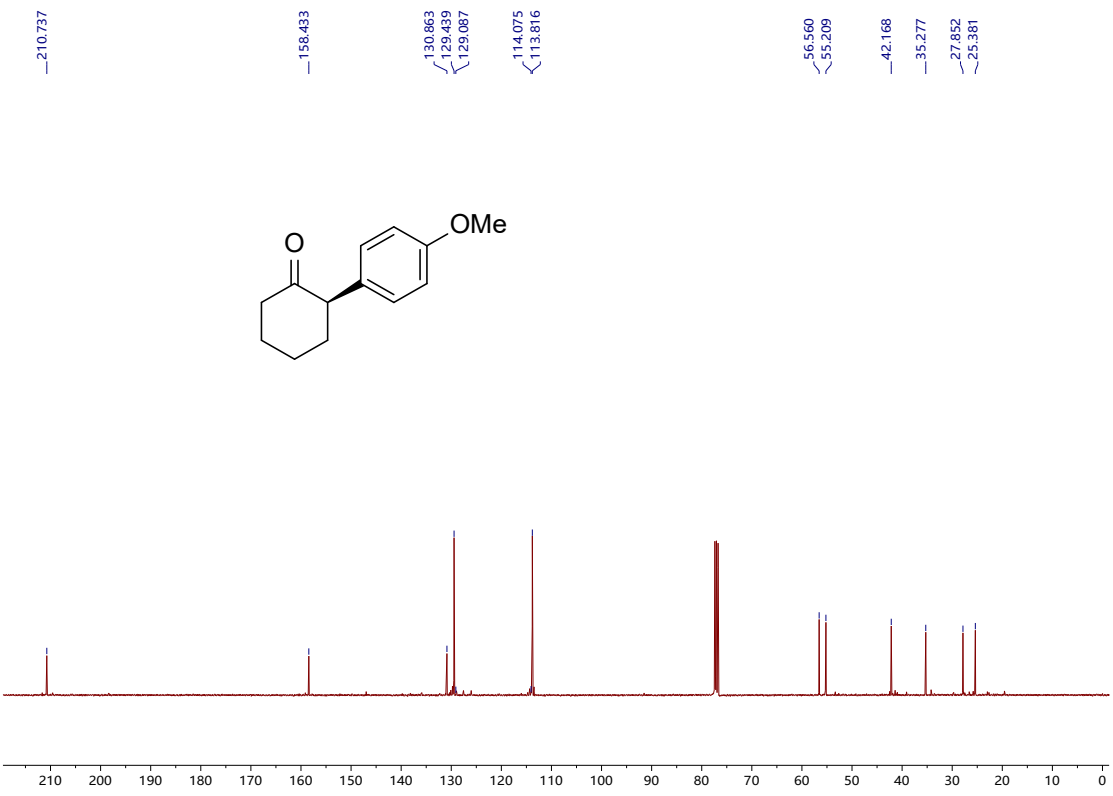
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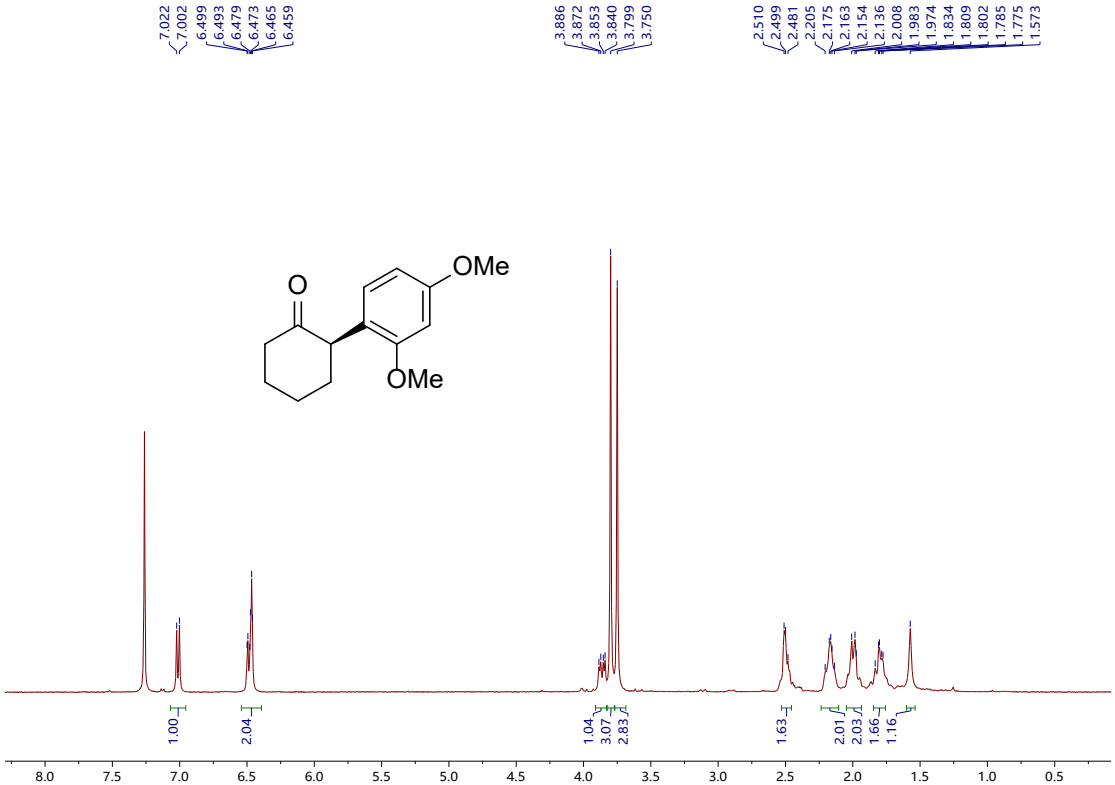
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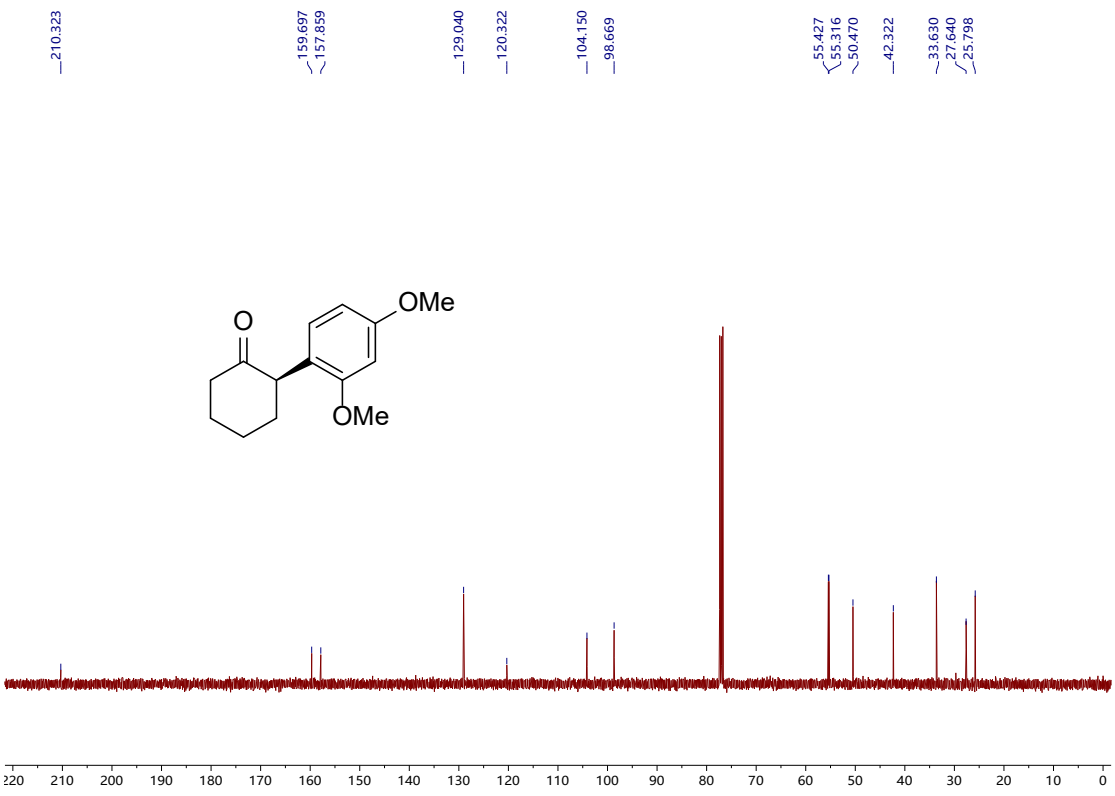
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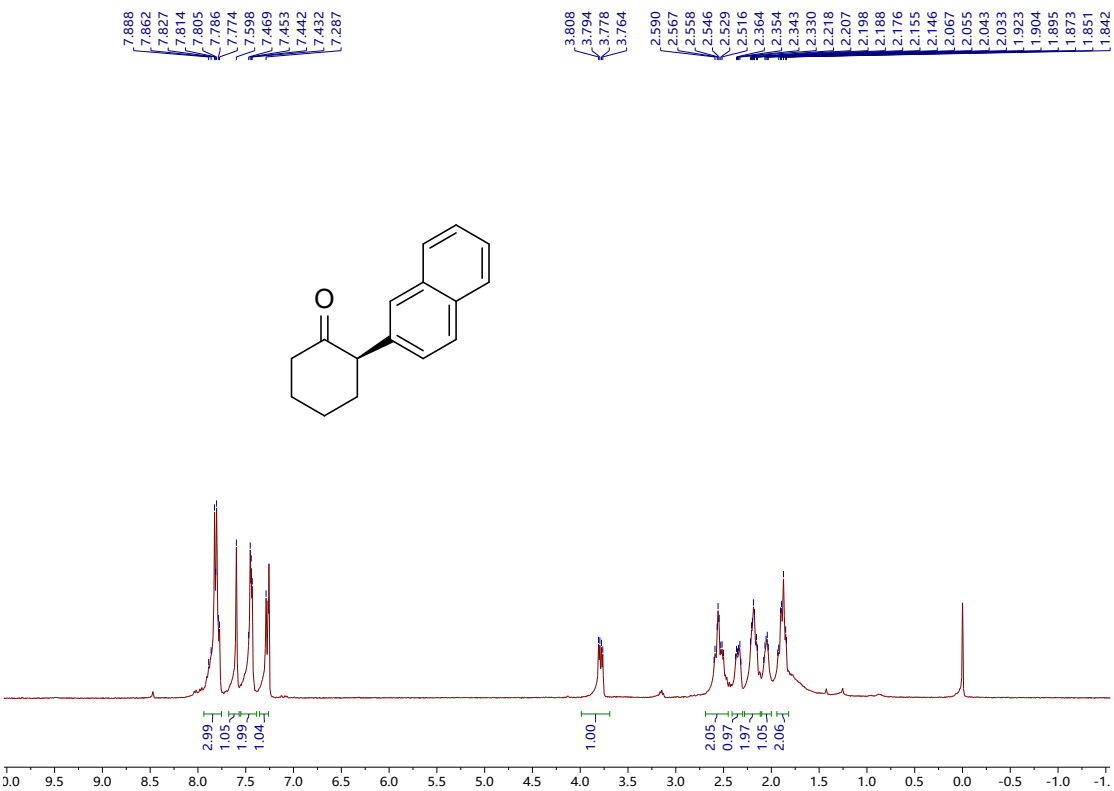
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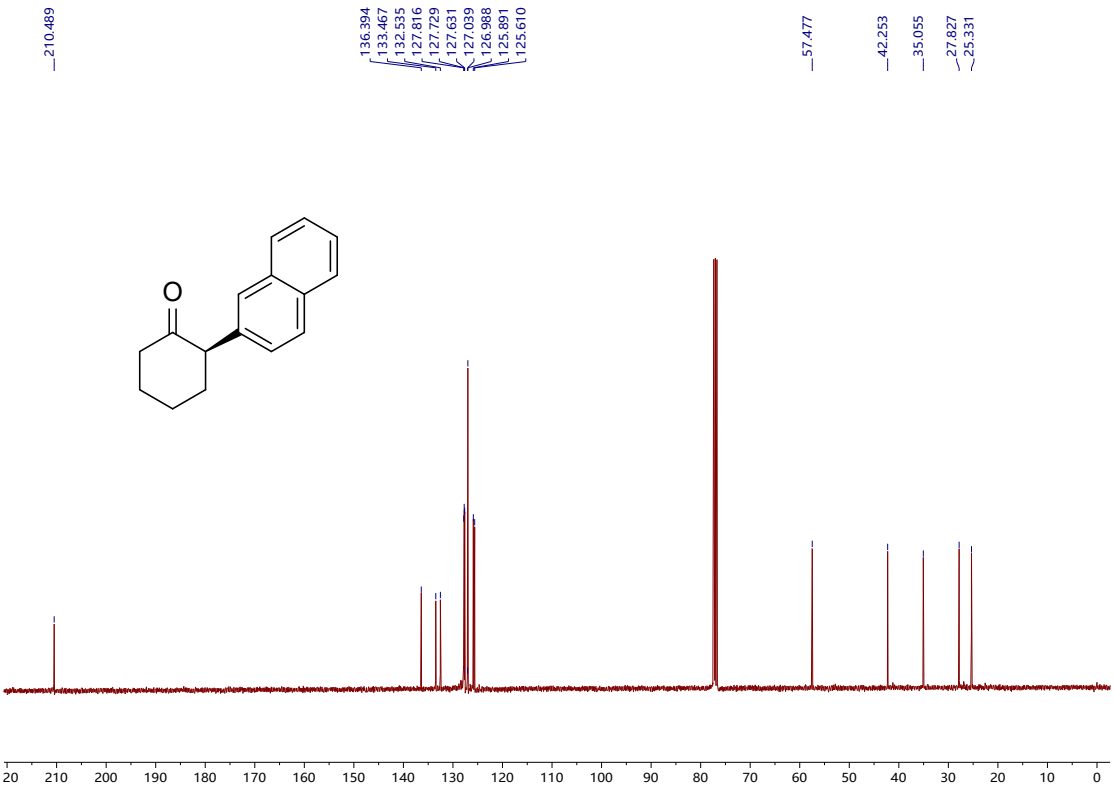
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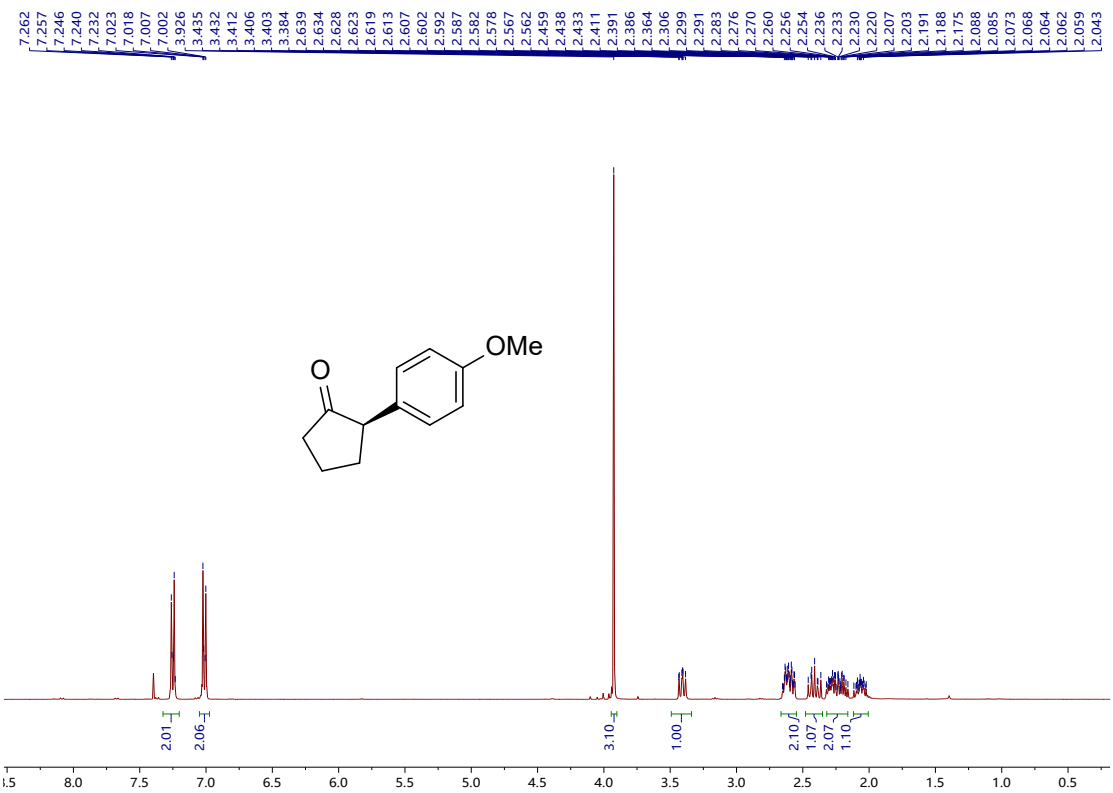
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2.06
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2.10
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1.10
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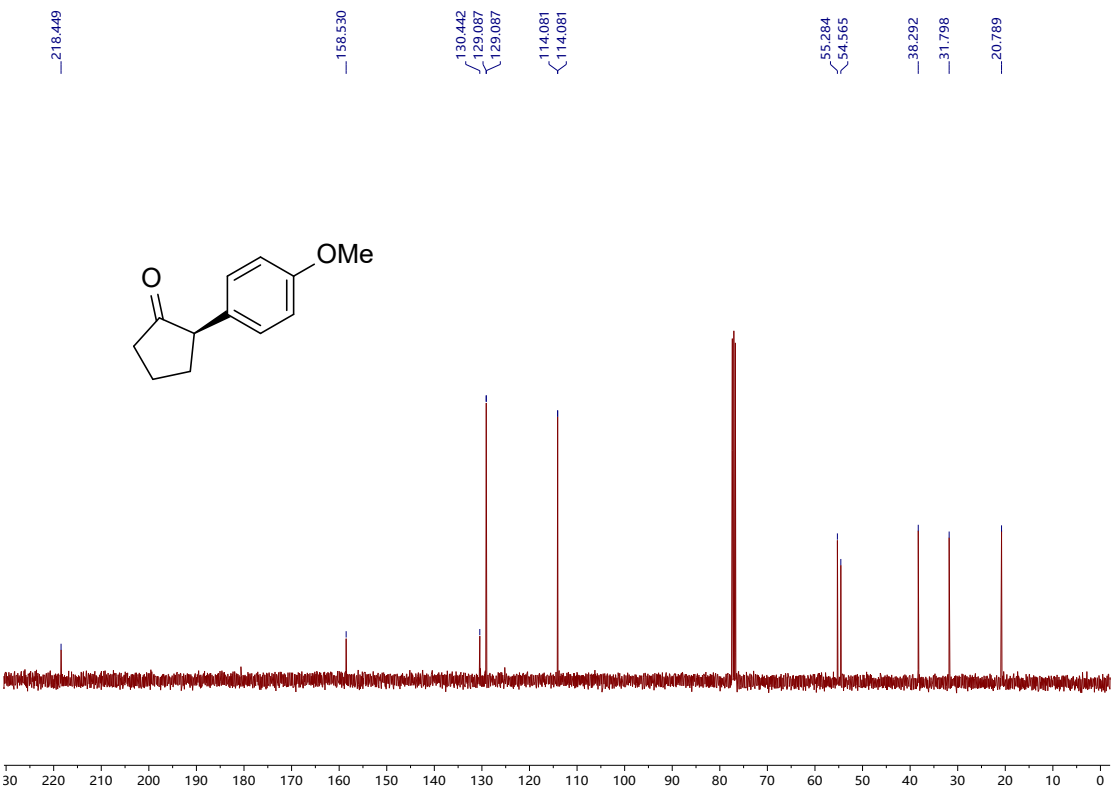
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120
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100
90
80
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60
50
40
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20
10
0


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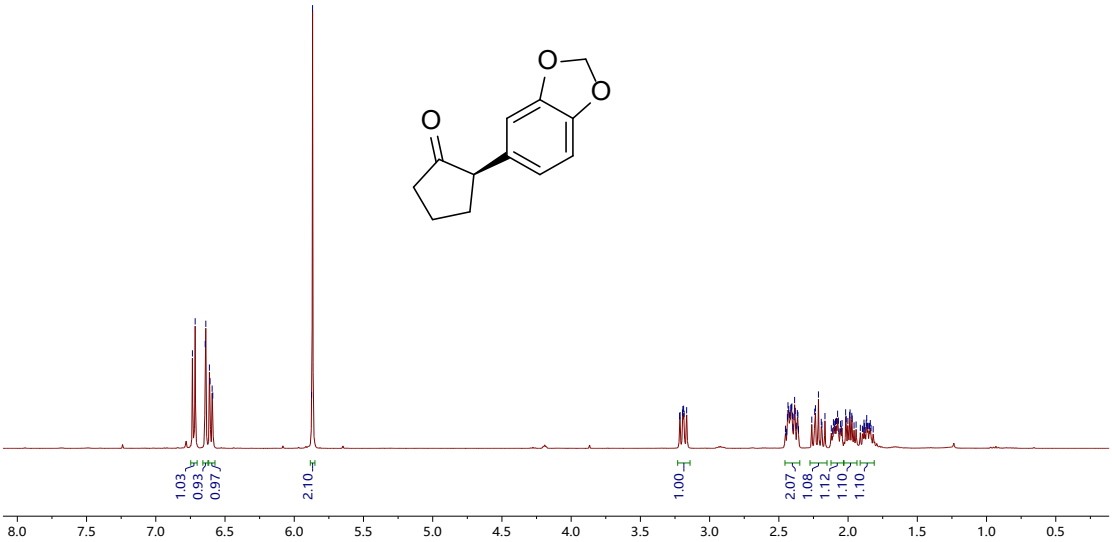
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2.07
1.08
1.12
1.10
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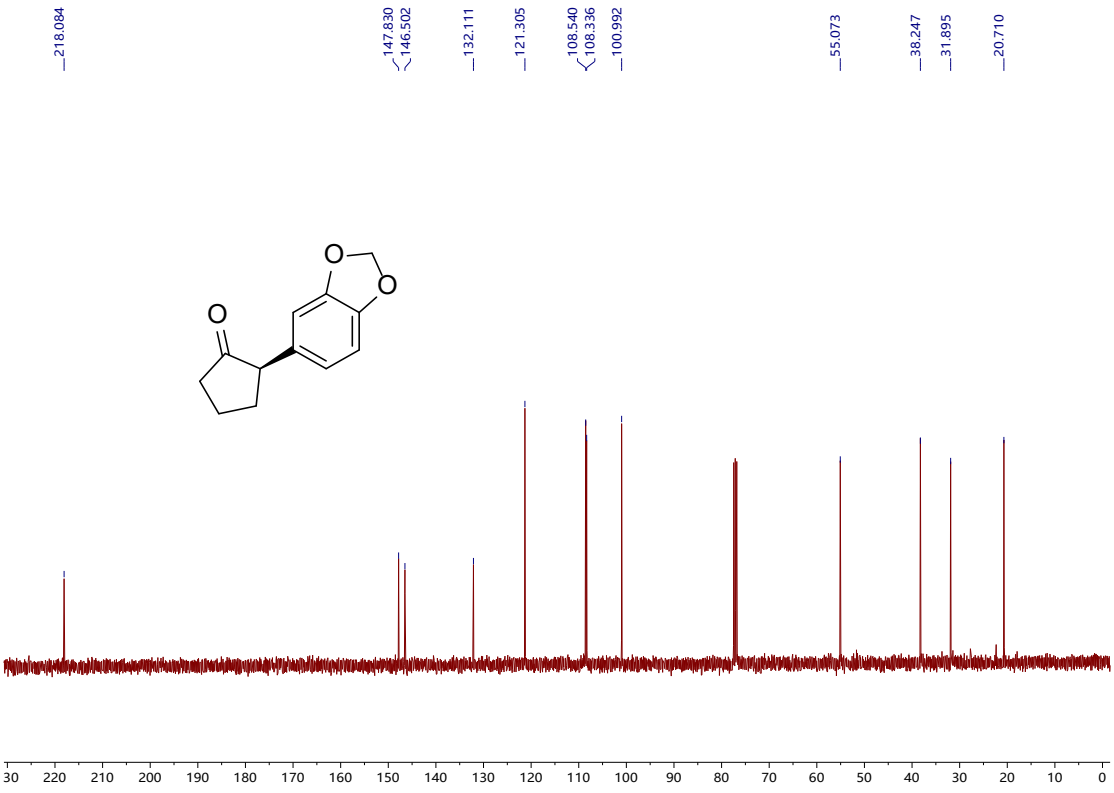
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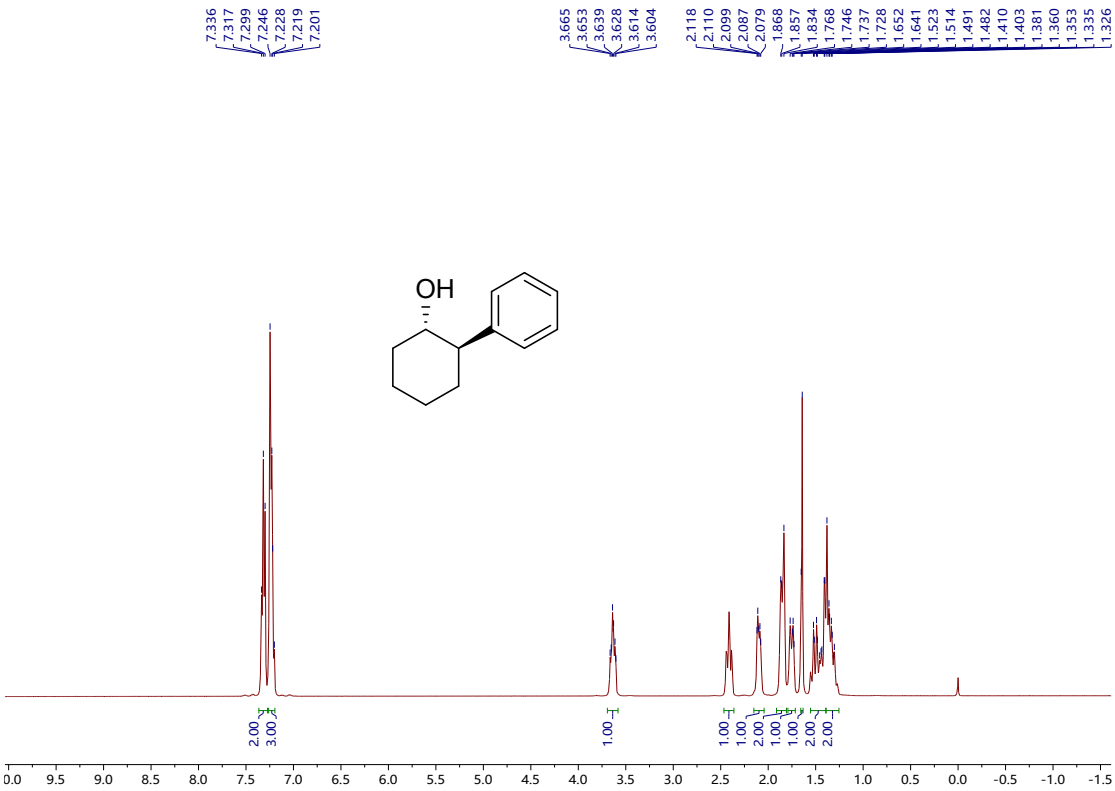
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2.110
2.099
2.087
2.079
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1.857
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3.00
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2.00
1.00
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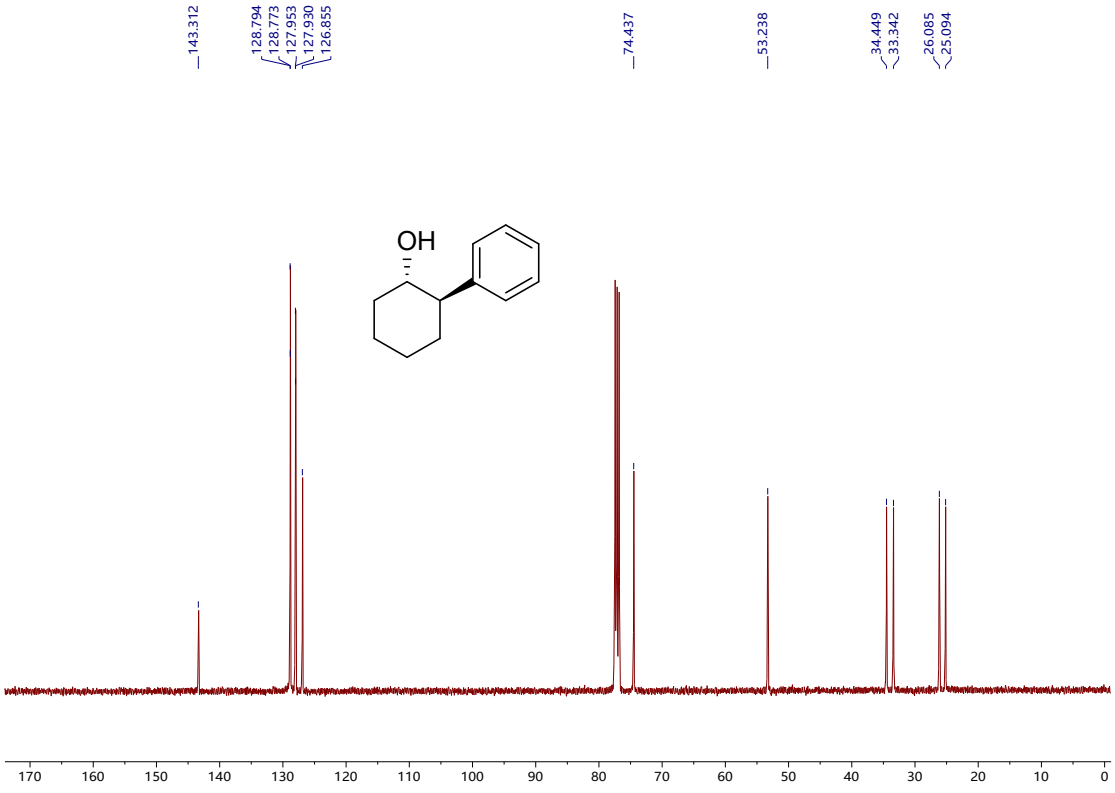
2.00
2.00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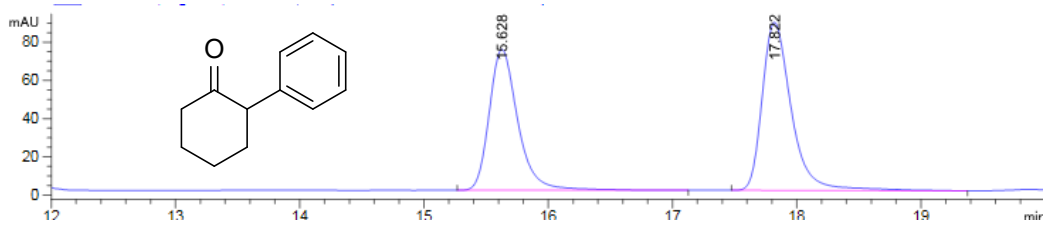
126.855
74.437
53.238
34.449
33.342
26.085
25.094
OH

HPLC traces for productions

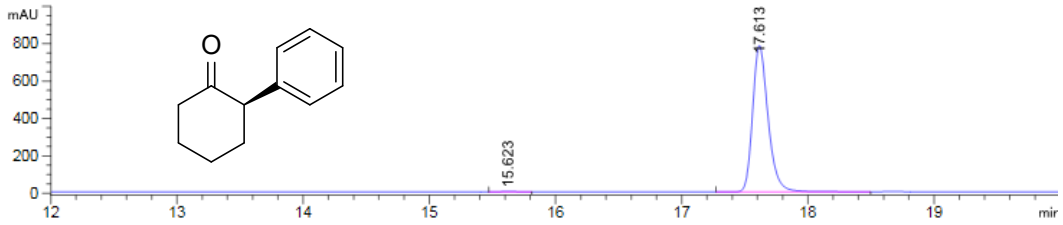
HPLC copies of compounds **2a**:

Rac-2a, OD-H, *i*PrOH/Hex 1/99, flow rate = 1.0 mL/min, λ = 210 nm



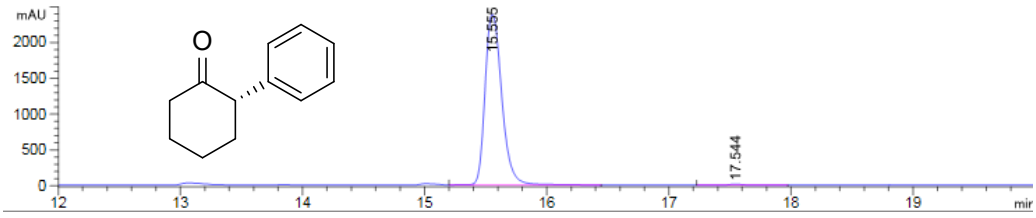
Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	15.628	0.2450	1183.21790	73.83742	45.0656
2	17.822	0.2491	1442.32629	88.03825	54.9344

(*R*)-2a, OD-H, *i*PrOH/Hex 1/99, flow rate = 1.0 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	15.623	0.1208	19.58880	2.51662	0.2927
2	17.613	0.1294	6673.47217	783.50177	99.7073

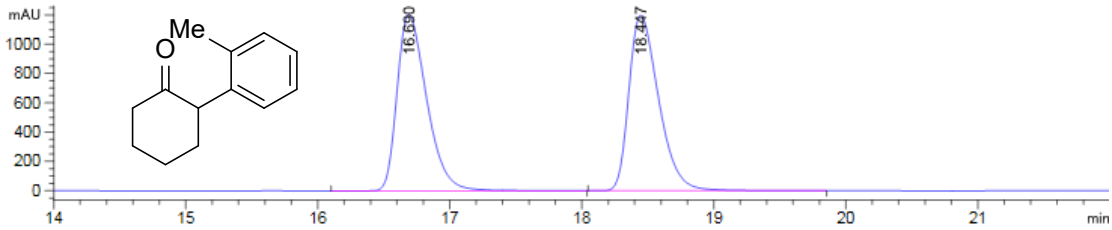
(*S*)-2a, OD-H, *i*PrOH/Hex 1/99, flow rate = 1.0 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	15.555	0.1468	2.26551e4	2385.68164	99.5863
2	17.544	0.1339	94.10821	10.36750	0.4137

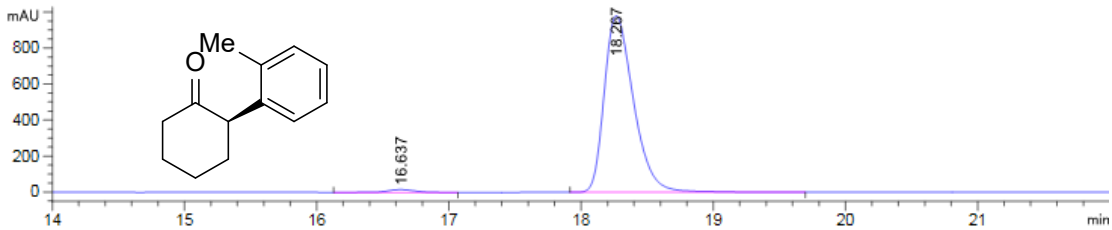
HPLC copies of compounds **2b**:

Rac-2b, OD-H, *i*PrOH/Hex 5/95, flow rate = 1.0 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	16.690	0.2421	1.87976e4	1204.26807	49.9261
2	18.447	0.2436	1.88533e4	1198.13977	50.0739

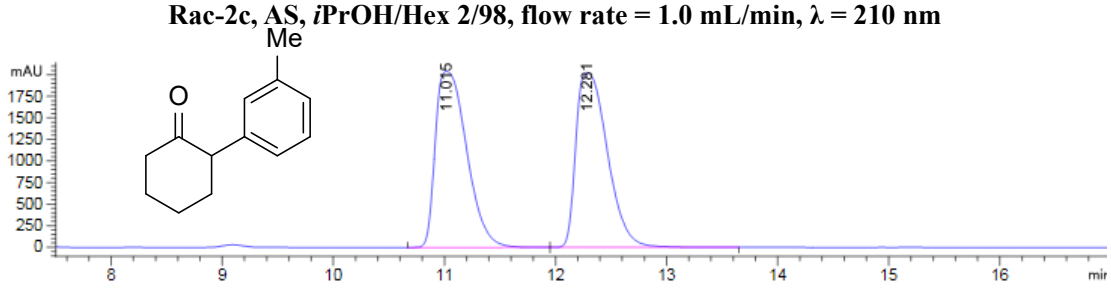
2b, OD-H, *i*PrOH/Hex 5/95, flow rate = 1.0 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	16.637	0.2281	234.48062	15.71052	1.5295
2	18.267	0.2377	1.50962e4	980.21338	98.4705

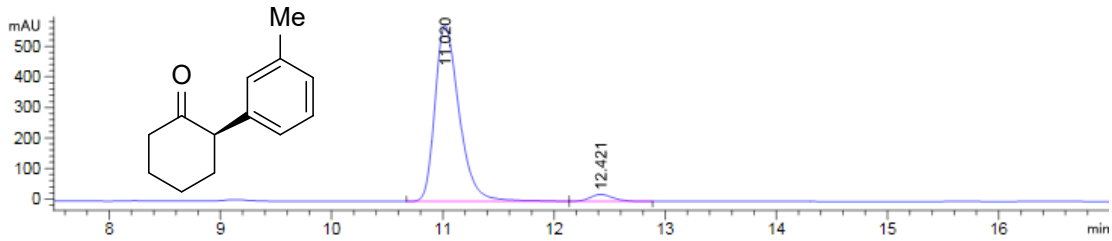
HPLC copies of compounds **2c**:

Rac-2c, AS, *i*PrOH/Hex 2/98, flow rate = 1.0 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	11.015	0.3101	3.99760e4	2044.78845	50.1007
2	12.281	0.3091	3.98154e4	2027.50916	49.8993

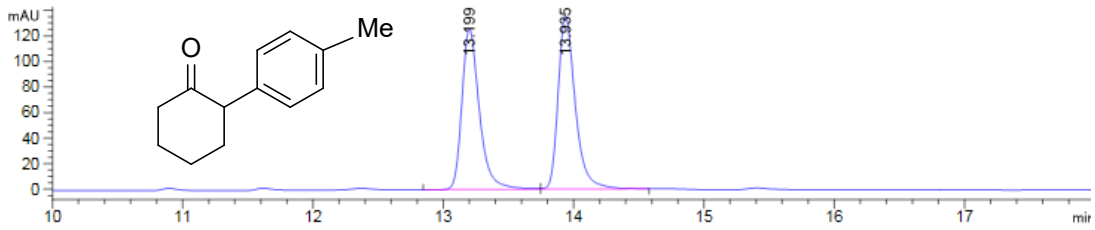
2c, AS, *i*PrOH/Hex 2/98, flow rate = 1.0 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	11.020	0.2328	8711.57910	574.88873	96.3097
2	12.421	0.2237	333.80634	22.95400	3.6903

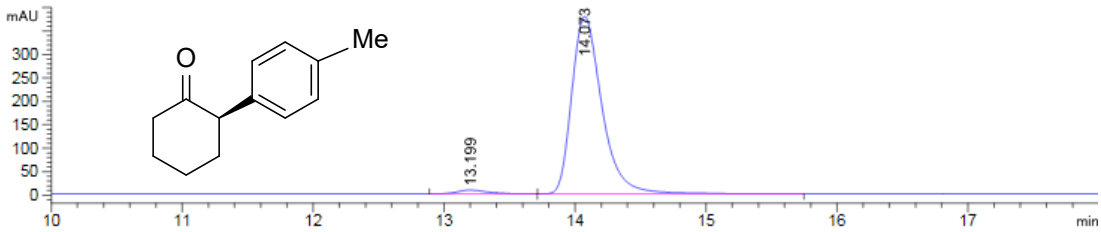
HPLC copies of compounds **2d**:

Rac-2d, OD-H, *i*PrOH/Hex 5/95, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	13.199	0.1428	1174.65479	125.91273	48.6372
2	13.935	0.1386	1240.48376	135.82240	51.3628

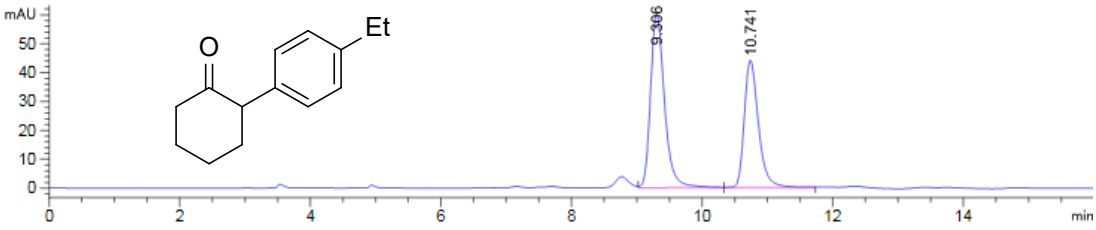
2d, OD-H, *i*PrOH/Hex 5/95, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	13.199	0.2473	795.46710	48.01775	2.2589
2	14.073	0.2635	34419.33213	2033.09351	97.7411

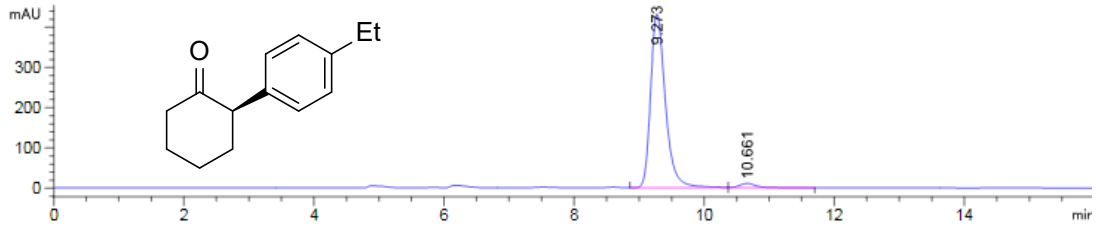
HPLC copies of compounds **2e**:

Rac-2e, AS, *i*PrOH/Hex 1/99, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	9.306	0.2287	889.55731	60.07897	57.5251
2	10.741	0.2283	656.82428	43.96044	42.4749

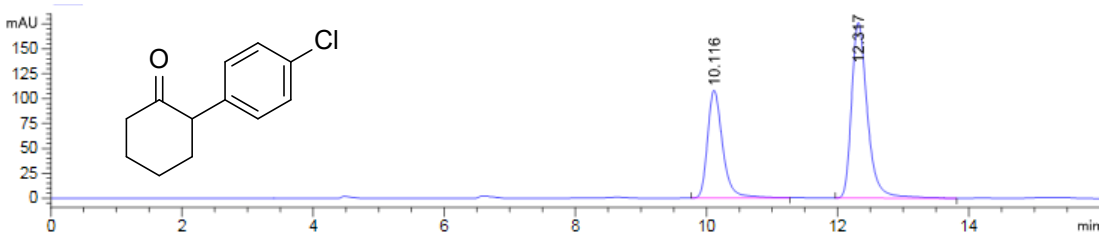
2e, AS, *i*PrOH/Hex 1/99, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	9.273	0.2423	6812.81055	431.28601	97.3250
2	10.661	0.2650	187.25218	10.65866	2.6750

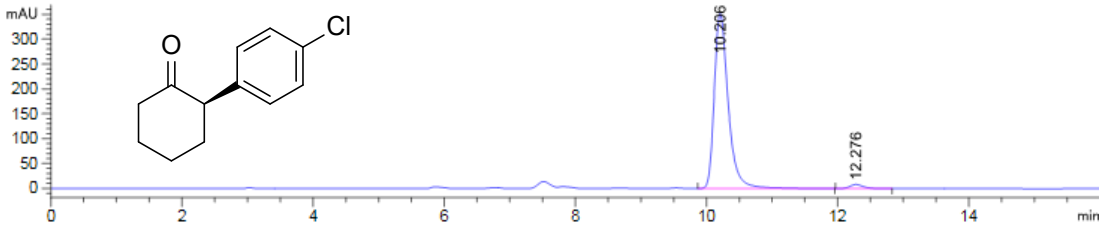
HPLC copies of compounds **2f**:

Rac-2f, AS, *i*PrOH/Hex 2/98, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	10.116	0.2439	1722.48718	108.11964	36.7925
2	12.317	0.2558	2959.13892	176.31015	63.2075

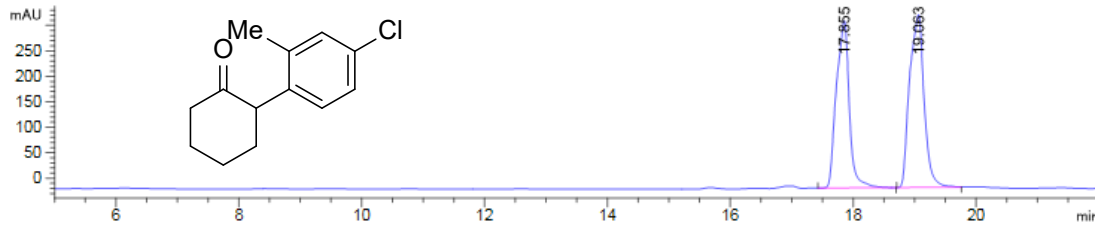
2f, AS, *i*PrOH/Hex 2/98, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	10.206	0.2239	5182.41846	351.65781	97.9618
2	12.276	0.2126	107.82544	7.83113	2.0382

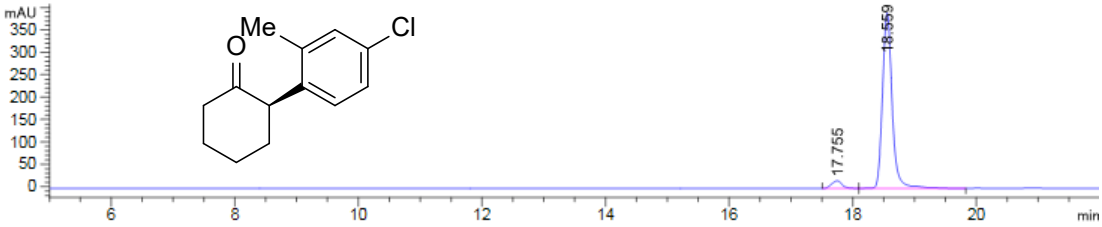
HPLC copies of compounds **2g**:

Rac-2g, OD-H, *i*PrOH/Hex 1/99, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	17.855	0.2019	4784.21924	328.57730	46.2928
2	19.063	0.2209	5550.47803	339.19559	53.7072

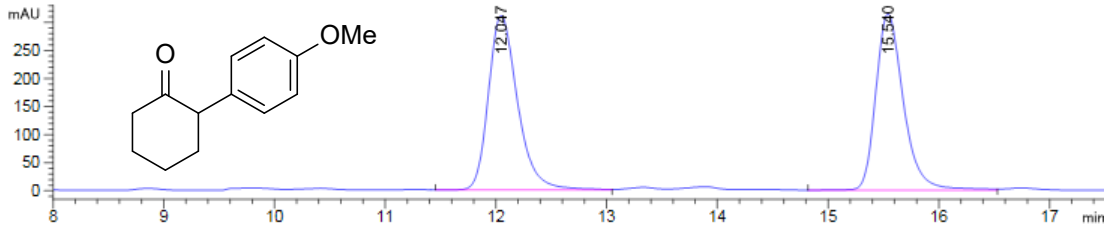
2g, OD-H, *i*PrOH/Hex 1/99, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	17.755	0.1855	193.23624	16.89090	4.3411
2	18.559	0.1648	4258.05762	391.92261	95.6589

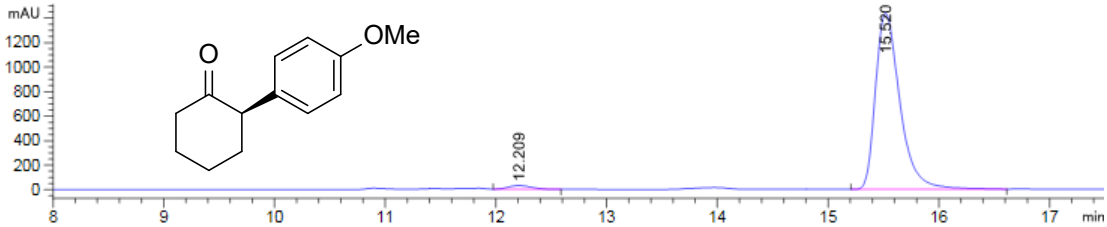
HPLC copies of compounds **2h**:

Rac-2h, OD-H, *i*PrOH/Hex 5/95, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	12.047	0.2795	5676.49219	310.20877	50.9977
2	15.540	0.2670	5454.37598	313.49872	49.0023

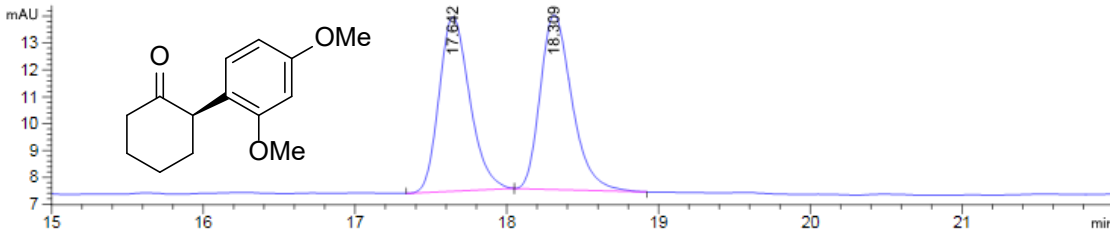
2h, OD-H, *i*PrOH/Hex 5/95, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	12.209	0.2217	447.86194	31.15390	1.9855
2	15.520	0.2354	22108.77064	1437.58264	98.0145

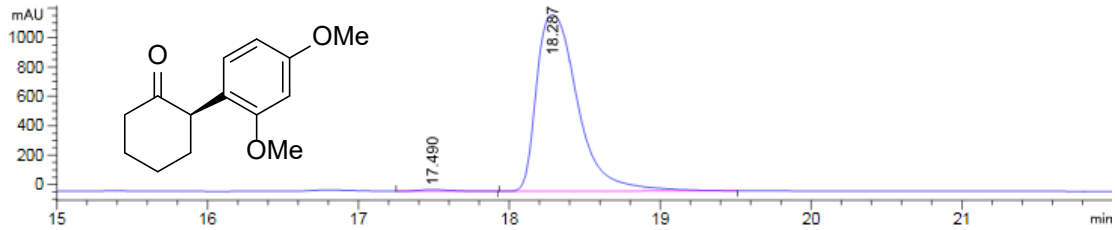
HPLC copies of compounds **2i**:

Rac-2i, OJ-H, *i*PrOH/Hex 1/99, flow rate = 0.7 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	17.642	0.2152	60.64426	4.33572	49.0542
2	18.309	0.2233	62.98291	4.33960	50.9458

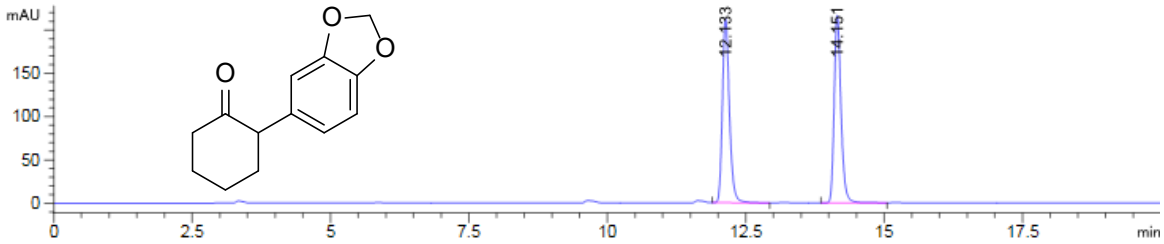
2i, OJ-H, *i*PrOH/Hex 1/99, flow rate = 0.7 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	17.490	0.2336	173.45973	10.90269	0.7559
2	18.287	0.2973	2.27746e4	1200.56995	99.2441

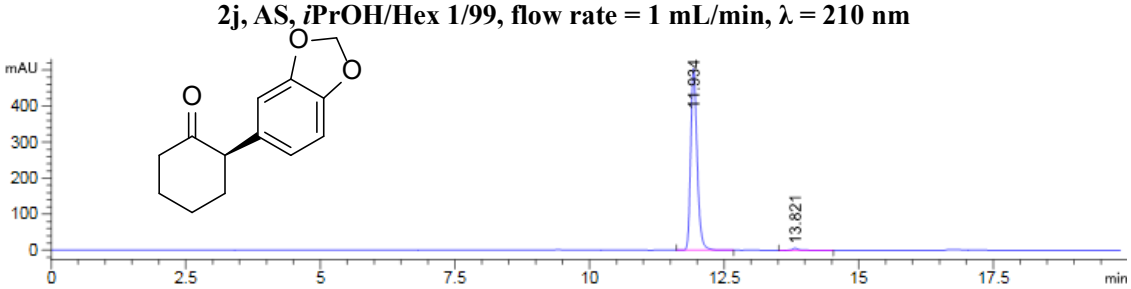
HPLC copies of compounds **2j**:

Rac-2j, AS, *i*PrOH/Hex 1/99, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	12.133	0.1325	1867.52844	212.47765	50.2050
2	14.151	0.1317	1852.27356	216.65186	49.7950

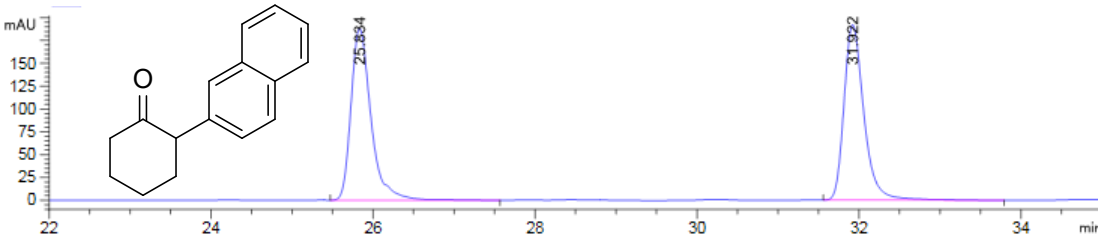
2j, AS, *i*PrOH/Hex 1/99, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	11.934	0.1275	4226.62695	505.74072	98.7956
2	13.821	0.1332	51.52543	5.82256	1.2044

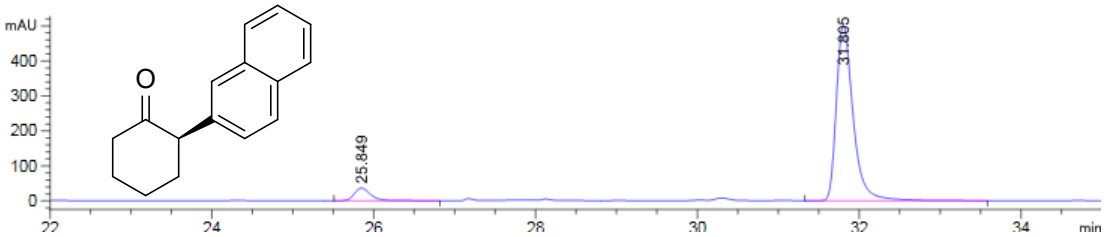
HPLC copies of compounds **2k**:

Rac-2k, OD-H, *i*PrOH/Hex 5/95, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	25.834	0.2632	3215.97388	187.83957	49.5562
2	31.922	0.2609	3273.58008	191.98599	50.4438

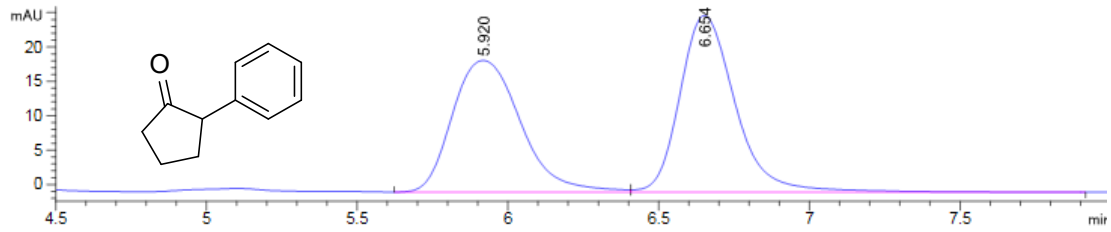
2k, OD-H, *i*PrOH/Hex 5/95, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	25.849	0.2153	349.92260	36.18599	4.6052
2	31.805	0.2206	7248.50098	501.52042	95.3948

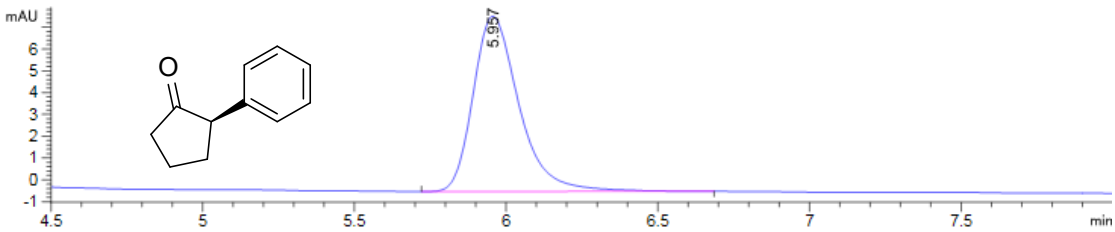
HPLC copies of compounds **2l**:

Rac-2l, AD, *i*PrOH/Hex 5/95, flow rate = 1.0 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	5.920	0.2495	300.99002	19.13783	47.7196
2	6.654	0.1997	329.75674	25.70044	52.2804

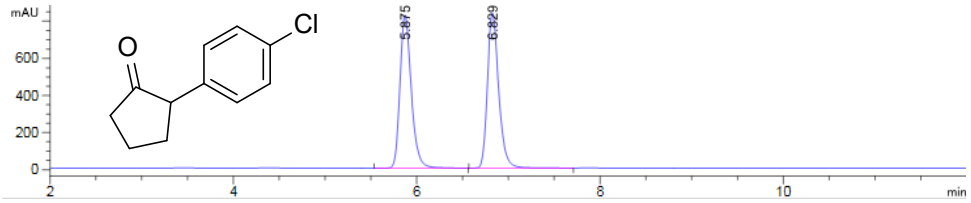
2l, AD, *i*PrOH/Hex 5/95, flow rate = 1.0 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	5.957	0.1608	84.68151	8.04246	100.0000

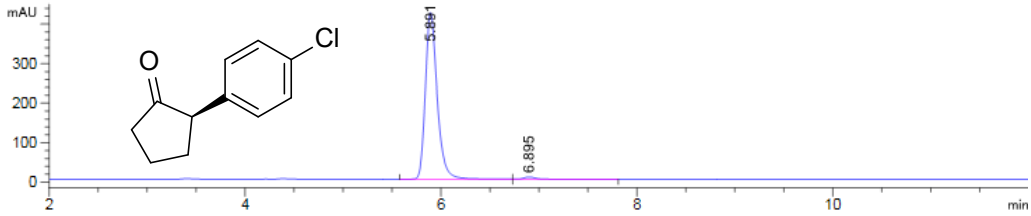
HPLC copies of compounds **2m**:

Rac-2m, AD, *i*PrOH/Hex 10/90, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	5.875	0.1323	7097.14404	825.23846	49.8097
2	6.829	0.1295	7151.37012	838.30890	50.1903

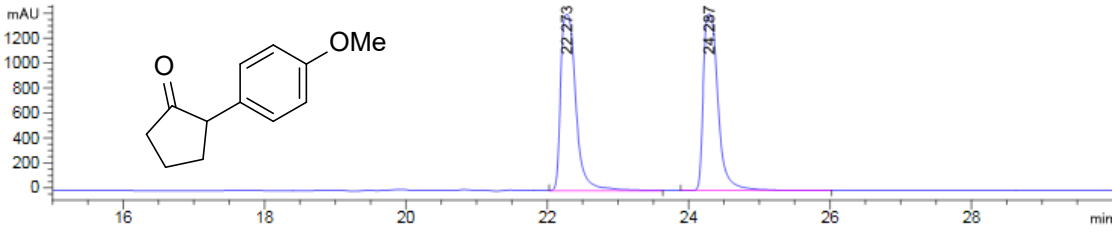
2m, AD, *i*PrOH/Hex 10/90, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	5.891	0.1285	3564.13916	422.15793	98.3966
2	6.895	0.1450	58.07900	5.99556	1.6034

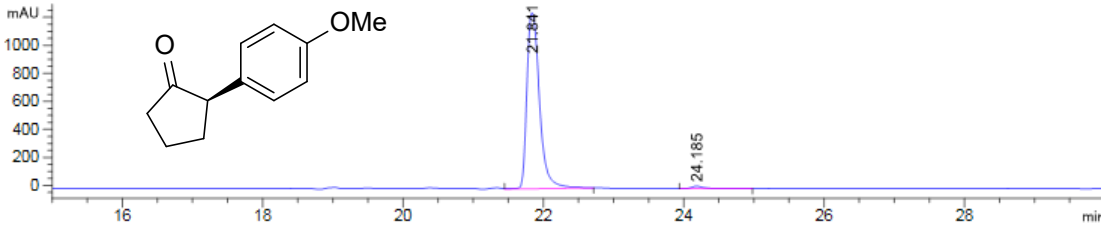
HPLC copies of compounds **2n**:

Rac-2n, AD, *i*PrOH/Hex 1/99, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	22.273	0.2340	2.10921e4	1414.23486	50.8719
2	24.287	0.2260	2.03691e4	1414.71008	49.1281

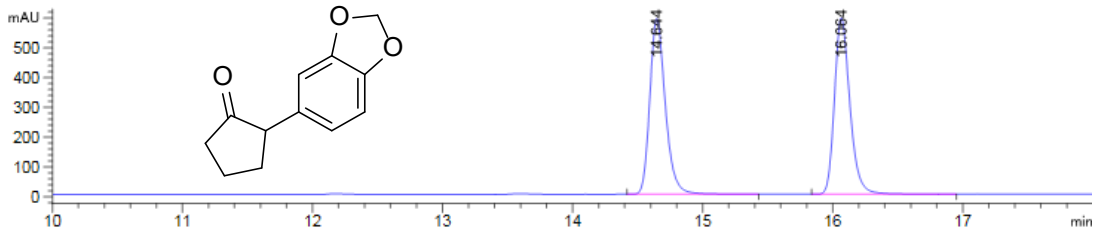
2n, AD, *i*PrOH/Hex 1/99, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	21.841	0.1980	1.56911e4	1253.61597	98.8079
2	24.185	0.1793	189.31450	15.85006	1.1921

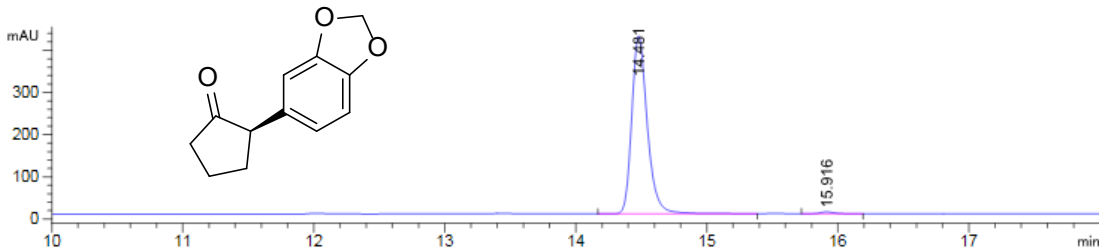
HPLC copies of compounds **2o**:

Rac-2o, AD, *i*PrOH/Hex 5/95, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	14.644	0.1274	4934.73193	590.93719	50.1272
2	16.064	0.1265	4909.68359	593.72943	49.8728

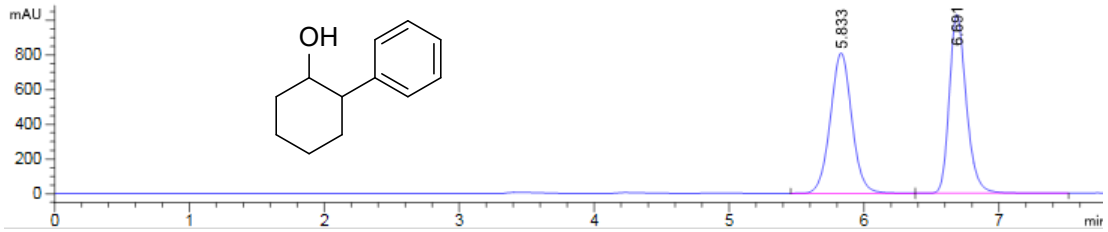
2o, AD, *i*PrOH/Hex 5/95, flow rate = 1 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	14.481	0.1266	3494.86841	422.00110	99.0289
2	15.916	0.1234	34.27315	4.28338	0.9711

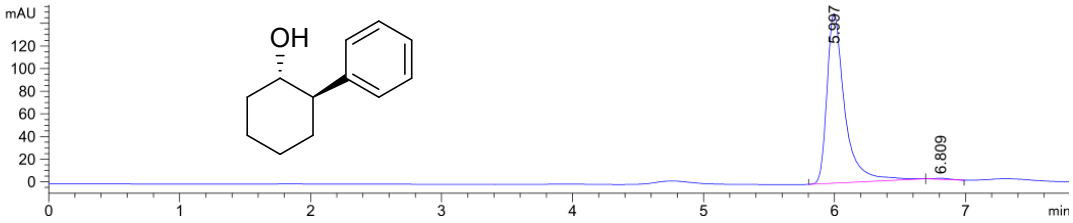
HPLC copies of compounds **4**:

Rac-4, OD-H, *i*PrOH/Hex 1/99, flow rate = 0.5 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	5.833	0.1694	8974.07520	809.22986	49.7725
2	6.691	0.1344	9056.11426	1031.94592	50.2275

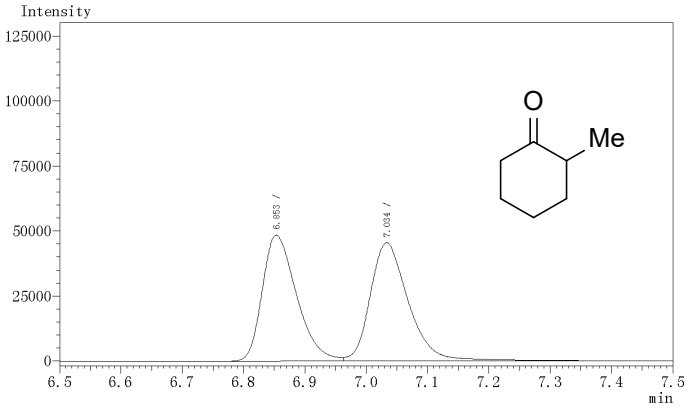
4, OD-H, *i*PrOH/Hex 1/99, flow rate = 0.5 mL/min, λ = 210 nm



Peak#	RetTime/min	Width/min	Area/mAU*s	Height/mAU	Area%
1	5.997	0.1400	1414.21558	149.95598	99.4005
2	6.809	0.1326	8.52946	1.00927	0.5995

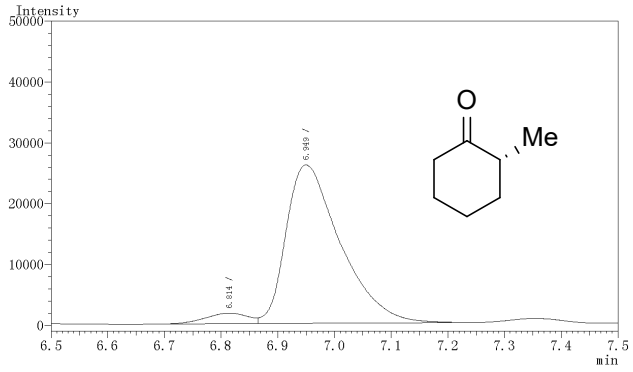
GC chromatogram of α-alkyl enones

2-methylcyclohexanone (*Rac*-3a)



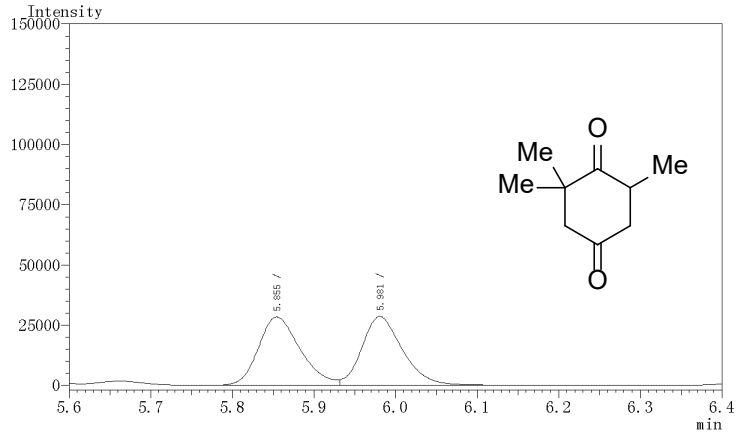
#	Time/min	Area	Height	Area%
1	6.853	188654	48402	48.895
2	7.034	197180	45293	51.105

(*R*)-2-methylcyclohexanone (3a)



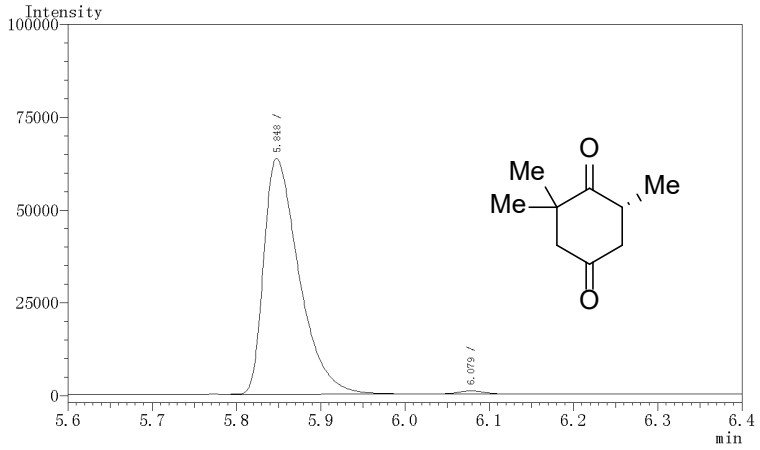
#	Time/min	Area	Height	Area%
1	6.814	7756	48402	4.268
2	6.949	173977	26037	95.732

levodione (*Rac*-3b)



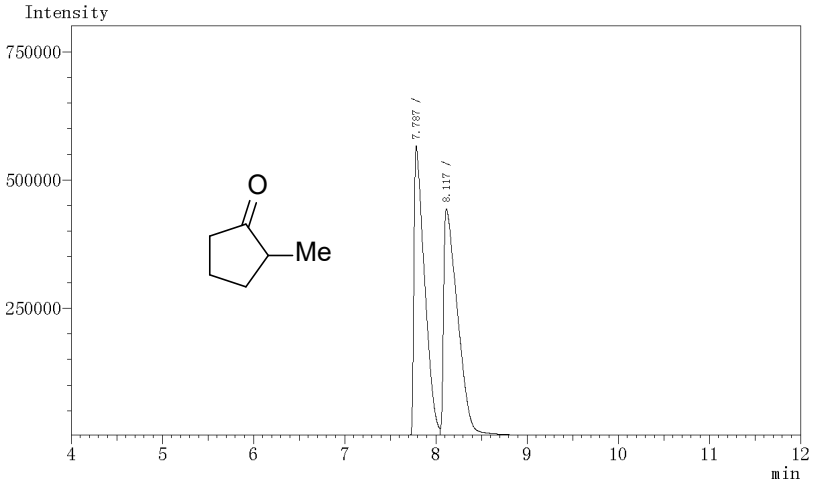
#	Time/min	Area	Height	Area%
1	5.855	100941	28276	50.726
2	5.981	98051	28519	49.274

(*R*)-levodione (3b)



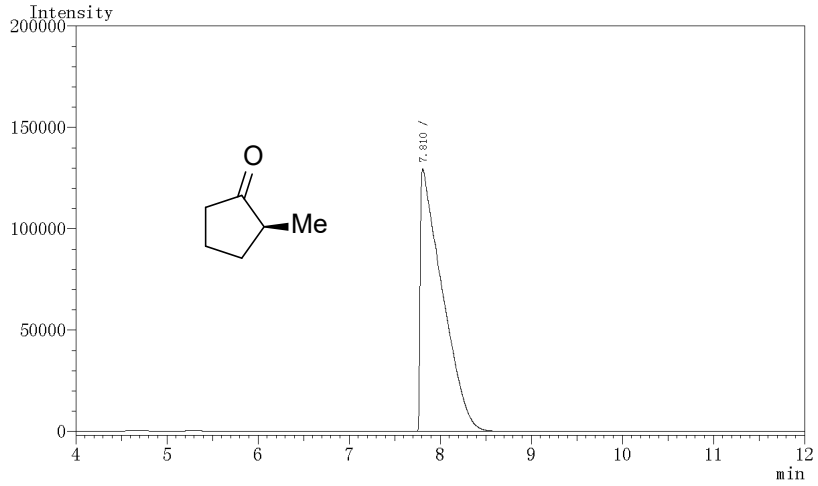
#	Time/min	Area	Height	Area%
1	5.848	185357	62994	98.889
2	6.079	2083	864	1.111

2-methylcyclopentanone (*Rac*-3c)



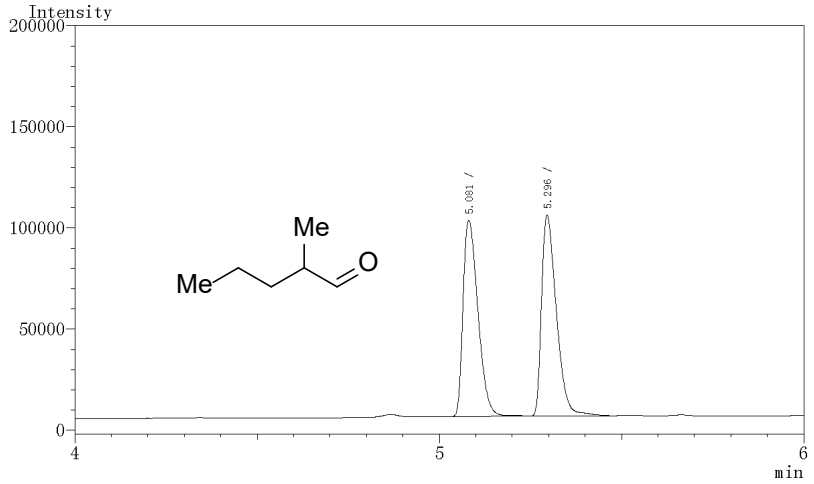
#	Time/min	Area	Height	Area%
1	7.787	4585982	565353	48.819
2	8.117	4807847	442887	51.181

(*S*)-2-methylcyclopentanone (3c)



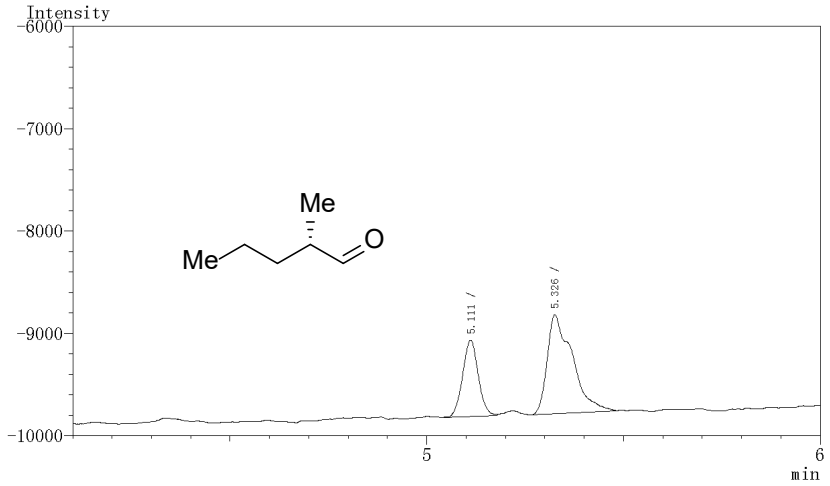
#	Time/min	Area	Height	Area%
1	7.810	2170801	129416	100

2-methylpentanal (*Rac*-3d)



#	Time/min	Area	Height	Area%
1	5.081	276817	96857	49.564
2	5.296	281684	99119	50.436

(*S*)-2-methylpentanal (3d)



#	Time/min	Area	Height	Area%
1	5.111	2.92	745	32.766
2	5.326	4292	958	67.234