Electronic Supplementary Information

Ruthenium-catalyzed dynamic kinetic asymmetric transfer hydrogenation: stereoselective access to 2-(1,2,3,4-tetrahydro-1-isoquinolyl)ethanol derivatives

Long-Sheng Zheng, Phannarath Phansavath* and Virginie Ratovelomanana-Vidal*

PSL Research University, Chimie ParisTech-CNRS
Institut de Recherche de Chimie Paris 75005 Paris, France
E-mail: phannarath.phansavath@chimie-paristech.fr, virginie.vidal@chimie-paristech.fr

Contents

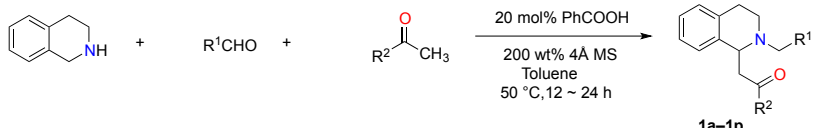
I. General informations 1
II. General procedure for the preparation of THIQ-derived β-amino ketones **1a**–**1q** 2
III. Analytical data for compounds **1k**–**1o**……2
IV. General procedure for the ATH-DKR of THIQ-derived β-amino ketones **1a**–**1q**…….....5
V. Analytical data for compounds **2a**–**2p** 5
VI. NMR spectra of compounds **1k**–**1o** 15
VII. NMR spectra and HPLC or SFC chromatograms for **2a**–**2p**……...20
VIII. Debenzylation of compound **2a**……...……...53

I. General informations

All manipulations were carried out under an argon atmosphere. Dichloromethane was distilled from calcium hydride. Reactions were monitored by thin layer chromatography carried out on precoated silica gel plates (E. Merck ref. 5554 60 F254) and revealed with either a ultra-violet lamp (λ = 254 nm) or a potassium permanganate solution. The nuclear magnetic resonance spectra were recorded on Bruker AV300 or AV400 instruments. The chemical shifts are expressed in parts per million (ppm) referenced to residual chloroform (7.26 ppm for ^{1}H and 77.16 ppm for ^{13}C). Coupling constants (*J*) are given in Hz and refer to apparent peak multiplicities. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal. Melting points were determined with a Kofler Heizbank 7841 apparatus and are uncorrected. Mass spectrometry analyses (direct introduction by chemical ionization with ammoniac or electrospray) were performed at Chimie ParisTech. High resolution mass spectra were performed at the University Pierre and Marie Curie (Paris). Sigma-Aldrich Silica gel (high-purity grade, pore size 60 Å, 230-400 mesh particle size, 40-63 μm particle size) was employed for flash column chromatography. Analytical thin layer chromatography (TLC) was carried out using commercial silica-gel plates (Merck 60 F254), spots were detected with UV light (254 nm) and revealed with a $KMnO_4$ or ninhydrin stain solution. All reagents were used as received from commercial sources.

II. General procedure for the preparation of THIQ-derived β-amino ketones 1a–1q[1]

A 100 mL round-bottom flask was charged with 4Å molecular sieves (200 wt% of aldehyde), benzoic acid (2.4 mmol, 0.2 equiv), toluene (60 mL), aldehyde (12.0 mmol, 1 equiv), aryl methyl ketone (18.0 mmol, 1.5 equiv) or acetone (3.0 equiv) and tetrahydroisoquinoline (THIQ) (18.0 mmol, 1.5 equiv). The mixture was stirred at 50 °C for 12–24 h at which time the aldehyde was consumed as detected by TLC analysis. The reaction mixture was allowed to cool to room temperature and filtered through a short pad of celite that was then rinsed with EtOAc (100 mL). The filtrate was washed with saturated aqueous $NaHCO_3$ (3 x 40 mL). The combined aqueous layers were extracted with EtOAc (3 x 40 mL), and the combined organic layers were washed with water (100 mL), brine (100 mL), and dried over anhydrous $MgSO_4$ or Na_2SO_4. Solvent was then removed under reduced pressure and the residue purified by silica gel chromatography. After column chromatography, the remaining impurity was removed using a Kugelrohr apparatus (0.001 mbar, 100 °C).



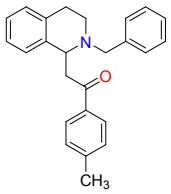
1a–1p

1a: $R^1 = C_6H_5$, $R^2 = C_6H_5$
1b: $R^1 = p\text{-}ClC_6H_4$, $R^2 = C_6H_5$
1c: $R^1 = m\text{-}ClC_6H_4$, $R^2 = C_6H_5$
1d: $R^1 = o\text{-}ClC_6H_4$, $R^2 = C_6H_5$
1e: $R^1 = p\text{-}BrC_6H_4$, $R^2 = C_6H_5$
1f: $R^1 = p\text{-}OCH_3IC_6H_4$, $R^2 = C_6H_5$
1g: $R^1 = m\text{-}OCH_3C_6H_4$, $R^2 = C_6H_5$
1h: $R^1 = p\text{-}CH_3C_6H_4$, $R^2 = C_6H_5$
1i: R^1 = 2-thienyl, $R^2 = C_6H_5$
1j: R^1 = 2-naphthyl, $R^2 = C_6H_5$
1k: $R^1 = C_6H_5$, $R^2 = p\text{-}CH_3C_6H_5$
1l: $R^1 = C_6H_5$, $R^2 = p\text{-}FC_6H_5$
1m: $R^1 = C_6H_5$, $R^2 = p\text{-}BrC_6H_5$
1n: $R^1 = C_6H_5$, $R^2 = p\text{-}OCH_3C_6H_5$
1o: $R^1 = C_6H_5$, R^2 = 2-naphthyl
1p: $R^1 = C_6H_5$, $R^2 = CH_3$

Compounds **1a**–**1j** and **1p** were synthesized according to the general procedure and their NMR data matched those reported.[1]

III. Analytical data for compounds 1k–1o

2-(2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(p-tolyl)ethan-1-one (1k)

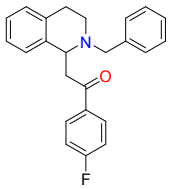


Synthesized according to the general procedure: 1.3 g (37% yield), pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (d, J = 8.2 Hz, 2H), 7.26–7.11 (m, 11H), 4.60 (dd, J = 7.3, 5.8 Hz, 1H), 3.75 (d, J = 13.3 Hz, 1H), 3.68 (d, J = 13.3 Hz, 1H), 3.59 (dd, J = 15.7, 7.8 Hz, 1H), 3.23–3.12 (m, 2H), 3.04–2.93 (m, 1H), 2.80 (ddd, J = 12.8, 5.4, 2.2 Hz, 1H), 2.58 (ddd, J = 16.9, 4.4, 2.4 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.7, 143.7, 139.3, 138.5, 135.2, 134.4, 129.4 (2C), 129.3, 128.9 (2C), 128.5 (2C),

[1] W. Chen, D. Seidel, *Org. Lett.* **2014**, *16*, 3158–3161.

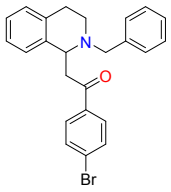
128.2 (2C), 127.8, 127.0, 126.4, 126.1, 58.5, 58.0, 45.7, 42.4, 24.5, 21.8.

2-(2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(4-fluorophenyl)ethan-1-one (1l)



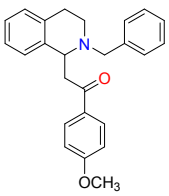
Synthesized according to the general procedure: 1.4 g (39% yield), pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96–7.90 (m, 2H), 7.20–7.06 (m, 11H), 4.54 (dd, *J* = 7.5, 5.6 Hz, 1H), 3.73 (d, *J* = 13.3 Hz, 1H), 3.62 (d, *J* = 13.3 Hz, 1H), 3.55 (dd, *J* = 15.4, 7.9 Hz, 1H), 3.24–3.11 (m, 2H), 3.05–2.94 (m, 1H), 2.85–2.78 (m, 1H), 2.61–2.53 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.5, 165.7 (d, J_{CF} = 252.8 Hz), 139.1, 138.1, 134.4, 134.0 (d, J_{CF} = 2.4 Hz), 131.0 (d, J_{CF} = 9.2 Hz, 2C), 129.4, 128.9 (2C), 128.2 (2C), 127.8, 127.1, 126.6, 126.2, 115.7 (d, J_{CF} = 21.8 Hz, 2C), 58.4, 58.0, 45.9, 42.5, 24.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ –106.7.

2-(2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(4-bromophenyl)ethan-1-one (1m)



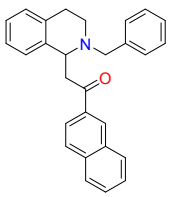
Synthesized according to the general procedure: 1.4 g (39% yield), pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.6 Hz, 2H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.23–7.07 (m, 9H), 4.52 (dd, *J* = 7.9, 5.5 Hz, 1H), 3.73 (d, *J* = 13.2 Hz, 1H), 3.65 (d, *J* = 13.2 Hz, 1H), 3.53 (dd, *J* = 15.4, 8.2 Hz, 1H), 3.25–3.10 (m, 2H), 3.05–2.94 (m, 1H), 2.82 (ddd, *J* = 13.1, 5.8, 2.0 Hz, 1H), 2.57 (ddd, *J* = 16.4, 4.4, 2.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.1, 139.0, 137.9, 136.3, 134.4, 132.0 (2C), 129.9 (2C), 129.4, 128.9 (2C), 128.3 (2C), 128.1, 127.7, 127.1, 126.6, 126.2, 58.4, 58.0, 45.9, 42.5, 24.2.

2-(2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(4-methoxyphenyl)ethan-1-one (1n)



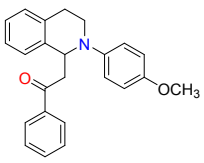
Synthesized according to the general procedure: 1.48 g (40% yield), pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.8 Hz, 2H), 7.26–7.12 (m, 9H), 6.91 (d, *J* = 8.8 Hz, 2H), 4.62–4.57 (m, 1H), 3.88 (s, 3H), 3.76 (d, *J* = 13.4 Hz, 1H), 3.69 (d, *J* = 13.4 Hz, 1H), 3.57 (dd, *J* = 15.6, 7.5 Hz, 1H), 3.24–3.10 (m, 2H), 2.99 (ddd, *J* = 16.4, 10.8, 5.5 Hz, 1H), 2.84–2.77 (m, 1H), 2.63–2.55 (m, 1H);^{13}C NMR (75 MHz, $CDCl_3$) δ 197.6, 163.5, 139.3, 138.5, 134.4, 130.7, 130.6 (2C), 129.3, 128.9 (2C), 128.2 (2C), 127.8, 127.0, 126.4, 126.1, 113.8 (2C), 58.6, 58.1, 55.6, 45.5, 42.6, 24.6.

2-(2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(naphthalen-2-yl)ethan-1-one (1o)



Synthesized according to the general procedure: 0.7 g (30% yield), pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.05 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.93–7.88 (m, 3H), 7.64–7.52 (m, 2H), 7.21–7.11 (m, 9H), 4.66 (dd, *J* = 7.7, 5.5 Hz, 1H), 3.80–3.68 (m, 3H), 3.31 (dd, *J* = 15.6, 5.2 Hz, 1H), 3.26–3.20 (m, 1H), 3.01 (ddd, *J* = 16.7, 10.8, 5.9 Hz, 1H), 2.86–2.79 (m, 1H), 2.64–2.56 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.0, 139.2, 138.4, 135.7, 135.0, 134.5, 132.7, 130.0, 129.7, 129.4, 128.9 (2C), 128.52, 128.47, 128.2 (2C), 127.9, 127.8, 127.0, 126.8, 126.5, 126.2, 124.3, 58.6, 58.1, 46.0, 42.5, 24.5.

1-phenyl-2-(2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)ethan-1-one (1q)[2]



A mixture of DDQ (10 mol%, 33.1 mg, 146.0 μmol), AIBN (24.0 mg, 14.6 μmol), *N*-4-methoxyphenyl tetrahydroisoquinoline (350 mg, 1.46 mmol) and acetophenone (877 mg, 7.30 mmol) in MeOH (6 mL) were heated at 60 ℃ under an oxygen atmosphere (balloon) for 24 h. The solvent was removed under vacuum, then water was added. After extraction with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (ethyl acetate/hexane: 1/20 to 1/10) to afford the desired product **1q** (220 mg, 42% yield) as a pale yellow solid. Analytical data of **1q** matched those reported in the literature.[3]

[2] K. Alagiri, P. Devadig, K. R. Prabhu, *Chem. Eur. J.* **2012**, *18*, 5160–5164

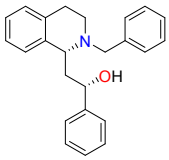
[3] Y. Shen, M. Li, S. Wang, T. Zhan, Z. Tan, C.-C. Guo, *Chem. Commun.* **2009**, 953.

IV. General procedure for the ATH-DKR of THIQ-derived β-amino ketones 1a–1q

In a round-bottom tube, charged with complex (*S*,*S*)-**4b** (5.0 μmol, 0.012 equiv) was added under argon a solution of the ketone **1** (0.42 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (1.3 mL), then HCO$_2$H/NEt$_3$ (5:2) azeotropic mixture (97 μL, 1.15 mmol, 2.75 equiv) was added dropwise. The mixture was stirred at 30 °C for 24 h, then filtered through a short pad of silica gel (ethyl acetate/petroleum ether: 1/4) and concentrated. The residue was purified by flash column chromatography (ethyl acetate/petroleum ether: 1/10 to 1/8) to afford compounds **2**:**3** as a mixture of diastereomers.

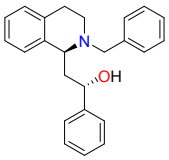
V. Analytical data for compounds 2a–2p

(*S*)-2-((*R*)-2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (2a)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.59 (br s, 1H), 7.42–6.93 (m, 14H), 4.95 (d, *J* = 10.6 Hz, 1H), 4.12 (dd, *J* = 11.8, 2.6 Hz, 1H), 3.92, 3.84 (ABq, *J* = 12.9 Hz, 2H), 3.60–3.47 (m, 1H), 3.17–2.99 (m, 2H), 2.55 (dd, *J* = 16.4, 4.8 Hz, 1H), 2.23–2.11 (m, 1H), 1.90–1.83 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*syn*) δ 144.8, 137.7, 136.4, 133.2, 129.5, 129.4 (2C), 128.8 (2C), 128.3 (2C), 127.8, 127.1, 126.7, 126.5, 125.8 (2C), 125.5, 75.5, 62.2, 57.3, 44.6, 40.8, 21.5.

(*S*)-2-((*S*)-2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (3a)



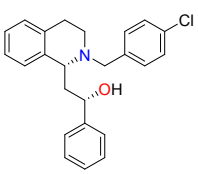
^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.59 (br s, 1H), 7.42–6.93 (m, 14H), 4.87 (dd, *J* = 6.5, 3.1 Hz, 1H), 4.03–3.95 (m, 2H), 3.60–3.47 (m, 1H, $H_{16'}$), 3.31 (ddd, *J* = 12.8, 7.9, 4.7 Hz, 1H), 2.92–2.73 (m, 2H), 2.72–2.63 (m, 1H), 2.46 (ddd, *J* = 14.8, 8.1, 3.2 Hz, 1H), 2.27–2.15 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*anti*) δ 145.4, 137.7, 136.6, 134.9, 129.3 (2C), 129.1, 128.8 (2C), 128.2 (2C), 127.8, 127.7, 126.7, 126.4, 125.8, 125.5 (2C), 72.3, 60.3, 58.3, 43.5, 42.2, 25.0.

Colourless oil, (**2a**:**3a**): 76% yield, dr (*syn/anti*) = 68/32, ee_{syn} = 98%, ee_{anti} = 99%.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{24}H_{26}NO$ 344.2014, found 344.2016.

HPLC (**2a**:**3a**): Chiralpak IC, Hexane : *i*-PrOH = 90:10, 1.0 mL/min, λ = 215 nm; t_R (*anti*) 10.38 min, t_R (*syn*) 13.94 min (major), t_R (*syn*) 25.38 min (minor).

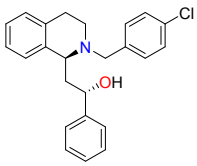
(*S*)-2-((*R*)-2-(4-chlorobenzyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (2b)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.51–6.86 (m, 14H), 4.92 (d, *J* = 9.3 Hz, 1H), 4.11–4.01 (dd, *J* = 11.9, 2.9 Hz, 1H), 3.89, 3.78 (ABq, *J* = 12.9 Hz, 2H), 3.50 (d, *J* = 12.9 Hz, 1H), 3.16–2.95 (m,

2H), 2.56 (dd, J = 16.8, 4.8 Hz, 1H), 2.22–2.10 (m, 1H), 1.92–1.79 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.7, 136.2, 136.1, 133.6, 133.0, 130.7 (2C), 129.1, 129.0 (2C), 128.3 (2C), 127.4, 127.2, 126.7, 126.5, 125.7 (2C), 75.5, 62.2, 56.5, 44.6, 41.0, 21.5.

(*S*)-2-((*S*)-2-(4-chlorobenzyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (3b)



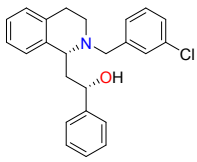
^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.67–6.74 (m, 14H), 4.86 (dd, J = 6.1, 3.1 Hz, 1H), 3.95–3.91 (m, 2H), 3.61–3.53 (m, 1H), 3.35–3.27 (m, 1H), 2.91–2.77 (m, 2H), 2.73–2.64 (m, 1H), 2.46 (ddd, J = 14.9, 8.3, 3.2 Hz, 1H), 2.25–2.15 (d, J = 11.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1, 136.3, 134.7, 133.6, 133.0, 130.8 (2C), 129.4 (2C), 129.1, 128.2 (2C), 127.4, 127.2, 126.7, 126.5, 125.4 (2C), 72.2, 60.1, 57.5, 43.7, 42.1, 24.9.

Colourless oil, (**2b**:**3b**): 73% yield, dr (*syn/anti*) = 66/34, ee_{syn} = 97%, ee_{anti} = 99%.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{24}H_{25}ClNO$ 378.1624, found 378.1627.

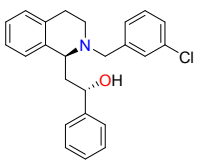
HPLC (**2b**:**3b**): Chiralpak IC, Hexane : *i*-PrOH = 90:10, 1.0 mL/min, λ = 215 nm; t_R (*anti*) 11.15 min, t_R (*syn*) 14.00 min (major), t_R (*syn*) 27.63 min (minor).

(*S*)-2-((*R*)-2-(3-chlorobenzyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (2c)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.42–6.94 (m, 14H), 4.96 (d, J = 10.5 Hz, 1H), 4.09 (dd, J = 11.7, 2.6 Hz, 1H), 3.98–3.81 (m, 2H), 3.61–3.49 (m, 1H), 3.15–2.99 (m, 2H), 2.58 (dd, J = 16.7, 4.8 Hz, 1H), 2.27–2.13 (m, 1H), 1.92–1.86 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*syn*) δ 144.7, 139.8, 136.1, 134.6, 133.0, 130.3, 129.5, 129.4, 128.4 (2C), 128.2, 128.0, 127.5, 127.3, 126.8, 126.6, 125.8 (2C), 75.5, 62.5, 56.8, 44.7, 40.9, 21.5.

(*S*)-2-((*S*)-2-(3-chlorobenzyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (3c)



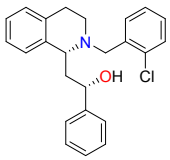
^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.42–6.94 (m, 14H), 4.88 (dd, J = 6.5, 3.1 Hz, 1H), 3.98–3.81 (m, 2H), 3.61–3.49 (m, 1H), 3.33 (ddd, J = 12.8, 7.9, 4.8 Hz, 1H), 2.93–2.76 (m, 2H), 2.74–2.66 (m, 1H), 2.53–2.42 (m, 1H), 2.27–2.13 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*anti*) δ 145.2, 139.8, 136.4, 134.7, 134.6, 130.2, 129.6, 129.1, 128.4 (2C), 128.0, 127.6, 127.5, 126.8, 126.6, 126.5, 125.4 (2C), 72.2, 60.2, 57.8, 43.7, 42.2, 25.0.

Colourless oil, (**2c**:**3c**): 70% yield, dr (*syn/anti*) = 66/34, ee_{syn} = 96%, ee_{anti} = 98%.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{24}H_{25}ClNO$ 378.1624, found 378.1626.

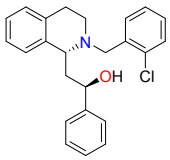
HPLC (**2c**:**3c**): Chiralpak IB, Hexane : *i*-PrOH = 90:10, 0.5 mL/min, λ = 215 nm; t_R (*anti*) 10.54 min, t_R (*anti*) 13.35 min, t_R (*syn*) 14.97 min (major), t_R (*syn*) 17.34 min (minor).

(*S*)-2-((*R*)-2-(2-chlorobenzyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (2d)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.38–6.70 (m, 14H), 4.76 (dd, *J* = 5.2, 3.8 Hz, 1H), 4.01 (dd, *J* = 12.0, 2.9 Hz, 1H), 3.85–3.68 (m, 2H), 3.55–3.41 (m, 1H), 3.15–2.98 (m, 1H), 2.91–2.78 (m, 1H), 2.50 (dd, *J* = 16.0, 4.4 Hz, 1H), 2.11–1.97 (m, 1H), 1.77–1.70 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*syn*) δ 144.8, 136.5, 135.5, 135.2, 133.2, 131.6, 130.0, 129.2, 129.1, 128.3 (2C), 127.7, 127.1, 126.7, 126.5 (2C), 125.8, 125.4, 75.5, 62.0, 55.0, 44.2, 41.8, 22.0.

(*S*)-2-((*S*)-2-(2-chlorobenzyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (3d)



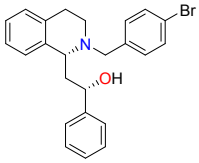
^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.38–6.70 (m, 14H), 4.66 (dd, *J* = 10.5, 1.2 Hz, 1H), 3.96 (d, *J* = 13.0 Hz, 1H), 3.85–3.68 (m, 2H), 3.38–3.31 (m, 1H), 3.15–2.98 (m, 1H), 2.92–2.77 (m, 1H), 2.71–2.61 (m, 1H), 2.44–2.35 (m, 1H), 2.11–1.97 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*anti*) δ 145.2, 136.6, 135.6, 135.3, 134.5, 131.7, 130.1, 129.4, 129.1, 128.3 (3C), 127.2, 127.0, 126.5 (2C), 125.8, 125.4, 72.2, 58.9, 54.4, 45.0, 42.4, 24.6.

Colourless oil, (**2d**:**3d**): 61% yield, dr (*syn/anti*) = 51/49, ee_{syn} = 96%, ee_{anti} = 98%.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{24}H_{25}ClNO$ 378.1624, found 378.1630.

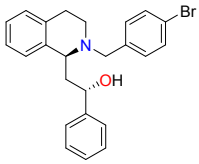
HPLC (**2d**:**3d**): Chiralpak IA, Hexane : *i*-PrOH = 90:10, 0.5 mL/min, λ = 215 nm; t_R (*syn*) 15.19 min (minor), t_R (*syn*) 16.48 min (major), t_R (*anti*) 22.05 min (minor), t_R (*anti*) 27.42 min (major).

(*S*)-2-((*R*)-2-(4-bromobenzyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (2e)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.52–6.91 (m, 14H), 4.91 (d, *J* = 10.4 Hz, 1H), 4.06 (dd, *J* = 11.7, 2.7 Hz, 1H), 3.87, 3.76 (ABq, *J* = 12.9 Hz, 2H), 3.59–3.46 (m, 1H), 3.13–2.97 (m, 2H), 2.59–2.52 (m, 1H), 2.21–2.09 (m, 1H), 1.85 (dd, *J* = 12.6, 2.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*syn*) δ 144.7, 136.8, 136.1, 133.0, 132.0 (2C), 131.1 (2C), 129.4, 128.3 (2C), 127.2, 126.8, 126.5, 125.7 (2C), 125.4, 121.7, 75.5, 62.2, 56.6, 44.6, 41.0, 21.5.

(*S*)-2-((*S*)-2-(4-bromobenzyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (3e)



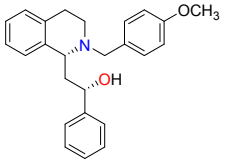
^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.52–6.91 (m, 14H), 4.85 (dd, *J* = 6.3, 3.1 Hz, 1H), 3.92–3.87 (m, 2H), 3.59–3.46 (m, 1H), 3.35–3.26 (m, 1H), 2.90–2.72 (m, 2H), 2.71–2.63 (m, 1H), 2.50–2.40 (m, 1H), 2.24–2.14 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*anti*) δ 145.1, 136.8, 136.3, 134.6, 132.0 (2C), 131.2 (2C), 129.1, 128.2 (2C), 127.4, 126.8, 126.5, 125.7 (2C), 125.4, 121.7, 72.2, 60.0, 57.6, 43.7, 42.1, 24.9.

Colourless oil, (**2e**:**3e**): 75% yield, dr (*syn/anti*) = 67/33, ee_{syn} = 98%, ee_{anti} = 99%.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{24}H_{25}BrNO$ 422.1119, found 422.1119.

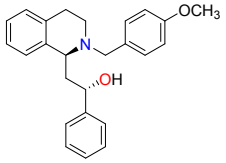
HPLC (**2e**:**3e**): Chiralpak IC, Hexane : *i*-PrOH = 90:10, 1.0 mL/min, λ = 215 nm; t_R (*anti*) 11.12 min, t_R (*syn*) 14.03 min (major), t_R (*syn*) 30.17 min (minor).

(*S*)-2-((*R*)-2-(4-methoxybenzyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (2f)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.60 (br s, 1H), 7.41–6.91 (m, 13H), 4.92 (d, *J* = 10.4 Hz, 1H), 4.13–4.07 (m, 1H), 3.85–3.76 (m, 2H), 3.83 (s, 3H), 3.59–3.45 (m, 1H), 3.15–2.99 (m, 2H), 2.53 (dd, *J* = 16.9, 5.0 Hz, 1H), 2.21–2.08 (m, 1H), 1.85 (dd, *J* = 14.6, 1.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*syn*) δ 159.2, 144.9, 136.4, 133.3, 130.6 (2C), 129.8, 129.3, 128.3 (2C), 128.2, 127.1, 126.6, 126.4, 125.8 (2C), 114.2 (2C), 75.5, 61.9, 56.5, 55.4, 44.6, 40.8, 21.5.

(*S*)-2-((*S*)-2-(4-methoxybenzyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (3f)



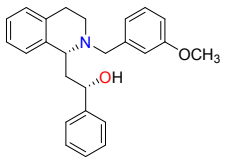
^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.60 (br s, 1H), 7.41–6.91 (m, 13H), 4.86 (dd, *J* = 6.1, 3.0 Hz, 1H), 3.96–3.91 (m, 2H), 3.85 (s, 3H), 3.59–3.45 (m, 1H), 3.30 (ddd, *J* = 12.2, 7.7, 4.3 Hz, 1H), 2.91–2.74 (m, 2H), 2.72–2.62 (m, 1H), 2.46–2.40 (m, 1H), 2.25–2.13 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*anti*) δ 159.2, 145.4, 136.6, 135.0, 130.7 (2C), 129.7, 129.0, 128.3, 128.2 (2C), 127.4, 126.7, 126.4, 125.5 (2C), 114.2 (2C), 72.3, 60.0, 57.5, 55.4, 43.4, 42.1, 25.1.

Colourless oil, (**2f**:**3f**): 83% yield, dr (*syn/anti*) = 68/32, ee_{syn} = 97%, ee_{anti} = 99%.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{25}H_{28}NO_2$ 374.2120, found 374.2121.

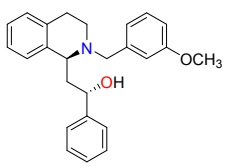
HPLC (**2f**:**3f**): Chiralpak IA, Hexane : *i*-PrOH = 90:10, 0.8 mL/min, λ = 215 nm; t_R (*syn*) 11.58 min (major), t_R (*syn*) 14.30 min (minor), t_R (*anti*) 41.11 min.

(*S*)-2-((*R*)-2-(3-methoxybenzyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (2g)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ) 7.62–6.81 (m, 14H), 4.94 (d, *J* = 9.5 Hz, 1H), 4.10 (dd, *J* = 11.9, 2.3 Hz, 1H), 4.01–3.77 (m, 2H), 3.83 (s, 3H) 3.61–3.45 (m, 1H), 3.17–3.00 (m, 2H), 2.61–2.50 (m, 1H), 2.23–2.10 (m, 1H), 1.85 (d, *J* = 15.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*syn*) δ 160.0, 144.9, 139.4, 136.4, 133.2, 129.8, 129.4, 128.3 (2C), 127.2, 126.7, 126.5, 125.8 (2C), 125.5, 121.7, 114.6, 113.6, 75.5, 62.1, 57.3, 55.4, 44.7, 41.1, 21.6.

(*S*)-2-((*S*)-2-(3-methoxybenzyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (3g)



^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.62–6.81 (m, 14H), 4.87 (dd, *J* = 6.6, 3.2 Hz, 1H), 4.01–3.77 (m, 2H), 3.86 (s, 3H), 3.61–3.45 (m, 1H), 3.36–3.27 (m, 1H), 2.92–2.77 (m, 2H), 2.72–2.67

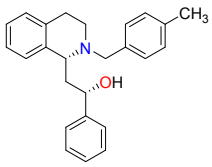
(m, 1H), 2.49–2.40 (m, 1H), 2.26–2.15 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*anti*) 160.0, 145.4, 139.4, 136.6, 134.9, 129.8, 129.1, 128.2 (2C), 127.4, 126.7, 126.5, 125.8 (2C), 125.5, 121.7, 114.9, 113.3, 72.3, 60.3, 58.3, 55.4, 43.6, 42.3, 25.1.

Colourless oil, (**2g**:**3g**): 70% yield, dr (*syn/anti*) = 65/35, ee_{syn} = 98%, ee_{anti} = 99%.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{25}H_{28}NO_2$ 374.2120, found 374.2124.

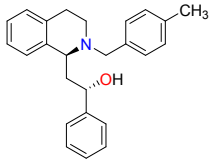
HPLC (**2g**:**3g**): Chiralpak IC, Hexane : *i*-PrOH = 90:10, 1.0 mL/min, λ = 215 nm; t_R (*anti*) 11.74 min, t_R (*syn*) 17.62 min (major), t_R (*syn*) 27.27 min (minor).

(*S*)-2-((*R*)-2-(4-methylbenzyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (2h)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.61 (br s, 1H), 7.41–6.92 (m, 13H), 4.94 (dd, *J* = 10.6, 1.5 Hz, 1H), 4.11 (dd, *J* = 11.8, 2.8 Hz, 1H), 3.88, 3.80 (ABq, *J* = 12.6 Hz, 2H), 3.57–3.45 (m, 1H), 3.16–2.99 (m, 2H), 2.59–2.49 (m, 1H), 2.38 (s, 3H), 2.22–2.09(m,1H), 1.89–1.82 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*syn*) δ 144.9, 137.4, 136.5, 134.7, 133.3, 129.5 (2C), 129.4 (2C), 128.3 (2C), 127.1, 126.7, 126.6, 126.4, 125.8 (2C), 125.5, 75.5, 62.1, 56.9, 44.6, 40.8, 21.5, 21.3.

(*S*)-2-((*S*)-2-(4-methylbenzyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (3h)



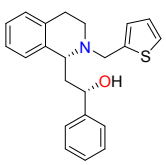
^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.61 (br s, 1H), 7.41–6.92 (m, 13H), 4.86 (dd, *J* = 6.4, 3.1 Hz, 1H), 3.98–3.92 (m, 2H), 3.57–3.45 (m, 1H), 3.31 (ddd, *J* = 12.7, 8.5, 4.6 Hz, 1H), 2.91–2.73 (m, 2H), 2.72–2.64 (m, 1H), 2.48–2.43 (m, 1H), 2.40 (s, 3H), 2.26–2.14 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*anti*) δ 145.4, 137.4, 136.6, 134.9, 134.60, 129.5 (2C), 129.4 (2C), 129.0, 128.2 (2C), 127.4, 126.7, 126.4, 125.8 (2C), 125.5, 72.4, 60.2, 57.9, 43.4, 42.1, 25.0, 21.3.

Colourless oil, (**2h**:**3h**): 85% yield, dr (*syn/anti*) = 67/33, ee_{syn} = 98%, ee_{anti} = 99%.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{25}H_{28}NO$ 358.2170, found 358.2172.

HPLC (**2h**:**3h**): Chiralpak ID, Hexane : *i*-PrOH = 90:10, 1.0 mL/min, λ = 215 nm; t_R (*syn*) 9.35 min (major), t_R (*syn*) 10.51 min (minor), t_R (*anti*) 22.34 min.

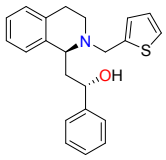
(*S*)-1-phenyl-2-((*R*)-2-(thiophen-2-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)ethan-1-ol (2i)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.43–6.92 (m, 13H), 5.01 (dd, *J* = 10.5, 1.4 Hz, 1H), 4.16 (dd, *J* = 11.8, 2.9 Hz, 1H), 4.12–3.90 (m, 2H), 3.56 (ddd, *J* = 15.6, 13.3, 5.1 Hz, 1H), 3.16–3.02 (m, 2H), 2.61–2.53 (m, 1H), 2.24–2.12 (m, 1H), 1.88 (ddd, *J* = 14.9, 3.1, 1.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*syn*) δ 144.8, 141.4, 136.3, 133.1, 129.4, 128.3 (3C), 127.2, 126.8 (2C), 126.7, 126.5, 125.81 (2C), 125.77, 75.4, 62.0,

51.6, 44.9, 41.2, 21.5.

(*S*)-1-phenyl-2-((*S*)-2-(thiophen-2-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)ethan-1-ol (3i)



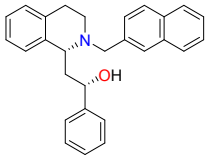
^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.43–6.92 (m, 13H), 4.89 (dd, *J* = 6.8, 3.0 Hz, 1H), 4.12–3.90 (m, 3H), 3.38–3.29 (m, 1H), 2.95–2.75 (m, 3H), 2.47–2.41 (m, 1H), 2.24–2.12 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*anti*) δ 145.3, 140.8, 136.5, 134.8, 129.1, 128.4 (3C), 127.4, 126.8 (2C), 126.7, 126.5, 125.6 (3C), 72.2, 59.7, 52.2, 43.3, 42.4, 25.0.

Colourless oil, (**2i**:**3i**): 59% yield, dr (*syn/anti*) = 71/29, ee_{syn} = 99%, ee_{anti} = 99%.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{22}H_{24}NOS$ 350.1578, found 350.1581.

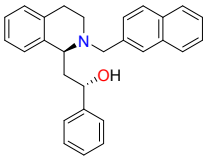
HPLC (**2i**:**3i**): Chiralpak IC, Hexane : *i*-PrOH = 90:10, 1.0 mL/min, λ = 215 nm; t_R (*syn*) 13.89 min (minor), t_R (*syn*)18.01 min (major), t_R (*anti*) 32.66 min.

(*S*)-2-((*R*)-2-(naphthalen-2-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (2j)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.94–6.93 (m, 17H), 4.95–4.88 (m, 1H), 4.18–3.98 (m, 3H), 3.62–3.51 (m, 1H), 3.23–3.03 (m, 2H), 2.56 (dd, *J* = 16.8, 4.7 Hz, 1H), 2.27–2.12 (m, 1H), 1.89–1.83 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.8, 136.4, 135.2, 133.4, 133.2, 133.1, 129.4, 128.8, 128.3 (4C), 127.9 (2C), 127.2 (2C), 126.7, 126.5, 126.3, 126.1, 125.8 (2C), 75.5, 62.1, 57.5, 44.7, 41.1, 21.6.

(*S*)-2-((*S*)-2-(naphthalen-2-ylmethyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenylethan-1-ol (3j)



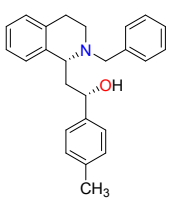
^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.94–6.93 (m, 17H), 4.95–4.88 (m, 1H), 4.18–3.98 (m, 2H), 3.70 (d, *J* = 12.9 Hz, 1H), 3.41–3.32 (m, 1H), 2.94–2.85 (m, 1H), 2.80–2.70 (m, 2H), 2.51–2.45 (m, 1H), 2.27–2.12 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.3, 136.6, 134.8, 133.2, 133.1, 129.1, 128.8, 128.3 (4C), 128.4, 127.9, 127.5, 127.3, 127.2, 126.7, 126.5, 126.4, 126.1, 125.5 (2C), 72.4, 60.1, 58.4, 43.6, 42.2, 24.9.

Colourless oil, (**2j**:**3j**): 78% yield, dr (*syn/anti*) = 68/32, ee_{syn} = 99%, ee_{anti} = 99%.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{28}H_{28}NO$ 394.2170, found 394.2173.

HPLC (**2j**:**3j**): Chiralpak IC, Hexane : *i*-PrOH = 90:10, 1.0 mL/min, λ = 215 nm; t_R (*syn*) 13.89 min (minor), t_R (*syn*)18.01 min (major), t_R (*anti*) 32.66 min.

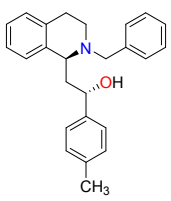
(*S*)-2-((*R*)-2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(p-tolyl)ethan-1-ol (2k)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.55 (br s, 1H), 7.46–6.93 (m, 13H), 4.91 (d, *J* = 10.6 Hz, 1H), 4.10 (dd, *J* = 11.8, 2.7 Hz, 1H), 3.91, 3.83 (ABq, *J* = 12.6 Hz, 2H), 3.55–3.45 (m, 1H), 3.16–2.98 (m, 2H), 2.54 (dd, *J* = 16.6, 4.8 Hz, 1H),

2.32 (s, 3H), 2.27–2.09 (m, 1H), 1.88–1.81 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) (*syn*) δ 141.9, 137.7, 136.7, 136.5, 133.2, 129.4 (2C), 129.3, 129.0 (2C), 128.8 (2C), 128.2, 127.7, 126.6, 126.4, 125.7 (2C), 75.4, 62.3, 57.3, 43.4, 40.8, 21.5, 21.2

(*S*)-2-((*S*)-2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(p-tolyl)ethan-1-ol (3k)



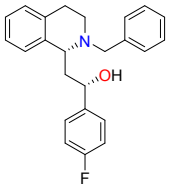
^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.55 (br s, 1H), 7.46–6.93 (m, 13H), 4.84 (dd, *J* = 6.5, 2.9 Hz, 1H), 4.01 (d, *J* = 12.9 Hz, 1H), 3.96 (dd, *J* = 8.2, 2.8 Hz, 1H), 3.55–3.45 (m, 1H), 3.29 (ddd, *J* = 12.8, 8.0, 4.7 Hz, 1H), 2.91–2.72 (m, 2H), 2.70–2.62 (m, 1H), 2.48–2.37 (m, 1H), 2.36 (s, 3H), 2.27–2.09 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*anti*) δ 142.4, 137.7, 136.7, 136.2, 134.9, 129.5 (2C), 129.3, 129.0 (2C), 128.8 (2C), 127.7, 127.4, 126.4, 126.3, 125.4 (2C), 72.2, 60.4, 58.3, 44.7, 42.2, 25.0, 21.2.

Colourless oil, (**2k**:**3k**): 78% yield, dr (*syn/anti*) = 64/36, ee_{syn} = 99%, ee_{anti} = 95%.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{25}H_{28}NO$ 358.2170, found 358.2173.

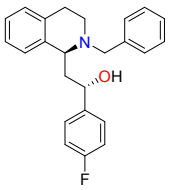
HPLC (**2k**:**3k**): Chiralpak IB, Hexane : *i*-PrOH = 97:3, 0.5 mL/min, λ = 215 nm; t_R (*anti*) 19.89 min, t_R (*syn*) 23.40 min (major), t_R (*syn*) 30.20 min (minor).

(*S*)-2-((*R*)-2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(4-fluorophenyl)ethan-1-ol (2l)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.48 (br s, 1H), 7.30–6.82 (m, 13H), 4.80 (d, *J* = 9.7 Hz, 1H), 3.99 (dd, *J* = 11.8, 2.6 Hz, 1H), 3.82, 3.71 (ABq, *J* = 12.8 Hz, 2H), 3.46 – 3.34 (m, 1H), 3.07–2.89 (m, 2H), 2.44 (dd, *J* = 16.4, 4.7 Hz, 1H), 2.08–1.95 (m, 1H), 1.74–1.68 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*syn*) δ 160.2 (*J* = 242.8 Hz), 140.7, 137.7, 136.2, 133.2, 129.6, 129.4 (2C), 128.8 (2C), 128.2, 127.8, 127.4, 127.3, 126.5 (2C), 115.0 (*J* = 21.1 Hz, 2C), 74.9, 62.1, 57.3, 44.7, 40.9, 21.5.

(*S*)-2-((*S*)-2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(4-fluorophenyl)ethan-1-ol (3l)



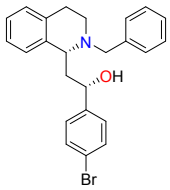
^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.48 (br s, 1H), 7.30–6.82 (m, 13H), 4.71 (dd, *J* = 6.4, 2.9 Hz, 1H), 3.89 (d, *J* = 12.9 Hz, 1H), 3.87–3.84 (m, 1H), 3.46–3.34 (m, 1H), 3.21 (ddd, *J* = 12.6, 7.5, 5.0 Hz, 1H), 2.81–2.63 (m, 2H), 2.63–2.54 (m, 1H), 2.35–2.26 (m, 1H), 2.11–1.95 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*anti*) δ 163.5 (*J* = 233.9 Hz), 141.1, 137.6, 136.4, 134.9, 129.4 (2C), 129.1, 128.8 (2C), 128.2, 127.8, 127.1, 127.0, 126.7 (2C), 115.0 (*J* = 21.1 Hz, 2C), 71.7, 60.1, 58.4, 44.0, 42.2, 25.3.

Colourless oil, (**2l**:**3l**): 71% yield, dr (*syn/anti*) = 68/32, ee_{syn} = 98%, ee_{anti} = 98%.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{24}H_{25}FNO$ 362.1920, found 362.1923.

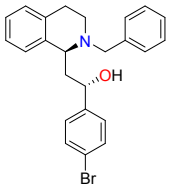
HPLC (**2l**:**3l**): Chiralpak IB, Hexane : *i*-PrOH = 97:3, 0.5 mL/min, λ = 215 nm; t_R (*anti*) 18.05 min (minor), t_R (*anti*) 19.00 min (major), t_R (*syn*) 21.38 min (major), t_R (*syn*) 24.97 min (minor).

(*S*)-2-((*R*)-2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(4-bromophenyl)ethan-1-ol (2m)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.72 (br s, 1H), 7.45–6.90 (m, 13H), 4.88 (d, *J* = 10.2 Hz, 1H), 4.10 (dd, *J* = 11.7, 2.5 Hz, 1H), 3.91, 3.81 (ABq, *J* = 12.9 Hz, 2H), 3.56–3.43 (m, 1H), 3.16–3.09 (m, 2H), 2.55 (dd, *J* = 16.4, 4.7 Hz, 1H), 2.21–2.03 (m, 1H), 1.84–1.77 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*syn*) δ 143.9, 137.6, 136.1, 133.2, 131.4 (2C), 129.6, 129.4 (2C), 128.9 (2C), 128.2, 127.8, 127.5 (2C), 126.8, 126.5, 120.8, 74.9, 62.1, 57.2, 44.5, 40.9, 21.5.

(*S*)-2-((*S*)-2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(4-bromophenyl)ethan-1-ol (3m)



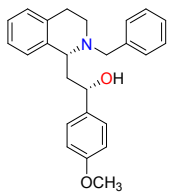
^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.72 (br s, 1H), 7.45–6.90 (m, 13H), 4.79 (dd, *J* = 6.2, 3.0 Hz, 1H), 3.98–3.92 (m, 2H), 3.56–3.43 (m, 1H), 3.37–3.33 (m, 1H), 2.92–2.77 (m, 2H), 2.73–2.66 (m, 1H), 2.49–2.38 (m, 1H), 2.21–2.03 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*anti*) δ 144.5, 137.6, 136.1, 134.8, 131.4 (2C), 129.4 (2C), 129.1, 128.9 (2C), 128.2, 127.8, 127.3 (2C), 126.8, 126.5, 120.3, 71.8, 59.9, 58.3 , 43.9, 41.9, 25.0.

Colourless oil, (**2m**:**3m**): 60% yield, dr (*syn/anti*) = 69/31, ee_{syn} = 96%, ee_{anti} = 98%.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{24}H_{25}BrNO$ 422.1119, found 422.1120.

HPLC (**2m**:**3m**): Chiralpak IB, Hexane : *i*-PrOH = 97:3, 0.5 mL/min, λ = 215 nm; t_R (*anti*) 16.47 min (minor), t_R (*anti*) 18.53 min (major), t_R (*syn*) 19.67 min (major), t_R (*syn*) 23.50 min (minor).

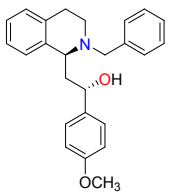
(*S*)-2-((*R*)-2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(4-methoxyphenyl)ethan-1-ol (2n)



Sticky yellow oil, (**2n**:**3n**): 79% yield, dr (*syn/anti*) = 61/39, ee_{syn} = 98%, ee_{anti} = 99%.

^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.43–7.25 (m, 8H), 7.20–7.13 (m, 3H), 7.06–7.03 (m, 1H), 6.91–6.85 (m, 2H), 4.92–4.89 (m, 1H), 4.10 (dd, *J* = 11.7, 2.5 Hz, 1H), 3.93–3.84 (m, 2H), 3.80 (s, 3H), 3.56–3.47 (m, 1H), 3.17–2.99 (m, 2H), 2.55 (dd, *J* = 16.7, 4.9 Hz, 1H), 2.25–2.11 (m, 1H), 1.87–1.80 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) (*syn*) δ 158.8, 137.7, 137.2, 136.4, 133.2, 129.4 (2C), 129.3, 128.8 (2C), 128.2, 127.7, 126.9 (2C), 126.6, 126.4, 113.7 (2C), 75.1, 62.2, 57.2, 55.3, 44.7, 40.8, 21.5.

(*S*)-2-((*S*)-2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(4-methoxyphenyl)ethan-1-ol (3n)



^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.43–7.25 (m, 8H), 7.20–7.13 (m, 3H), 6.97–6.94 (m, 1H), 6.91–6.85 (m, 2H), 4.83 (dd, *J* = 6.4, 2.8 Hz, 1H), 4.04–3.97 (m, 2H) 3.82 (s, 3H), 3.56–3.47 (m, 1H), 3.30 (ddd, *J* = 12.6, 7.7, 4.7 Hz, 1H), 2.92–2.74 (m, 2H), 2.71–2.63 (m, 1H), 2.42 (ddd, *J* = 14.8, 8.1, 3.1 Hz, 1H), 2.25–2.11 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) (*anti*) δ 158.4, 137.6, 137.5, 136.6, 134.9,

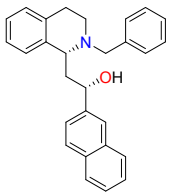
129.5 (2C), 129.0, 128.8 (2C), 128.7, 127.4, 126.9 (2C), 126.6, 126.3, 113.7 (2C), 71.8, 60.3, 58.3, 55.3, 43.5, 42.2, 25.1.

MS (ESI): *m/z* = 374 $[M + H]^+$.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{25}H_{28}NO_2$ 374.2120, found 374.2121.

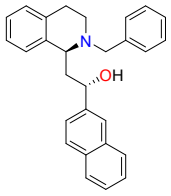
HPLC : Chiralpak IE, Hexane : *i*-PrOH = 95:5, 1.0 mL/min, λ = 215 nm; t_R [*syn* – (*R,S*)] = 48.55 min, t_R [*syn* – (*S,R*)] = 52.45 min, t_R (*anti*) = 58.91 min, t_R (*anti*) = 90.98 min.

(*S*)-2-((*R*)-2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(naphthalen-2-yl)ethan-1-ol (2o)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.92–7.81 (m, 5H), 7.54–7.34 (m, 8H), 7.22–6.93 (m, 4H), 5.13 (d, *J* = 9.3 Hz, 1H), 4.18 (dd, *J* = 11.8, 2.7 Hz, 1H), 3.95, 3.88 (ABq, *J* = 12.8 Hz, 2H), 3.63–3.51 (m, 1H), 3.19–3.03 (m, 2H), 2.60–2.50 (m, 1H), 2.37–2.18 (m, 1H), 2.00–1.93 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*syn*) δ 142.3, 137.7, 136.3, 133.6, 133.2, 132.9, 129.5 (2C), 129.4, 128.8 (2C), 128.2, 128.1, 128.0, 127.8, 127.7, 126.7, 126.5, 125.9, 125.5, 124.3, 124.2, 75.6, 62.3, 57.3, 44.5, 40.7, 21.5.

(*S*)-2-((*S*)-2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-(naphthalen-2-yl)ethan-1-ol (3o)



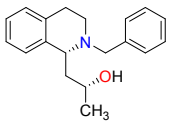
^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.92–7.81 (m, 5H), 7.54–7.34 (m, 8H), 7.22–6.93 (m, 4H), 5.06 (dd, *J* = 6.1, 3.1 Hz, 1H), 4.04–3.97 (m, 2H), 3.63–3.51 (m, 1H), 3.34 (ddd, *J* = 12.8, 7.9, 4.6 Hz, 1H), 2.93–2.75 (m, 2H), 2.74–2.66 (m, 1H), 2.60–2.50 (m, 1H), 2.37–2.18 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) (*anti*) δ 142.8, 137.6, 136.5, 134.9, 133.6, 132.7, 129.5 (2C), 129.1, 128.8 (2C), 128.1 (2C), 128.0, 127.8, 127.4, 126.5, 126.4, 126.0, 125.5, 124.1, 124.0, 72.4, 60.5, 58.3, 43.4, 42.0, 25.0.

Colourless oil, (**2o**:**3o**): 75% yield, dr (*syn/anti*) = 63/37, ee_{syn} = 94%, ee_{anti} = 98%.

HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{28}H_{28}NO$ 394.2170, found 394.2173.

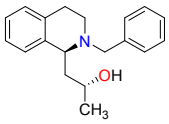
HPLC (**2o**:**3o**): Chiralpak IB, Hexane : *i*-PrOH = 94:6, 0.7 mL/min, λ = 215 nm; t_R (*anti*) 14.63 min (minor), t_R (*syn*) 17.05 min (major), t_R (*anti*) 18.41 min (major), t_R (*syn*) 38.77 min (minor).

(*R*)-1-((*R*)-2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-ol (2p)



^{1}H NMR (300 MHz, $CDCl_3$) (*syn*) δ 7.39–7.00 (m, 10H), 4.04–3.96 (m, 1H), 3.91 (dd, *J* = 12.0, 2.8 Hz, 1H), 3.79 (q, *J* = 12.7 Hz, 2H), 3.47–3.36 (m, 1H), 3.13–3.01 (m, 1H), 2.93 (dd, *J* = 14.0, 6.2 Hz, 1H), 2.51 (dd, *J* = 17.1, 4.9 Hz, 1H), 1.95–1.82 (m, 1H), 1.67–1.60 (m, 1H), 1.15 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) (*syn*) δ 137.8, 136.7, 133.2, 129.3 (3C), 128.7 (2C), 128.2, 127.6, 126.5, 126.4, 69.1, 62.1, 57.2, 43.8, 40.8, 23.5, 21.5.

(*R*)-1-((*S*)-2-benzyl-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-ol (3p)



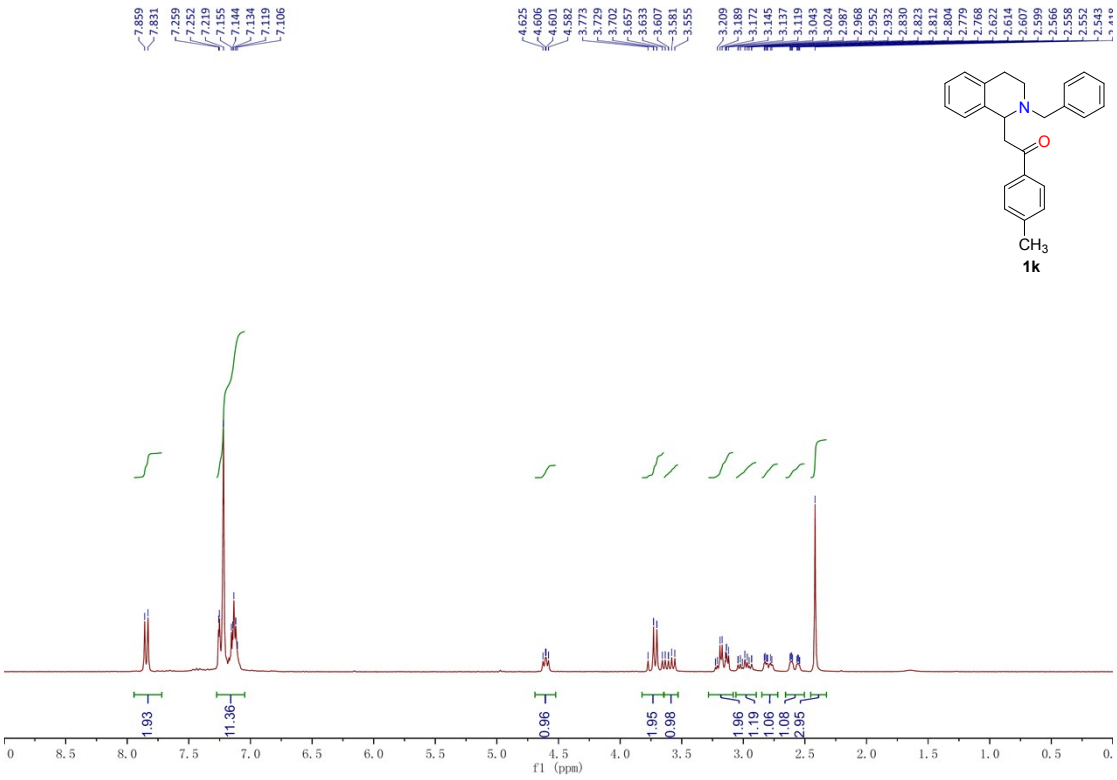
^{1}H NMR (300 MHz, $CDCl_3$) (*anti*) δ 7.37 – 7.03 (m, 9H), 6.23 (br s, 1H), 4.15 – 4.06 (m, 2H), 3.75 (dd, *J* = 10.4, 5.5 Hz, 1H), 3.48 (d, *J* = 12.8 Hz, 1H), 3.21 (dt, *J* = 11.7, 5.3 Hz, 1H), 2.83 – 2.77 (m, 2H), 2.58 – 2.50 (m, 1H), 2.05 – 2.01 (m, 2H), 1.10 (d, *J* = 6.3 Hz, 3H).

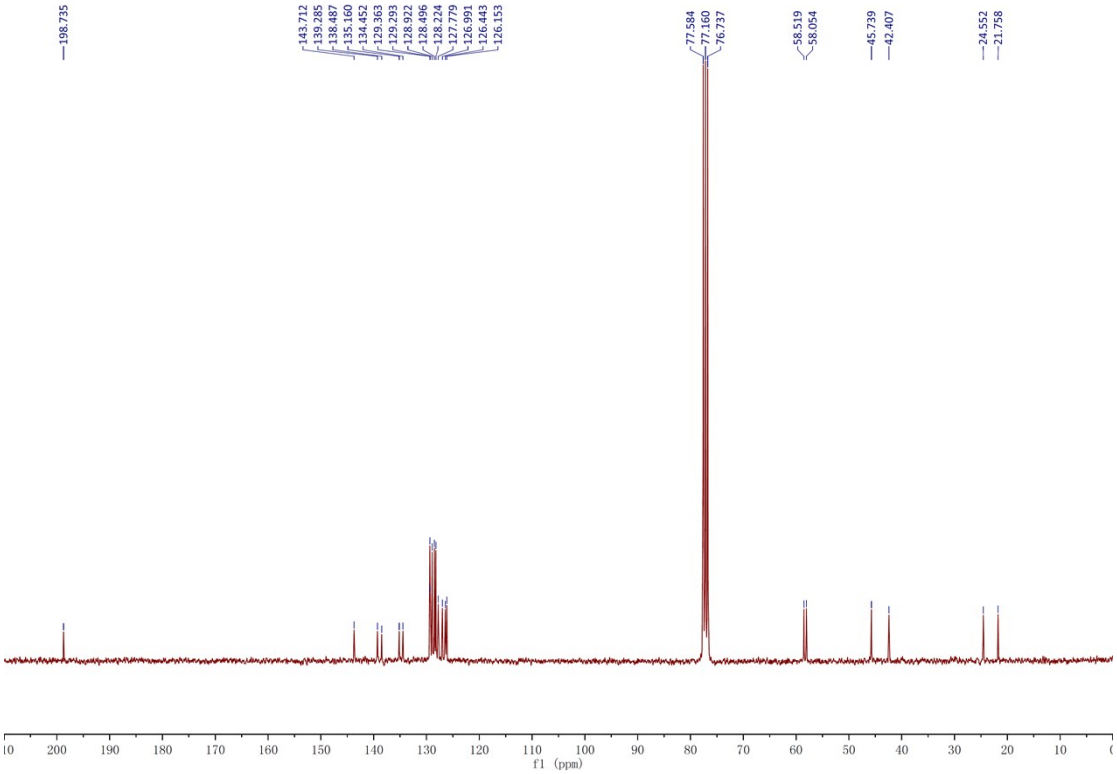
Colourless oil, (**2p**:**3p**): 65% yield, dr (*syn/anti*) = 71/29, ee_{syn} = 81%, ee_{anti} = 99%.

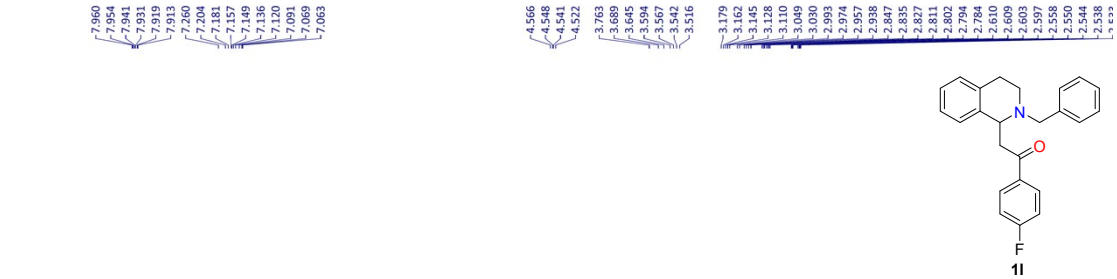
HRMS (ESI/ion trap): *m/z* $[M + H]^+$ calcd for $C_{19}H_{24}NO$ 282.1858, found 282.1861.

HPLC (**2p**:**3p**) : Chiralpak IA, Hexane : *i*-PrOH = 96 : 4, 0.6 mL/min, λ = 215 nm; t_R (*syn*) 14.29 min (major), t_R (*syn*) 17.17 min (minor), t_R (*anti*) 18.57 min.

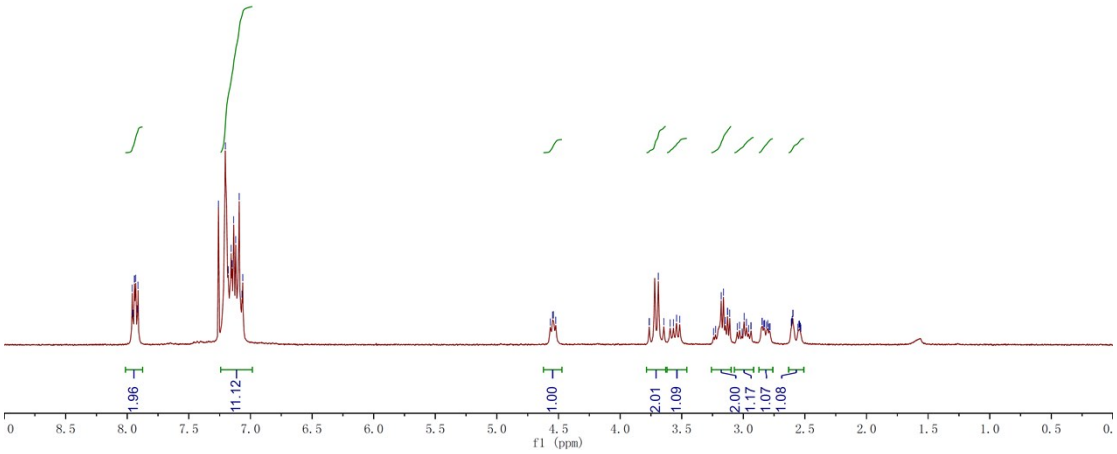
VI. NMR spectra of compounds 1k–1o

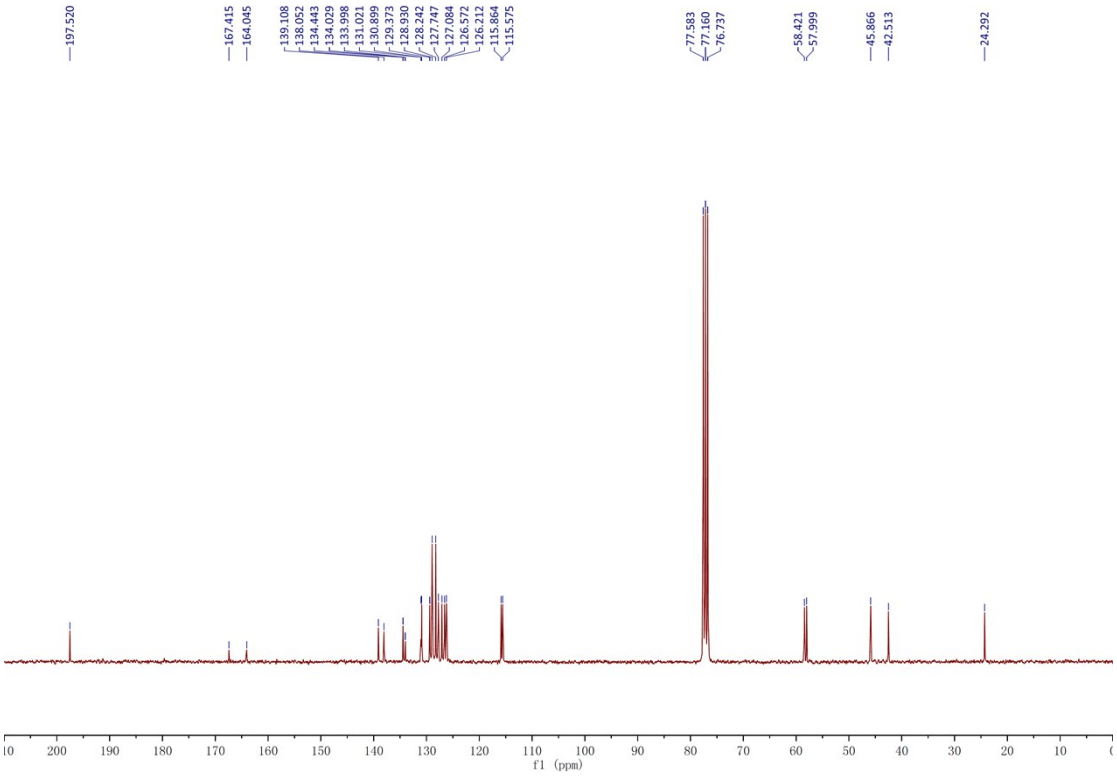


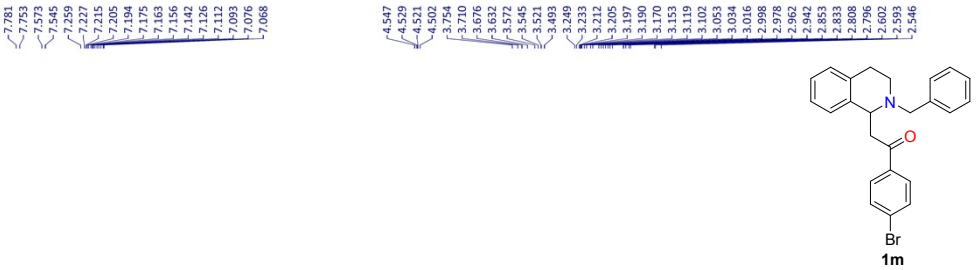



7.960
7.954
7.941
7.931
7.919
7.913
7.260
7.204
7.181
7.157
7.149
7.136
7.120
7.091
7.069
7.063
4.566
4.548
4.541
4.522
3.763
3.689
3.645
3.594
3.567
3.542
3.516
3.179
3.162
3.145
3.128
3.110
3.049
3.030
2.993
2.974
2.957
2.938
2.847
2.835
2.827
2.811
2.802
2.794
2.784
2.610
2.609
2.603
2.597
2.558
2.550
2.544
2.538
N
O
F

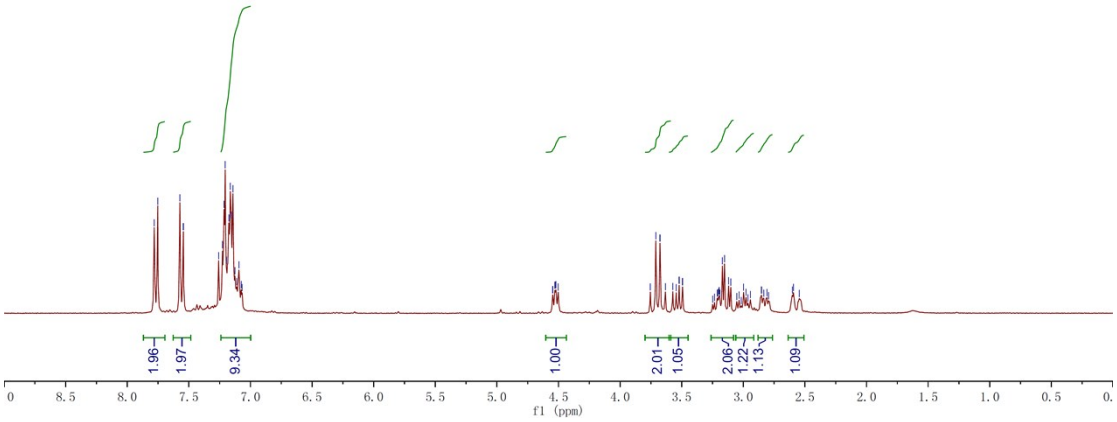
1l

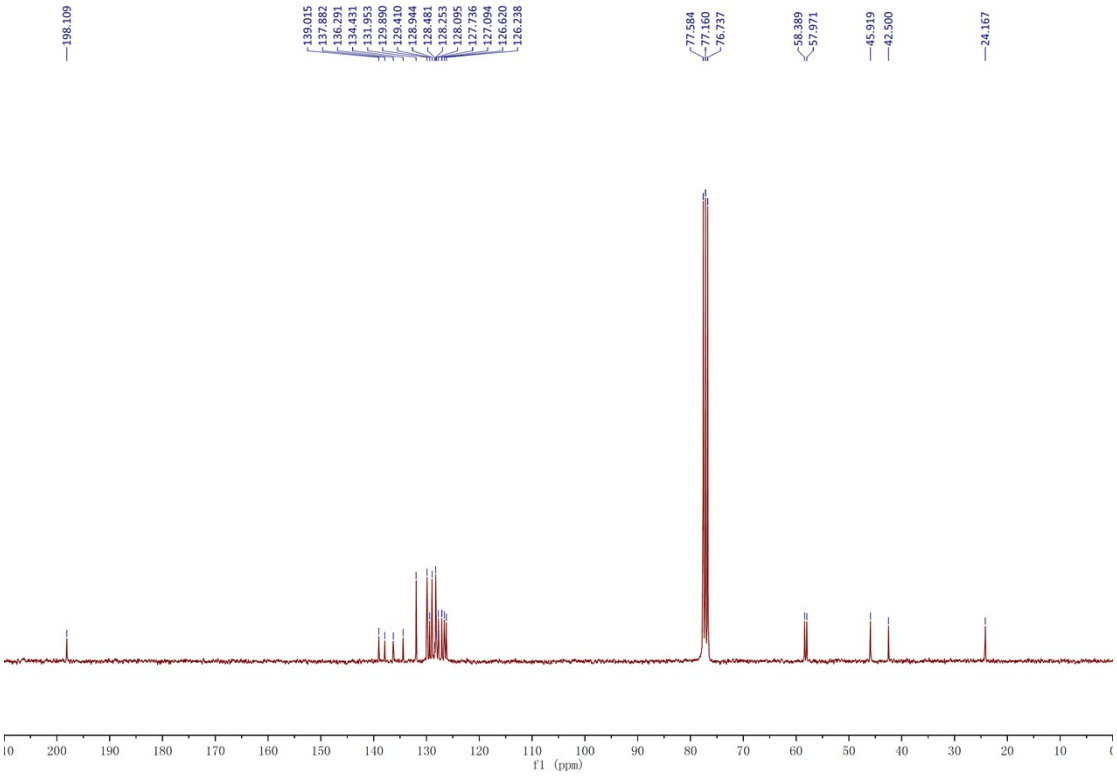

1.96
11.12
1.00
2.01
1.09
2.00
1.17
1.07
1.08
f1 (ppm)

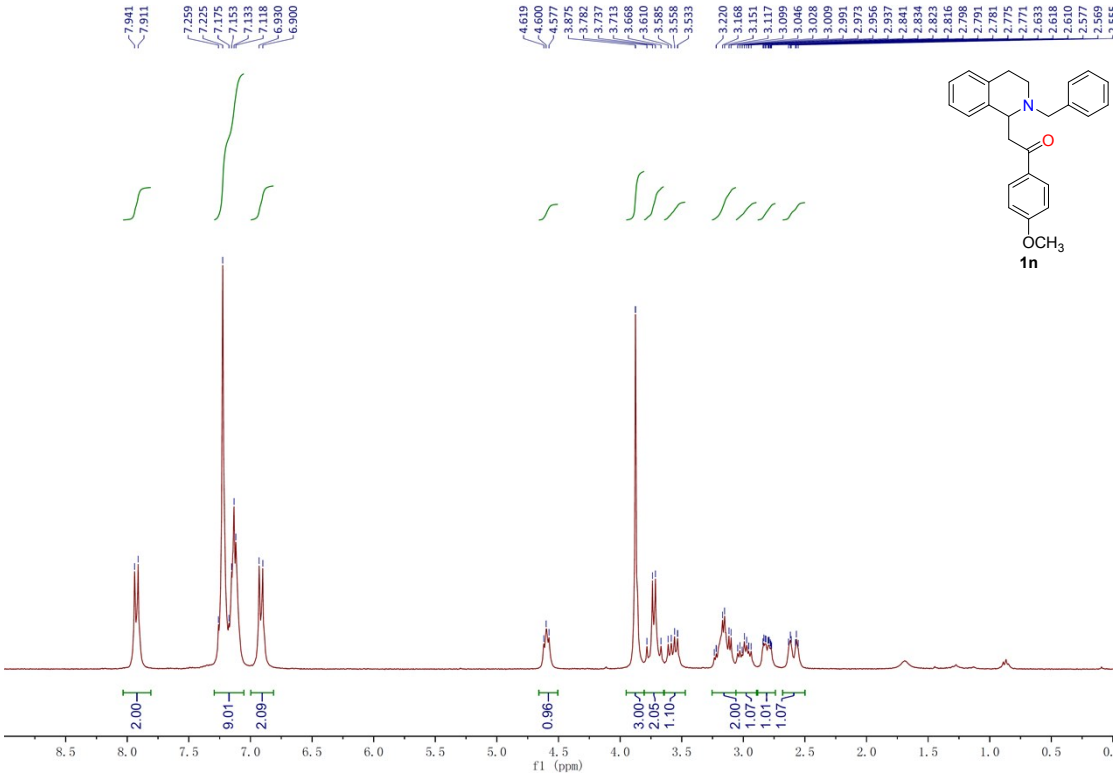

197.520
167.415
164.045
139.108
138.052
134.443
134.029
133.998
131.021
130.899
129.373
128.930
128.242
127.747
127.084
126.572
126.212
115.864
115.575
77.583
77.160
76.737
58.421
57.999
45.866
42.513
24.292
f1 (ppm)

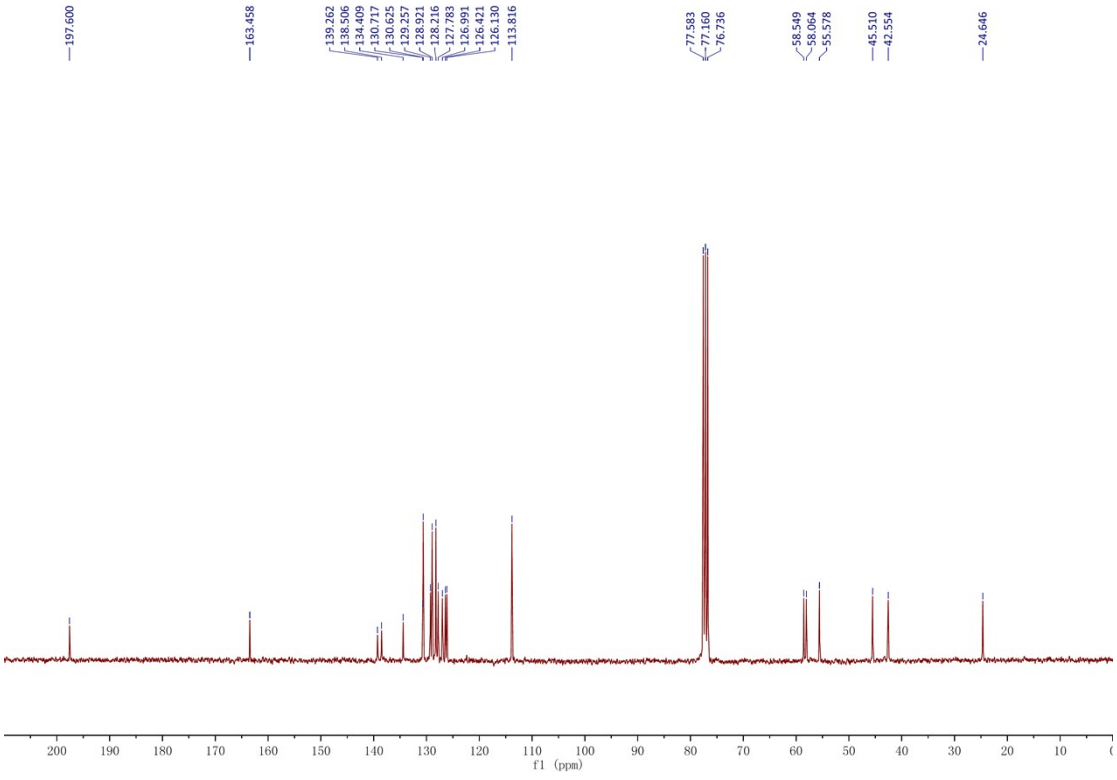

7.781
7.753
7.573
7.545
7.259
7.227
7.215
7.205
7.194
7.175
7.163
7.156
7.142
7.126
7.112
7.093
7.076
7.068
4.547
4.529
4.521
4.502
3.754
3.710
3.676
3.632
3.572
3.545
3.521
3.493
3.249
3.233
3.212
3.205
3.197
3.190
3.170
3.153
3.119
3.102
3.053
3.034
3.016
2.998
2.978
2.962
2.942
2.853
2.833
2.808
2.796
2.602
2.593
2.546
N
O
Br

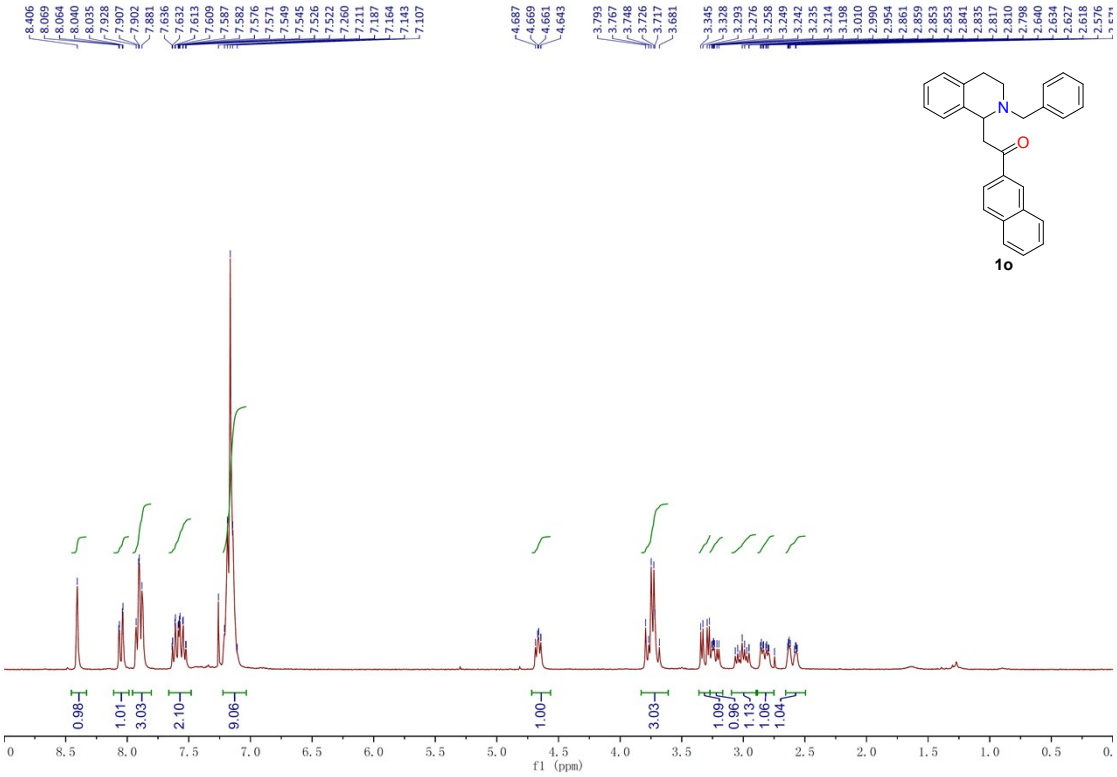
1m

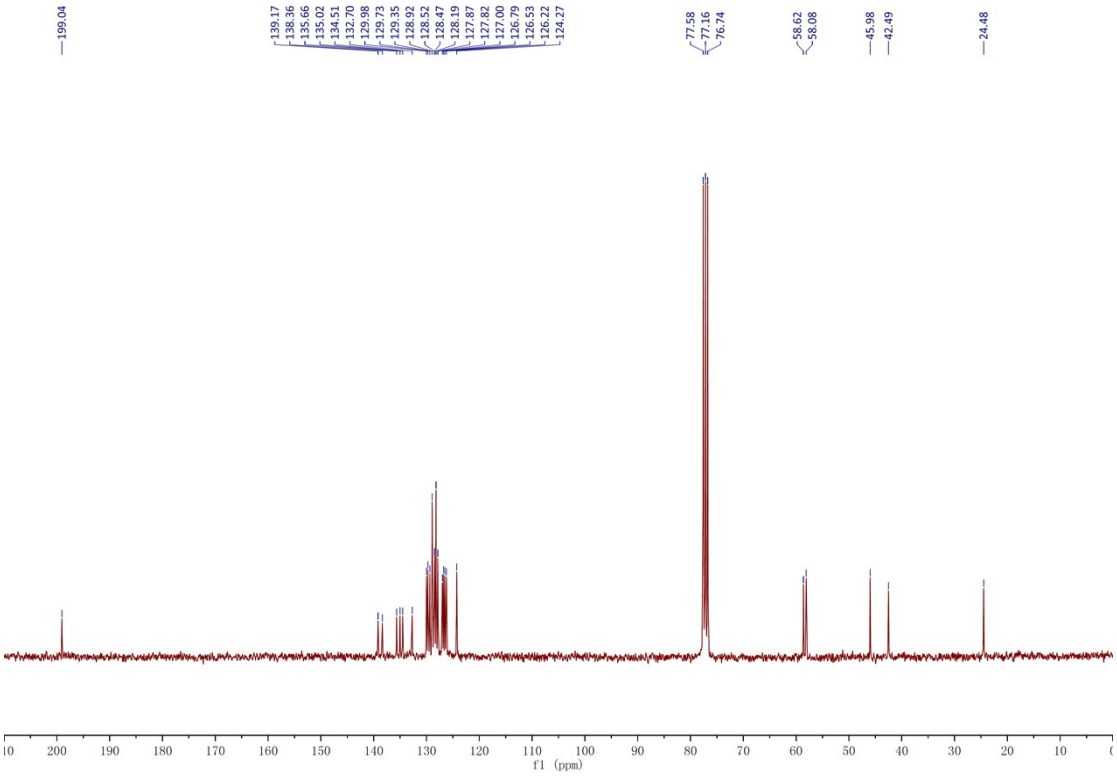

1.96
1.97
9.34
1.00
2.01
1.05
2.06
1.22
1.13
1.09
f1 (ppm)


198.109
139.015
137.882
136.291
134.431
131.953
129.890
129.410
128.944
128.461
128.253
128.095
127.736
127.094
126.620
126.238
77.584
77.160
76.737
58.389
57.971
45.919
42.500
24.167
f1 (ppm)

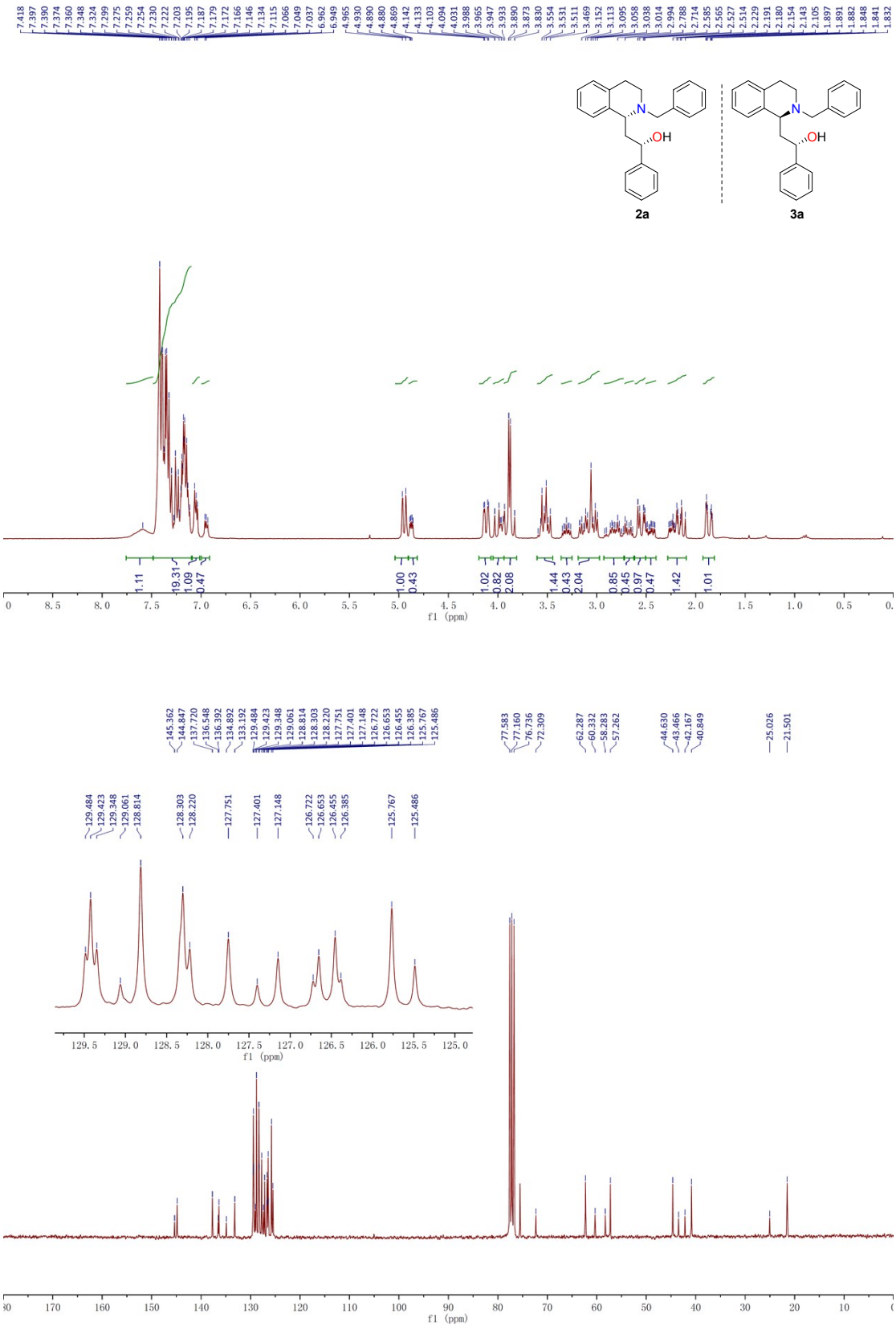

7.941
7.911
7.259
7.225
7.175
7.153
7.133
7.118
6.930
6.900
4.619
4.600
4.577
3.875
3.782
3.737
3.713
3.668
3.610
3.585
3.558
3.533
3.220
3.168
3.151
3.117
3.099
3.046
3.028
3.009
2.991
2.973
2.956
2.937
2.841
2.834
2.823
2.816
2.798
2.791
2.781
2.775
2.771
2.633
2.618
2.610
2.577
2.569
N
O
OCH3
1n
2.00
9.01
2.09
0.96
3.00
2.05
1.10
2.00
1.07
1.01
1.07
f1 (ppm)

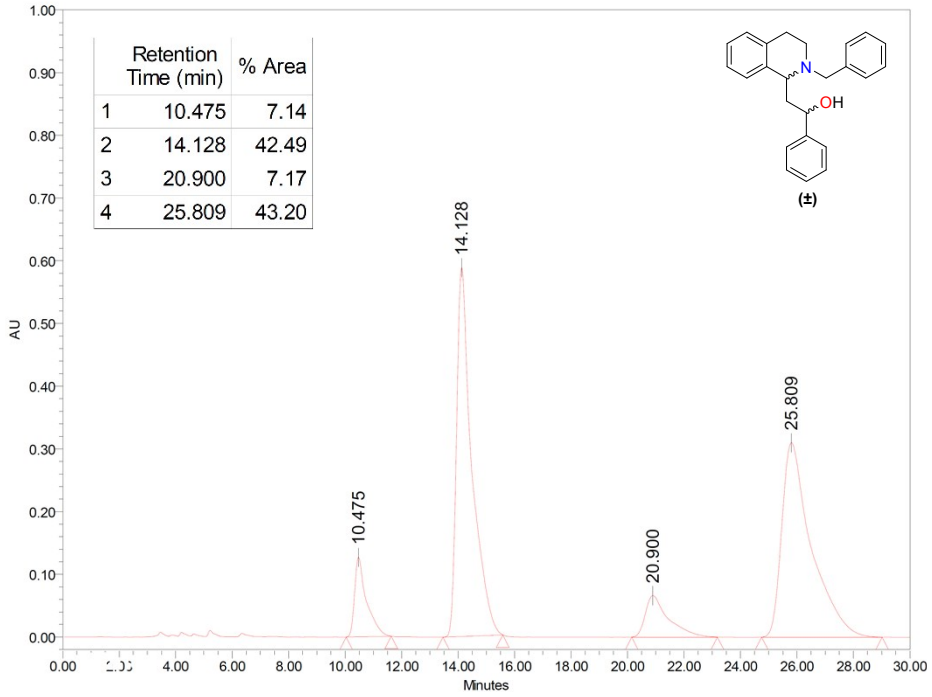

197.600
163.458
139.262
138.506
134.409
130.717
130.625
129.257
128.921
128.216
127.783
126.991
126.421
126.130
113.816
77.583
77.160
76.736
58.549
58.064
55.578
45.510
42.554
24.646
f1 (ppm)

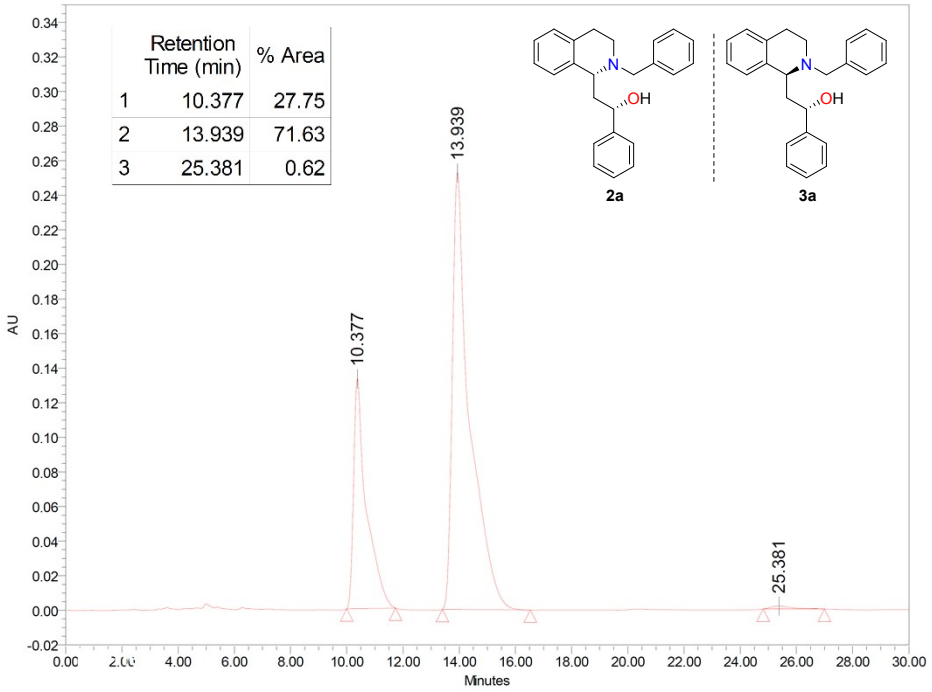

8.406
8.069
8.064
8.040
8.035
7.928
7.907
7.902
7.881
7.636
7.632
7.613
7.609
7.587
7.582
7.576
7.571
7.549
7.545
7.526
7.522
7.260
7.211
7.187
7.164
7.143
7.107
4.687
4.669
4.661
4.643
3.793
3.767
3.748
3.726
3.717
3.681
3.345
3.328
3.293
3.276
3.258
3.249
3.242
3.235
3.214
3.198
3.010
2.990
2.954
2.861
2.859
2.853
2.841
2.835
2.817
2.810
2.798
2.640
2.634
2.627
2.618
O
1o
0.98
1.01
3.03
2.10
9.06
1.00
3.03
1.09
0.96
1.13
1.06
1.04
f1 (ppm)

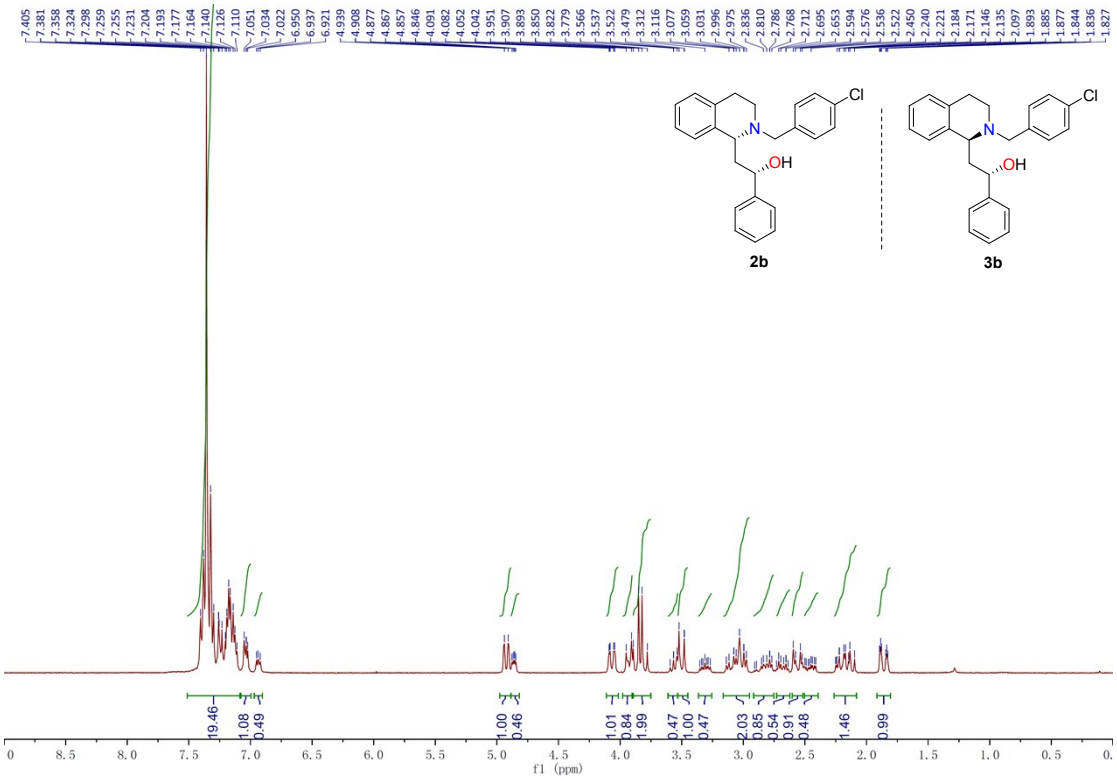

199.04
139.17
138.36
135.66
135.02
134.51
132.70
129.98
129.73
129.35
128.92
128.52
128.47
128.19
127.87
127.82
127.00
126.79
126.53
126.22
124.27
77.58
77.16
76.74
58.62
58.08
45.98
42.49
24.48
f1 (ppm)

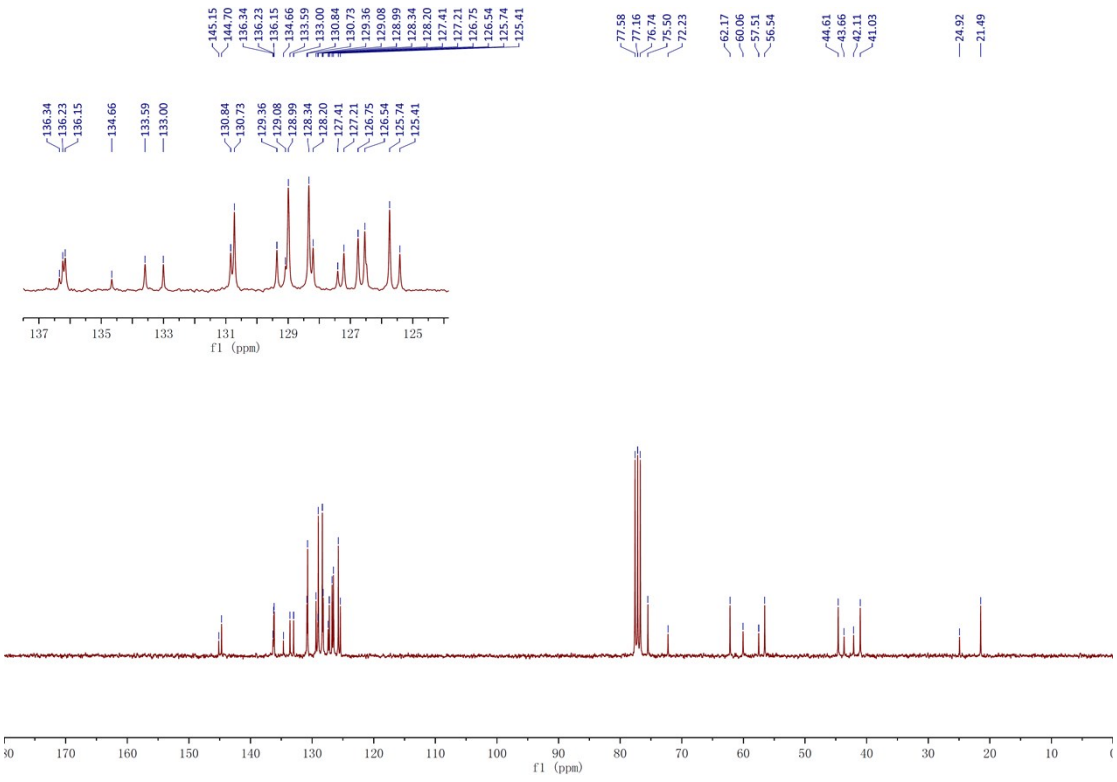
VII. NMR spectra and HPLC or SFC chromatograms for 2a–2p



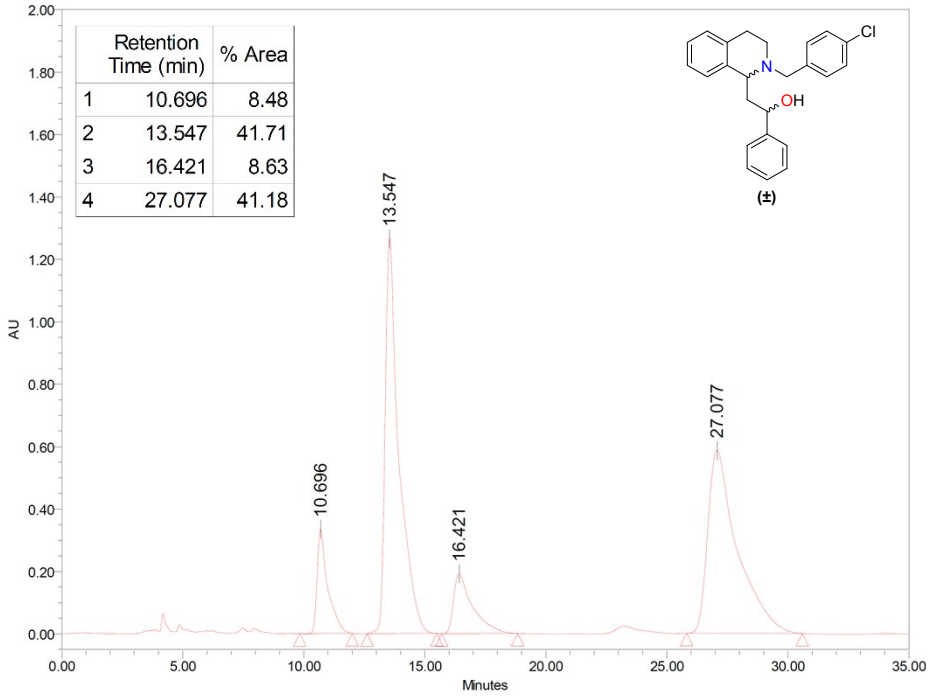

Retention Time (min) | % Area
1 | 10.475 | 7.14
2 | 14.128 | 42.49
3 | 20.900 | 7.17
4 | 25.809 | 43.20
(±)
AU
Minutes
10.475
14.128
20.900
25.809

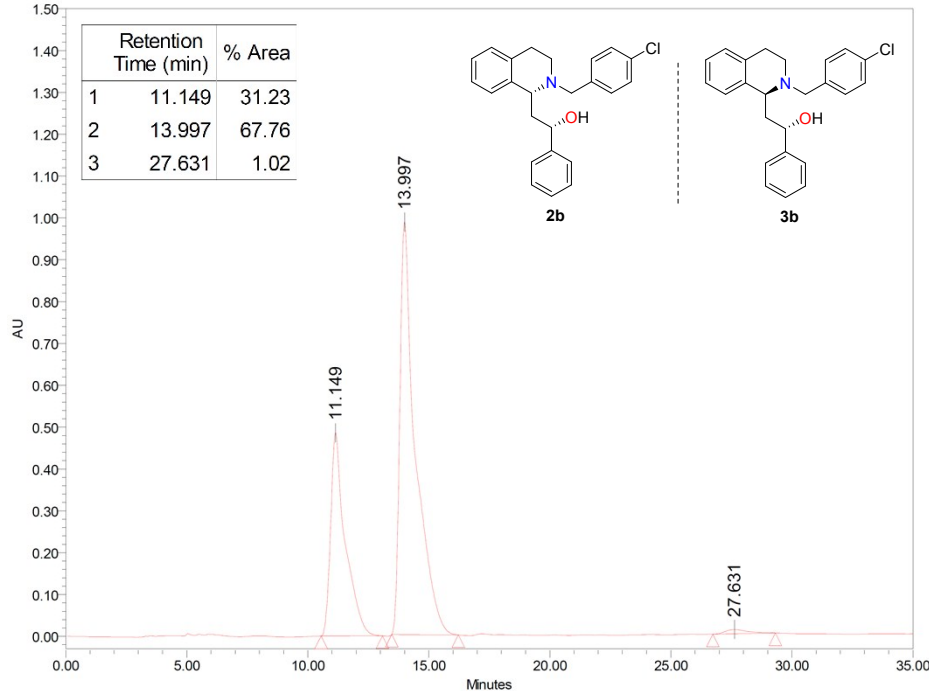

Retention Time (min) | % Area
1 | 10.377 | 27.75
2 | 13.939 | 71.63
3 | 25.381 | 0.62
2a
3a
AU
Minutes
10.377
13.939
25.381

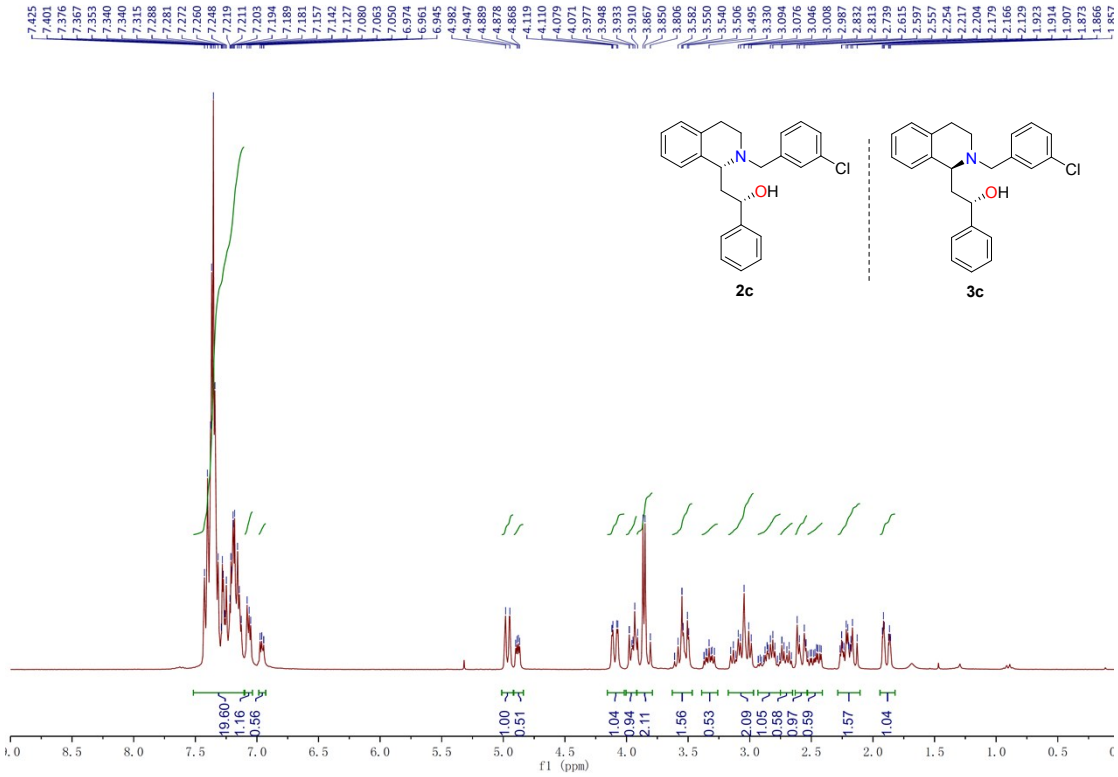

Cl
N
OH
2b
Cl
N
OH
3b
f1 (ppm)

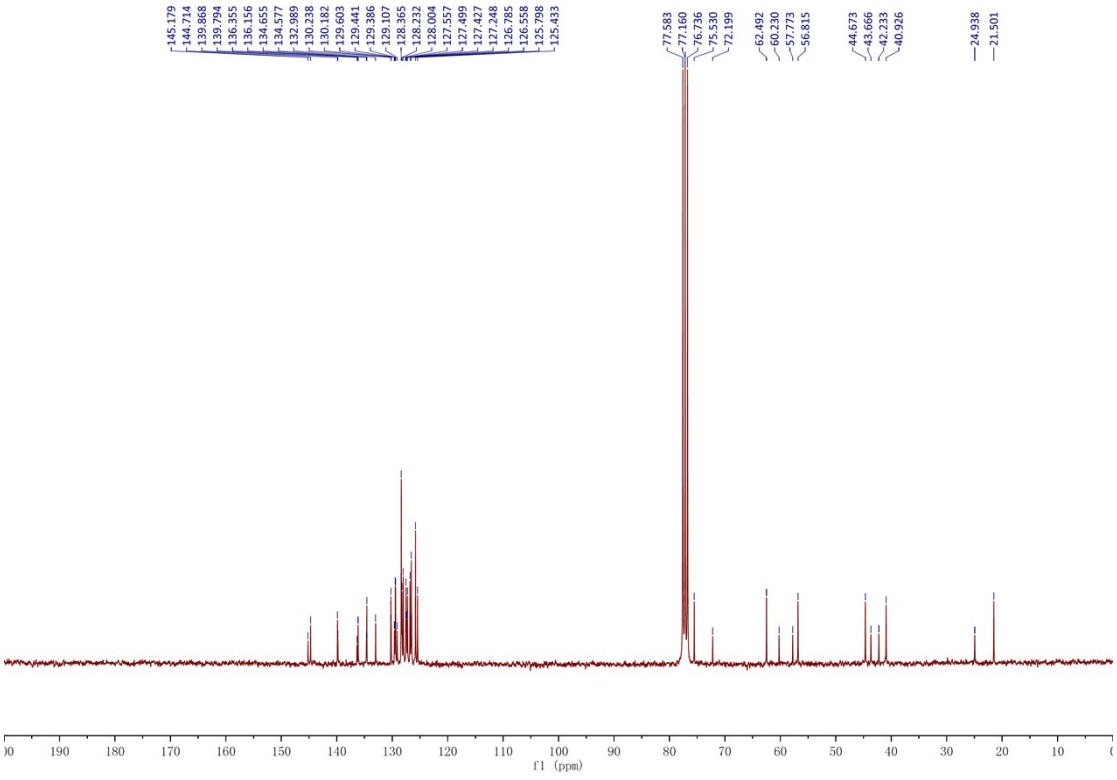

f1 (ppm)

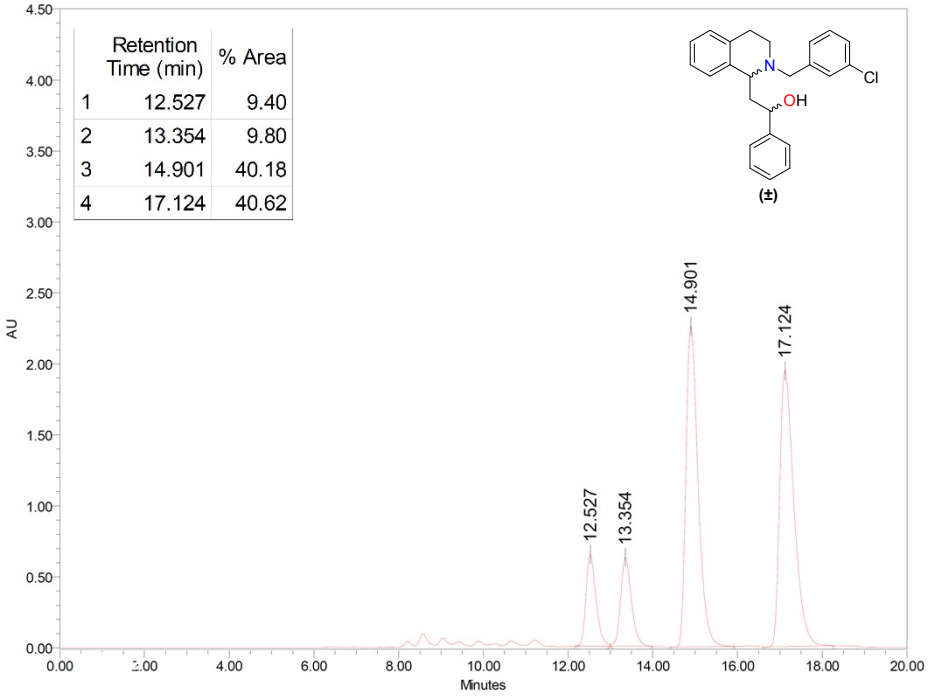
f1 (ppm)

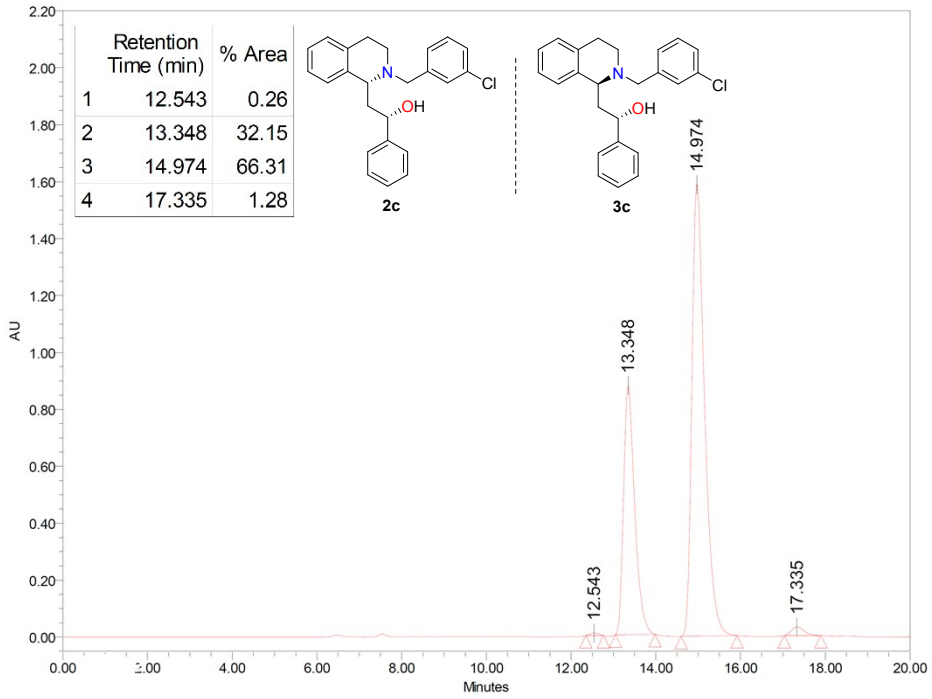

Retention Time (min) | % Area
1 10.696 8.48
2 13.547 41.71
3 16.421 8.63
4 27.077 41.18
Cl
N
OH
(±)
AU
Minutes
10.696
13.547
16.421
27.077

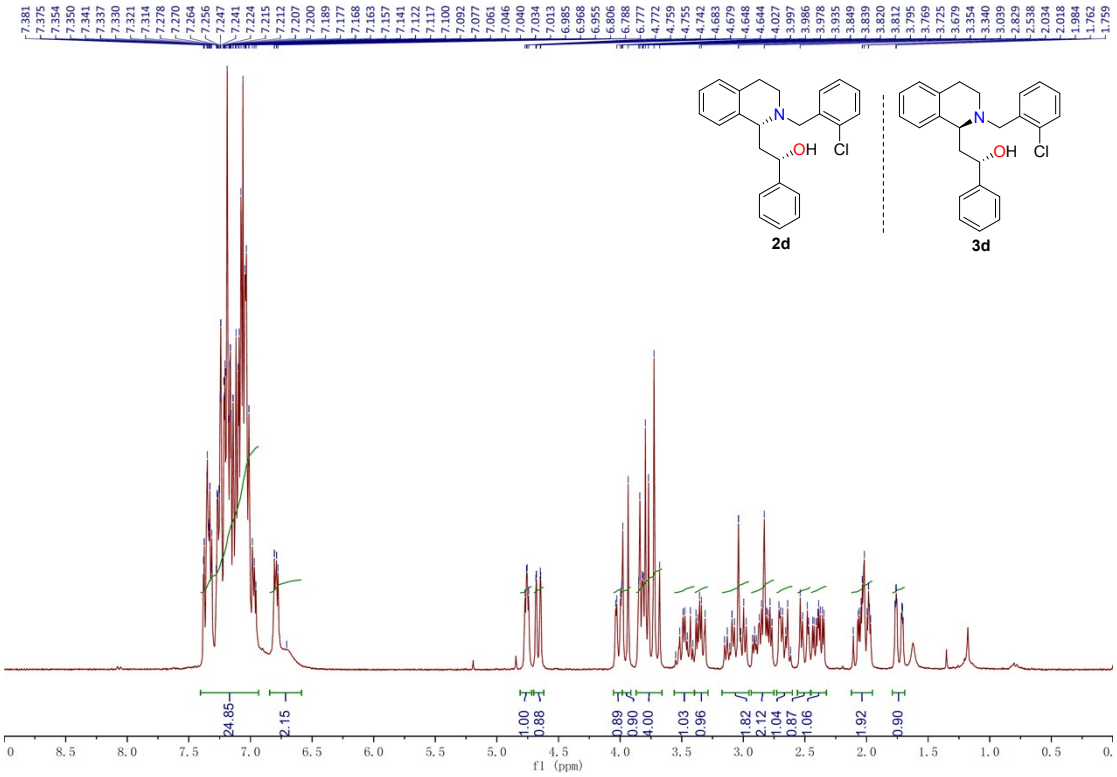

Retention Time (min) | % Area
1 11.149 31.23
2 13.997 67.76
3 27.631 1.02
Cl
N
OH
2b
3b
AU
Minutes
11.149
13.997
27.631

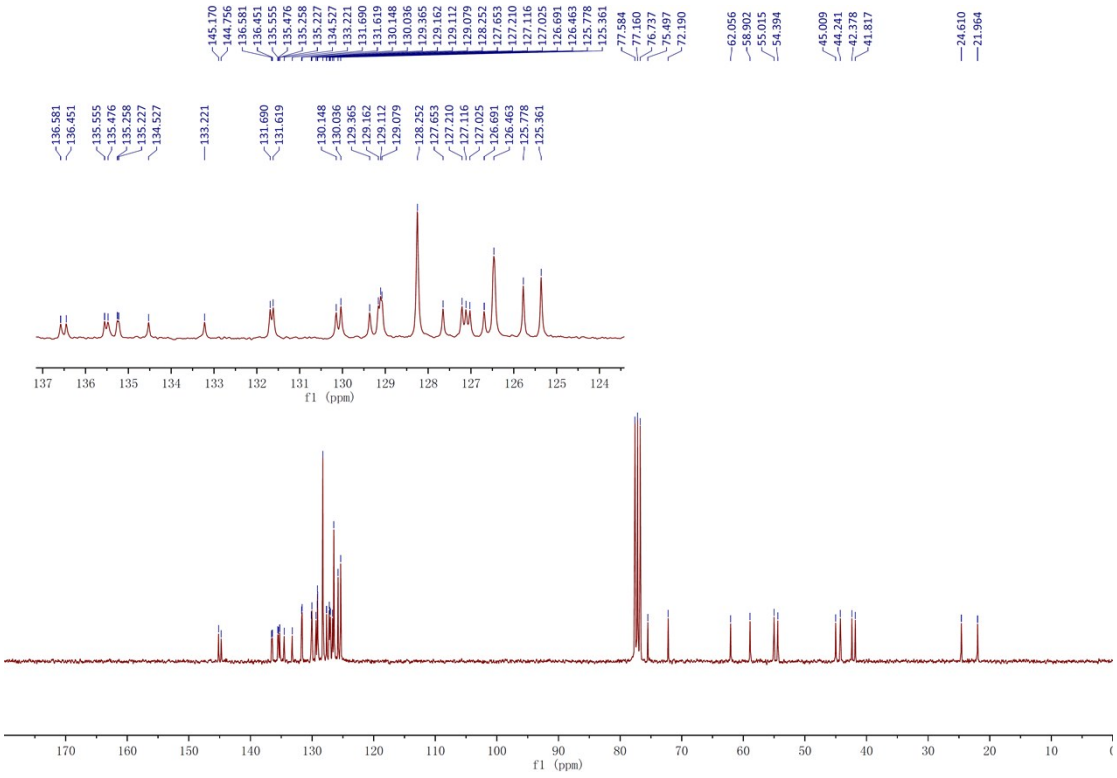

7.425 7.401 7.376 7.367 7.353 7.340 7.340 7.315 7.288 7.281 7.272 7.260 7.248 7.219 7.211 7.203 7.194 7.189 7.181 7.157 7.142 7.127 7.080 7.063 7.050 6.974 6.961 6.945 4.982 4.947 4.889 4.878 4.868 4.119 4.110 4.079 4.071 3.977 3.948 3.933 3.910 3.867 3.850 3.806 3.582 3.550 3.540 3.506 3.495 3.330 3.094 3.076 3.046 3.008 2.987 2.832 2.813 2.739 2.615 2.597 2.557 2.254 2.217 2.204 2.179 2.166 2.129 1.923 1.914 1.907 1.873 1.866
N
Cl
OH
2c
3c
19.60 1.16 0.56 1.00 0.51 1.04 0.94 2.11 1.56 0.53 2.09 1.05 0.58 0.97 0.59 1.57 1.04
f1 (ppm)

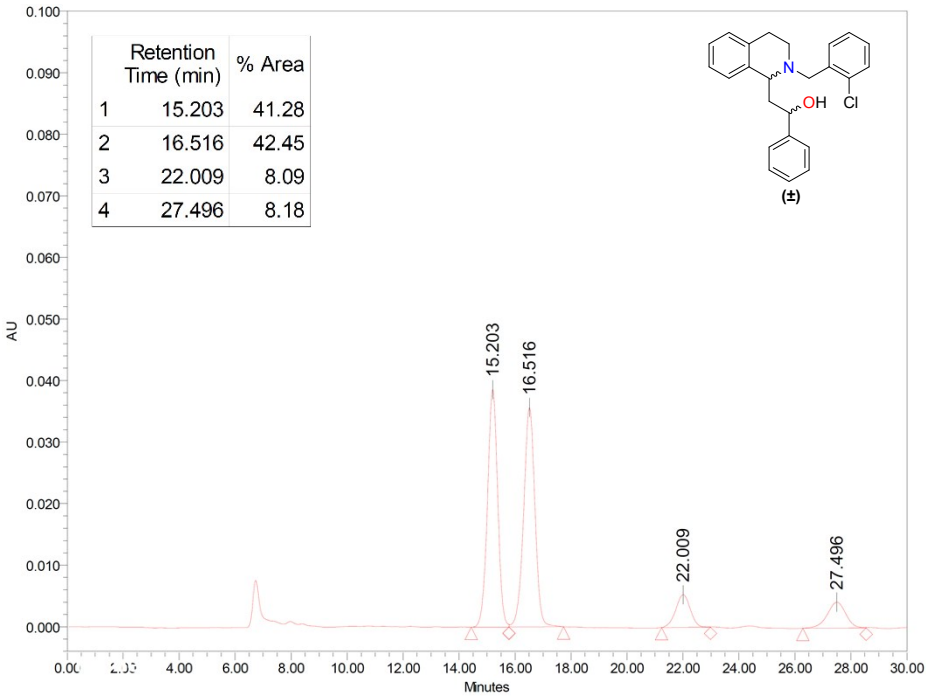

145.179 144.714 139.868 139.794 136.355 136.156 134.655 134.577 132.989 130.238 130.182 129.603 129.441 129.386 129.107 128.365 128.232 128.004 127.557 127.499 127.427 127.248 126.785 126.558 125.798 125.433
77.583 77.160 76.736 75.530 72.199 62.492 60.230 57.773 56.815 44.673 43.666 42.233 40.926 24.938 21.501
f1 (ppm)

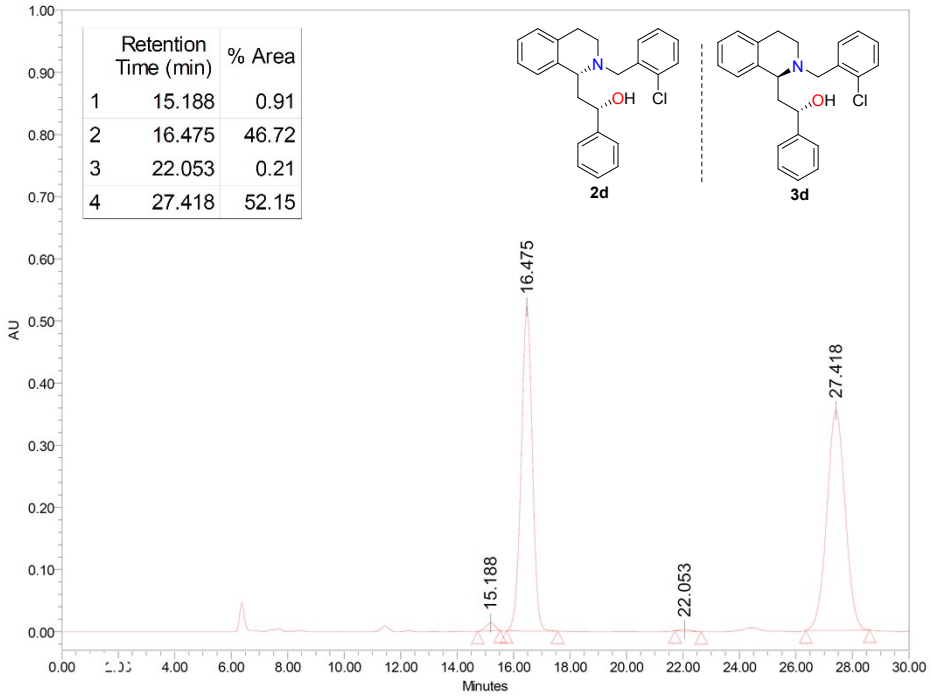

Retention Time (min) % Area
1 12.527 9.40
2 13.354 9.80
3 14.901 40.18
4 17.124 40.62
(±)
AU
Minutes
12.527
13.354
14.901
17.124

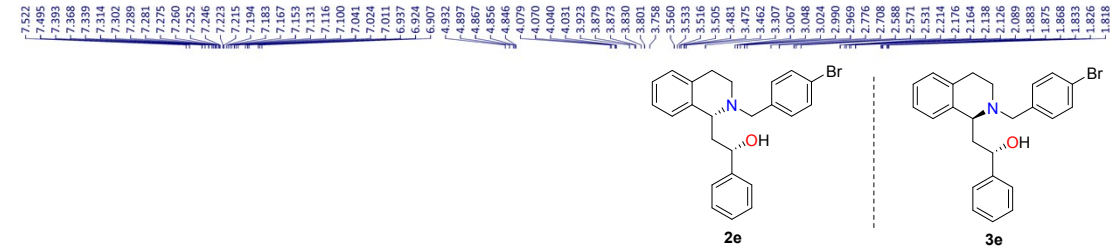

Retention Time (min) % Area
1 12.543 0.26
2 13.348 32.15
3 14.974 66.31
4 17.335 1.28
2c
3c
AU
Minutes
12.543
13.348
14.974
17.335

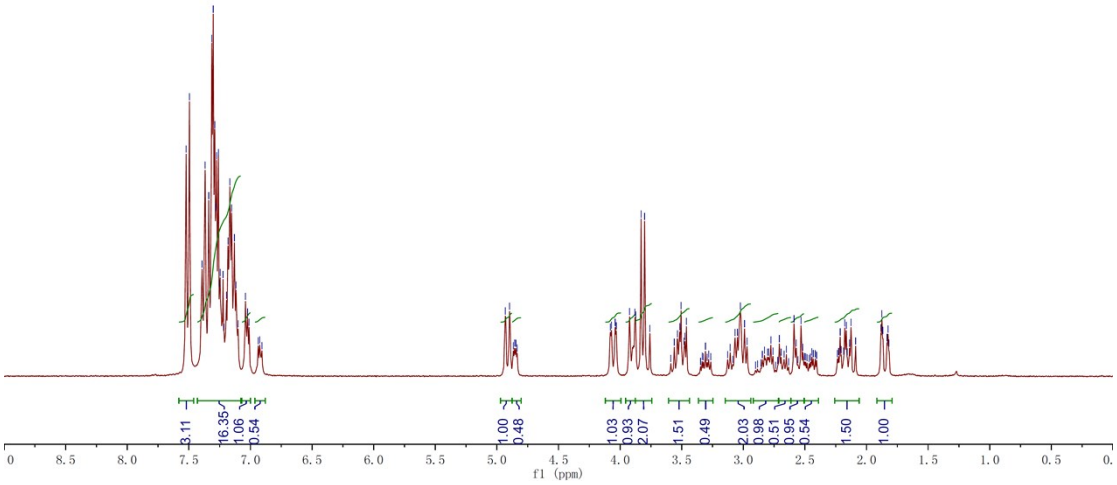

2d
3d
f1 (ppm)

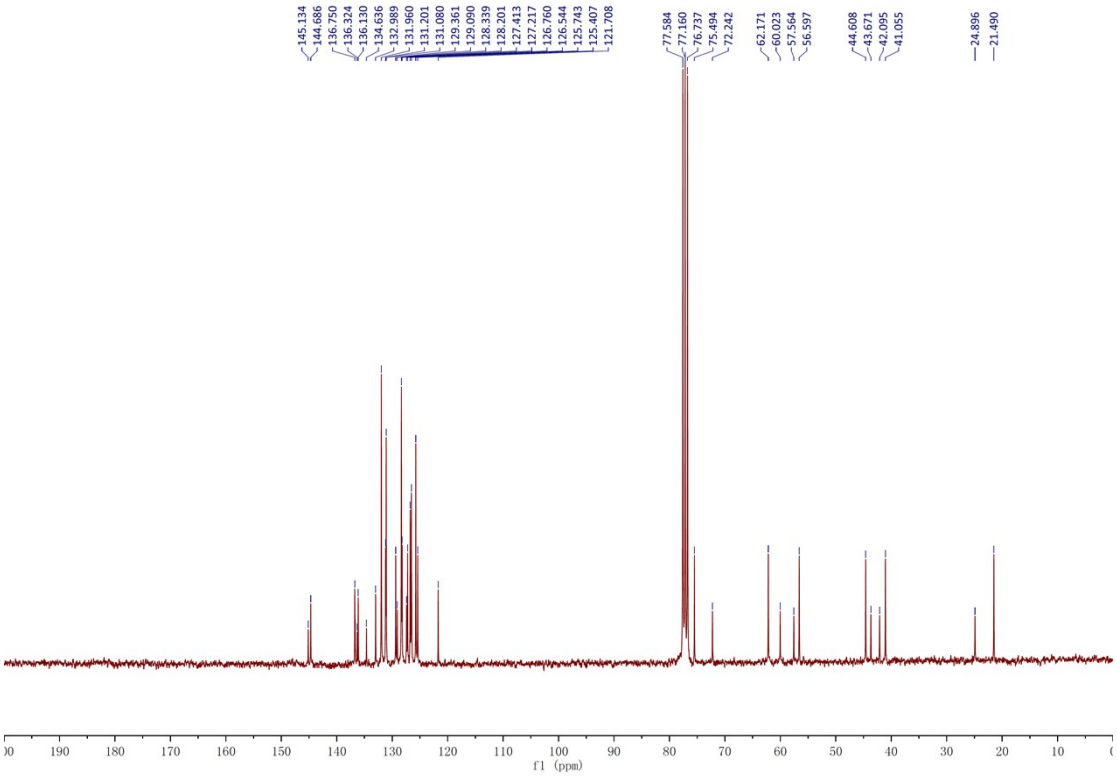

f1 (ppm)

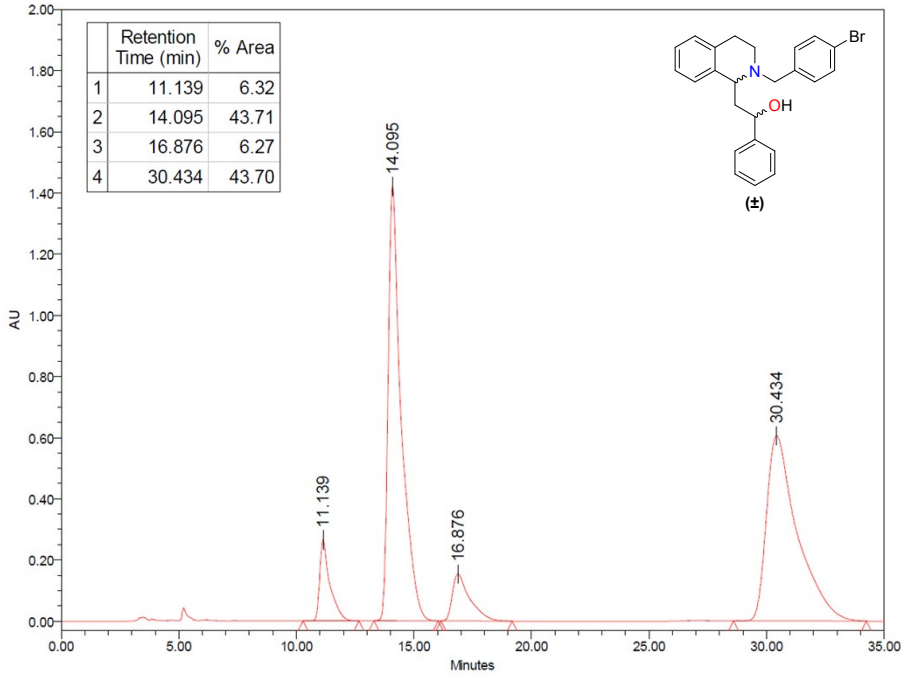

Retention Time (min) % Area
1 15.203 41.28
2 16.516 42.45
3 22.009 8.09
4 27.496 8.18
(±)
AU
Minutes
15.203
16.516
22.009
27.496

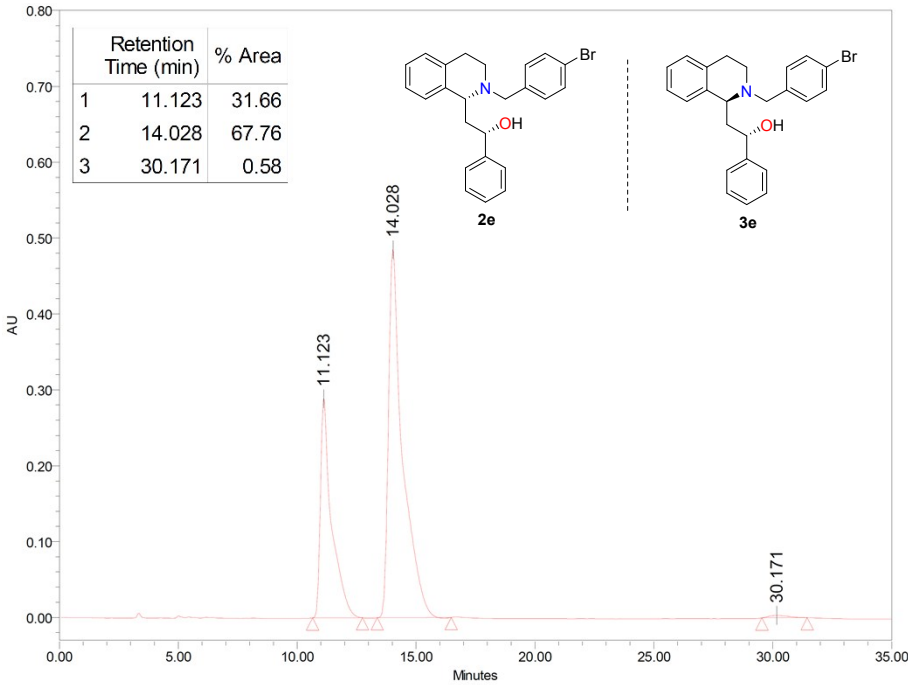

Retention Time (min) % Area
1 15.188 0.91
2 16.475 46.72
3 22.053 0.21
4 27.418 52.15
2d
3d
AU
Minutes
15.188
16.475
22.053
27.418

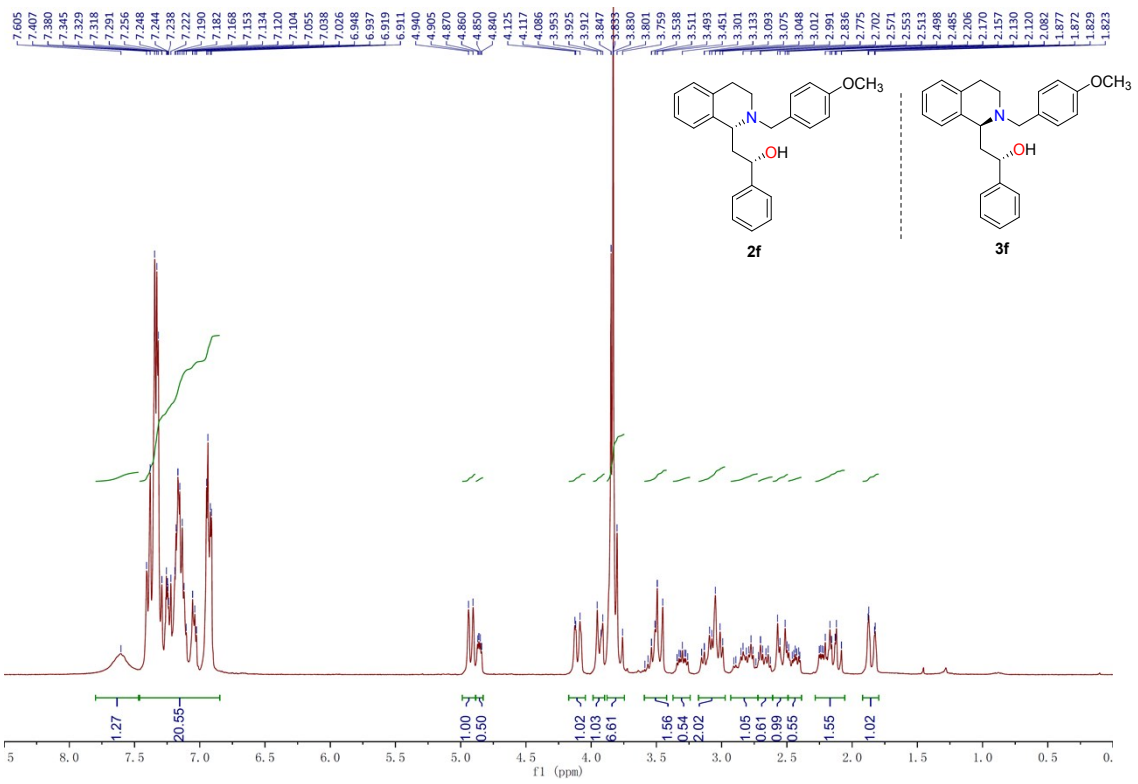

Br
N
OH
2e
Br
N
OH
3e

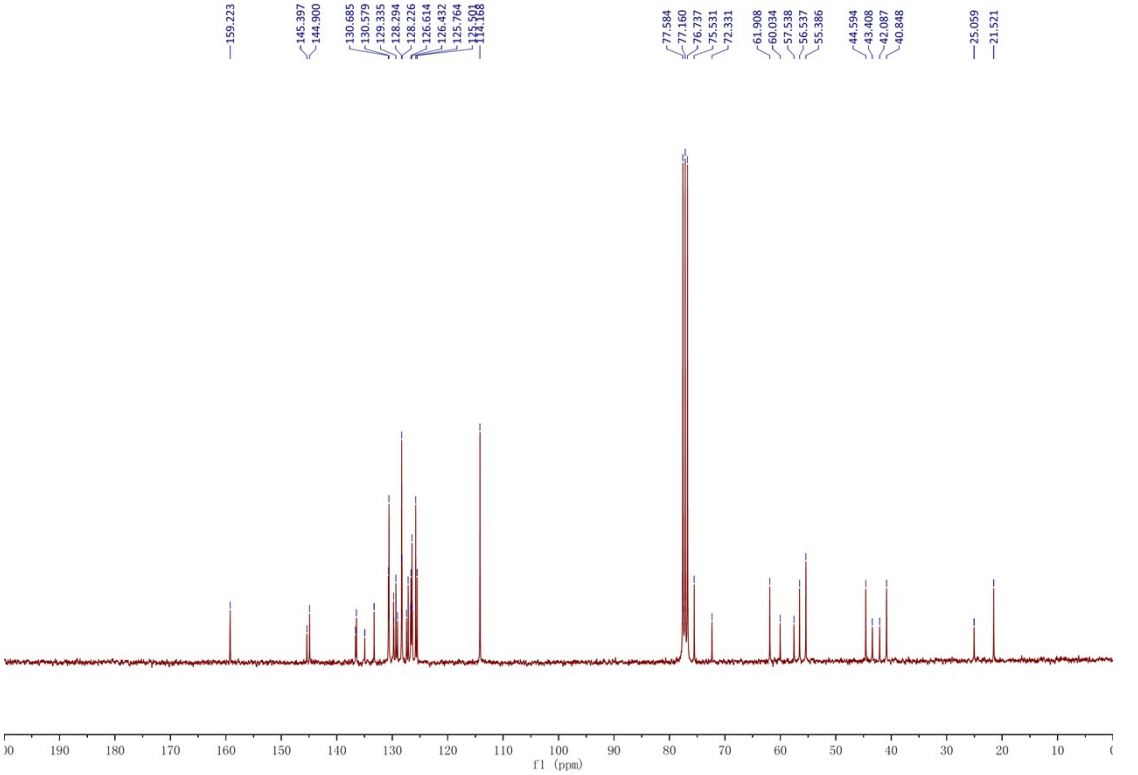

3.11
16.35
1.06
0.54
1.00
0.48
1.03
0.93
2.07
1.51
0.49
2.03
0.98
0.51
0.95
0.54
1.50
1.00
f1 (ppm)

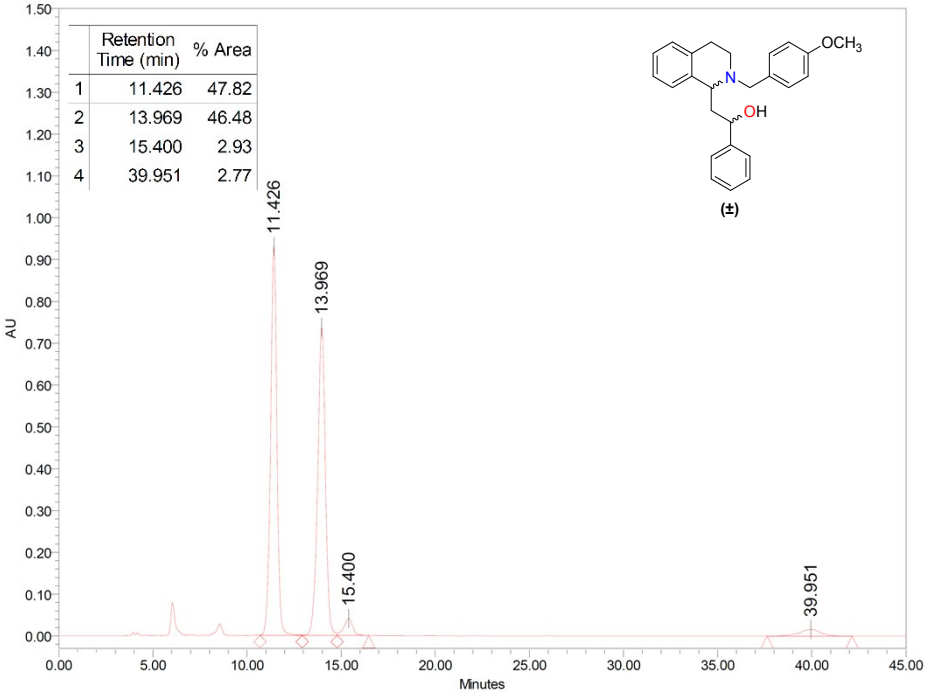

f1 (ppm)

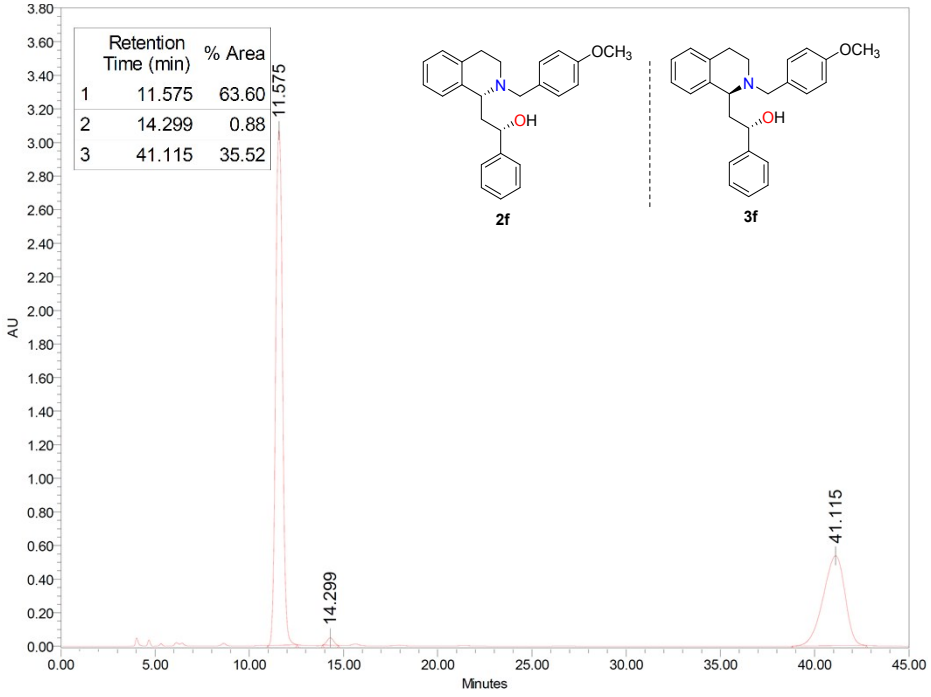

Retention Time (min) | % Area
1 | 11.139 | 6.32
2 | 14.095 | 43.71
3 | 16.876 | 6.27
4 | 30.434 | 43.70
Br
N
OH
(±)
14.095
11.139
16.876
30.434
AU
Minutes

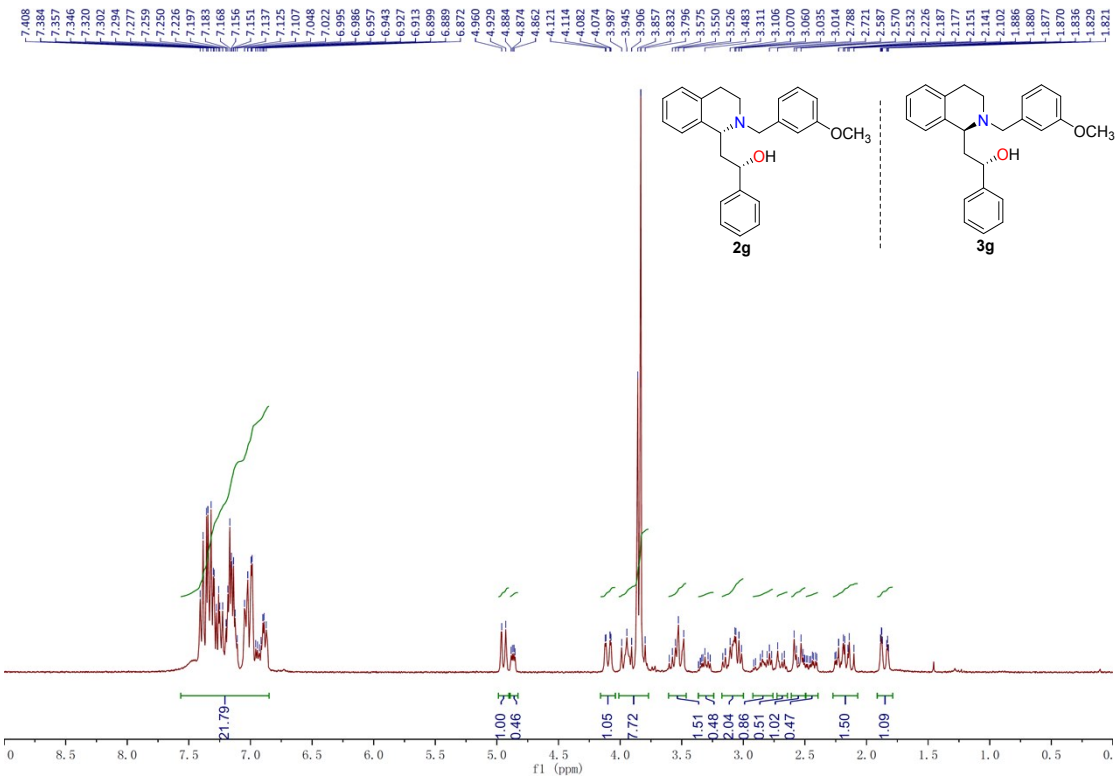

Retention Time (min) | % Area
1 | 11.123 | 31.66
2 | 14.028 | 67.76
3 | 30.171 | 0.58
Br
N
OH
2e
3e
14.028
11.123
30.171
AU
Minutes

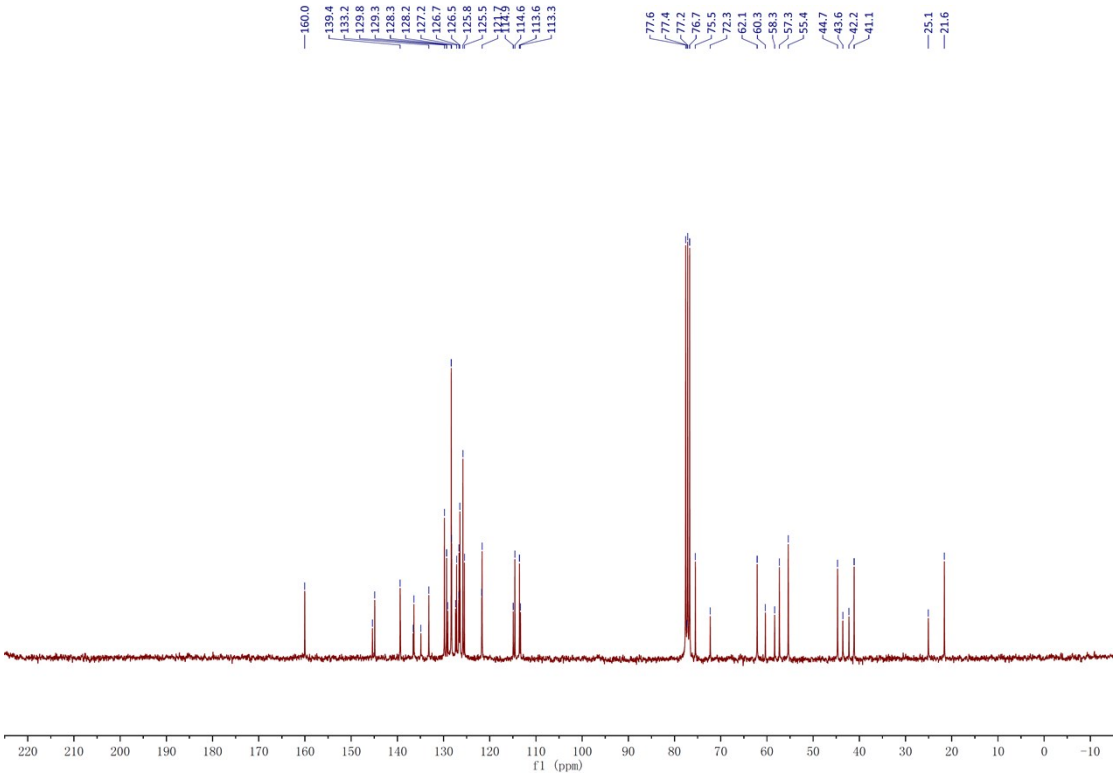

OCH3
OH
2f
OCH3
OH
3f
f1 (ppm)

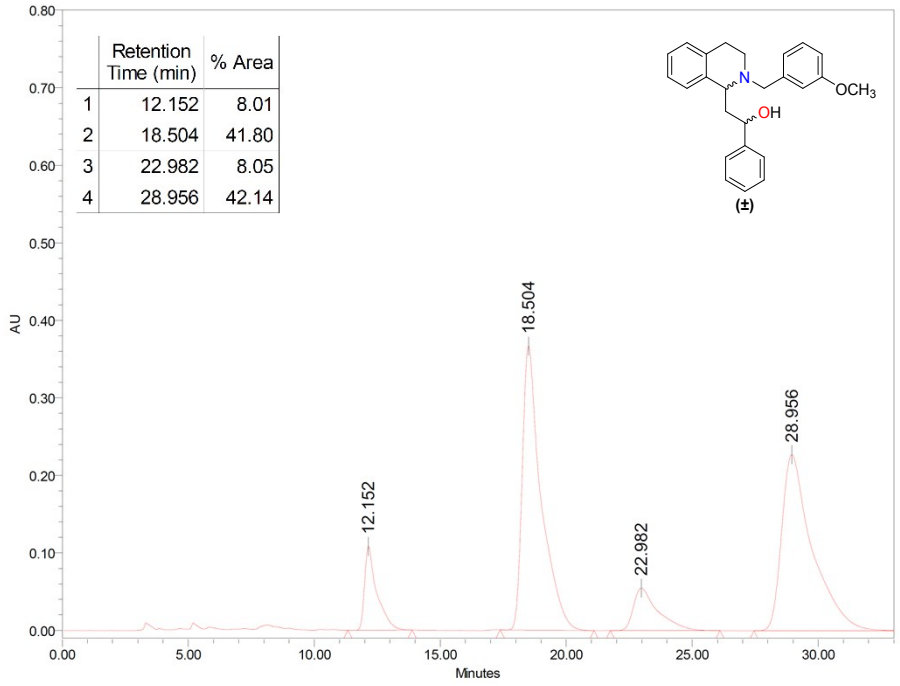

f1 (ppm)

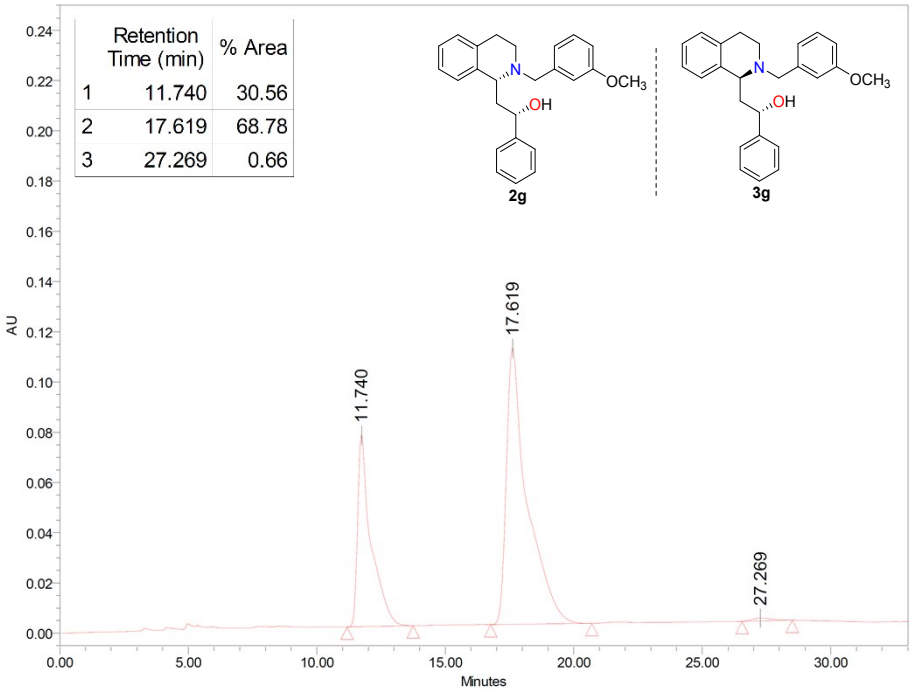

Retention Time (min) % Area
1 11.426 47.82
2 13.969 46.48
3 15.400 2.93
4 39.951 2.77
11.426
13.969
15.400
39.951
AU
Minutes
OCH3
OH
N
(±)

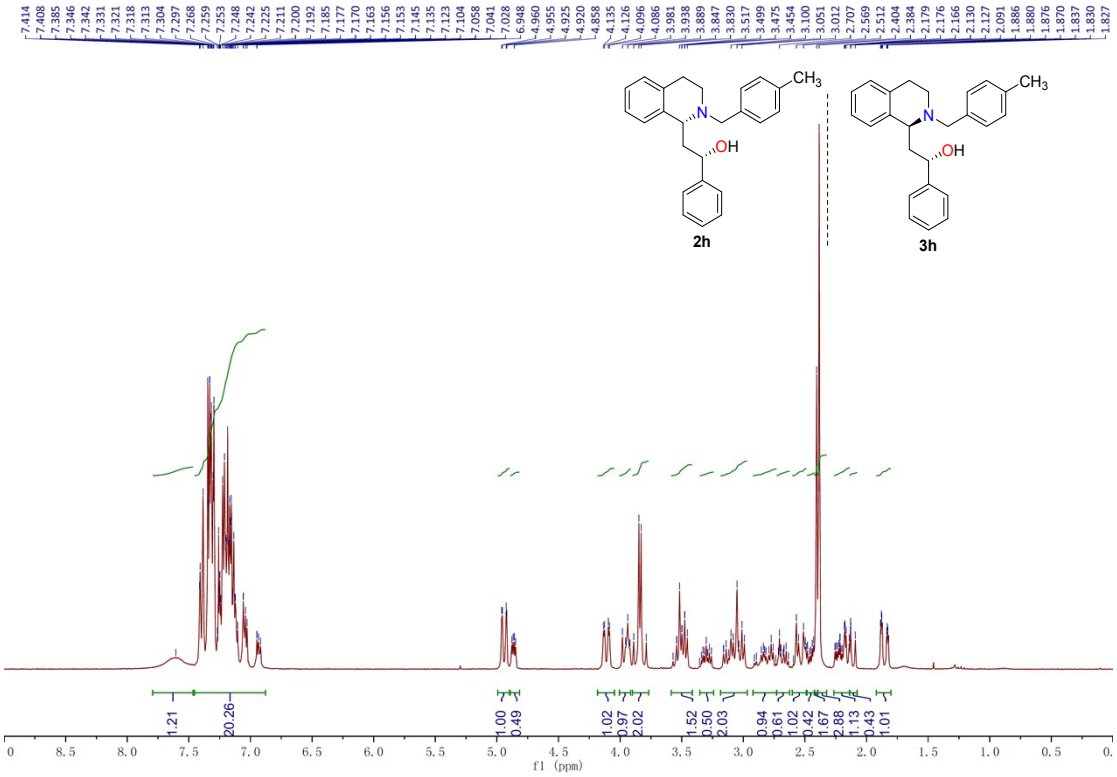

Retention Time (min) % Area
1 11.575 63.60
2 14.299 0.88
3 41.115 35.52
11.575
14.299
41.115
AU
Minutes
OCH3
OH
N
2f
3f

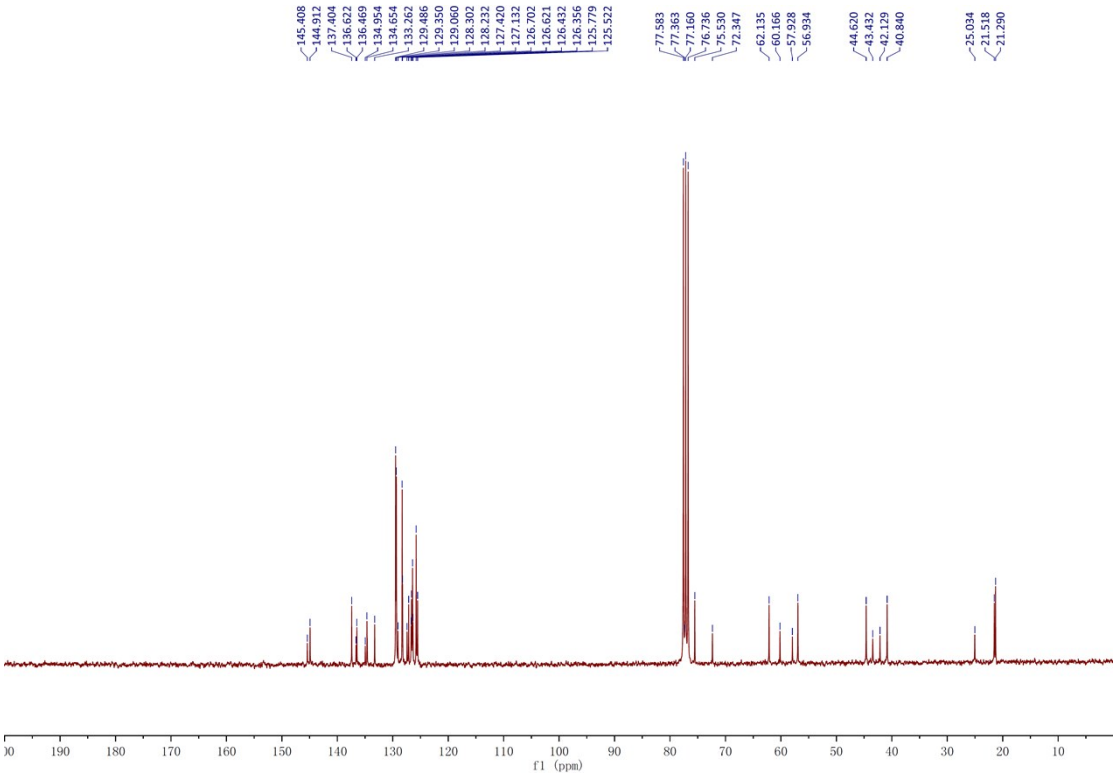

7.408 7.384 7.357 7.346 7.320 7.302 7.294 7.277 7.259 7.250 7.226 7.197 7.183 7.168 7.156 7.151 7.137 7.125 7.107 7.048 7.022 6.995 6.986 6.957 6.943 6.927 6.913 6.899 6.889 6.872 4.960 4.929 4.884 4.874 4.862 4.121 4.114 4.082 4.074 3.987 3.945 3.906 3.857 3.832 3.796 3.575 3.550 3.526 3.483 3.311 3.106 3.070 3.060 3.035 3.014 2.788 2.721 2.587 2.570 2.532 2.226 2.187 2.177 2.151 2.141 2.102 1.886 1.880 1.877 1.870 1.836 1.829 1.821
OCH3
OH
2g
3g
21.79
1.00
0.46
1.05
7.72
1.51
0.48
2.04
0.86
0.51
1.02
0.47
1.50
1.09
f1 (ppm)

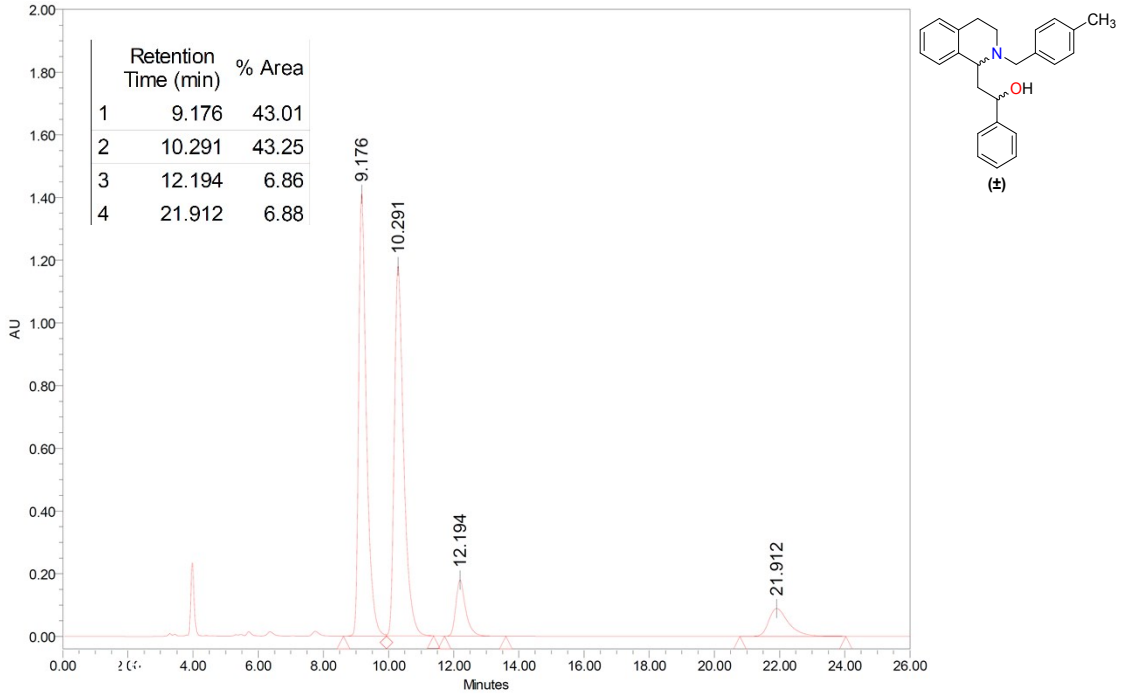

160.0 139.4 133.2 129.8 129.3 128.3 128.2 127.2 126.7 126.5 125.8 125.5 114.9 114.6 113.6 113.3
77.6 77.4 77.2 76.7 75.5 72.3 62.1 60.3 58.3 57.3 55.4 44.7 43.6 42.2 41.1
25.1 21.6
f1 (ppm)

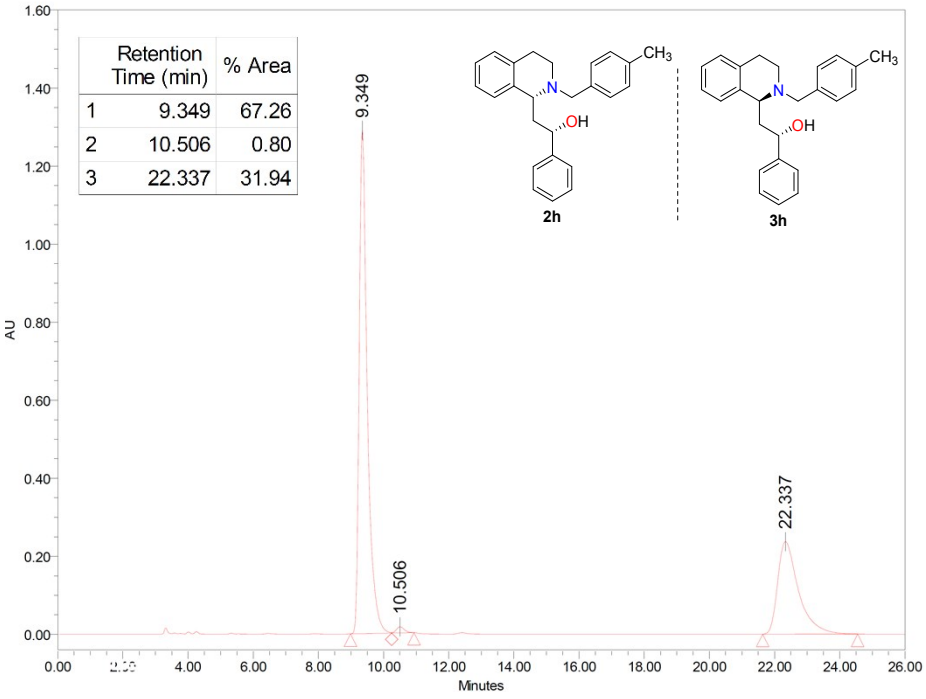

Retention Time (min) | % Area
1 | 12.152 | 8.01
2 | 18.504 | 41.80
3 | 22.982 | 8.05
4 | 28.956 | 42.14
OCH3
OH
N
(±)
AU
Minutes
12.152
18.504
22.982
28.956

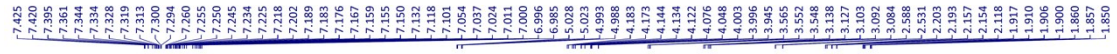

Retention Time (min) | % Area
1 | 11.740 | 30.56
2 | 17.619 | 68.78
3 | 27.269 | 0.66
OCH3
OH
N
2g
3g
AU
Minutes
11.740
17.619
27.269

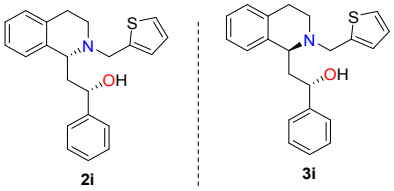

2h
3h
f1 (ppm)


f1 (ppm)

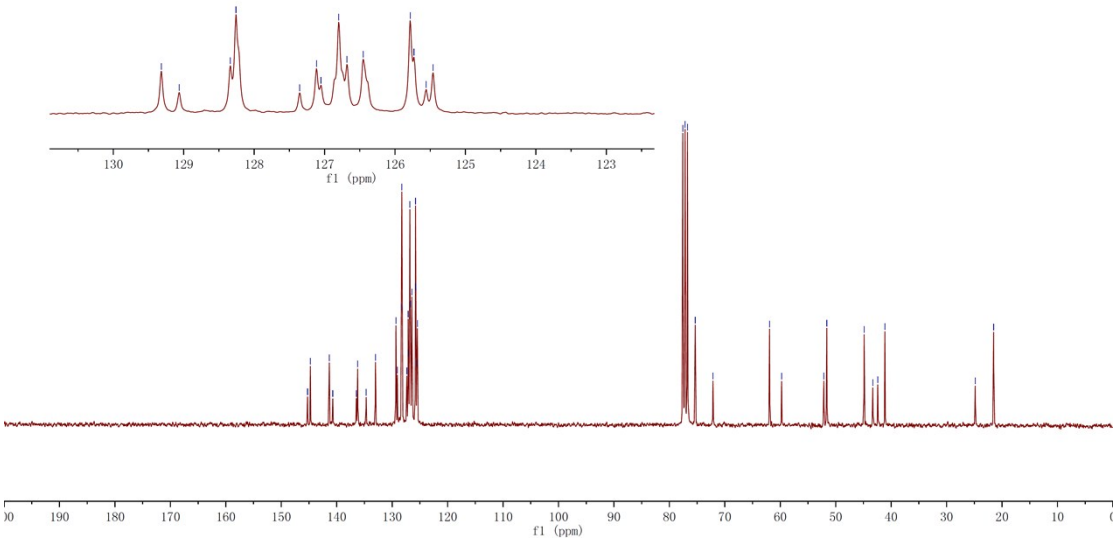

Retention Time (min) % Area
1 9.176 43.01
2 10.291 43.25
3 12.194 6.86
4 21.912 6.88
9.176
10.291
12.194
21.912
AU
Minutes
(±)

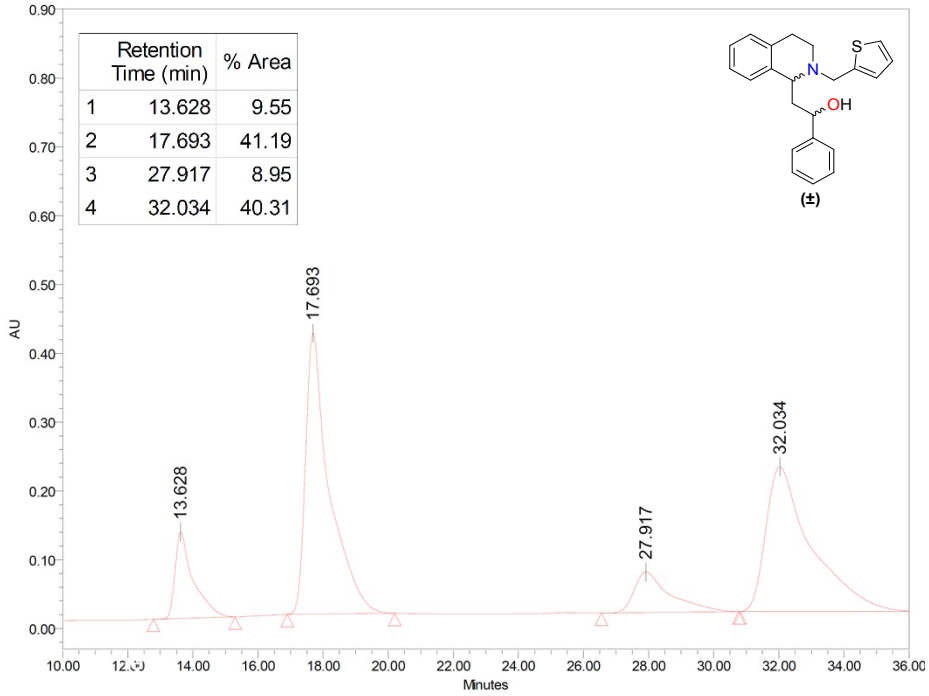

Retention Time (min) % Area
1 9.349 67.26
2 10.506 0.80
3 22.337 31.94
9.349
10.506
22.337
AU
Minutes
2h
3h

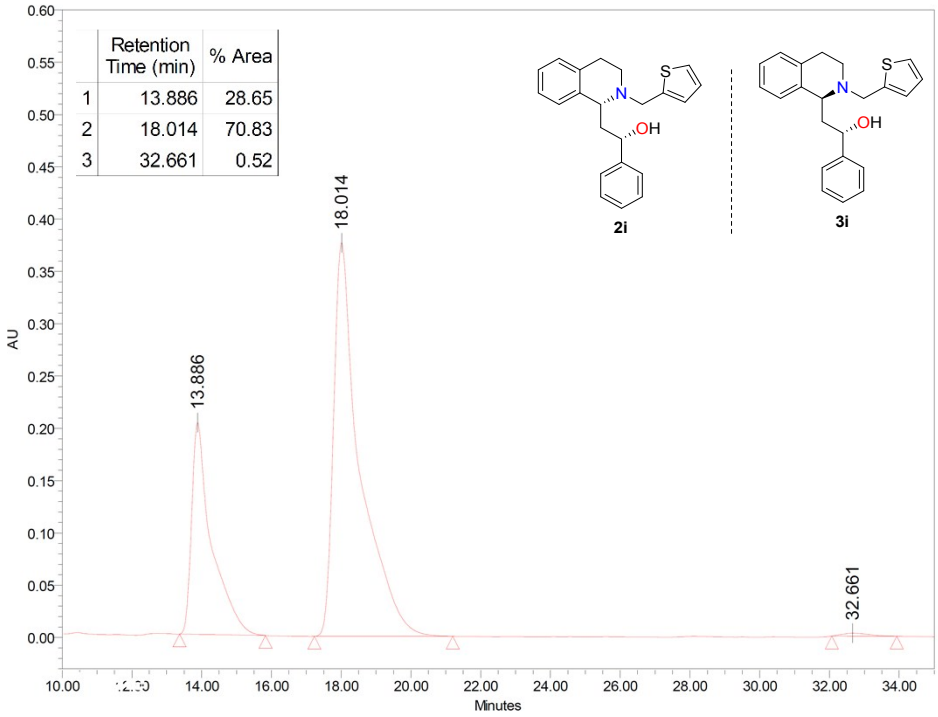


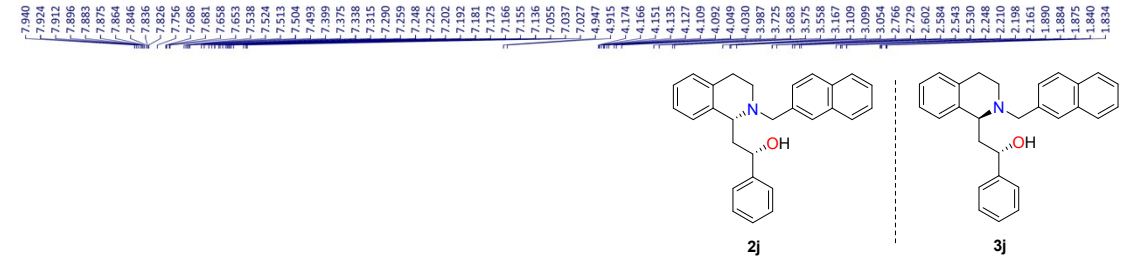

N
S
OH
2i
3i

15.57
1.00
0.17
0.94
2.66
1.03
0.19
2.09
0.60
1.03
0.21
1.20
1.04
f1 (ppm)


f1 (ppm)

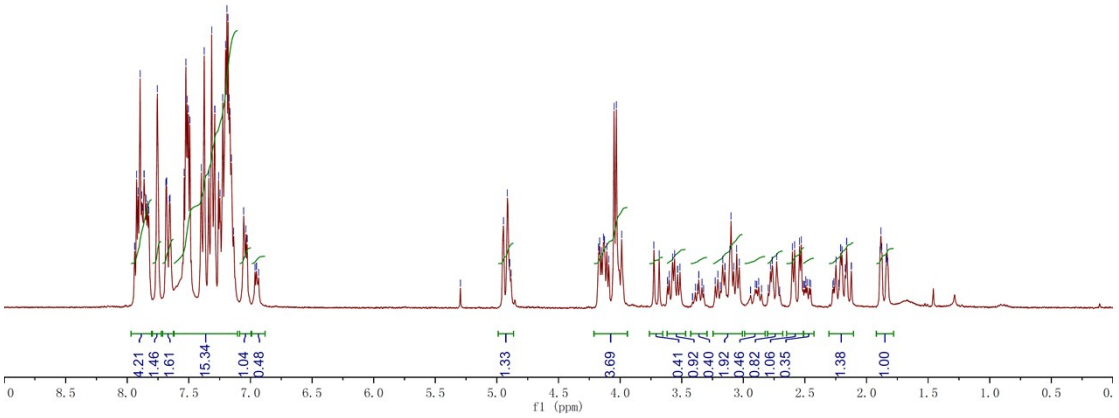

Retention Time (min) % Area
1 13.628 9.55
2 17.693 41.19
3 27.917 8.95
4 32.034 40.31
(±)
AU
Minutes
13.628
17.693
27.917
32.034

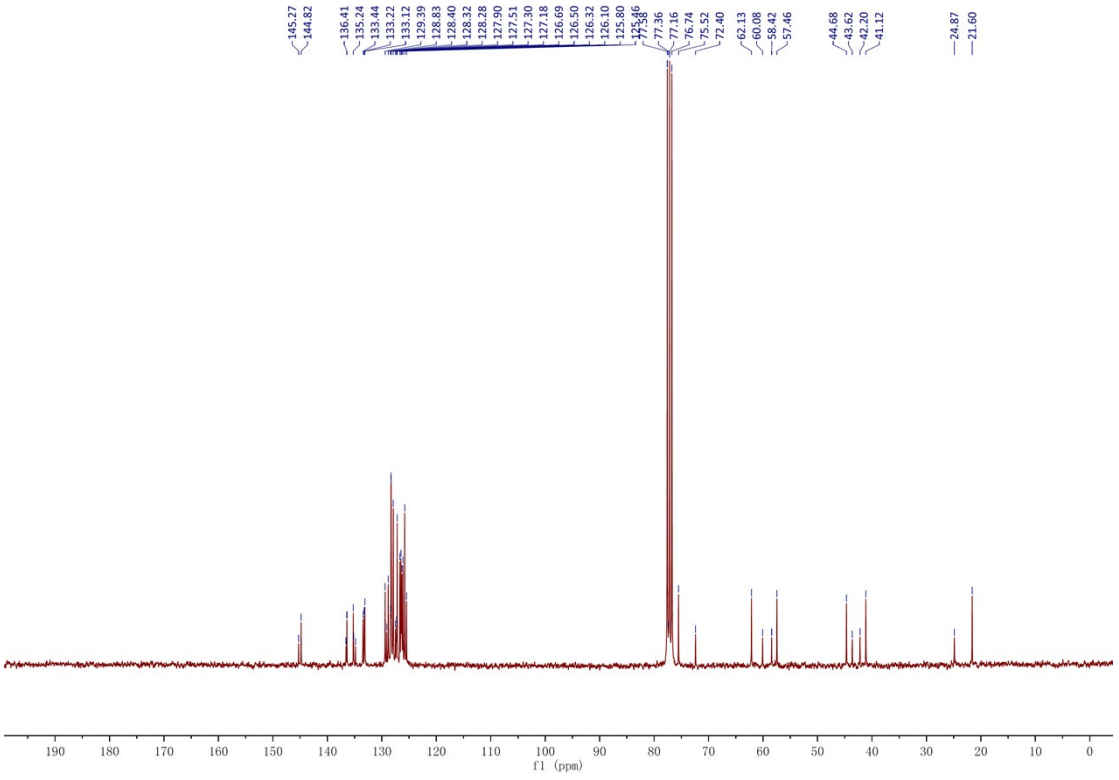

Retention Time (min) % Area
1 13.886 28.65
2 18.014 70.83
3 32.661 0.52
2i
3i
AU
Minutes
13.886
18.014
32.661

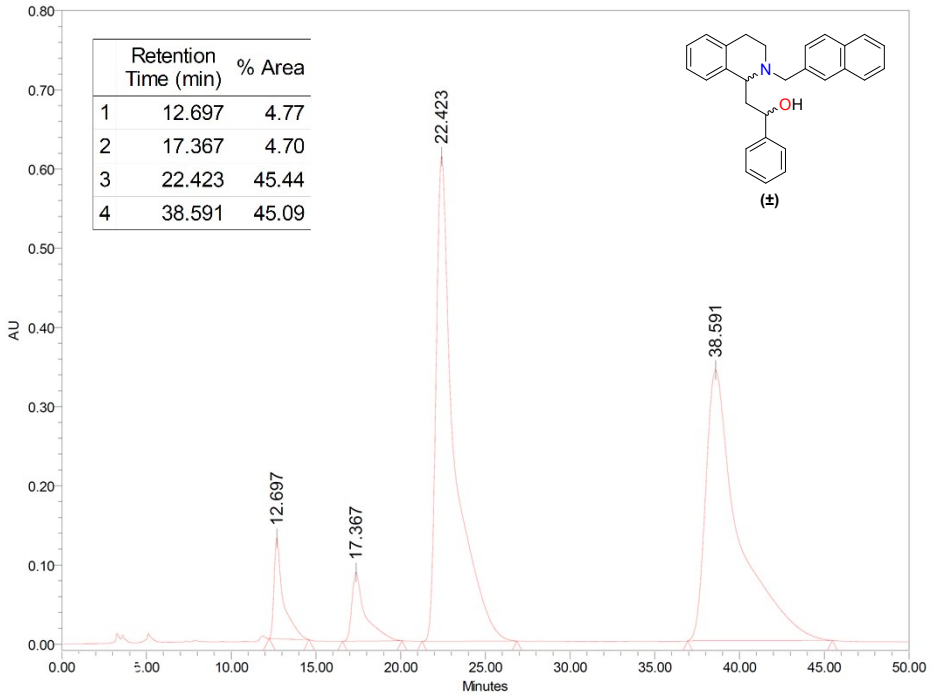

7.940 7.924 7.912 7.896 7.883 7.875 7.864 7.846 7.836 7.826 7.756 7.686 7.681 7.658 7.653 7.538 7.524 7.513 7.504 7.493 7.399 7.375 7.338 7.315 7.290 7.259 7.248 7.225 7.202 7.192 7.181 7.173 7.166 7.155 7.136 7.055 7.037 7.027 4.947 4.915 4.174 4.166 4.151 4.135 4.127 4.109 4.092 4.049 4.030 3.987 3.725 3.683 3.575 3.558 3.167 3.109 3.099 3.054 2.766 2.729 2.602 2.584 2.543 2.530 2.248 2.210 2.198 2.161 1.890 1.884 1.875 1.840 1.834

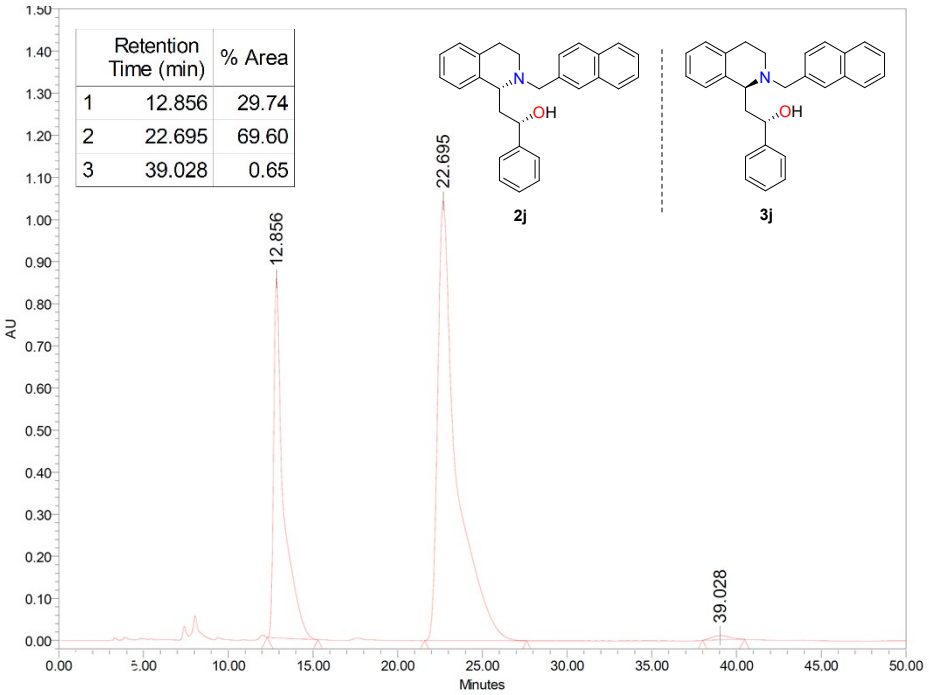
N
OH
N
OH

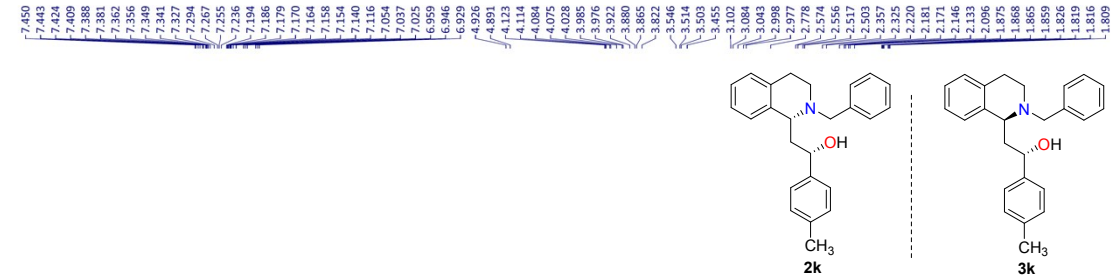
2j **3j**


4.21 1.46 1.61 15.34 1.04 0.48 1.33 3.69 0.41 0.92 0.40 1.92 0.46 0.82 1.06 0.35 1.38 1.00
0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)


145.27 144.82 136.41 135.24 133.44 133.22 133.12 129.39 128.83 128.40 128.32 128.28 127.90 127.51 127.30 127.18 126.69 126.50 126.32 126.10 125.80 125.46 77.58 77.36 77.16 76.74 75.52 72.40 62.13 60.08 58.42 57.46 44.68 43.62 42.20 41.12 24.87 21.60
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

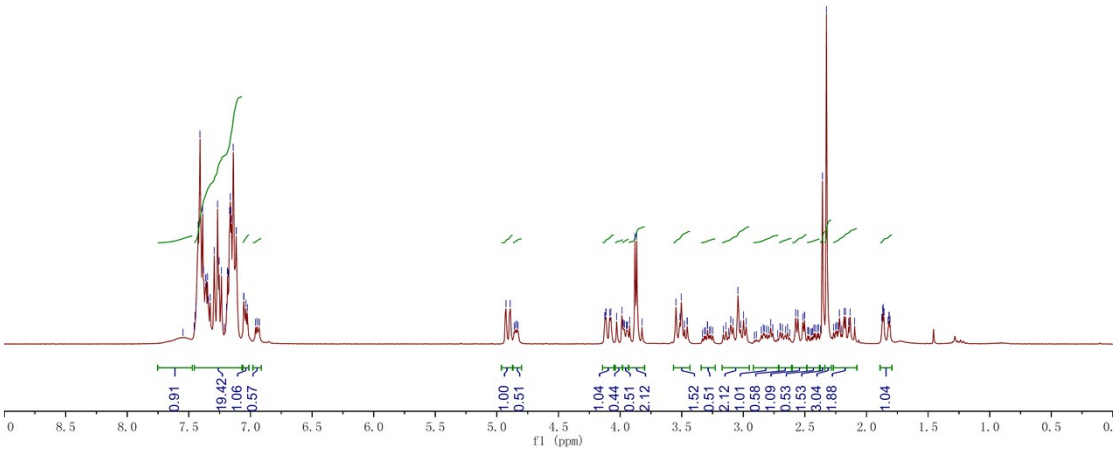

Retention Time (min) % Area
1 12.697 4.77
2 17.367 4.70
3 22.423 45.44
4 38.591 45.09
22.423
38.591
12.697
17.367
OH
(±)
AU
Minutes


Retention Time (min) % Area
1 12.856 29.74
2 22.695 69.60
3 39.028 0.65
12.856
22.695
39.028
OH
2j
3j
AU
Minutes


7.450
7.443
7.424
7.409
7.388
7.381
7.362
7.356
7.349
7.341
7.327
7.294
7.267
7.255
7.236
7.194
7.186
7.179
7.170
7.164
7.158
7.154
7.140
7.116
7.054
7.037
7.025
6.959
6.946
6.929
4.926
4.891
4.123
4.114
4.084
4.075
4.028
3.985
3.976
3.922
3.880
3.865
3.822
3.546
3.514
3.503
3.455
3.102
3.084
3.043
2.998
2.977
2.778
2.574
2.556
2.517
2.503
2.357
2.325
2.220
2.181
2.171
2.146
2.133
2.096
1.875
1.868
1.865
1.859
1.826
1.819
1.816
1.809

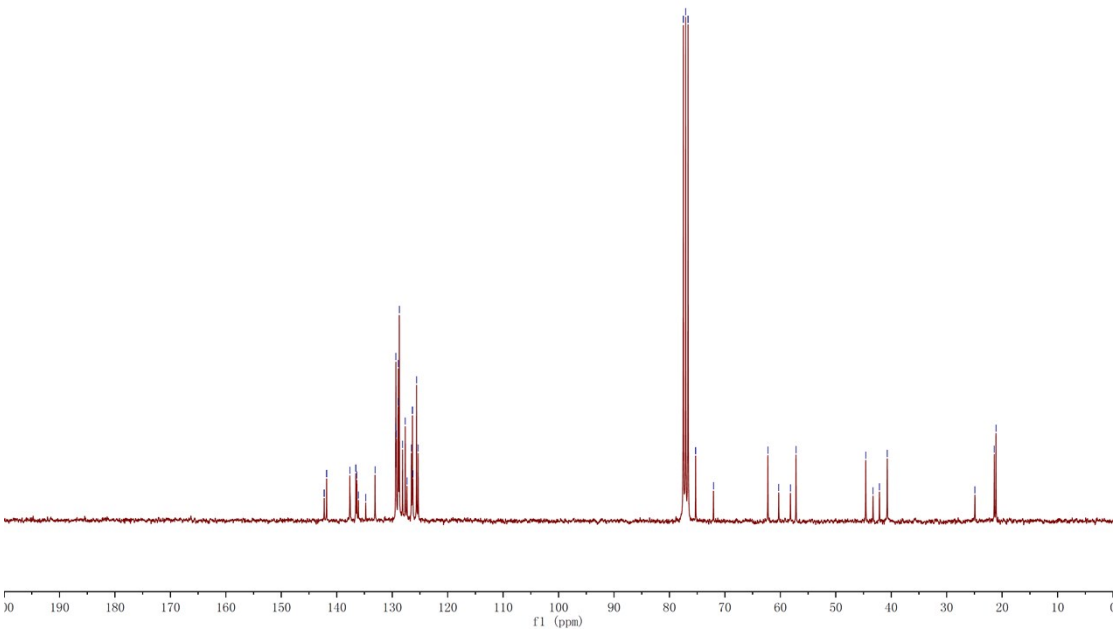
N
OH
CH3
N
OH
CH3

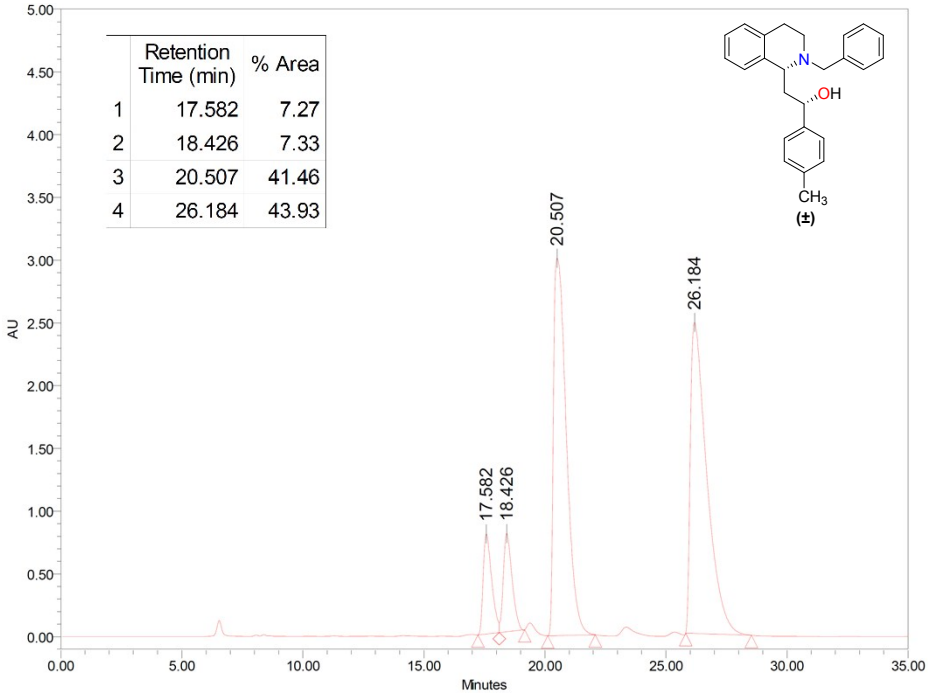
2k **3k**

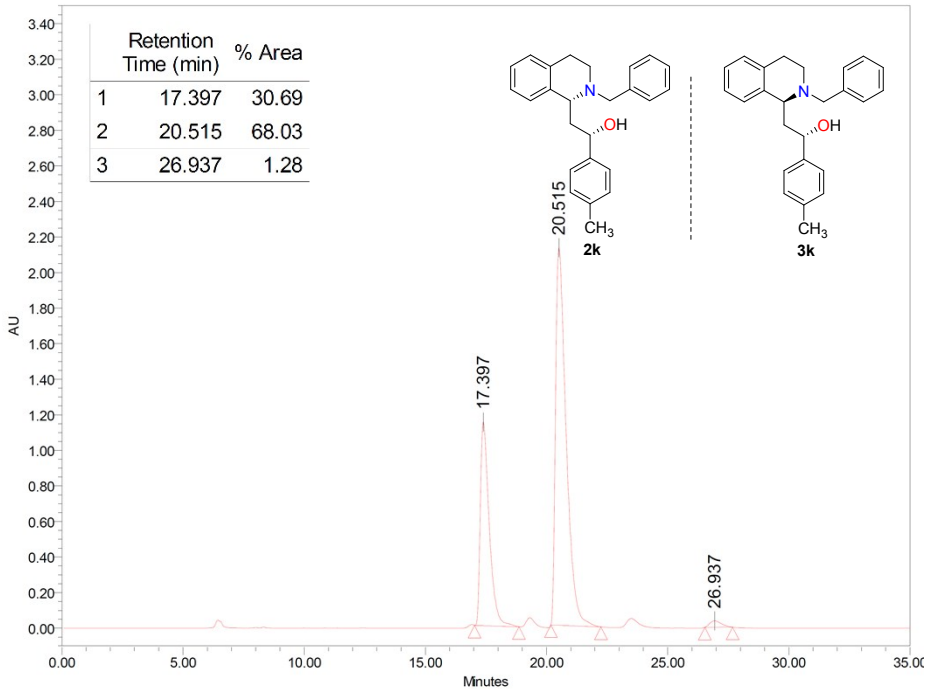

0.91
19.42
1.06
0.57
1.00
0.51
1.04
0.44
0.51
2.12
1.52
0.51
2.12
1.01
0.58
1.09
0.53
1.53
3.04
1.88
1.04
f1 (ppm)

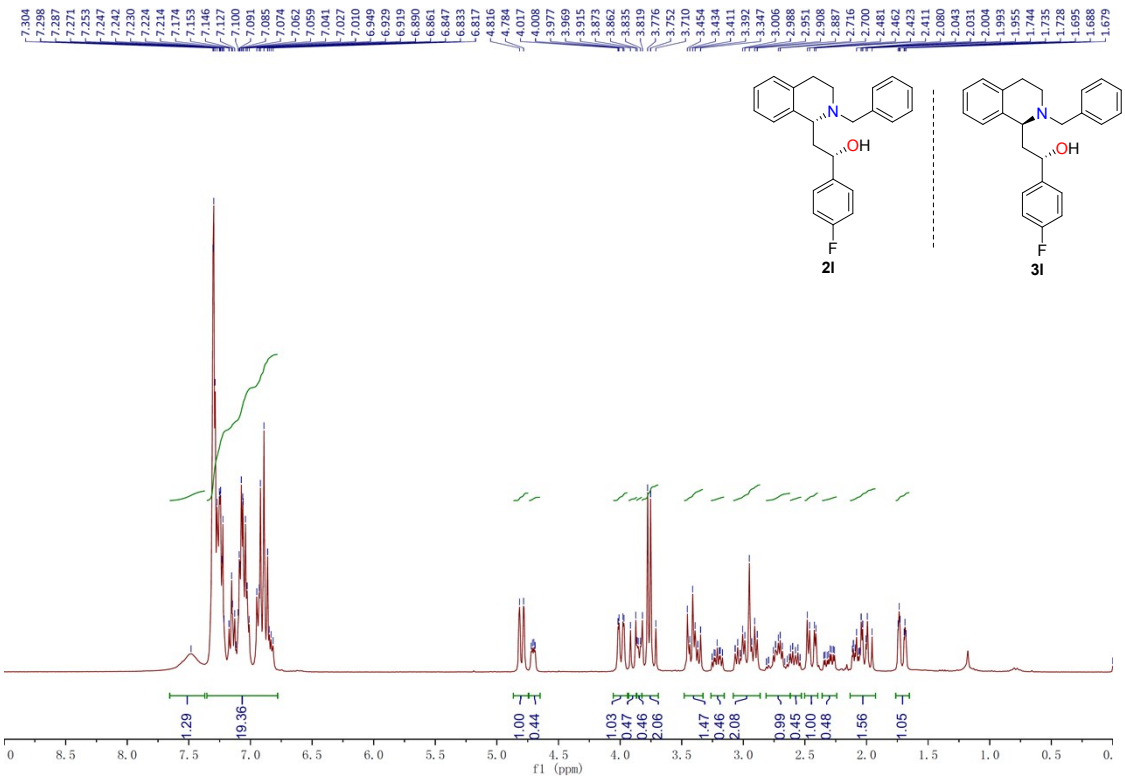

142.268
141.829
137.638
136.561
136.370
136.088
134.777
133.098
129.389
129.337
129.248
128.950
128.890
128.716
128.137
127.649
127.340
126.533
126.350
126.265
125.608
125.324

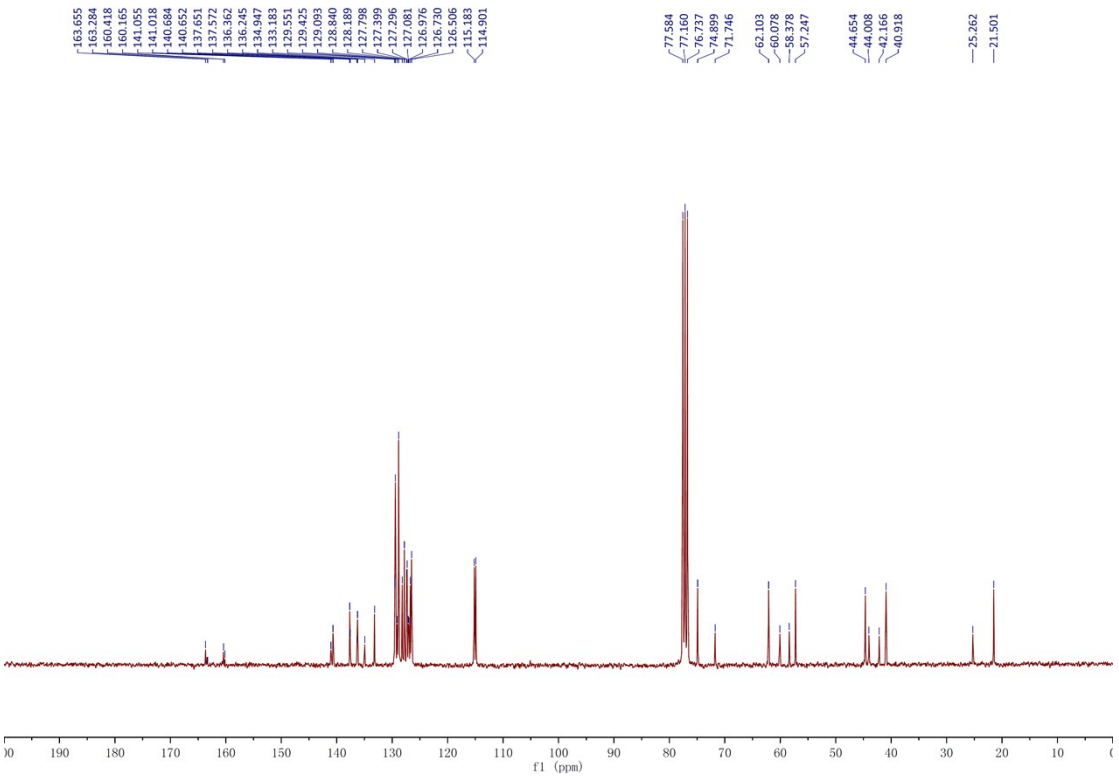

77.493
77.070
76.646
75.279
72.058
62.248
60.293
58.182
57.177
44.596
43.285
42.128
40.717
24.912
21.413
21.113

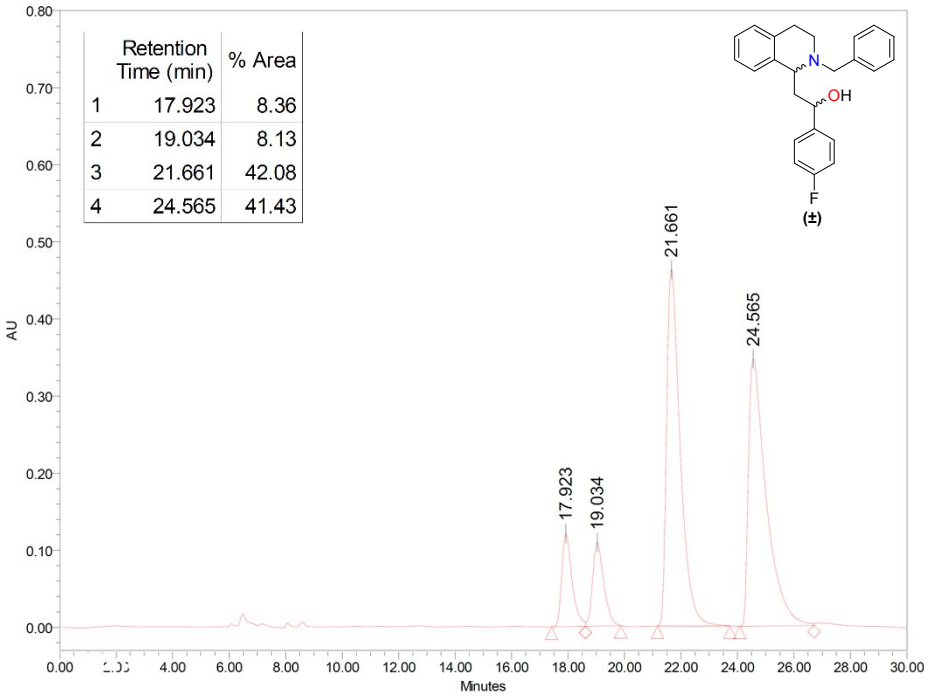

f1 (ppm)

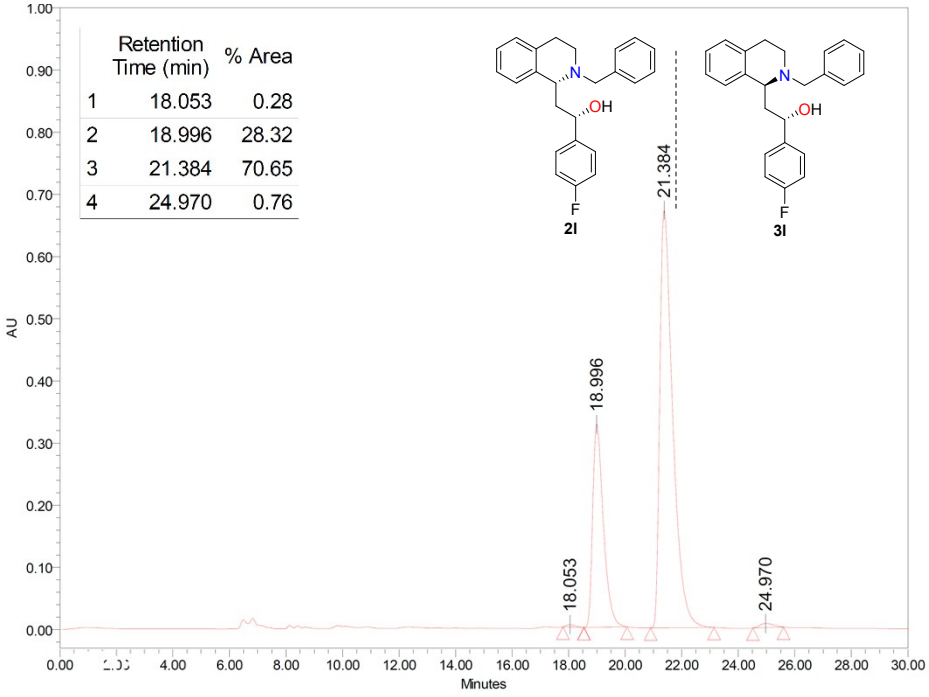

Retention Time (min) % Area
1 17.582 7.27
2 18.426 7.33
3 20.507 41.46
4 26.184 43.93
20.507
26.184
17.582
18.426
AU
Minutes
(±)

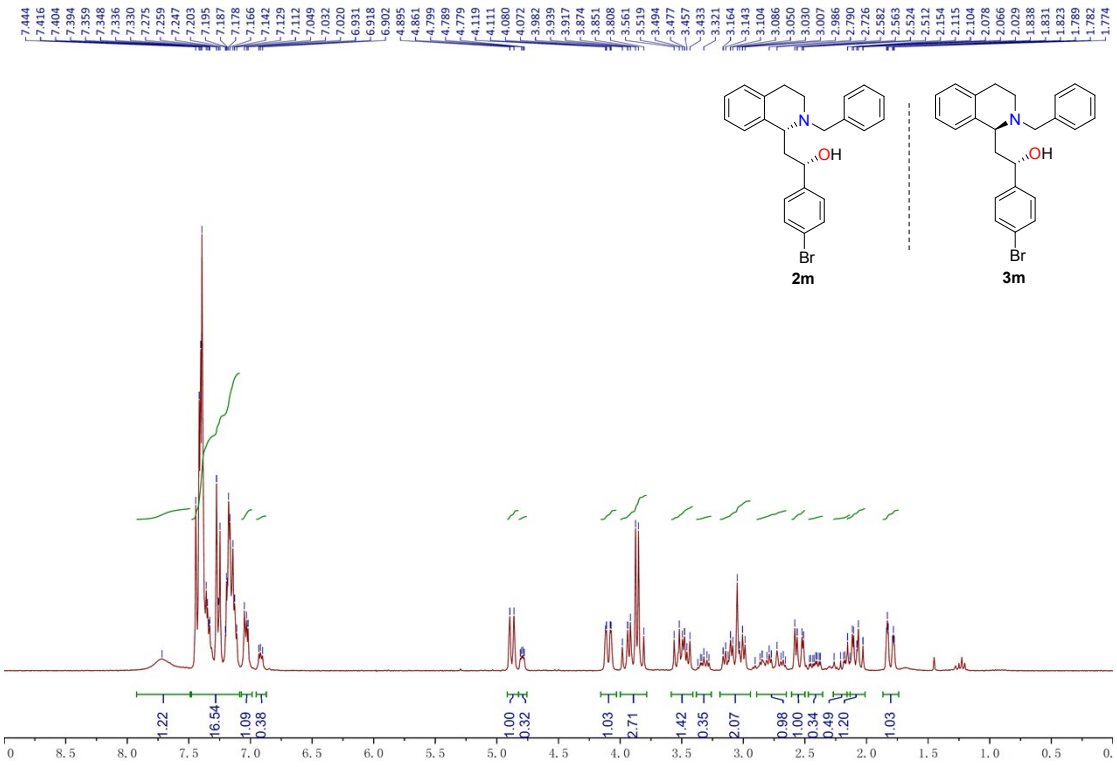

Retention Time (min) % Area
1 17.397 30.69
2 20.515 68.03
3 26.937 1.28
20.515
17.397
26.937
AU
Minutes
2k
3k

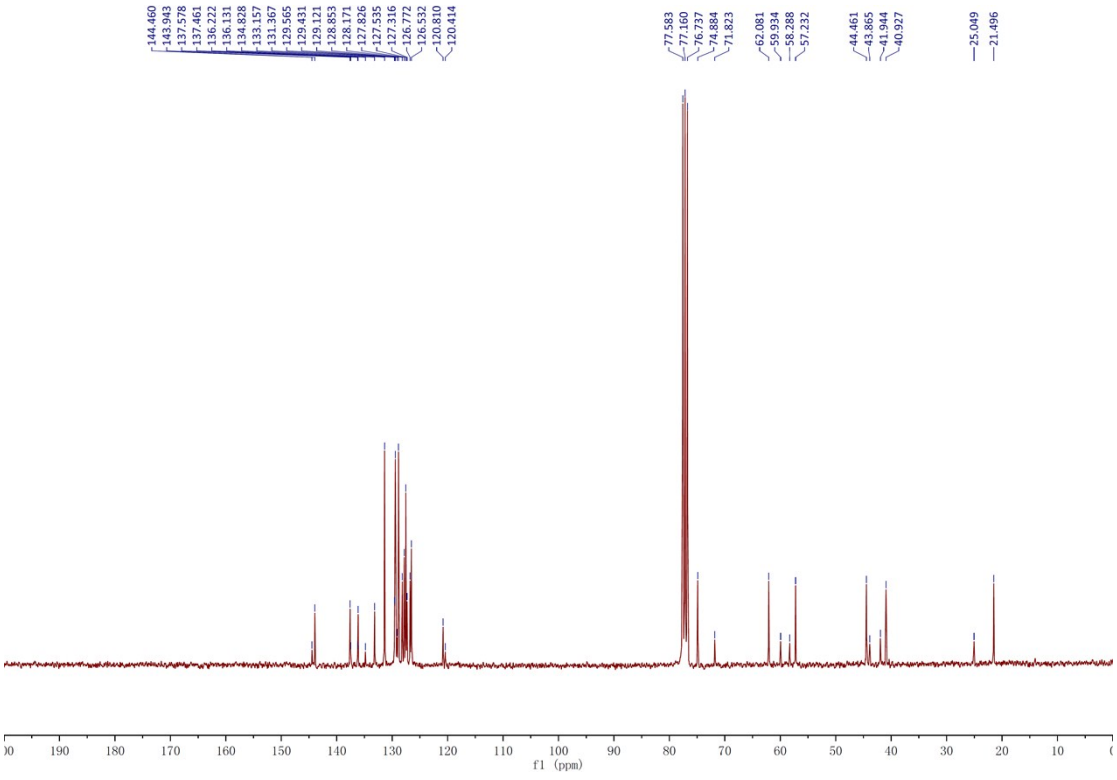

7.304 7.298 7.287 7.271 7.253 7.247 7.242 7.230 7.224 7.214 7.174 7.153 7.146 7.127 7.100 7.091 7.085 7.074 7.062 7.059 7.041 7.027 7.010 6.949 6.929 6.919 6.890 6.861 6.847 6.833 6.817 4.816 4.784 4.017 4.008 3.977 3.969 3.915 3.873 3.862 3.835 3.819 3.776 3.752 3.710 3.454 3.434 3.411 3.392 3.347 3.006 2.988 2.951 2.908 2.887 2.716 2.700 2.481 2.462 2.423 2.411 2.080 2.043 2.031 2.004 1.993 1.955 1.744 1.735 1.728 1.695 1.688 1.679
N
OH
F
2l
N
OH
F
3l
1.29 19.36 1.00 0.44 1.03 0.47 0.46 2.06 1.47 0.46 2.08 0.99 0.45 1.00 0.48 1.56 1.05
f1 (ppm)

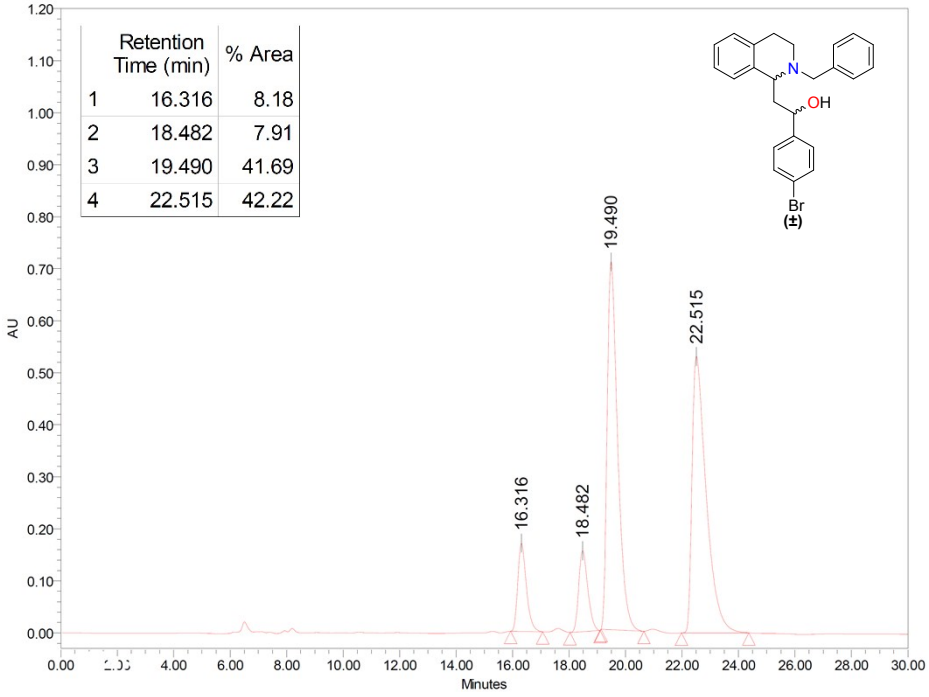

163.655 163.284 160.418 160.165 141.055 141.018 140.684 140.652 137.651 137.572 136.362 136.245 134.947 133.183 129.551 129.425 129.093 128.840 128.189 127.798 127.399 127.296 127.081 126.976 126.730 126.506 115.183 114.901
77.584 77.160 76.737 74.899 71.746 62.103 60.078 58.378 57.247 44.654 44.008 42.166 40.918 25.262 21.501
f1 (ppm)

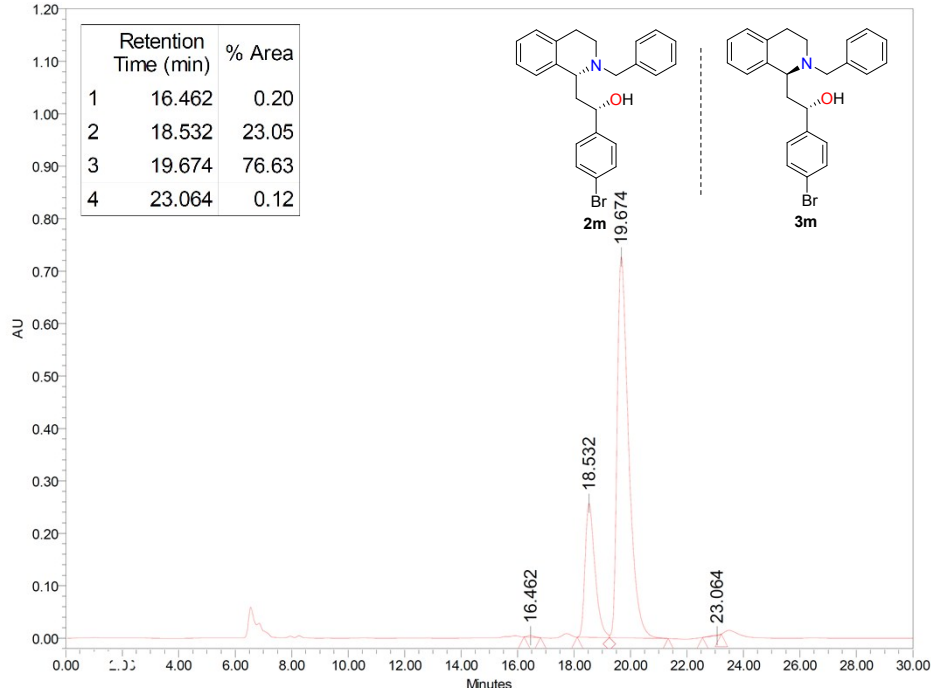

Retention Time (min) % Area
1 17.923 8.36
2 19.034 8.13
3 21.661 42.08
4 24.565 41.43
(±)
17.923
19.034
21.661
24.565
AU
Minutes

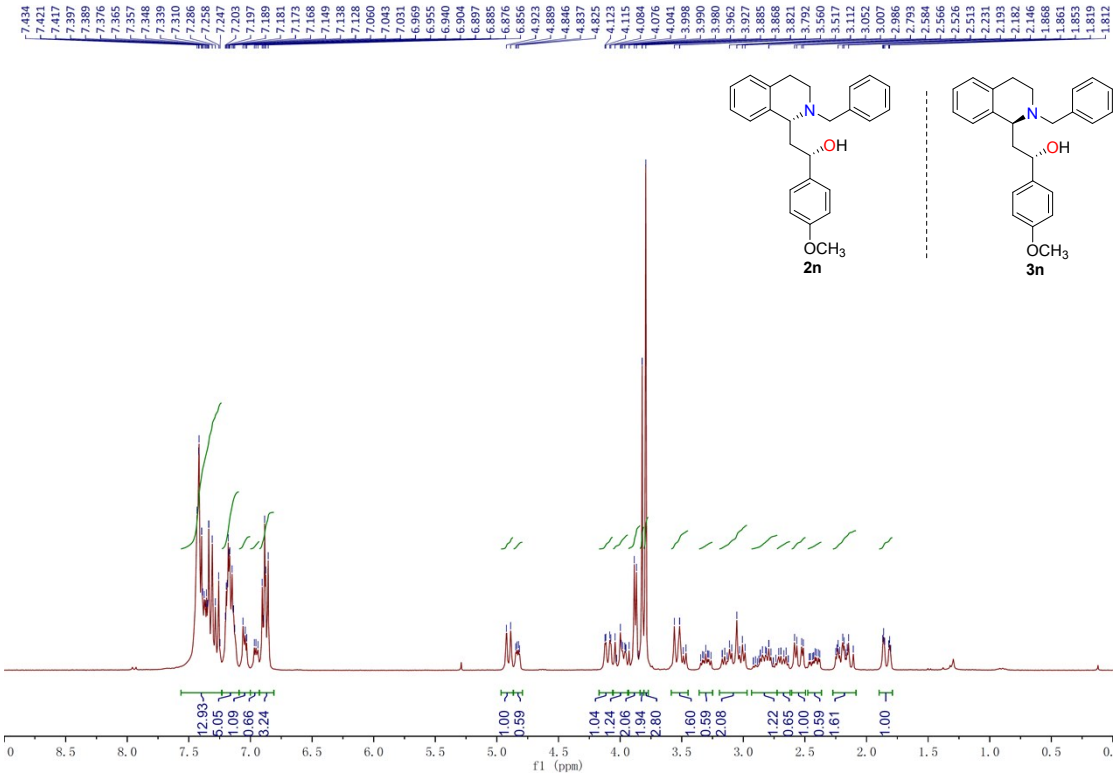

Retention Time (min) % Area
1 18.053 0.28
2 18.996 28.32
3 21.384 70.65
4 24.970 0.76
2l
3l
18.053
18.996
21.384
24.970
AU
Minutes

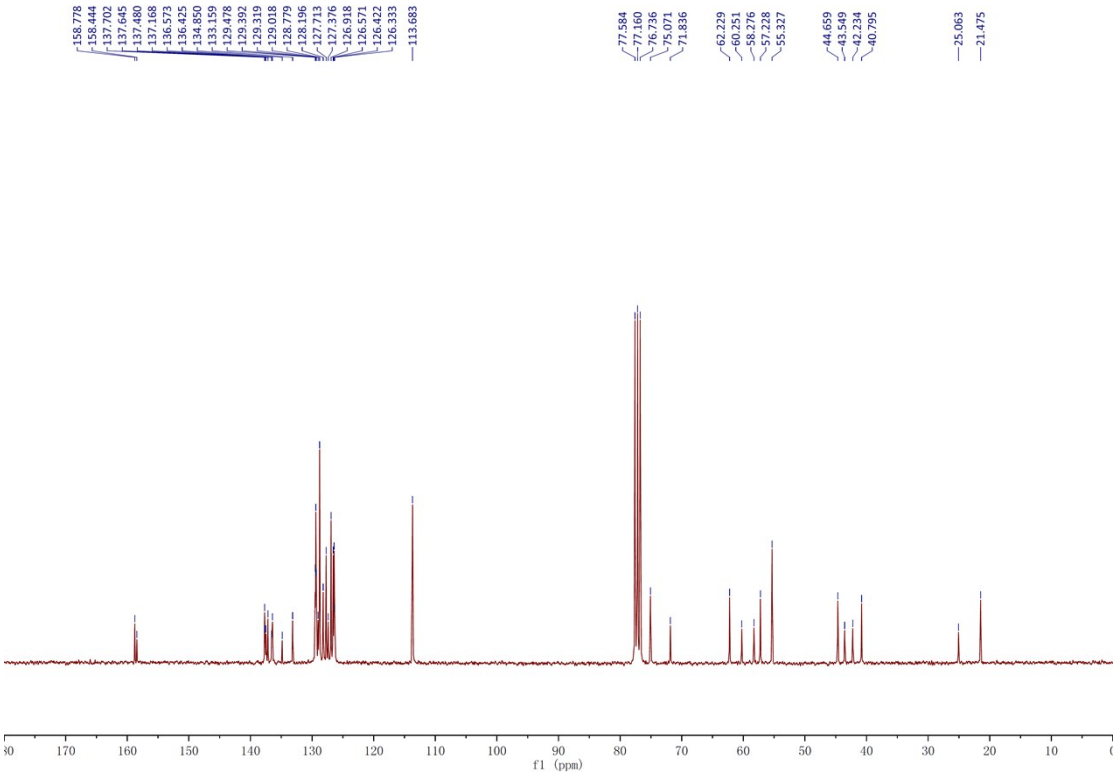

7.444 7.416 7.404 7.394 7.359 7.348 7.336 7.330 7.275 7.259 7.247 7.203 7.195 7.187 7.178 7.166 7.142 7.129 7.112 7.049 7.032 7.020 6.931 6.918 6.902 4.895 4.861 4.799 4.789 4.779 4.119 4.111 4.080 4.072 3.982 3.939 3.917 3.874 3.851 3.808 3.561 3.519 3.494 3.477 3.457 3.433 3.321 3.164 3.143 3.104 3.086 3.050 3.030 3.007 2.986 2.790 2.726 2.582 2.563 2.524 2.512 2.154 2.115 2.104 2.078 2.066 2.029 1.838 1.831 1.823 1.789 1.782 1.774
N
OH
Br
2m
N
OH
Br
3m
1.22 16.54 1.09 0.38 1.00 0.32 1.03 2.71 1.42 0.35 2.07 0.98 1.00 0.34 0.49 1.20 1.03
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

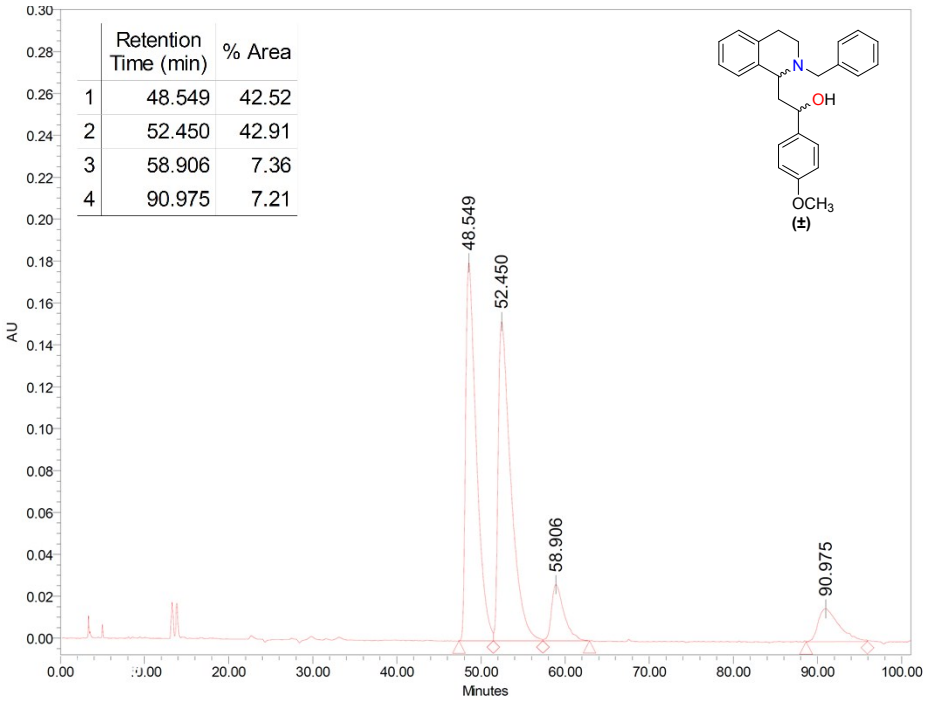

144.460 143.943 137.578 137.461 136.222 136.131 134.828 133.157 131.367 129.565 129.431 129.121 128.853 128.171 127.826 127.535 127.316 126.772 126.532 120.810 120.414
77.583 77.160 76.737 74.884 71.823 62.081 59.934 58.288 57.232 44.461 43.865 41.944 40.927 25.049 21.496
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

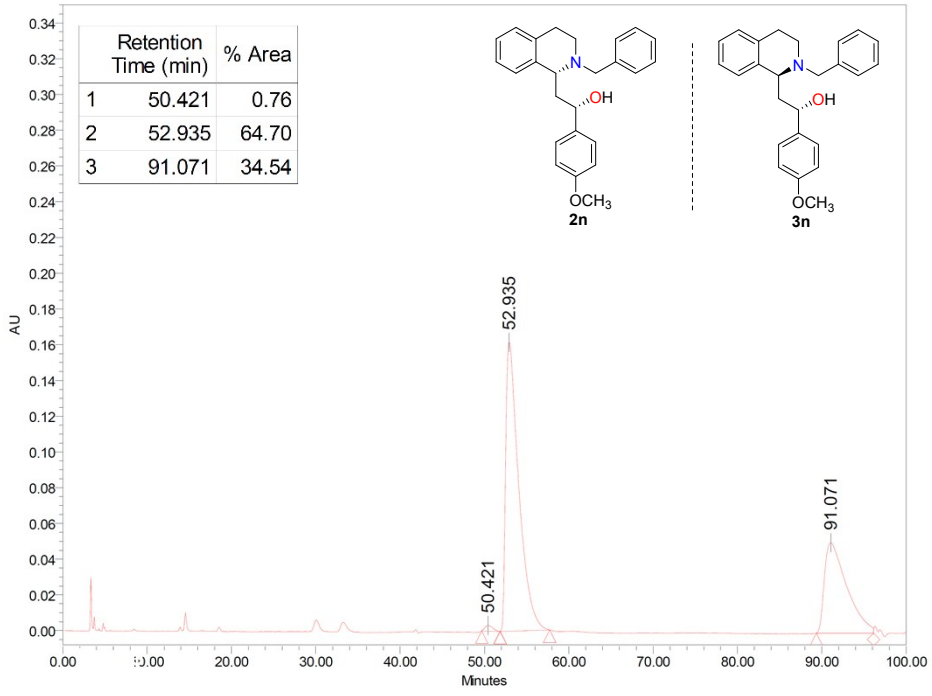

Retention Time (min) % Area
1 16.316 8.18
2 18.482 7.91
3 19.490 41.69
4 22.515 42.22
OH
Br
(±)
19.490
22.515
16.316
18.482
AU
Minutes

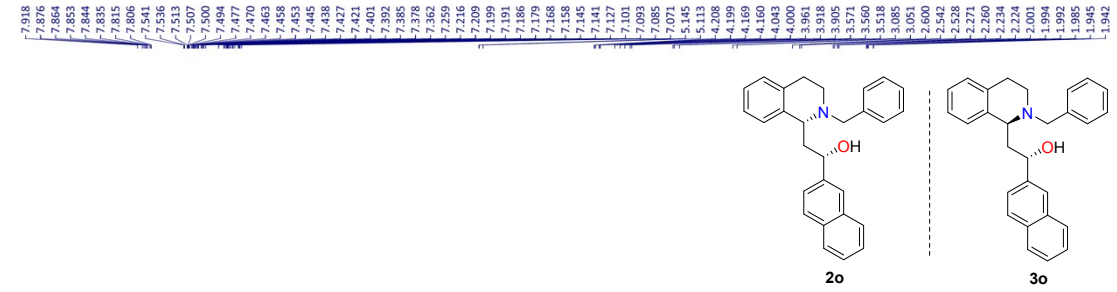

Retention Time (min) % Area
1 16.462 0.20
2 18.532 23.05
3 19.674 76.63
4 23.064 0.12
OH
Br
2m
OH
Br
3m
19.674
18.532
16.462
23.064
AU
Minutes


7.434 7.421 7.417 7.397 7.389 7.376 7.365 7.357 7.348 7.339 7.310 7.286 7.258 7.247 7.203 7.197 7.189 7.181 7.173 7.168 7.149 7.138 7.128 7.060 7.043 7.031 6.969 6.955 6.940 6.904 6.897 6.885 6.876 6.856 4.923 4.889 4.846 4.837 4.825 4.123 4.115 4.084 4.076 4.041 3.998 3.990 3.980 3.962 3.927 3.885 3.868 3.821 3.792 3.560 3.517 3.112 3.052 3.007 2.986 2.793 2.584 2.566 2.526 2.513 2.231 2.193 2.182 2.146 1.868 1.861 1.853 1.819 1.812
OH
OCH3
2n
3n
12.93 5.05 1.09 0.66 3.24 1.00 0.59 1.04 1.24 2.06 1.94 2.80 1.60 0.59 2.08 1.22 0.65 1.00 0.59 1.61 1.00
f1 (ppm)


158.778 158.444 137.702 137.645 137.480 137.168 136.573 136.425 134.850 133.159 129.478 129.392 129.319 129.018 128.779 128.196 127.713 127.376 126.918 126.571 126.422 126.333 113.683
77.584 77.160 76.736 75.071 71.836 62.229 60.251 58.276 57.228 55.327 44.659 43.549 42.234 40.795 25.063 21.475
f1 (ppm)

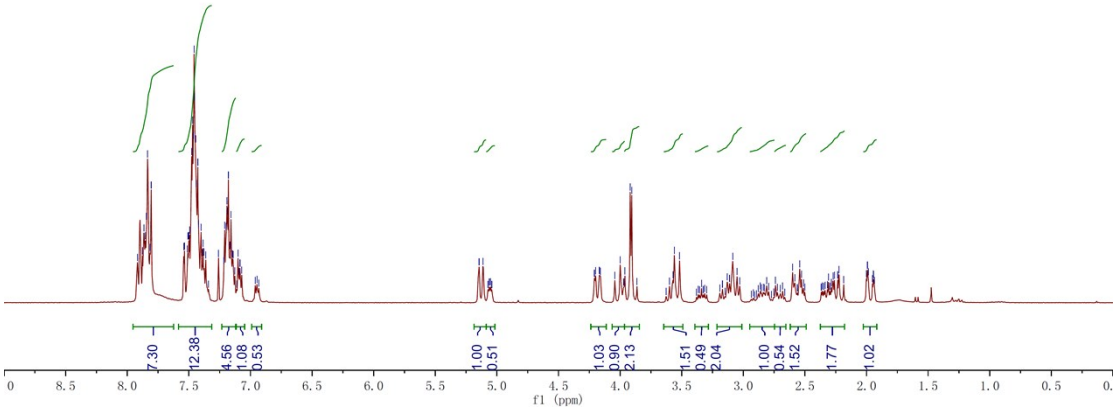

Retention Time (min) % Area
1 48.549 42.52
2 52.450 42.91
3 58.906 7.36
4 90.975 7.21
OH
OCH3
(±)
48.549
52.450
58.906
90.975
AU
Minutes

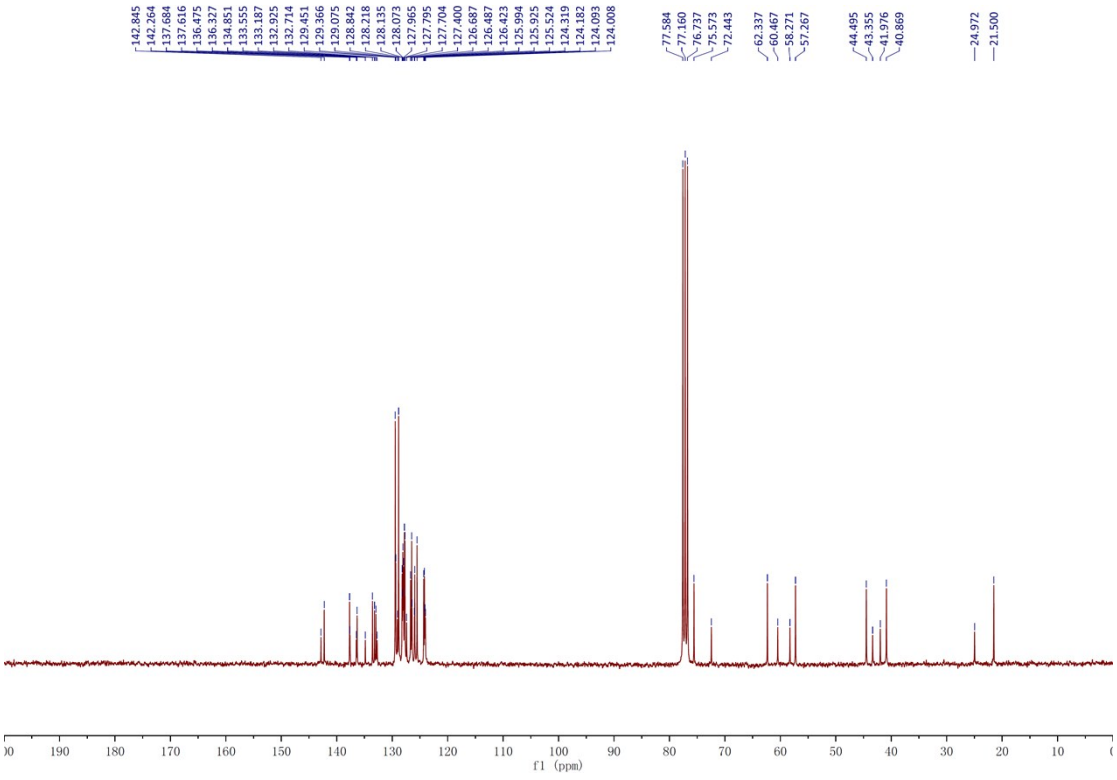

Retention Time (min) % Area
1 50.421 0.76
2 52.935 64.70
3 91.071 34.54
OH
OCH3
2n
3n
52.935
91.071
50.421
AU
Minutes

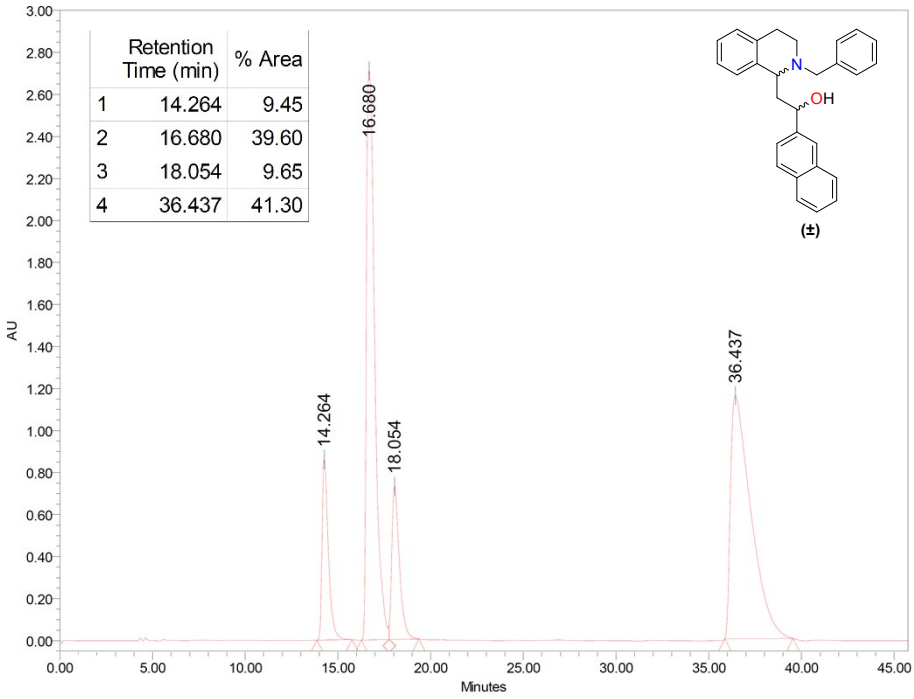

7.918
7.876
7.864
7.853
7.844
7.835
7.815
7.806
7.541
7.536
7.513
7.507
7.500
7.494
7.477
7.470
7.463
7.458
7.453
7.445
7.438
7.427
7.421
7.401
7.392
7.385
7.378
7.362
7.259
7.216
7.209
7.199
7.191
7.186
7.179
7.168
7.158
7.145
7.141
7.127
7.101
7.093
7.085
7.071
5.145
5.113
4.208
4.199
4.169
4.160
4.043
4.000
3.961
3.918
3.905
3.571
3.560
3.518
3.085
3.051
2.600
2.542
2.528
2.271
2.260
2.234
2.224
2.001
1.994
1.992
1.985
1.945
1.942

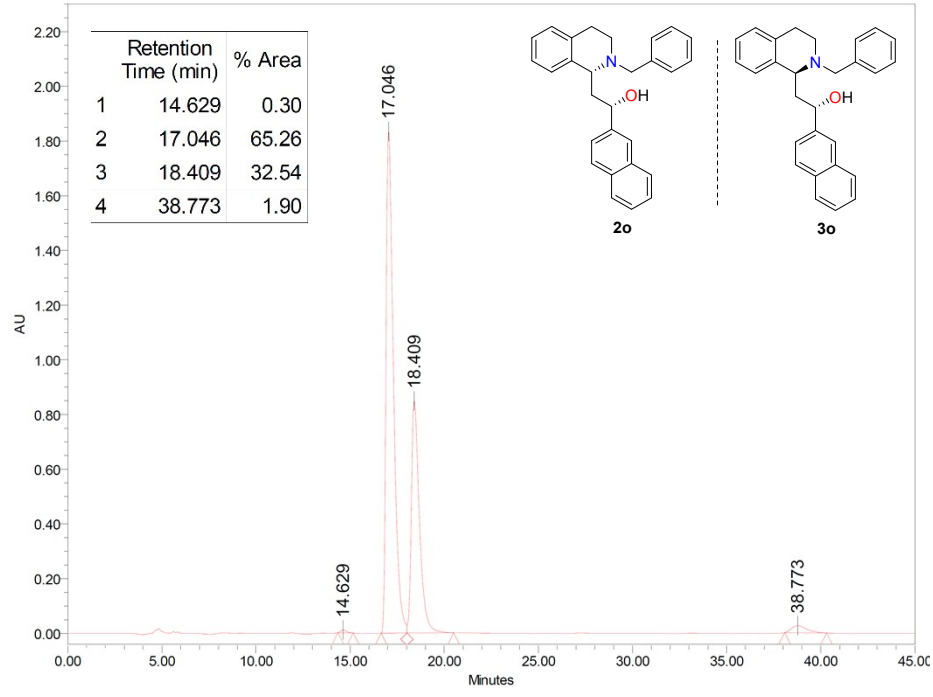
N
OH
N
OH

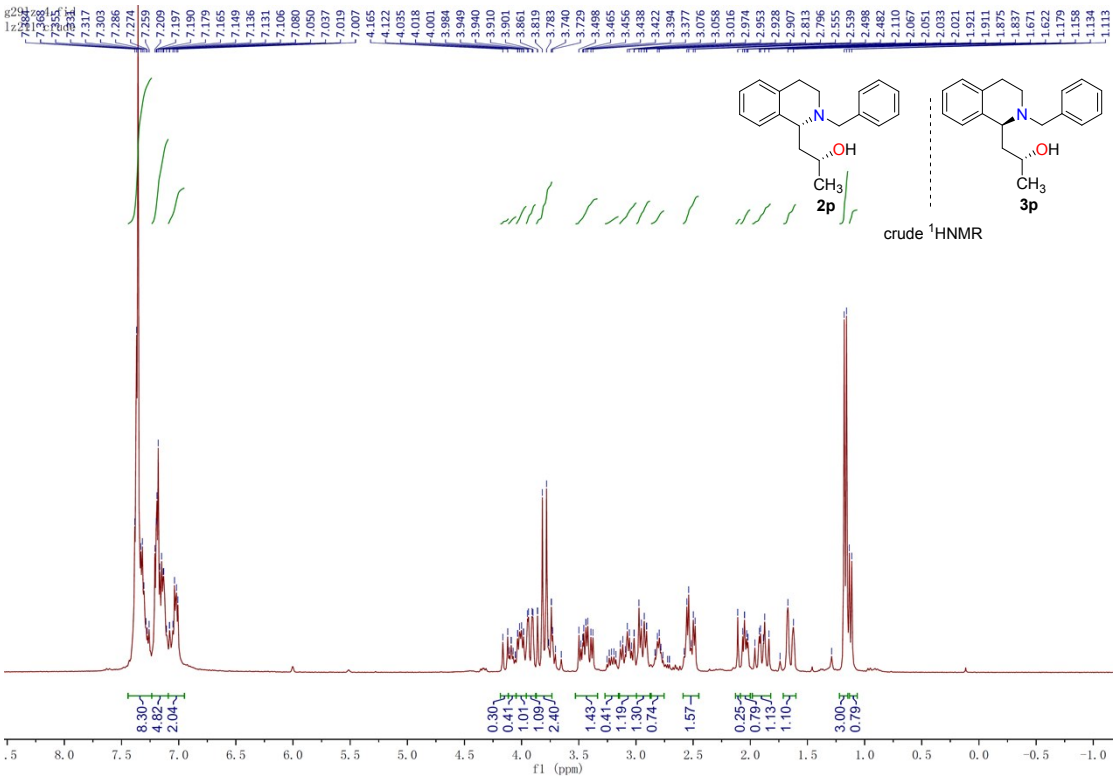
2o **3o**

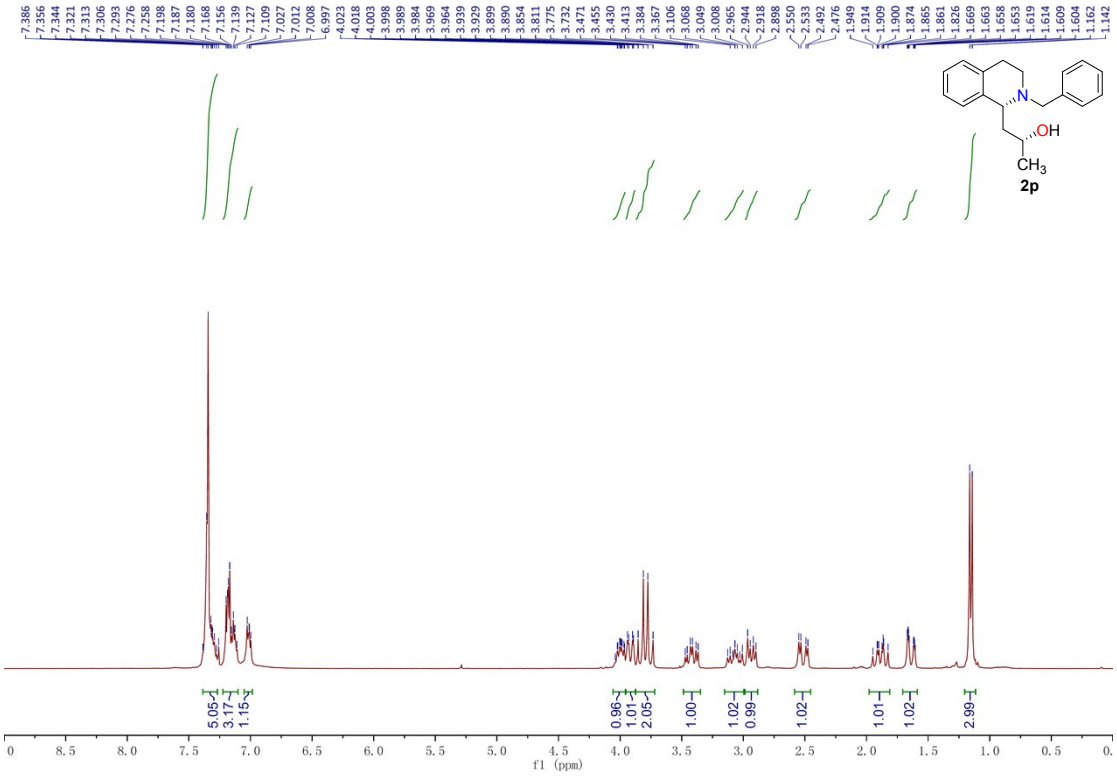

7.30
12.38
4.56
1.08
0.53
1.00
0.51
1.03
0.90
2.13
1.51
0.49
2.04
1.00
0.54
1.52
1.77
1.02
f1 (ppm)

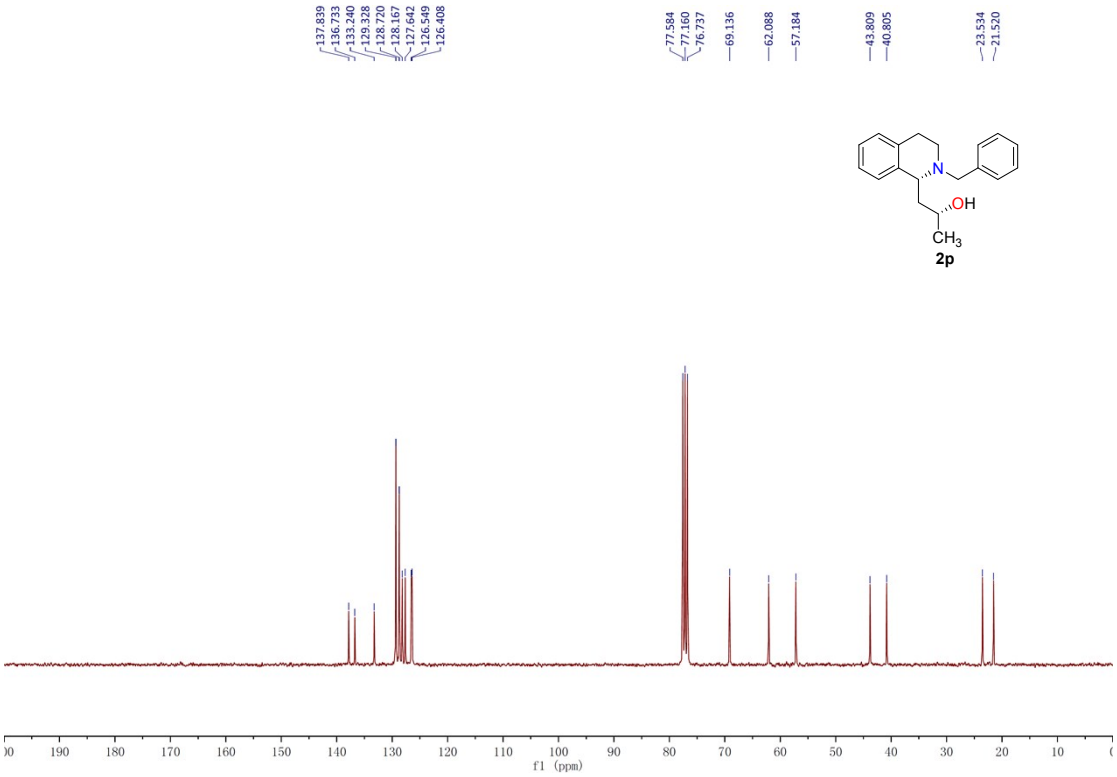

142.845
142.264
137.684
137.616
136.475
136.327
134.851
133.555
133.187
132.925
132.714
129.451
129.366
129.075
128.842
128.218
128.135
128.073
127.965
127.795
127.704
127.400
126.687
126.487
126.423
125.994
125.926
125.524
124.319
124.182
124.093
124.008
77.584
77.160
76.737
75.573
72.443
62.337
60.467
58.271
57.267
44.495
43.355
41.976
40.869
24.972
21.500
f1 (ppm)

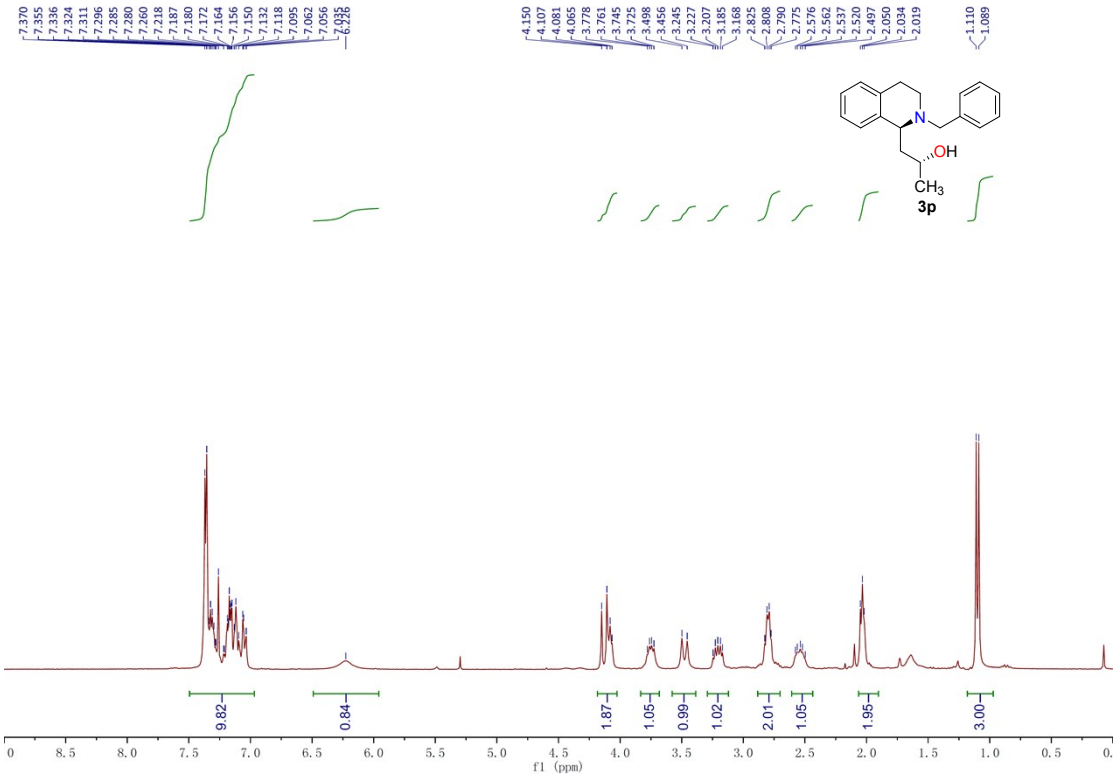

Retention Time (min) % Area
1 14.264 9.45
2 16.680 39.60
3 18.054 9.65
4 36.437 41.30
16.680
14.264
18.054
36.437
AU
Minutes
(±)

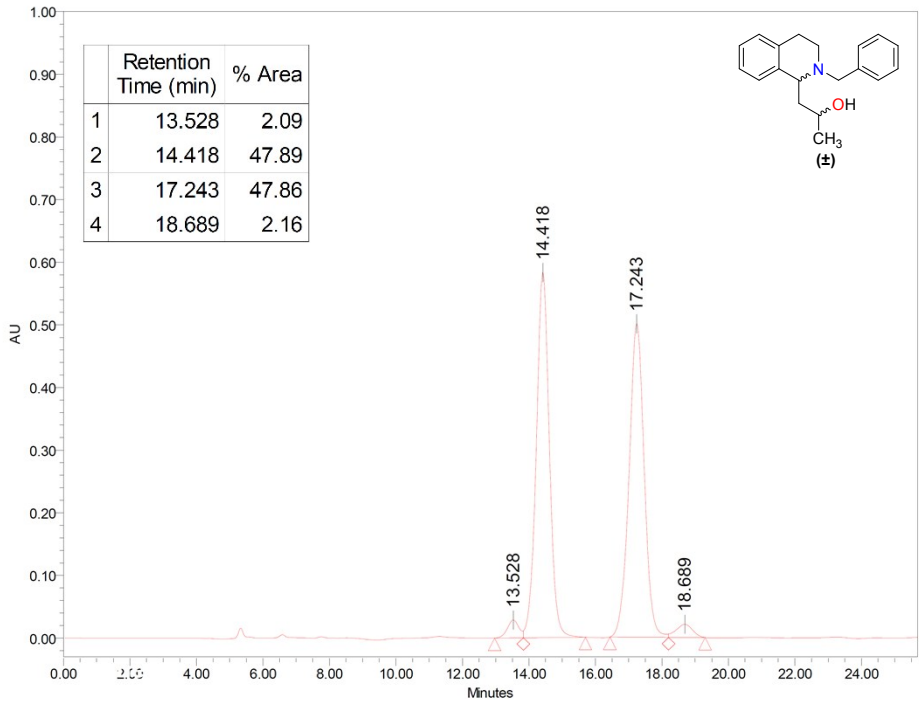

Retention Time (min) % Area
1 14.629 0.30
2 17.046 65.26
3 18.409 32.54
4 38.773 1.90
17.046
18.409
14.629
38.773
AU
Minutes
2o
3o

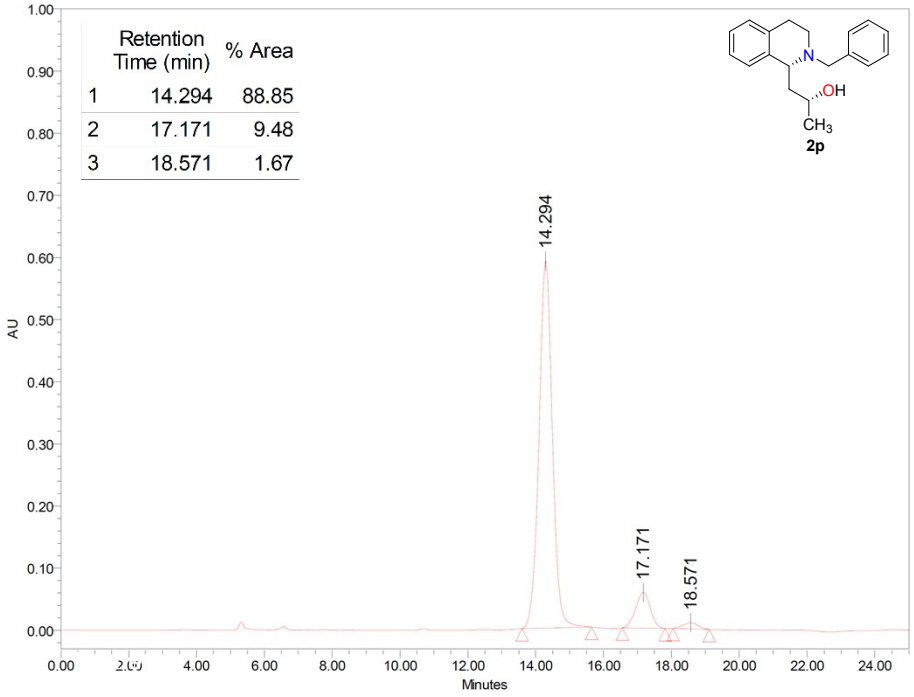

2p
3p
crude ^{1}HNMR
f1 (ppm)


2p
f1 (ppm)

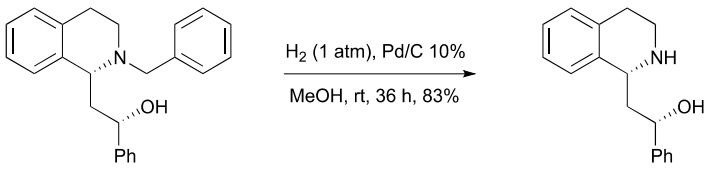

137.839
136.733
133.240
129.328
128.720
128.167
127.642
126.549
126.408
77.584
77.160
76.737
69.136
62.088
57.184
43.809
40.805
23.534
21.520
N
OH
CH3
2p
f1 (ppm)


7.370
7.355
7.336
7.324
7.311
7.296
7.285
7.280
7.260
7.218
7.187
7.180
7.172
7.164
7.156
7.150
7.132
7.118
7.095
7.062
7.056
7.035
6.226
4.150
4.107
4.081
4.065
3.778
3.761
3.745
3.725
3.498
3.456
3.245
3.227
3.207
3.185
3.168
2.825
2.808
2.790
2.775
2.576
2.562
2.537
2.520
2.497
2.050
2.034
2.019
1.110
1.089
N
OH
CH3
3p
9.82
0.84
1.87
1.05
0.99
1.02
2.01
1.05
1.95
3.00
f1 (ppm)


Retention Time (min) % Area
1 13.528 2.09
2 14.418 47.89
3 17.243 47.86
4 18.689 2.16
N
OH
CH3
(±)
14.418
17.243
13.528
18.689
AU
Minutes

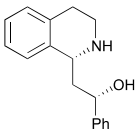

Retention Time (min) % Area
1 14.294 88.85
2 17.171 9.48
3 18.571 1.67
N
OH
CH3
2p
14.294
17.171
18.571
AU
Minutes

VIII. Debenzylation of compound 2a



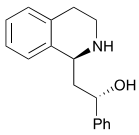
2a/3a

In a Schlenk tube, to a solution of **2a/3a** (0.32 mmol, 110 mg) in degassed MeOH (4 mL) was added Pd/C 10% (0.05 mmol, 17 mg). The system was purged with hydrogen and the reaction mixture was stirred at room temperature for 60 h under an atmospheric pressure of hydrogen (balloon). The suspension was then filtered on a celite pad and concentrated under reduced pressure. The residue was purified by flash column (petroleum ether/ethyl acetate: 1/1 to CH_2Cl_2/MeOH: 40/1 to 20/1) to afford the deprotected amino alcohol as a white solid (68 mg, 83% yield).



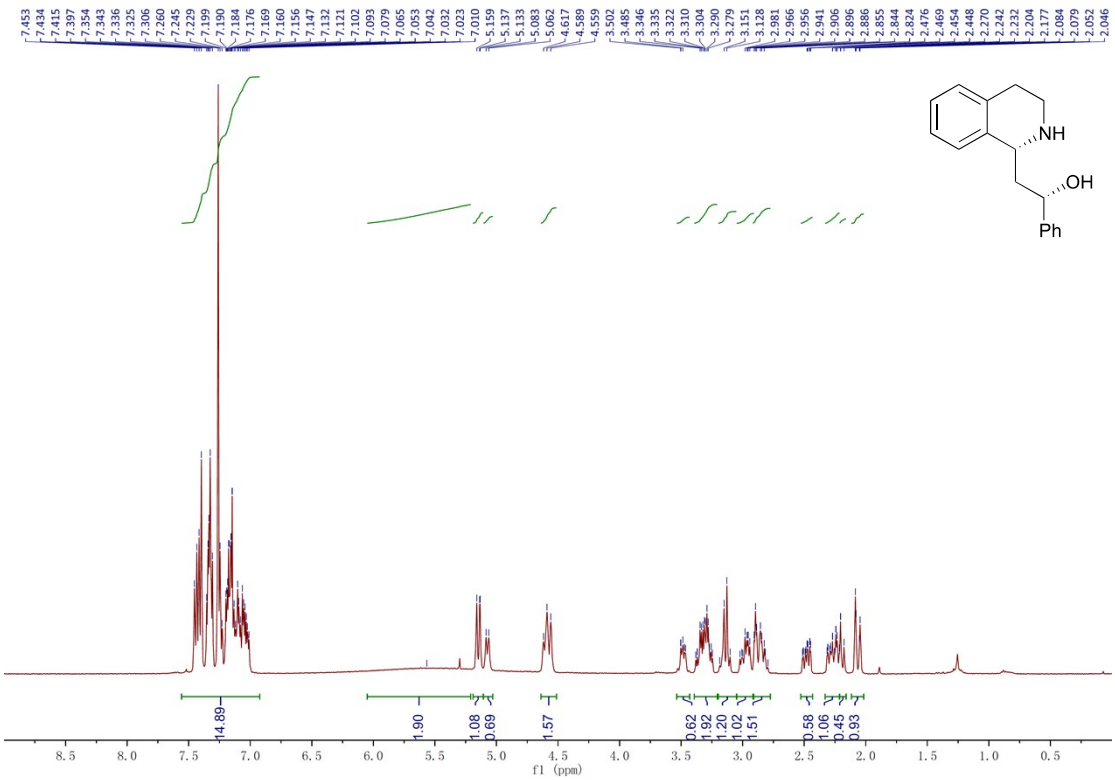
^{1}H NMR (400 MHz, $CDCl_3$) (*syn*) δ 7.45–7.01 (m, 9H), 5.16–5.13 (m, 1H), 4.62–4.56 (m, 1H), 3.38–3.24 (m, 2H), 2.98 (ddd, *J* = 15.7, 9.7, 5.7 Hz, 1H), 2.91–2.79 (m, 1H), 2.31–2.22 (m, 1H), 2.08–2.05 (m, 1H);

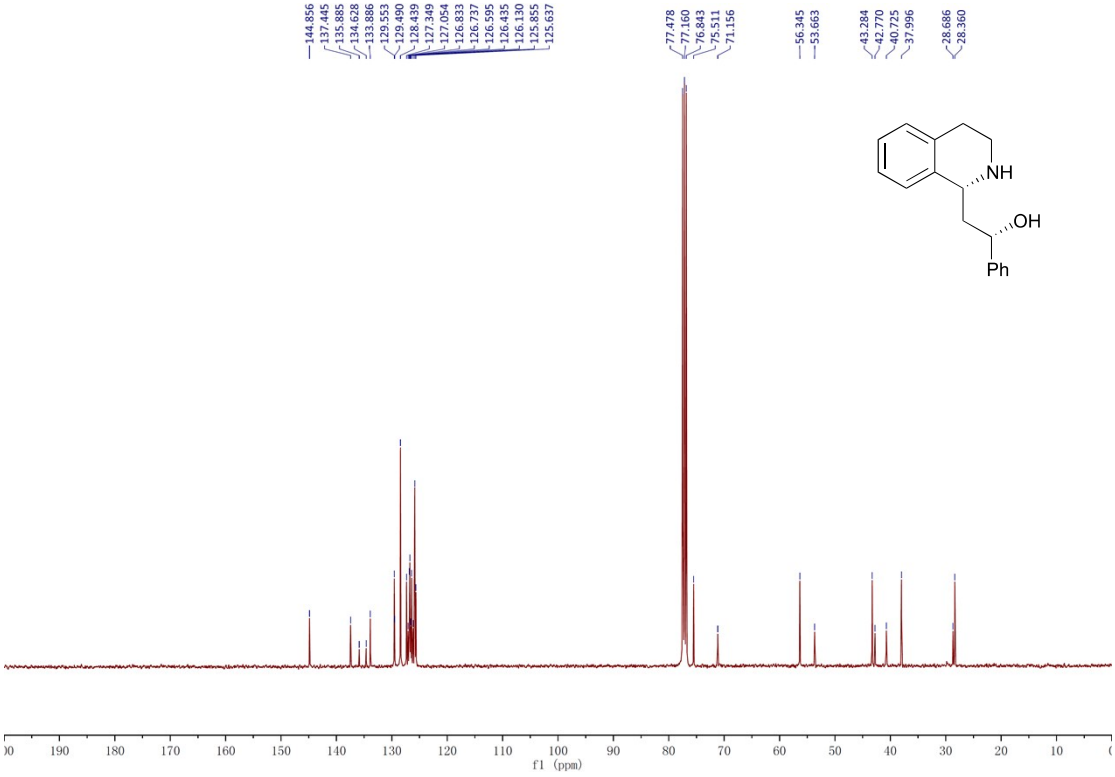
^{13}C NMR (101 MHz, $CDCl_3$) (*syn*) δ 144.9, 137.4, 133.9, 129.6, 128.4 (2C), 127.3, 126.8, 126.7, 126.4, 125.9 (2C), 75.5, 56.3, 43.3, 38.0, 28.4.



^{1}H NMR (400 MHz, $CDCl_3$) (*anti*) δ 7.45–7.01 (m, 9H), 5.07 (d, *J* = 8.4 Hz, 1H), 4.62–4.56 (m, 1H), 3.50–3.46 (m, 1H), 3.19–3.10 (m, 2H), 2.91–2.79 (m, 1H), 2.48 (ddd, *J* = 14.9, 8.4, 2.6 Hz, 1H), 2.20–2.18 (m, 1H);

^{13}C NMR (101 MHz, $CDCl_3$) (*anti*) δ 144.9, 135.9, 134.6, 129.5, 128.4 (2C), 127.1, 126.7, 126.6, 126.1, 125.6 (2C), 71.2, 53.7, 42.8, 40.7, 28.7.


NH
OH
Ph
f1 (ppm)


NH
OH
Ph
f1 (ppm)