Electronic Supplementary Information (ESI)

Bifunctional organic sponge photocatalyst for efficient cross-dehydrogenative coupling of tertiary amines to ketones

*Teng Zhang, Weiwei Liang, Yuxing Huang, Xingrong Li, Yizhen Liu, Bo Yang, Chuanxin He, Xuechang Zhou and Junmin Zhang**

College of Chemistry and Environmental Engineering, Shenzhen University, Shenzhen, 518060, P. R. China

E-mail: zhangjm@szu.edu.cn

Index of Contents

I. General Information

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Varian 400 (400 MHz) spectrometers. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00) or chloroform (δ = 7.26, singlet). ^{1}H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets); m (multiplets), and etc. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Varian 400 (100 MHz) spectrometers.

Commercially available materials purchased from Aladdin or Sigma-Aldrich were used as received. The amino acids (protected or free) were obtained from GL Biochem Ltd. (Shanghai, China). The organic solvents were commercially available and were distilled before application. Elemental analysis is performed by MikroLab Kolbe, Mülheim an der Ruhr, Germany. The isolated yields were obtained from Biotage medium pressure liquid chromatography (MPLC). High resolution mass spectral analysis (HRMS) was performed AB SEIX TOF/TOF™ 5800 System. Infrared (IR) spectra were recorded on a FT-IR spectrometer. Surface-enhanced visible absorption spectrum was conducted by Pekin Elmer instrument with an internally illuminated integrating sphere. The determination of enantiomeric excess was performed via chiral phase HPLC analysis using Thermo U-3000 HPLC workstation with an AS-H column or OD-H column. SEM images were measured and analyzed on a scanning electron microscope (Hitachi S-3400N). TLC measurements were performed on silica gel GF254 plates. Compounds were visualized by irradiation with UV light or by treatment with 0.05 g/ml ninhydrin in ethanol or potassium iodide reagent. All of the photocatalytic reactions were conducted using a green light-emitting diode (LED belt, 12 W) as the visible-light source.

Abbreviations: ACN, acetonitrile; Boc-, tert-butyloxycarbonyl; Boc_2O, di-*tert*-butylpyrocarbonate; CDC, cross-dehydrogenative coupling; DCC, N, N'-dicyclohexylcarbodiimide; DCM, Dichloromethane; DIEA, diisopropylethylamine; DMSO, dimethyl sulfoxide; EA, ethyl acetate; EDC·HCl, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride; DMF, dimethylformamide; Et_3N, triethylamine; EtOH, ethyl alcohol; Fmoc, fluorenylmethoxycarbonyl; HOBt, 1-Hydroxybenzotriazole; HPLC, high performance liquid chromatography; MPLC, medium pressure liquid chromatography; Na_2CO_3, sodium carbonate; $NaHCO_3$, sodium bicarbonate; Nin, ninhydrin; NMM, N-methylmorpholine; NMP, 1-Methyl-2-pyrrolidinone; PDMS, polydimethylsiloxane; PE, petroleum ether; RB, rose bengal; RT, room temperature; SEM, scanning electron microscopy; SPPS, solid pahse peptide synthesis; TAA, TBTU, 2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate; tBu, tert-Butyl; triethylamine; THF, tetrahydrofuran.

II. Preparation of bifunctional organic sponge photocatalyst

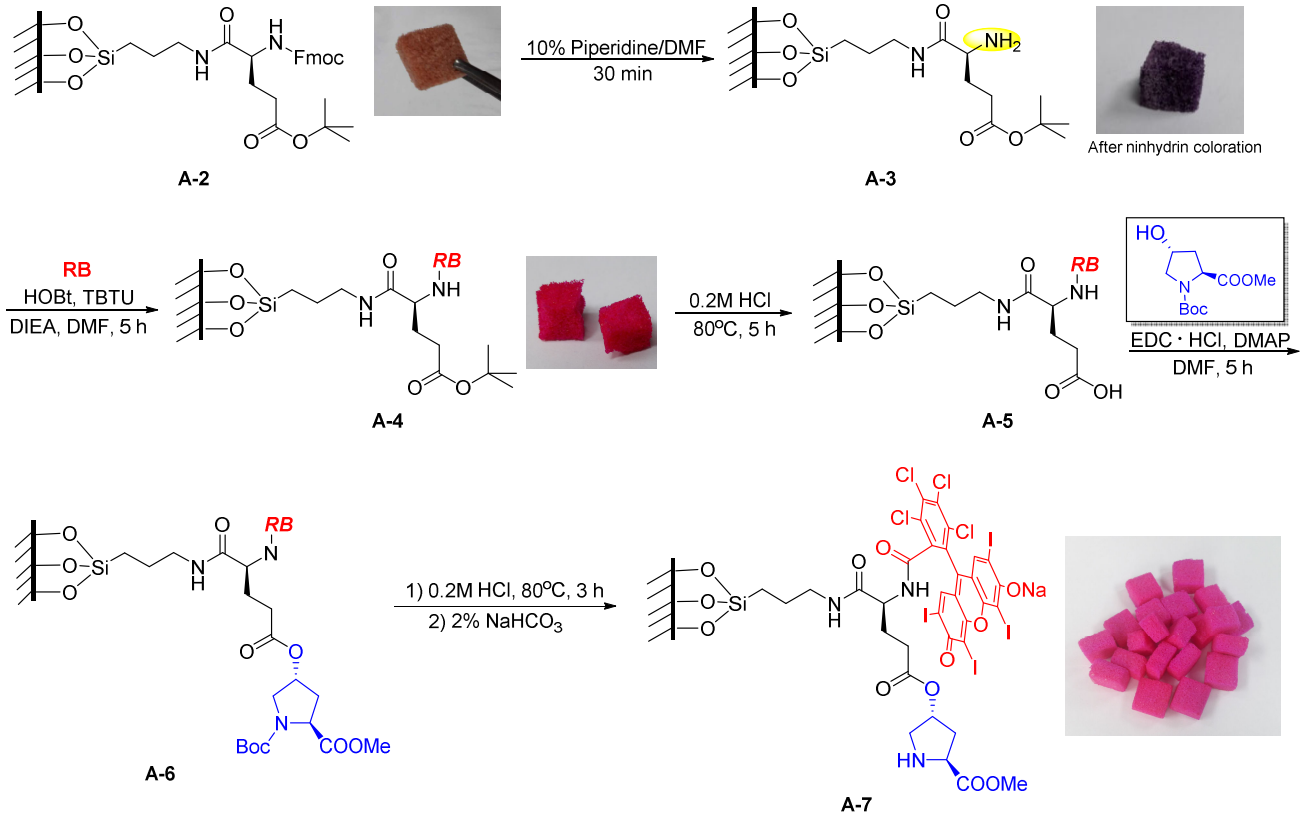
Ⅱ-1. Fabrication of poly(dimethlysiloxane) (PDMS) sponge

PDMS sponges were prepared by our group using sugar cubes as template.[S1] Details as below: PDMS prepolymer and curing agent at a weight ratio of 10:1 (Sylgard 184, Dow Corning Corporation, Midland, MI, USA) were mixed to immerse the cube sugars, followed by degassing in a vacuum for 2 h. The mixture infiltrated into the sugar cubes. After curing at 60 °C atmospheric conditions for 3 h, PDMS on the surface of the sugar template was excised out to expose the sugar. The sugar was then dissolved in water and washed away at 60 °C under stirring. Finally, PDMS sponges were obtained after drying at 60 °C atmospheric conditions for 10 h.

Ⅱ-2. The optimized SPPS of bifunctional organic sponge photocatalyst

The preparation of sponge photocatalyst is based on the technology of polymer surface modification and classic solid-phase peptide synthesis (SPPS), as illustrated in Scheme S1. After air plasma treatment for 7 min to drive the surface of PDMS sponges hydrophilic, sponges (5 g) were then immersed in 200 mL 3-aminopropyltrimethoxysilane/toluene solution (5%, v/v), the mixture was stirred at at RT to allow the reaction of silane molecules with hydroxyl groups, it was easily detected by treatment sponges with 0.05 g/ml ninhydrin in ethanol. After 2 h, sponges were filtered off and washed with EtOH (4×100 mL), then transferred to the vacuum dry oven at 60 ^{o}C for 30min to get **A-1**. Next, **A-1** were immersed in 150 mL dry DMF in ice bath, Fmoc-Glu(OtBu)-OH (2.13 g, 5 mmol), HOBT (1.02 g, 7.5 mmol), TBTU (2.4g, 7.5 mmol) were added in order and DIEA (41.4 μL, 0.25mmol) was dropwise added at last during which time the ice bath expired. Under the protection of nitrogen, the mixture was stirred at RT for another 5 h. After finished the coupling, the sponges were washed with EtOH (3×100 mL) to remove the unreacted materials, dried at vacuum to get **A-2**. Fmoc- group on **A-2** were easily removed by 10% piperidine in DMF (v/v, 100 mL) under stirring at RT for 30 min, following washed with EtOH (5×100 mL) and dried at vacuum to acquired the free **A-3**. By coupling **A-3** with RB (5.0g, 5 mmol) as the same conditions for prepared **A-2**, the product **A-4** were obtained, the unreacted RB was easily removed by washing with water until the water was colorless. **A-4** were then added in 100 mL 0.2 M HCl aqueous and stirred at 80 °C for 5h,[S2,S3] then washed with water and dried at vacuum to get the free **A-5**. After that, **A-5** were immersed in 150 mL dry DMF in ice bath, HO-Boc-Pro-OMe (1.23 g, 5 mmoL),[S4] DMAP (0.03g, 0.25mmol) and EDC·HCl (1.34 g, 7 mmoL) were added respectively. Under the protection of nitrogen, the mixture was stirred at RT for another 5 h. After completed, the sponges were washed with EtOH (3×100 mL) to remove the unreacted materials and dried at vacuum to acquired **A-6**. The Boc- group on **A-6** was easily removed by 0.2 M HCl aqueous as the same conditions for prepared **A-5**,[S5] after washing with 2 % $NaHCO_3$ aqueous (g/100mL, 2×100 mL) and EtOH (1×100 mL), as a result, the final product **A-7** were obtained.

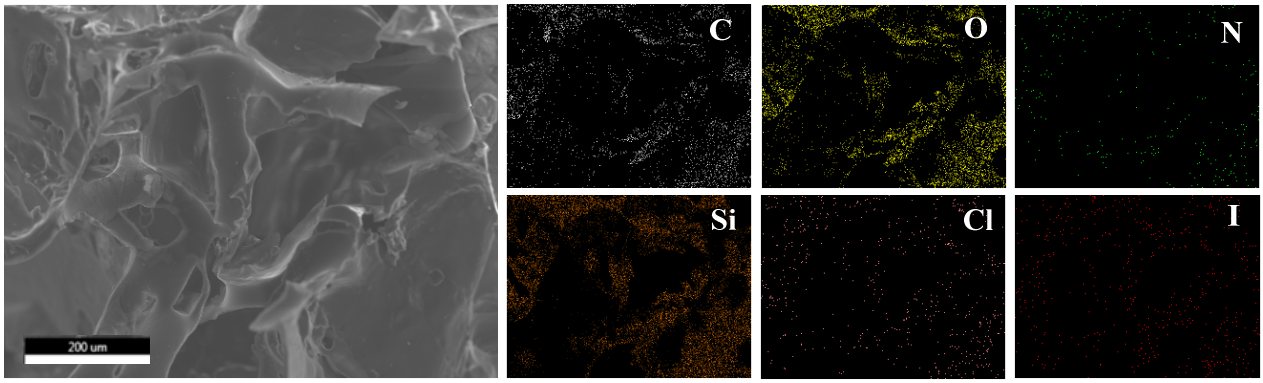
The size of the sponge catalyst is consistent with the sugar cube due to using sugar cube as template, about 10×10×5 mm, 750mg for each piece. In batch reactor, each sponge was divided into smaller pieces to satisfy the different catalytic reaction.



Scheme S1. Preparation of bifunctional organic sponge photocatalyst (**A-7**).

Ⅱ-3. Characterization of bifunctional organic sponge photocatalyst

The morphology of the obtained sponge photocatalyst was characterized by scanning electron microscopy (SEM), which showed that PDMS sponge is a 3D-interconnected porous material (Figure S1a). The corresponding SEM elemental mapping images further proved the homogenous distribution of Si, C, N, O, Cl and I elements throughout the PDMS sponge (Figure S1b). Catalyst loading on PDMS sponge, as determined by elemental analysis via measuring chlorine content in the sponge catalyst, is 0.0176 mmol/g.



(a) (b)

Figure S1. Characterization of bifunctional organic sponge photocatalyst: (a) SEM image and (b) SEM X-ray elemental mapping showing the presence of constituting elements, carbon (C), oxygen (O), nitrogen (N), silicon (Si), chlorine (Cl) and iodine (I). The scale bar represents 200 μm.

We have performed the control experiments to investigate proline's role on the sponge photocatalytic system (*Table S1*). The results showed that without proline moiety on the catalyst (**A-4** and **A-5**) led to 5% and 10% yields respectively; with N-protected proline moiety on the catalyst (**A-6**) gave only 11% yield. In addition, only 19% yield was observed even when **A-4** combined with proline methyl ester. These results indicated that proline moiety on the catalyst (**A-7**) could greatly accelerate the CDC reaction.

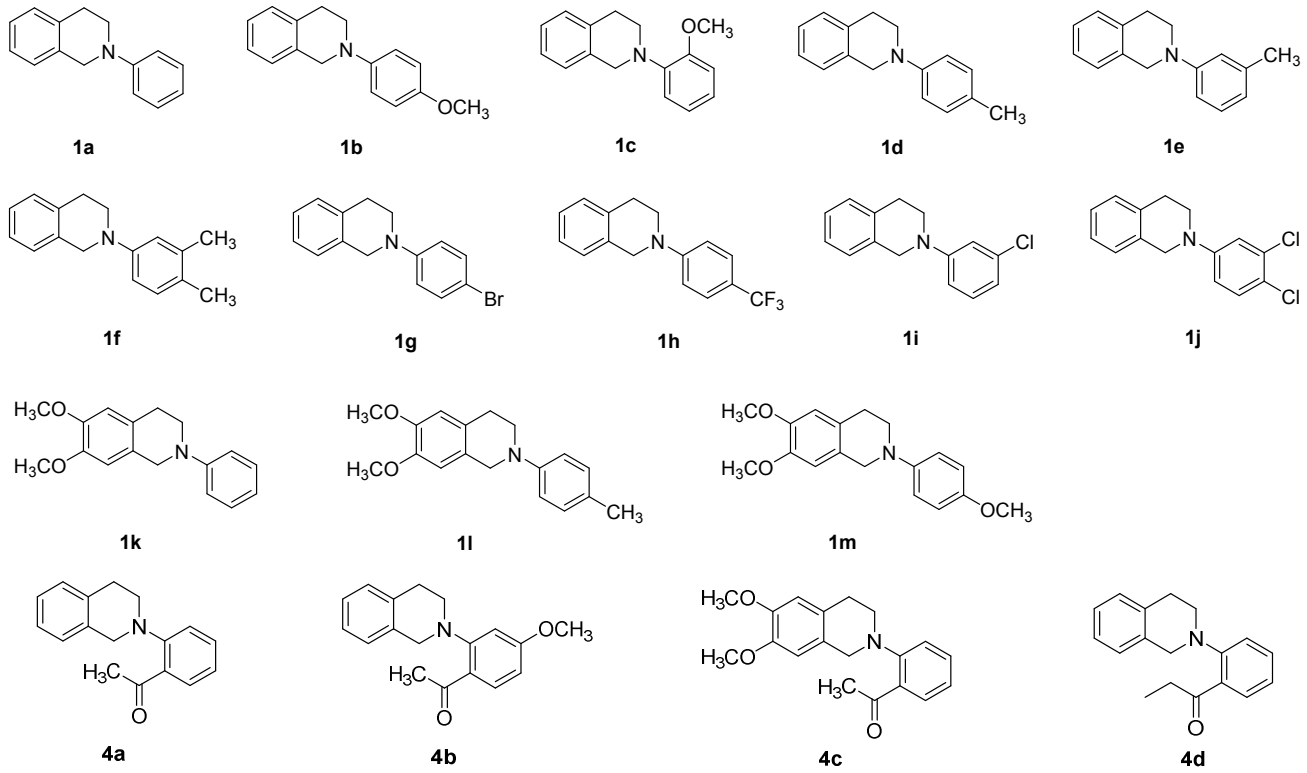
Table S1. Control experiments on the role of proline in the bifunctional sponge photocatalyst.[a]

Entr	x	Solvent	Yield (%)
1	**A-7**	**H_2O**	**95**
2	**A-4**	H_2O	5
3	**A-5**	H_2O	10
4	**A-6**	H_2O	11
5	**A-4/Pro-OMe**	H_2O	19

[a] Reactions were performed using **1a** (0.1 mmol) and **2a** (1.0 mmol) in 2 mL of H_2O and were catalyzed by sponge catalyst at room temperature with a 12 W green LED light for 24 hours. Yield was determined by ^{1}H NMR with 1,3,5-trimethoxybenzene as an internal standard.

III. General procedures

III-1. Synthesis of the substrates

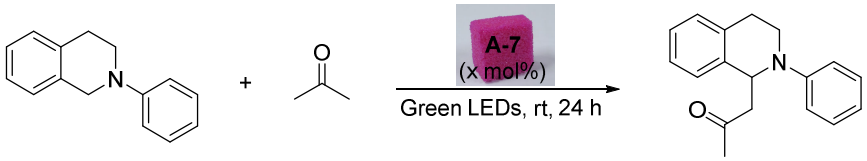


The substrates **1a-m** were synthesized according to literature procedures.[S6] A typical procedure is described as following for the synthesis of **1a**: Copper(I) iodide (200 mg, 1.0 mmol) and potassium phosphate (4.25 g, 20.0 mmol) were added to a Schlenk tube. The tube was evacuated and back filled

with nitrogen. 2-Propanol (10.0 mL), ethylene glycol (1.11 mL, 20.0 mmol), 1,2,3,4-tetrahydro-isoquinoline (2.00 g, 15 mmol) and Iodobenzene (1.11 mL, 10.0 mmol) were added successively via a micro-syringe at room temperature. The reaction mixture was heated at 85-90 °C and kept for 24 h and then allowed to cool to room temperature. Diethyl ether (20 mL) and water (20 mL) were then added. The aqueous layer was extracted by diethyl ether (2×20 mL). The combined organic phases were washed with brine and dried over magnesium sulfate. The solvent was removed via rotary evaporation, and the remaining residue was purified via MPLC (PE/EA, 2%-10%) to give the desired product **1a** with 95% yield. **1b-1m** were also synthesized according to the similar method.

Substrate **4a-b** were prepared by adopting reported procedures,[S7] A typical procedure is described as following for the synthesis of **4a**: To a solution of potassium carbonate (1.58 g, 11.5 mmol) in DMF (10 mL), 1,2,3,4-tetrahydro isoquinoline (1.53 g, 11.5 mmol) and 1-(2-fluorophenyl) ethanone (1.38 g, 10 mmol) were added. The reaction mixture were stirred at 140 °C for 12 h. After the completion of the reaction as shown by TLC, water (50 mL) was used to dilute the reaction. The organic layer was extracted with ethyl acetate (3×30 mL), the combined organic layer was washed with saturated NH_4Cl (2×30 mL), dried over anhydrous magnesium sulfate and concentrated in vacuum. The crude product was purified via MPLC (PE/EA, 2%-20%) to give the desired product **4a** with 89% yields. **4b-4d** were also synthesized according to the similar method.

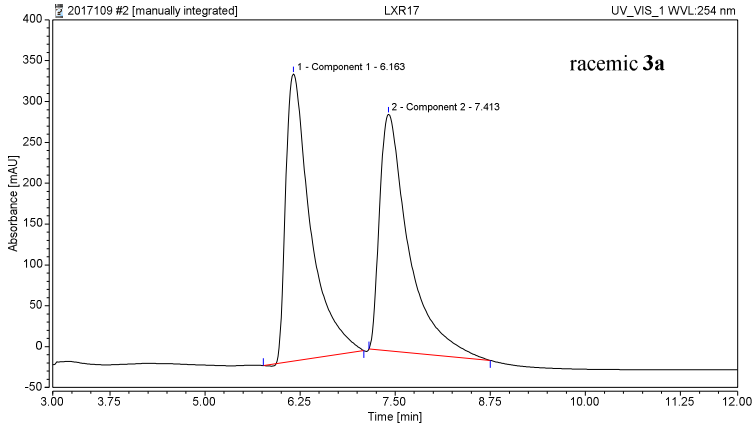
III-2. General reaction conditions for sponge photocatalytic CDC reactions



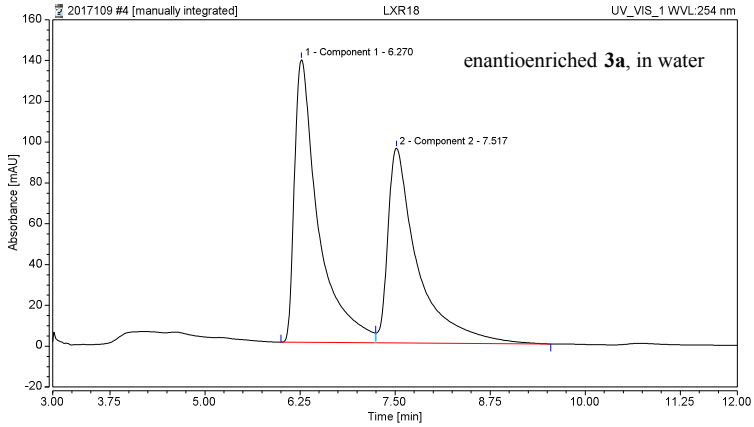
1a **2a** **3a**

Generally, N-phenyl-tetrahydroisoquinoline **1a** (20.9 mg, 0.1 mmol), acetone **2a** (74.04 μL, 1.0 mmol), sponge photocatalyst (x mol%) and solvent (2 mL) were added to a 10 mL test tube, the mixture was then stirred at RT with the irradiation of a 12 W green LED light. After 24 h, the sponge photocatalyst was filtered off and washed with EtOH (3×5 mL). All solvents were combined together and evaporated to get crude product. The reaction yield was determined by ^1H NMR with 1,3,5-trimethoxybenzene as an internal standard. The isolated yield was obtained by MPLC (PE/EA, 2%-10%). The enantiomeric excess of **3a** was determined by chiral HPLC analysis on an AS-H column (*n*-Hexane/*i*PrOH = 90/10, flow rate 1.0 mL/min, 254nm) and the result is 7.4%, as follows:

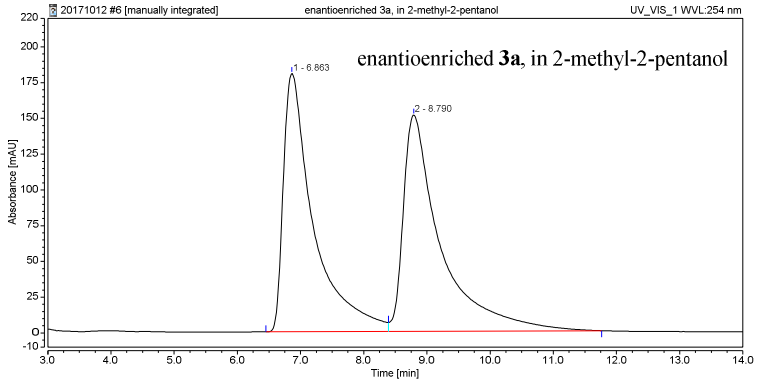
HPLC chromatogram: racemic + enantioenriched (**3a**)



No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	Component 1	6.163	133.360	351.356	50.90	54.85	n.a.
2	Component 2	7.413	128.650	289.202	49.10	45.15	n.a.
Total:			**262.010**	**640.558**	**100.00**	**100.00**	



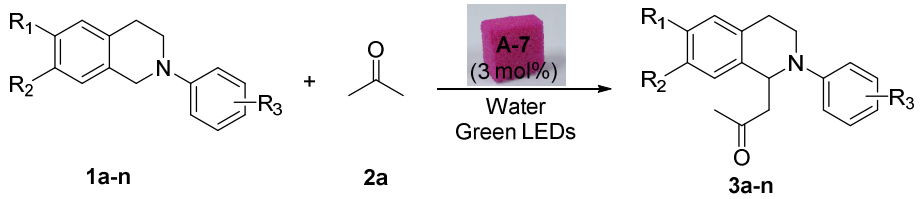
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1	Component 1	6.270	50.222	138.502	53.71	59.20	n.a.
2	Component 2	7.517	43.282	95.466	46.29	40.80	n.a.
Total:			**93.504**	**233.968**	**100.00**	**100.00**	



No.	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1	6.863	99.672	180.564	49.08	54.42	n.a.
2	8.790	103.414	151.251	50.92	45.58	n.a.
Total:		**203.086**	**331.815**	**100.00**	**100.00**	

III-3. Substrate scope for CDC reactions via bifunctional organic sponge photocatalysis

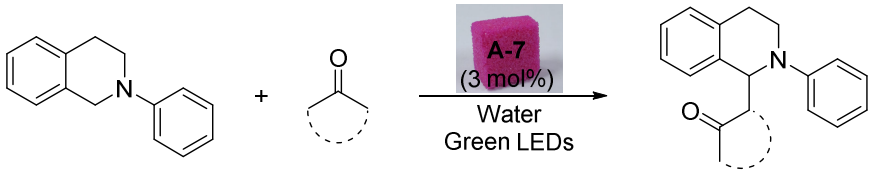
CDC reaction of N-phenyl-tetrahydroisoquinoline derivatives and acetone:



1a-n **2a** **3a-n**

Generally, N-phenyl-tetrahydroisoquinoline **1a-n** (0.5 mmol), acetone **2a** (370.0 μL, 5.0 mmol) and sponge photocatalyst (850 mg, 3 mol%) were added in 5 mL H_2O, the mixture was then stirred at RT or 50 °C with the irradiation of a 12 W green LED light. After finished the reaction (monitored by TLC), the sponge was filtered off and washed with EA (3×10 mL). The aqueous layer was discarded, organic phases were combined together and removed via rotary evaporation, the remaining residue was purified via MPLC (PE/EA, 2%-10%) to give the desired product.

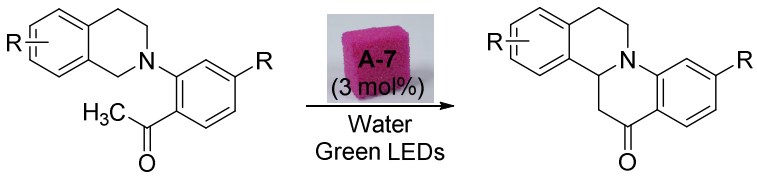
CDC reaction of N-phenyl-tetrahydroisoquinoline and varying ketones:



1a **2b-i** **3o-3v**

Generally, N-phenyl-tetrahydroisoquinoline **1a** (104.5 mg, 0.5 mmol), ketones **2b-i** (5.0 mmol) and sponge photocatalyst (850 mg, 3 mol%) were mixed in H_2O (5 mL), the mixture was then stirred at RT or 50 °C with the irradiation of a 12 W green LED light. The reaction was monitored by TLC, the post-treatment is the same as above.

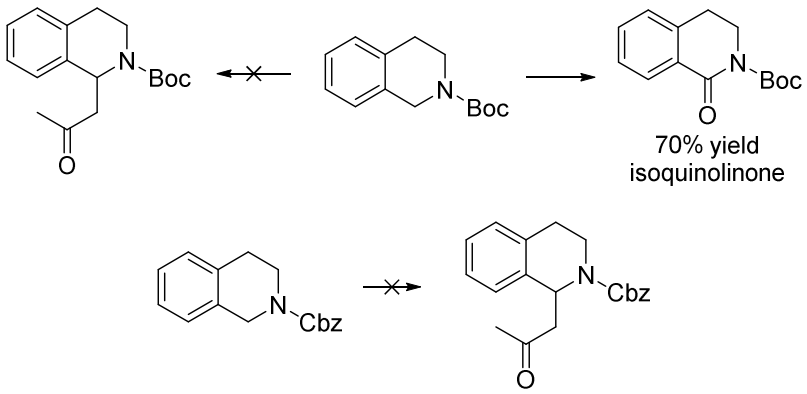
Intermolecular CDC reaction of N-phenyl-tetrahydroisoquinoline derivatives and acetone:



4a-d **5a-d**

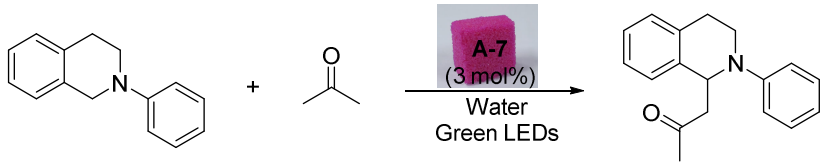
Generally, N-phenyl-tetrahydroisoquinoline derivatives **4a-d** (0.5 mmol) and sponge photocatalyst (850 mg, 3 mol%) were added in 5 mL H_2O and then stirred at RT with the irradiation of a 12 W green LED light. The reaction was monitored by TLC, the post-treatment is the same as above.

Other unsuccessful examples for organic sponge photocatalysis

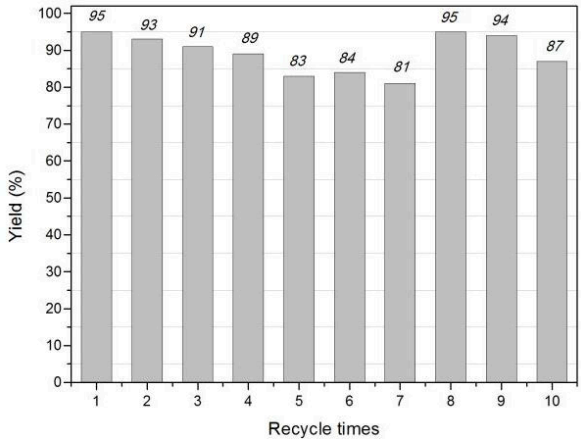


There was no desired product formed for N-Boc and N-Cbz THIQs. For N-Boc protected THIQ as substrate, the oxidized by-product (isoquinolinone) was found with 70% isolate yield. This result indicated that the sponge photocatalyst may not be efficient for this type of substrates.

III-4. Recycling and reuse of bifunctional organic sponge photocatalyst

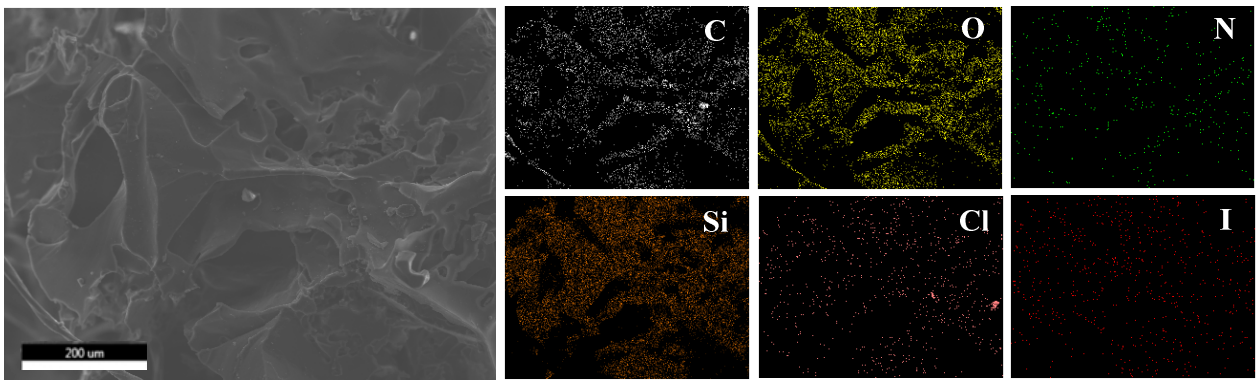


PDMS sponge photocatalyst was recovered as follows: To a 10 mL test tube equipped with a magnetic stir bar was charged with N-phenyl-tetrahydroisoquinoline **1a** (20.9 mg, 0.1 mmol), acetone **2a** (74.04 μL, 1.0 mmol), sponge photocatalyst (170 mg, 3 mol%) and 2 mL H_2O. The solution was stirred for 24h with the irradiation of a green LED light. After completion of the catalysis (monitored by TLC), sponge photocatalyst was grabbed out of the mixture and washed with EtOH (3×5 mL). The combined liquids were concentrated, the resulting residue was dried and determined by ^{1}H NMR with 1,3,5-trimethoxybenzene as an internal standard to get the reaction yield. Sponge photocatalyst was recovered by low temperature drying, ready for another run. Cycle time 1-7 were performed at room temperature, cycle time 8-10 were performed at 50 ^{o}C.



The SEM results showed that there was a slight break on the surface of PDMS sponge, so that catalyst deactivation after a long time of soaking and stirring in reaction mixture (Wate/EtOH/Acetone). When the scale bar was 200 μm, the corresponding elemental mapping

images still proved the homogenous distribution of Si, C, N, O, Cl and I elements throughout the material.



(a) (b)

Figure S2. Characterization of sponge photocatalyst after recycling: (a) SEM image and (b) SEM X-ray elemental mapping showing the presence of constituting elements, carbon (C), oxygen (O), nitrogen (N), silicon (Si), chlorine (Cl) and iodine (I). The scale bar represents 200 μm.

III-5. Gram scale reaction between N-phenyl tetrahydroisoquinoline and acetone

A circulating flow reactor was built up by connecting a peristaltic pump with a glass column (1×30 cm) filled with sponge photocatalyst (8.15 g, 3 mol%). N-phenyl tetrahydroisoquinoline (1.0 g, 4.78 mmol) was added into the glass column before the system was tightly sealed. A green LED belt was wrapped around the column (7×30 cm) for irradiation. The peristaltic pump was then started and the solvents of acetone (3.7 mL, 47.8 mmol) and H_2O (50 mL) was left for running (note: the up outlet of silicone tube connecting with peristaltic pump was immersed into the reaction solution). After 36 h the reaction was stopped (monitored by TLC), the product was isolated by MPLC (PE/EA, 2%-10%) and the yield was 91.0% (1.16 g).

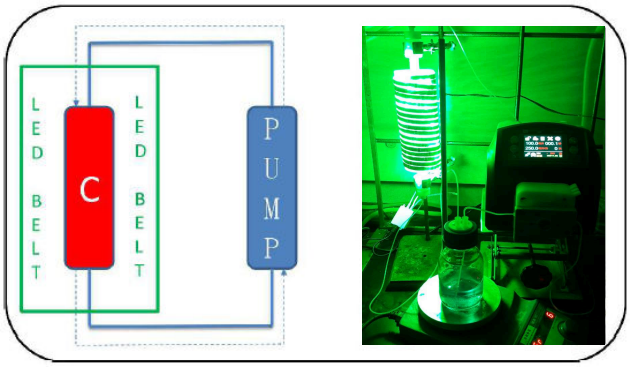
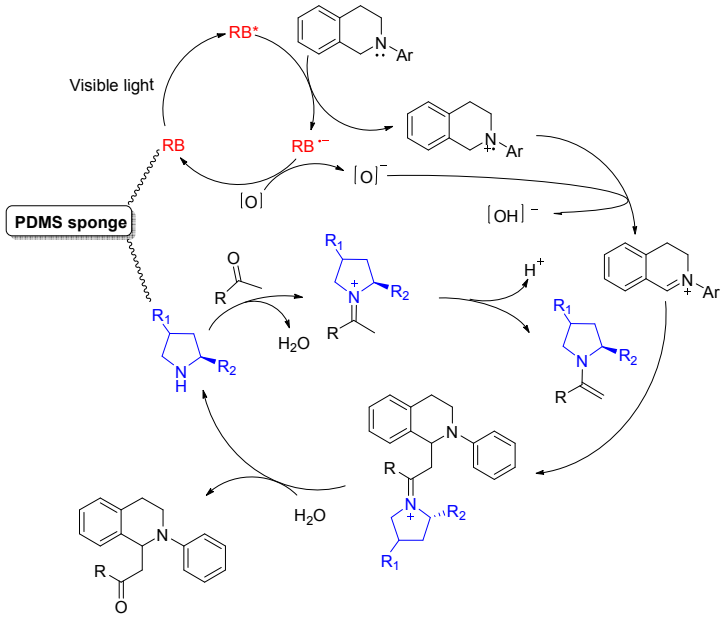


Figure S3. Schematic illustration of the circulating flow reactor and the picture of the setup, C stands for a glass column filled with bifunctional organic sponge photocatalyst.

III-6. Cooperative photocatalytic mechanism

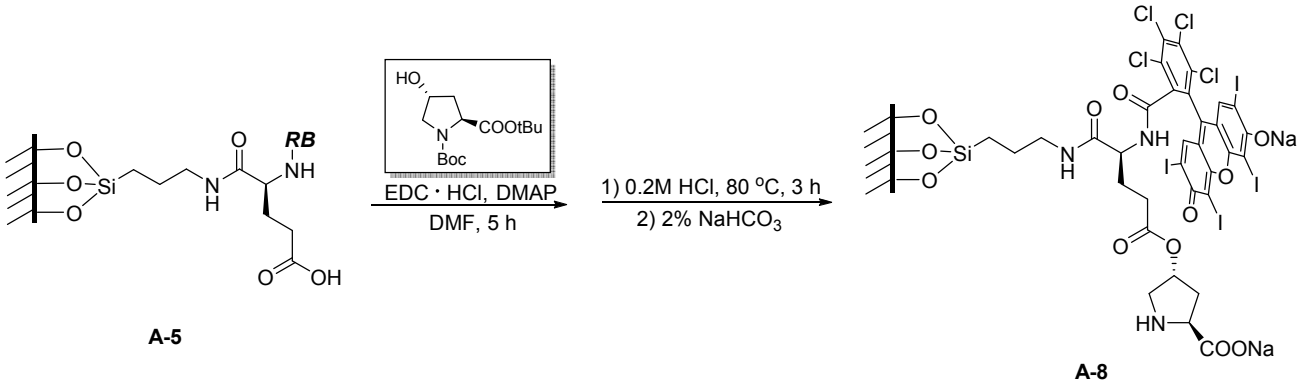
A plausible mechanism for this cooperative photocatalysis is illustrated in Scheme S2. In this catalytic system, it choose rose bengal (RB) as photocatalyst and proline as the enamine catalyst, in which tertiaryamine was directly converted into iminium and ketone was activated results in the formation of an enamine intermediate at the same time.



Scheme S2. Proposed mechanism of the cooperative catalytic CDC reaction mediated by bifunctional organic sponge photocatalyst.

III-7. Preliminary study on asymmetric CDC reactions

Synthesis of chiral bifunctional sponge photocatalyst (A-8):

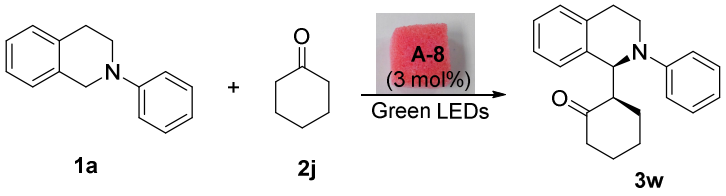


Scheme S3. Preparation of chiral bifunctional sponge photocatalyst (**A-8**).

A-5 were immersed in 150 mL dry DMF in ice bath, HO-Boc-Pro-O*t*Bu (1.44 g, 5 mmoL),[S4] DMAP (0.03g, 0.25mmol) and EDC·HCl (1.34 g, 7 mmoL) were added respectively. Under the protection of nitrogen, the mixture was stirred at RT for 5 h. Then, the sponges were washed with EtOH (3×100 mL) to remove the unreacted materials and dried at vacuum. After removed the Boc- and O*t*Bu groups with 0.2 M HCl aqueous at 80°C, the sponge photocatalyst was washed with 2 % $NaHCO_3$ aqueous (g/100mL, 2×100 mL) and EtOH (1×100 mL) to get the final product **A-8**.

Optimization of reaction conditions for asymmetric CDC reactions:

Table S2. Optimization of reaction conditions for asymmetric CDC reactions.[a]

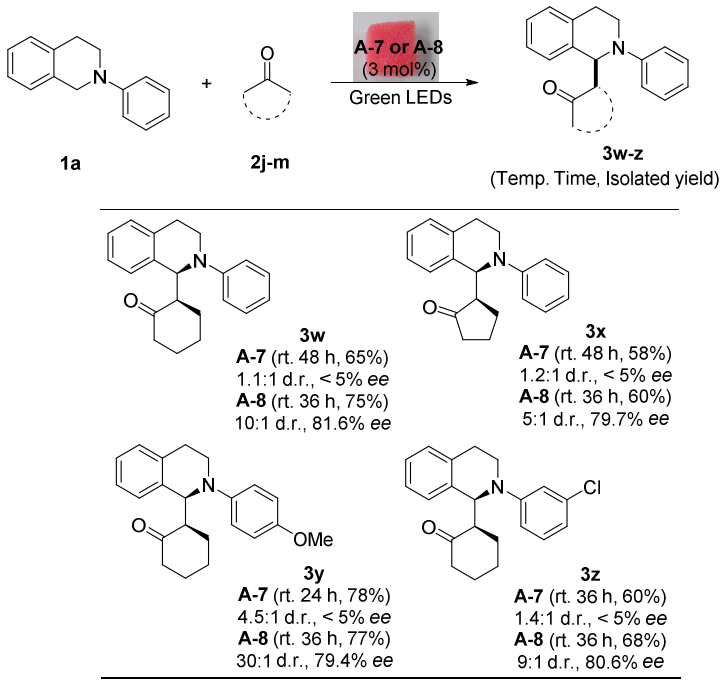


Entry	Solvent	Yield [%][b]	d.r.[c]	ee [%][d]
1	DMF	58	4.7 : 1	47.3
2	DCM	68	7.6 : 1	64.7
3	ACN	72	6.8 : 1	50.2
4	MeOH	45	3.5 : 1	31.7
5	**2-Methyl-2-pentanol**	**83**	**10 : 1**	**81.6**
6	H_2O	50	2 : 1	< 5

[a] Performed using **1a** (0.1 mmol) and **2j-m** (1.0 mmol) in 2 mL solvent catalyzed by 3 mol% chiral sponge catalyst **A-8** at room temperature with 12 W green LED light for 24 hours. [b] Determined by ^{1}H NMR with 1, 3, 5-trimethoxybenzene as internal standard. [c] The diastereomeric ratio, anti/syn, was determined by ^{1}HNMR analysis. [d] *D*etermined by chiral HPLC analysis.

The optimal solvent is 2-methyl-2-pentanol rather than water in asymmetric transformation. the reason may be concerned with the difference of hydrophobic and hydrophilic performance of catalysts and the substrates: a) the structure of catalyst is different as A-7 containing a carboxylic acid methyl ester is more hydrophobic, while A-8 containing a free carboxylic acid sodium salt is more hydrophilic; b) the substrate of ketone is different, for the asymmetric transformations cyclic ketone is generally more hydrophobic substrates, while acetone substrate in racemic reactions is hydrophilic. Based the different reaction system, the obtained results are different between them.

Asymmetric CDC reactions of N-phenyl-tetrahydroisoquinoline derivatives and ketones:



Generally, N-phenyl-tetrahydroisoquinoline **1a** (104.5 mg, 0.5 mmol), ketones **2j-m** (5.0 mmol) and chiral sponge photocatalyst (3 mol%) were mixed in 2-methyl-2-pentanol (3 mL), the mixture was then stirred at RT with the irradiation of a 12 W green LED light. After finished the reaction (monitored by TLC), the sponge was filtered off and washed with 2-methyl-2-pentanol (3×5 mL). The organic phases were combined together and removed via rotary evaporation. The remaining residue was purified via MPLC (PE/EA, 2%-10%) to give the desired product.

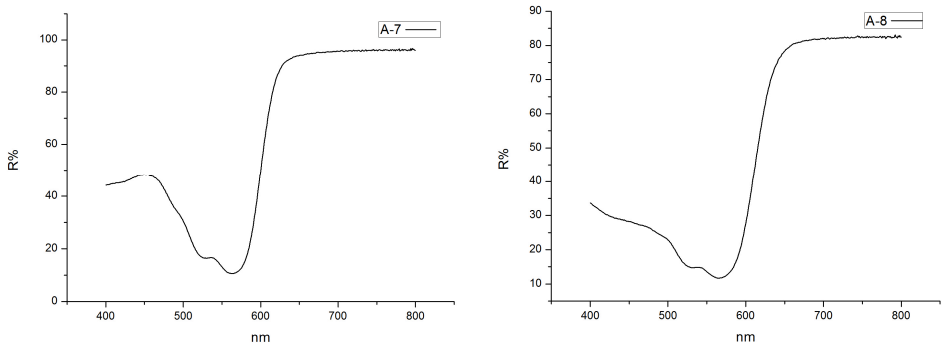
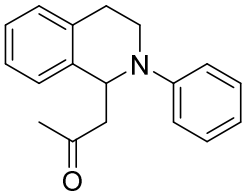


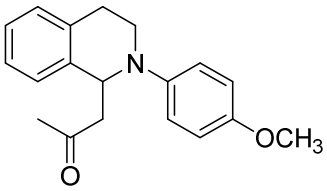
Figure S3. Visible absorption spectrum for photocatalysts **A-7** and **A-8**.

IV. ^{1}H and ^{13}C NMR data of substrates and products



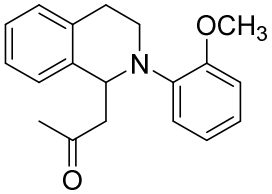
3a

1-(1,2,3,4-tetrahydro-2-phenyl-1-isoquinolinyl)-2-propanone (3a), known compound[S8,S10] : Yield 95%. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (t, *J* = 8.0 Hz, 2H), 7.14 – 7.00 (m, 4H), 6.87 (d, *J* = 8.2 Hz, 2H), 6.71 (t, *J* = 7.2 Hz, 1H), 5.34 (t, *J* = 6.3 Hz, 1H), 3.69 – 3.52 (m, 1H), 3.52 – 3.40 (m, 1H), 2.99 (dt, *J* = 11.2, 5.3 Hz, 2H), 2.83 – 2.66 (m, 2H), 2.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.26, 148.88, 138.28, 134.44, 129.35, 128.69, 126.84, 126.28, 118.27, 114.78, 54.80, 50.21, 42.07, 31.10, 27.22.



3b

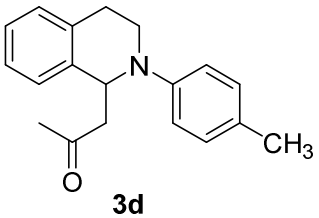
1-[1,2,3,4-tetrahydro-2-(4-methoxyphenyl)-1-isoquinolinyl]-2-propanone (3b), known compound[S8,S10] : Yield 87%. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (s, 4H), 6.91 (d, *J* = 8.9 Hz, 2H), 6.81 (d, *J* = 9.0 Hz, 2H), 5.24 (t, *J* = 6.3 Hz, 1H), 3.75 (s, 3H), 3.61 – 3.51 (m, 1H), 3.50 – 3.39 (m, 1H), 3.00 (dt, *J* = 13.0, 6.2 Hz, 2H), 2.81 – 2.68 (m, 2H), 2.06 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.31, 153.25, 143.64, 138.22, 134.26, 128.88, 126.74, 126.57, 126.12, 118.35, 114.59, 55.92, 55.55, 49.92, 42.84, 30.80, 26.70.



3c

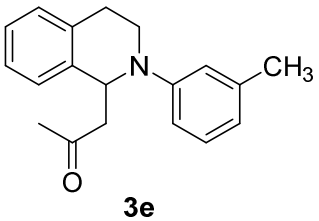
1-[1,2,3,4-tetrahydro-2-(2-methoxyphenyl)-1-isoquinolinyl]-2-propanone (3c): Yield 81%. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, *J* = 4.0 Hz, 3H), 7.01 (d, *J* = 4.2 Hz, 1H), 6.90 (d, *J* = 7.3 Hz, 1H), 6.76 (dd, *J* = 14.4, 7.3 Hz, 3H), 5.31 (t, *J* = 6.1 Hz, 1H), 3.84 (s, 3H), 3.47 – 3.41 (m, 2H), 2.98 (dd, *J* = 15.5, 6.9 Hz, 2H), 2.73 – 2.63 (m, 2H), 1.96 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.47, 152.99, 139.72, 138.82, 134.28, 129.06, 126.83, 126.32, 126.02,

123.37, 121.42, 120.72, 111.78, 55.61, 55.41–55.27, 49.83, 42.91, 30.46, 27.40. HRMS (ESI) *m/z*: calcd for $C_{19}H_{22}NO_2^+$ $[M+H]^+$: 296.1645, found: 296.1641. IR (KBr, cm^{-1}): 2918, 2846, 2358, 2335, 1234, 1107, 746.



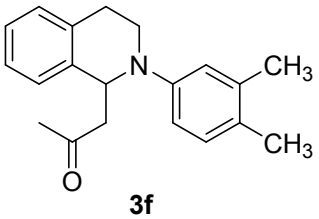
3d

1-[1,2,3,4-tetrahydro-2-(4-methylphenyl)-1-isoquinolinyl]-2-propanone (3d), known compound[S9,S10] : Yield 95%. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (s, 4H), 7.06 (d, *J* = 8.2 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.35 (t, *J* = 6.3 Hz, 1H), 3.70 – 3.58 (m, 1H), 3.49 (ddd, *J* = 34.6, 19.3, 14.5 Hz, 1H), 3.04 (dd, *J* = 15.9, 6.3 Hz, 2H), 2.86 – 2.72 (m, 2H), 2.26 (s, 3H), 2.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.41, 146.88, 138.28, 134.39, 129.82, 128.79, 127.96, 126.76, 126.18, 115.67, 55.16, 50.06, 42.18, 31.01, 26.98, 20.33.



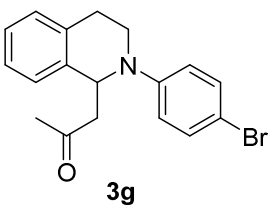
3e

1-[1,2,3,4-tetrahydro-2-(3-methylphenyl)-1-isoquinolinyl]-2-propanone (3e): Yield 92%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (dd, *J* = 12.9, 5.0 Hz, 5H), 6.77 (d, *J* = 8.1 Hz, 2H), 6.63 (d, *J* = 7.2 Hz, 1H), 5.41 (t, *J* = 6.3 Hz, 1H), 3.73 – 3.59 (m, 1H), 3.59 – 3.44 (m, 1H), 3.16 – 2.96 (m, 2H), 2.83 (dt, *J* = 16.0, 5.2 Hz, 2H), 2.33 (s, 3H), 2.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.33, 148.96, 139.01, 138.32, 134.46, 129.19, 128.68, 126.81, 126.23, 119.23, 115.62, 111.98, 54.84, 50.20, 42.05, 31.11, 27.24, 21.92. HRMS (ESI) *m/z*: calcd for $C_{19}H_{22}NO^+$ $[M+H]^+$: 280.1696, found: 280.1693. IR (KBr, cm^{-1}): 2922, 2850, 2358, 1708, 1597, 1485, 1098, 941, 758.



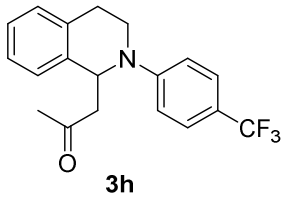
3f

1-[1,2,3,4-tetrahydro-2-(3,4-dimethylphenyl)-1-isoquinolinyl]-2-propanone (3f): Yield 88%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, *J* = 10.5 Hz, 4H), 7.00 (d, *J* = 8.2 Hz, 1H), 6.77 (s, 1H), 6.70 (dd, *J* = 8.1, 2.2 Hz, 1H), 5.34 (t, *J* = 6.3 Hz, 1H), 3.73 – 3.57 (m, 1H), 3.57 – 3.40 (m, 1H), 3.04 (ddd, *J* = 16.0, 10.2, 5.8 Hz, 2H), 2.78 (ddd, *J* = 12.4, 9.5, 5.5 Hz, 2H), 2.23 (s, 3H), 2.17 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.39, 147.28, 138.32, 137.26, 134.41, 130.30, 128.77, 126.82, 126.62, 126.12, 117.27, 113.08, 55.13, 50.05, 42.13, 30.98, 26.99, 20.28, 18.64. HRMS (ESI) *m/z*: calcd for $C_{20}H_{24}NO^+$ $[M+H]^+$: 294.1852, found: 294.1843. IR (KBr, cm^{-1}): 2922, 2850, 2358, 1603, 1111, 941, 796.



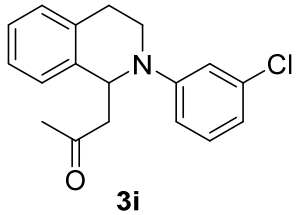
3g

1-[1,2,3,4-tetrahydro-2-(4-bromophenyl)-1-isoquinolinyl]-2-propanone (3g), known compound[S9,S10] : Yield 81%. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, *J* = 12.3 Hz, 2H), 7.16 (t, *J* = 5.2 Hz, 4H), 6.81 (d, *J* = 8.9 Hz, 2H), 5.35 (t, *J* = 6.2 Hz, 1H), 3.65 – 3.55 (m, 1H), 3.55 – 3.44 (m, 1H), 3.10 – 2.97 (m, 2H), 2.89 – 2.76 (m, 2H), 2.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.00, 147.79, 137.88, 134.18, 132.01, 128.67, 126.88, 126.40, 116.10, 110.05, 54.62, 50.11, 42.12, 31.13, 27.03.



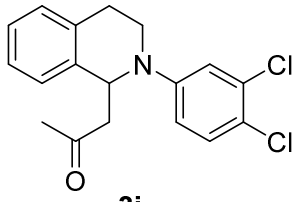
3h

1-[1,2,3,4-tetrahydro-2-(4-trifluoromethylphenyl)-1-isoquinolinyl]-2-propanone (3h), known compound[S10,S10] : Yield 79%. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.7 Hz, 2H), 7.24 – 7.12 (m, 4H), 6.95 (d, *J* = 8.7 Hz, 2H), 5.48 (dd, *J* = 7.3, 5.1 Hz, 1H), 3.69 – 3.54 (m, 2H), 3.13 – 3.00 (m, 2H), 2.91 (ddd, *J* = 16.8, 11.7, 6.9 Hz, 2H), 2.10 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.78, 150.63, 137.77, 134.20, 128.51, 127.19, 126.66, 125.09, 112.48, 54.11, 50.14, 42.16, 31.17, 27.38.



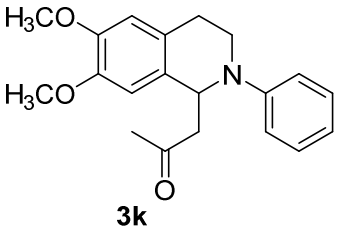
3i

1-[1,2,3,4-tetrahydro-2-(3-chlorophenyl)-1-isoquinolinyl]-2-propanone (3i): Yield 85%. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.09 (m, 6H), 6.86 (d, *J* = 9.0 Hz, 2H), 5.35 (t, *J* = 6.3 Hz, 1H), 3.60 (dt, *J* = 10.9, 5.4 Hz, 1H), 3.56 – 3.45 (m, 1H), 3.03 (dd, *J* = 16.4, 5.7 Hz, 2H), 2.90 – 2.73 (m, 2H), 2.02 (d, *J* = 51.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.04, 147.45, 137.91, 134.19, 129.11, 128.71, 126.87, 126.39, 122.92, 115.78, 54.76 , 50.12, 42.18, 31.12, 27.00. HRMS (ESI) *m/z*: calcd for $C_{18}H_{19}ClNO^+$ $[M+H]^+$: 300.1150, found: 300.1147. IR (KBr, cm^{-1}): 2916, 2850, 2358, 1715, 1492, 1104, 927, 817, 758.



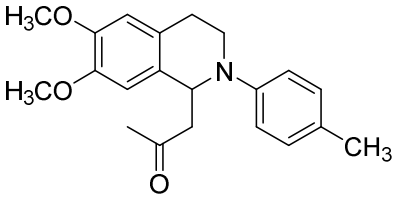
3j

1-[1,2,3,4-tetrahydro-2-(3,4-dichlorophenyl)-1-isoquinolinyl]-2-propanone (3j): Yield 82%. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 – 7.12 (m, 1H), 7.12 – 6.99 (m, 4H), 6.89 (d, *J* = 2.9 Hz, 1H), 6.69 (dd, *J* = 9.0, 2.9 Hz, 1H), 5.24 (t, *J* = 6.2 Hz, 1H), 3.52 – 3.36 (m, 2H), 3.01 – 2.87 (m, 2H), 2.80 – 2.70 (m, 2H), 2.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.66, 148.18, 137.57, 134.02, 132.90, 130.61, 128.66, 127.13, 126.77, 126.52, 120.44, 115.38, 113.66, 54.52, 50.12, 42.19 , 31.14, 27.00. HRMS (ESI) *m/z*: calcd for $C_{18}H_{18}Cl_2NO^+$ $[M+H]^+$: 334.0760, found: 334.0756. IR (KBr, cm^{-1}): 2925, 2851, 2365, 1703, 1596, 1481, 1130, 799.



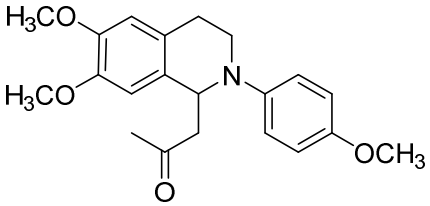
3k

1-(1,2,3,4-tetrahydro-6,7-dimethoxy-2-phenyl-1-isoquinolinyl)-2-propanone (3k), known compound[S9] **:** Yield 77%. White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.18 (m, 2H), 6.93 (d, *J* = 8.2 Hz, 2H), 6.79 (d, *J* = 7.3 Hz, 1H), 6.69 (s, 1H), 6.61 (s, 1H), 5.30 (t, *J* = 6.3 Hz, 1H), 3.84 (d, *J* = 3.9 Hz, 6H), 3.71 – 3.62 (m, 1H), 3.55 – 3.44 (m, 1H), 3.09 – 2.91 (m, 2H), 2.82 (dd, *J* = 16.3, 6.9 Hz, 1H), 2.70 (dt, *J* = 15.9, 4.3 Hz, 1H), 2.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.51, 143.80, 142.57, 142.18, 124.94, 124.11, 121.06, 113.22, 109.93, 106.11, 104.53, 50.72, 49.38, 44.94, 36.78 , 25.99, 21.39.



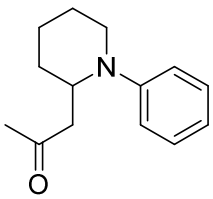
3l

1-(1,2,3,4-tetrahydro-6,7-dimethoxy-2-(4-methylphenyl)-1-isoquinolinyl)-2-propanone (3l): Yield 75%. Pale purplish oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, *J* = 7.3 Hz, 2H), 6.85 (d, *J* = 6.9 Hz, 2H), 6.68 (s, 1H), 6.59 (s, 1H), 5.23 (t, *J* = 6.1 Hz, 1H), 3.84 (s, 6H), 3.63 (d, *J* = 12.8 Hz, 1H), 3.51 – 3.38 (m, 1H), 2.97 (ddd, *J* = 15.7, 13.0, 5.5 Hz, 2H), 2.79 (dd, *J* = 16.2, 5.3 Hz, 1H), 2.63 (dd, *J* = 17.6, 9.3 Hz, 1H), 2.24 (s, 3H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.81, 147.72, 147.35, 147.01, 130.14, 129.78, 128.13, 126.24, 116.02, 114.02, 111.38, 109.68, 55.90, 54.96, 49.98, 42.12, 31.09, 26.37, 20.33. HRMS (ESI) *m/z*: calcd for $C_{21}H_{26}NO_3^+$ $[M+H]^+$: 340.1907, found: 340.1900. IR (KBr, cm^{-1}): 2969, 2922, 2850, 2358, 2312, 1092, 796.



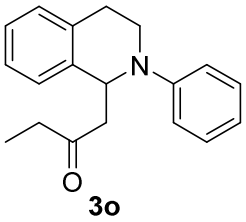
3m

1-(1,2,3,4-tetrahydro-6,7-dimethoxy-2-(4-methoxylphenyl)-1-isoquinolinyl)-2-propanone (3m), known compound[S11] **:** Yield 70%. White oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89 (d, *J* = 9.0 Hz, 1H), 6.81 (dd, *J* = 13.4, 6.5 Hz, 3H), 6.65 (s, 1H), 6.57 (s, 1H), 5.12 (t, *J* = 6.3 Hz, 1H), 4.00 (d, *J* = 4.5 Hz, 1H), 3.94 – 3.88 (m, 1H), 3.82 (s, 6H), 3.73 (s, 3H), 3.59 – 3.48 (m, 1H), 3.46 – 3.37 (m, 1H), 3.04 – 2.93 (m, 1H), 2.74 (dd, *J* = 16.1, 6.2 Hz, 1H), 2.06 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.83, 153.33, 147.71, 147.39, 143.74, 130.05, 126.17, 118.67, 115.54, 114.59, 111.45, 109.57, 69.89, 61.46, 49.85, 42.82, 30.95, 26.09.



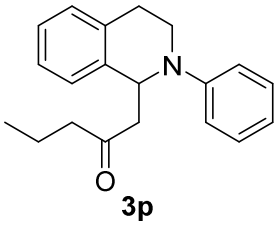
3n

1-(1-phenyl-2-piperidinyl)-2-propanone (3n), known compound[S12] **:** Yield 40%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (dd, *J* = 10.4, 5.0 Hz, 2H), 6.93 (d, *J* = 6.7 Hz, 2H), 6.83 (s, 1H), 4.35 (s, 1H), 3.32 (dd, *J* = 12.4, 3.9 Hz, 1H), 2.88 (d, *J* = 10.5 Hz, 1H), 2.72 (dd, *J* = 16.2, 9.6 Hz, 1H), 2.46 (dd, *J* = 16.3, 3.1 Hz, 1H), 2.05 (s, 3H), 1.93 – 1.83 (m, 1H), 1.75 (s, 1H), 1.61 (t, *J* = 14.0 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.03, 150.40, 129.22, 119.46, 117.09, 52.01, 44.71, 41.54, 30.69, 28.88, 25.54, 19.39.



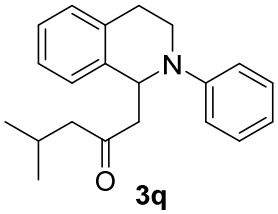
3o

1-(1,2,3,4-tetrahydro-2-phenyl-1-isoquinolinyl)-2-butanone (3o), known compound[S8] **:** Yield 85%. Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (dd, *J* = 8.1, 7.5 Hz, 2H), 7.19 (d, *J* = 11.4 Hz, 4H), 6.96 (d, *J* = 8.2 Hz, 2H), 6.80 (t, *J* = 7.1 Hz, 1H), 5.45 (t, *J* = 6.3 Hz, 1H), 3.73 – 3.62 (m, 1H), 3.60 – 3.49 (m, 1H), 3.07 (ddd, *J* = 15.7, 11.0, 4.5 Hz, 2H), 2.84 (ddd, *J* = 23.3, 12.8, 5.9 Hz, 2H), 2.46 – 2.21 (m, 2H), 1.01 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ δ 210.00, 148.85, 138.37, 134.46, 129.36, 128.67, 126.83, 126.25, 118.11, 114.58, 55.10, 48.95, 41.93, 37.29, 27.29, 7.54.



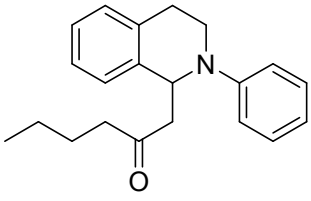
3p

1-(1,2,3,4-tetrahydro-2-phenyl-1-isoquinolinyl)-2-pentanone (3p), known compound[S8] **:** Yield 79%. Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (dd, *J* = 8.7, 7.3 Hz, 2H), 7.19 – 7.07 (m, 4H), 6.94 (d, *J* = 8.1 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 5.42 (t, *J* = 6.3 Hz, 1H), 3.70 – 3.59 (m, 1H), 3.58 – 3.45 (m, 1H), 3.10 – 2.96 (m, 2H), 2.88 – 2.70 (m, 2H), 2.36 – 2.16 (m, 2H), 1.52 (dt, *J* = 14.7, 7.3 Hz, 2H), 0.83 (t, *J* = 7.4 Hz, 3H). ^{1}H NMR (400 MHz, $CDCl_3$) δ 209.47, 148.82, 138.42, 134.40, 129.30, 128.59, 126.86, 126.73, 126.21, 118.07, 114.56, 54.88, 49.25, 45.98, 41.95, 27.29, 16.92, 13.62.



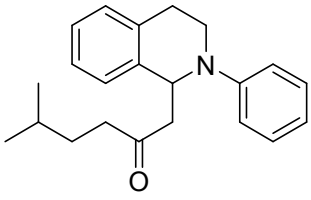
3q

4-methyl-1-(1,2,3,4-tetrahydro-2-phenyl-1-isoquinolinyl)-2-pentanone (3q), known compound[S8] **:** Yield 72%. Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.8 Hz, 2H), 7.14 (d, *J* = 4.3 Hz, 4H), 6.93 (d, *J* = 8.3 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 5.43 (t, *J* = 6.2 Hz, 1H), 3.64 (dt, *J* = 11.0, 5.3 Hz, 1H), 3.57 – 3.45 (m, 1H), 3.07 – 2.96 (m, 2H), 2.88 – 2.70 (m, 2H), 2.26 – 2.13 (m, 2H), 2.08 (dt, *J* = 19.8, 6.6 Hz, 1H), 0.84 (dd, *J* = 6.4, 2.9 Hz, 6H). ^{1}H NMR (400 MHz, $CDCl_3$) δ 209.15, 148.83, 138.48, 134.38, 129.30, 128.58, 126.88, 126.72, 126.21, 118.06, 114.57, 54.68, 53.03, 49.73, 42.01, 27.32, 24.37, 22.51.



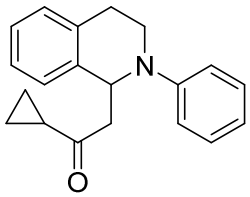
3r

1-(1,2,3,4-tetrahydro-2-phenyl-1-isoquinolinyl)-2-hexanone (3r), known compound[S8] **:** Yield 65%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.2 Hz, 2H), 7.14 (s, 4H), 6.94 (d, *J* = 8.0 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 5.42 (t, *J* = 6.2 Hz, 1H), 3.71 – 3.59 (m, 1H), 3.58 – 3.47 (m, 1H), 3.09 – 2.97 (m, 2H), 2.81 (ddd, *J* = 23.2, 12.8, 5.9 Hz, 2H), 2.37 – 2.18 (m, 2H), 1.46 (dd, *J* = 15.4, 7.5 Hz, 2H), 1.23 (dd, *J* = 15.6, 8.1 Hz, 2H), 0.84 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.60, 148.82, 138.41, 134.39, 129.30, 128.59, 126.79, 126.21, 118.07, 114.57, 54.89, 49.23, 43.79, 41.97, 27.31, 25.54, 22.18, 13.79.



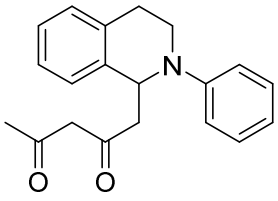
3s

5-methyl-1-(1,2,3,4-tetrahydro-2-phenyl-1-isoquinolinyl)-2-hexanone (3s), known compound[S8] **:** Yield 76%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (dd, *J* = 11.6, 4.2 Hz, 2H), 7.15 (s, 4H), 6.94 (d, *J* = 8.2 Hz, 2H), 6.77 (t, *J* = 7.2 Hz, 1H), 5.43 (t, *J* = 6.3 Hz, 1H), 3.64 (dd, *J* = 11.9, 6.0 Hz, 1H), 3.58 – 3.45 (m, 1H), 3.06 (ddd, *J* = 21.2, 9.9, 5.5 Hz, 2H), 2.82 (ddd, *J* = 23.6, 12.9, 5.9 Hz, 2H), 2.38 – 2.16 (m, 2H), 1.51 – 1.43 (m, 1H), 1.39 (dd, *J* = 14.4, 7.0 Hz, 2H), 0.82 (d, *J* = 6.3 Hz, 6H). ^{1}H NMR (400 MHz, $CDCl_3$) δ 209.72, 148.83, 138.41, 134.41, 129.31, 128.60, 126.86, 126.74, 126.22, 118.09, 114.59, 54.91, 49.24, 42.10, 41.98, 32.21, 27.53, 27.34, 22.28.



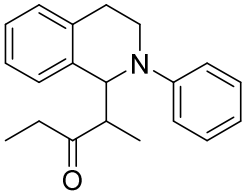
3t

1-cyclopropyl-2-(1,2,3,4-tetrahydro-2-phenyl-1-isoquinolinyl)-ethanone (3t), known compound[S8] **:** Yield 83%. Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (t, *J* = 7.9 Hz, 2H), 7.09 (d, *J* = 10.4 Hz, 4H), 6.90 (d, *J* = 8.4 Hz, 2H), 6.71 (t, *J* = 7.2 Hz, 1H), 5.48 – 5.31 (m, 1H), 3.59 (dd, *J* = 11.8, 6.1 Hz, 1H), 3.55 – 3.42 (m, 1H), 3.15 – 2.95 (m, 2H), 2.93 – 2.69 (m, 2H), 1.81 – 1.65 (m, 1H), 0.95 (t, *J* = 4.0 Hz, 2H), 0.80 – 0.63 (m, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 209.17, 148.87, 138.46, 134.48, 129.33, 128.60, 127.01, 126.78, 126.20, 117.99, 114.54, 54.86, 49.90, 42.03, 27.48, 21.56, 11.04.



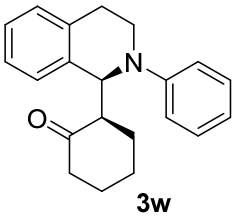
3u

1-(1,2,3,4-tetrahydro-2-phenyl-1-isoquinolinyl)-acetylacetone (3u), known compound[S8] **:** Yield 87%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, *J* = 7.3 Hz, 2H), 7.07 (d, *J* = 15.8 Hz, 4H), 6.92 (d, *J* = 7.9 Hz, 2H), 6.71 (d, *J* = 7.0 Hz, 1H), 5.29 – 5.20 (m, 1H), 3.57 (dd, *J* = 11.6, 5.9 Hz, 1H), 3.53 – 3.43 (m, 1H), 3.00 (dd, *J* = 15.2, 7.5 Hz, 1H), 2.87 (dd, *J* = 14.2, 5.7 Hz, 1H), 2.79 (d, *J* = 16.1 Hz, 1H), 2.51 (dd, *J* = 14.1, 7.2 Hz, 1H), 1.91 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.81, 190.51, 148.95, 137.69, 134.52, 129.35, 128.61, 127.15–126.75, 126.05, 118.05, 114.44, 101.57, 56.56, 44.86 , 41.67, 27.35, 25.02.



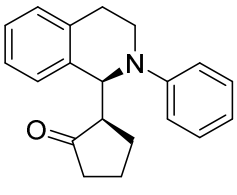
3v

2-(1,2,3,4-tetrahydro-2-phenyl-1-isoquinolinyl)-3-pentanone (3v), known compound[S8] **:** Yield 68%. White solid. Diastereomeric ratio = 5:1. ^{1}H NMR (major isomer, 400 MHz, $CDCl_3$) δ 7.19 (dd, *J* = 13.8, 6.5 Hz, 2H), 7.13 (dd, *J* = 10.8, 4.9 Hz, 4H), 6.92 (d, *J* = 8.1 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 4.91 (d, *J* = 9.3 Hz, 1H), 3.86 – 3.74 (m, 1H), 3.70 – 3.63 (m, 1H), 3.14 (dt, *J* = 13.9, 6.9 Hz, 1H), 3.08 – 2.99 (m, 1H), 2.97 – 2.84 (dt, *J* = 16.5, 4.7 Hz, 1H), 2.51 – 2.40 (m, 2H), 1.11 (d, *J* = 7.0 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (major isomer, 100 MHz, $CDCl_3$) δ 213.98, 149.43, 135.68, 134.90, 129.06, 128.37, 127.05, 125.35, 118.64, 115.64, 61.39, 51.26, 42.39, 34.92, 25.83, 15.36, 7.65.



3w

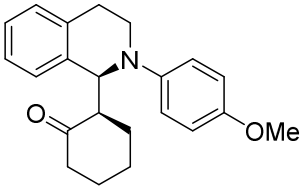
(*R*)-2-((*S*)-2-phenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)cyclohexanone (3w), known compound[S13] **:** Yield 75%. White solid. Syn/anti = 1:10. Isolated major isomer, enantiomeric excess: 81.6%, using an AS-H column (*n*-Hexane/*i*PrOH = 96/4, flow rate 0.8 mL/min, 25 °C, 254nm). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (dt, *J* = 10.5, 7.5 Hz, 3H), 7.12 (dd, *J* = 16.0, 5.2 Hz, 3H), 6.91 (d, *J* = 8.0 Hz, 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 5.61 (d, *J* = 4.2 Hz, 1H), 3.77 – 3.65 (m, 1H), 3.65 – 3.51 (m, 1H), 3.05 – 2.91 (m, 1H), 2.85 (ddd, *J* = 16.5, 10.1, 4.7 Hz, 2H), 2.46 (dd, *J* = 12.2, 7.3 Hz, 1H), 2.29 (dd, *J* = 14.4, 9.2 Hz, 1H), 1.95 – 1.78 (m, 2H), 1.66 (dd, *J* = 19.6, 10.2 Hz, 2H), 1.41 (dd, *J* = 19.9, 10.1 Hz, 1H), 1.27 (d, *J* = 9.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.84, 149.20, 135.94, 135.03, 129.25, 128.63, 127.91, 126.63, 125.75, 118.12, 114.89, 56.48, 54.95, 42.59, 41.35, 30.16, 27.27, 23.79.



3x

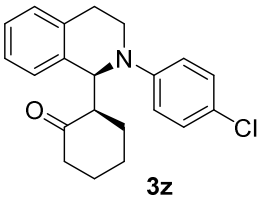
(*R*)-2-((*S*)-2-phenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)cyclopentanone (3x), known compound[S13] **:** Yield 60%. White solid. Syn/anti = 1:5. Isolated major isomer, enantiomeric excess: 79.7%, using an OD-H column (*n*-Hexane/*i*PrOH = 99/1, flow rate 1.0 mL/min, 25 °C, 254nm). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.23 (m, mixture of isomers), 7.19 – 7.14 (m, mixture of isomers), 7.13 – 7.06 (m, mixture of isomers), 7.04 (d, *J* = 8.2 Hz, 2H, major isomer), 6.95 (d, *J* = 7.6 Hz, 1H, major isomer), 6.81 (m, mixture of isomers), 5.63 (s, 1H, major isomer), 3.60 – 3.49 (m, 2H, major isomer), 3.10 – 2.93 (m, 2H, major isomer), 2.80 – 2.71 (m, 1H, major isomer), 2.30 (dd, *J* = 17.0, 7.7 Hz, 1H,

major isomer), 2.14 – 2.05 (m, 1H, major isomer), 1.91 – 1.79 (m, 1H, major isomer), 1.71 – 1.58 (m, 2H, major isomer), 1.30 (qd, *J* = 12.0, 6.0 Hz, 1H, major isomer). ^{13}C NMR (major isomer, 100 MHz, $CDCl_3$) δ 220.27, 148.51, 135.40, 129.45, 128.22, 126.92, 126.65, 126.37, 117.76 , 113.62, 57.52, 54.53, 42.53, 38.42, 28.86, 25.90, 20.63.



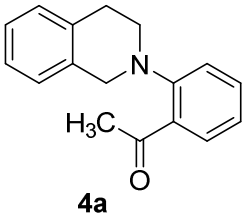
3y

(*R*)-2-((*S*)-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)cyclohexanone (3y), known compound[S13,S14] **:** Yield 77%. Yellow oil. Syn/anti = 1:30. Isolated major isomer, enantiomeric excess: 79.4%, using an AS-H column (*n*-Hexane/*i*PrOH = 96/4, flow rate 0.8 mL/min, 25 °C, 254nm). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 5.4 Hz, 3H), 7.11 (s, 1H), 6.90 (d, *J* = 8.3 Hz, 2H), 6.79 (d, *J* = 7.9 Hz, 2H), 5.37 (d, *J* = 5.3 Hz, 1H), 3.74 (d, *J* = 1.0 Hz, 3H), 3.71 – 3.61 (m, 1H), 3.49 (dd, *J* = 11.4, 6.4 Hz, 1H), 2.98 – 2.82 (m, 2H), 2.77 (d, *J* = 16.5 Hz, 1H), 2.45 (dd, *J* = 12.9, 6.7 Hz, 1H), 2.27 (t, *J* = 11.2 Hz, 1H), 1.90 – 1.82 (m, 2H), 1.75 (dd, *J* = 12.3, 6.9 Hz, 1H), 1.65 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.01, 153.08, 143.96, 136.10, 135.05, 128.89, 127.80, 126.56, 125.62, 118.28, 114.57, 56.37, 55.91, 55.55, 43.89, 41.07, 30.26, 27.50, 26.60, 23.37.



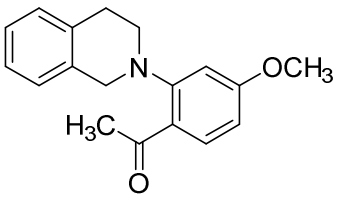
3z

(*R*)-2-((*S*)-2-(4-chlorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)cyclohexanone (3z), known compound[S13, S14] **:** Yield 68%. Yellow oil. Syn/anti= 1:9. Isolated major isomer, enantiomeric excess: 80.6%, using an AS-H column (*n*-Hexane/ *i*PrOH = 96/4, flow rate 0.8 mL/min, 25 °C, 254nm). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (dt, *J* = 12.6, 8.1 Hz, 6H), 6.80 (dd, *J* = 5.7, 3.2 Hz, 2H), 5.53 (d, *J* = 4.1 Hz, 1H), 3.62 (dd, *J* = 8.3, 4.9 Hz, 1H), 3.48 (dd, *J* = 12.8, 4.9 Hz, 1H), 2.99 – 2.86 (m, 1H), 2.80 (dd, *J* = 10.5, 5.1 Hz, 2H), 2.44 – 2.36 (m, 1H), 2.29 (d, *J* = 6.1 Hz, 2H), 1.86 (s, 1H), 1.68 (d, *J* = 3.6 Hz, 2H), 1.60 (d, *J* = 6.9 Hz, 1H), 1.33 (d, *J* = 10.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.95, 211.58, 147.78, 135.46, 134.71, 128.92, 128.63, 127.85, 126.76, 125.78 , 122.66, 115.91, 113.26, 56.26, 55.09, 42.55, 41.91, 41.44, 30.34, 27.28, 27.01, 24.93, 23.95.



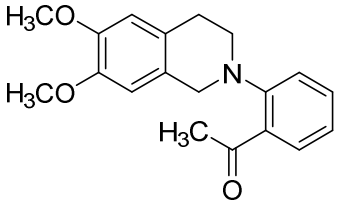
4a

1-[2-(3,4-Dihydro-2(1*H*)-isoquinolinyl)phenyl]ethanone (4a): Yield 88%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.45 – 7.39 (m, 1H), 7.18 (dt, *J* = 13.1, 6.0 Hz, 4H), 7.07 (dd, *J* = 8.9, 6.1 Hz, 2H), 4.22 (s, 2H), 3.36 (t, *J* = 5.8 Hz, 2H), 3.00 (t, *J* = 5.7 Hz, 2H), 2.62 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.27, 151.03, 135.12, 134.33, 134.13, 132.01, 129.36, 128.89, 126.50, 126.29, 126.02 , 122.35, 119.02, 55.03, 51.34, 29.29, 28.94.



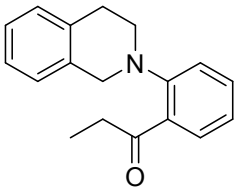
4b

1-[2-(3,4-Dihydro-2(1*H*)-isoquinolinyl)-4-methoxyphenyl]ethanone (4b): Yield 85%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.6 Hz, 1H), 7.15 (dd, *J* = 5.9, 2.8 Hz, 3H), 7.08 – 7.03 (m, 1H), 6.63 (d, *J* = 2.3 Hz, 1H), 6.55 (dd, *J* = 8.6, 2.3 Hz, 1H), 4.18 (s, 2H), 3.80 (s, 3H), 3.33 (t, *J* = 5.8 Hz, 2H), 3.00 (t, *J* = 5.7 Hz, 2H), 2.57 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.61, 163.04, 153.51, 134.16, 132.25, 128.83, 126.94, 126.49, 126.23, 125.98, 106.34, 105.20, 55.33, 55.01, 51.25, 28.89.



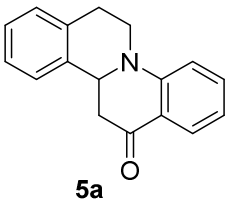
4c

1-[2-(3,4-Dihydro-6,7-dimethoxy-2(1*H*)-isoquinolinyl)phenyl]ethanone (4c): Yield 65%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (ddd, *J* = 15.5, 8.2, 1.2 Hz, 2H), 7.09 (d, *J* = 7.9 Hz, 1H), 7.02 (dd, *J* = 10.8, 4.1 Hz, 1H), 6.62 (s, 1H), 6.54 (s, 1H), 4.10 (s, 2H), 3.83 (d, *J* = 3.6 Hz, 6H), 3.30 (t, *J* = 5.7 Hz, 2H), 2.86 (t, *J* = 5.6 Hz, 2H), 2.58 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.43, 151.01, 147.66, 147.41, 134.98, 131.96, 129.28, 126.00, 122.20, 118.94, 111.49, 108.96, 60.33, 55.87, 54.70, 51.16, 29.16, 28.35, 20.98, 14.16.



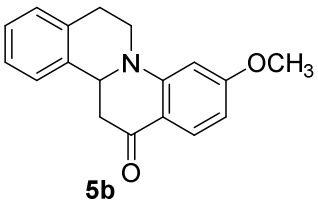
4d

1-[2-(3,4-Dihydro-2(1*H*)-isoquinolinyl)phenyl]-1-propanone (4d) : Yield 70%. Yellow oil. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.47 – 7.36 (m, 2H), 7.19 (t, *J* = 7.2 Hz, 4H), 7.13 – 7.04 (m, 2H), 4.22 (s, 2H), 3.34 (t, *J* = 4.4 Hz, 2H), 3.10 – 2.94 (m, 4H), 1.14 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.22, 150.54, 135.66, 134.41, 134.12, 131.48, 128.91, 126.43, 126.04, 122.58, 119.05, 54.86, 51.43, 34.91, 29.08, 27.00, 8.91.



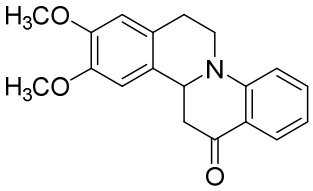
5a

6,7,11b,12-tetrahydro-13*H*-dibenzo[*a*,*f*]quinolizin-13-one (5a), known compound[S7a] **:** Yield 78%. Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.50 – 7.41 (m, 1H), 7.23 (dt, *J* = 15.9, 8.3 Hz, 5H), 7.00 (d, *J* = 8.5 Hz, 1H), 6.82 (t, *J* = 7.4 Hz, 1H), 4.74 (d, *J* = 11.5 Hz, 1H), 4.16 – 4.06 (m, 1H), 3.25 – 3.15 (m, 1H), 3.15 – 3.04 (m, 2H), 2.92 (d, *J* = 15.1 Hz, 1H), 2.80 (dd, *J* = 16.6, 13.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.94, 152.26, 135.51, 133.97, 128.72, 128.35, 126.82, 126.73, 125.66, 120.80, 117.82, 113.20, 57.74, 46.85, 42.35, 29.43.



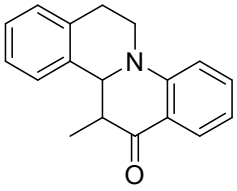
5b

6,7,11b,12-tetrahydro-3-methoxy-13*H*-dibenzo[*a*,*f*]quinolizin-13-one (5b), known compound[S7a] **:** Yield 81%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 9.3 Hz, 1H), 7.30 – 7.14 (m, 4H), 6.41 (d, *J* = 6.5 Hz, 2H), 4.73 (d, *J* = 13.8 Hz, 1H), 4.04 (d, *J* = 11.7 Hz, 1H), 3.87 (s, 3H), 3.22 – 3.09 (m, 2H), 3.03 (dd, *J* = 16.6, 3.0 Hz, 1H), 2.91 (d, *J* = 15.1 Hz, 1H), 2.85 – 2.69 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.56, 165.72, 154.05, 135.58, 133.85, 130.66, 128.66, 126.76, 125.68 , 115.33, 104.90, 97.51, 57.86, 55.38, 46.73, 44.30, 42.36, 29.42.



5c

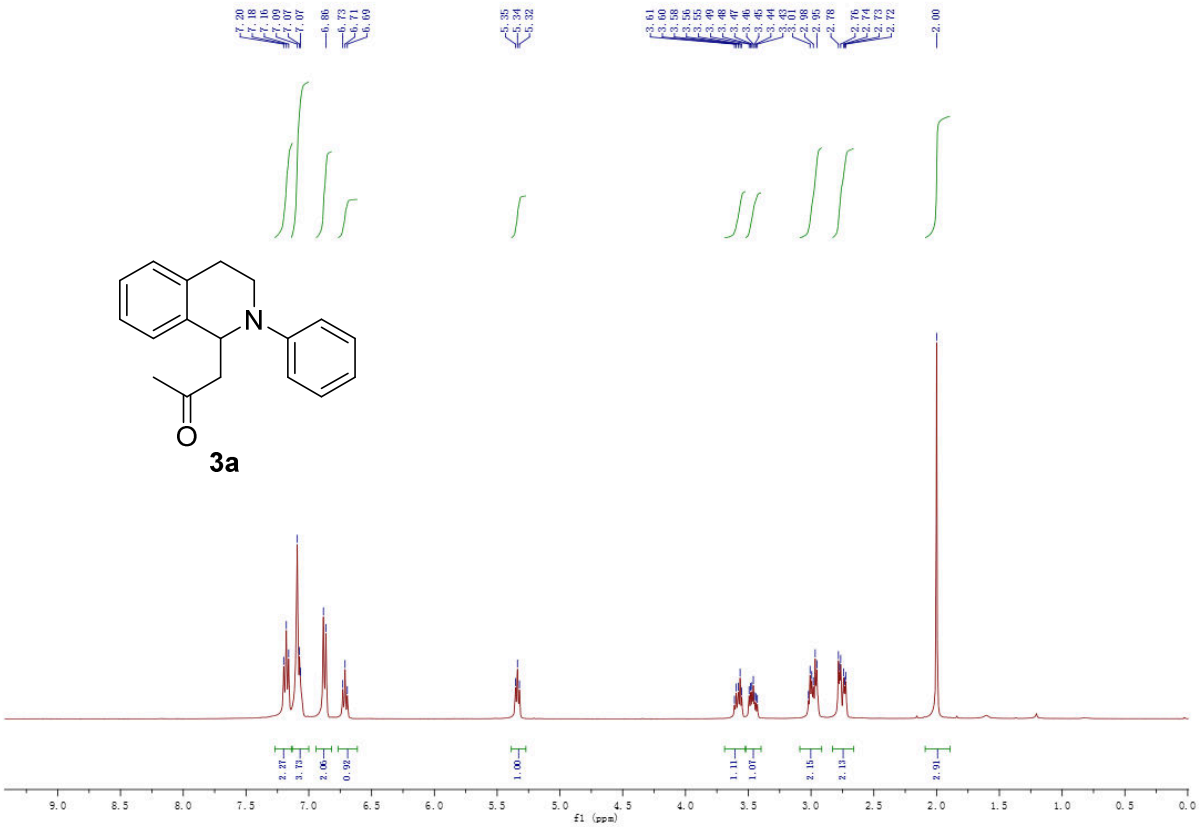
6,7,11b,12-tetrahydro-9,10-dimethoxy-13*H*-dibenzo[*a*,*f*]quinolizin-13-one (5c), known compound[S7a] **:** Yield 68%. Yellow oil. ^{1}H NMR (399 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.49 – 7.40 (m, 1H), 7.00 (d, *J* = 8.6 Hz, 1H), 6.81 (t, *J* = 7.4 Hz, 1H), 6.65 (d, *J* = 9.9 Hz, 2H), 4.64 (d, *J* = 11.7 Hz, 1H), 4.10 (dd, *J* = 12.2, 5.3 Hz, 1H), 3.87 (d, *J* = 4.9 Hz, 6H), 3.13 (s, 1H), 3.10 – 3.00 (m, 2H), 2.86 – 2.69 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.12, 152.34, 147.94, 135.55, 128.28, 127.19, 126.04, 120.70, 117.77, 113.22, 111.22, 108.34, 57.53, 55.96, 47.03, 42.37, 28.90, 14.18.

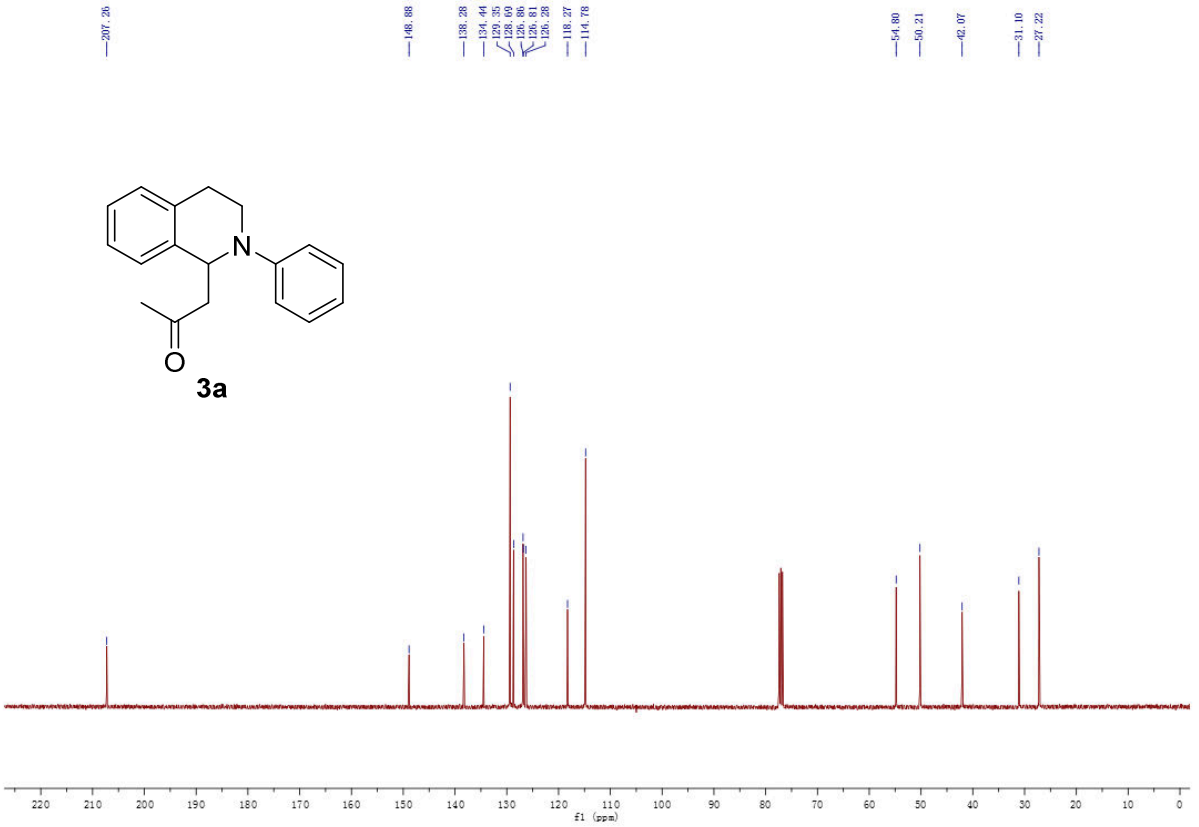


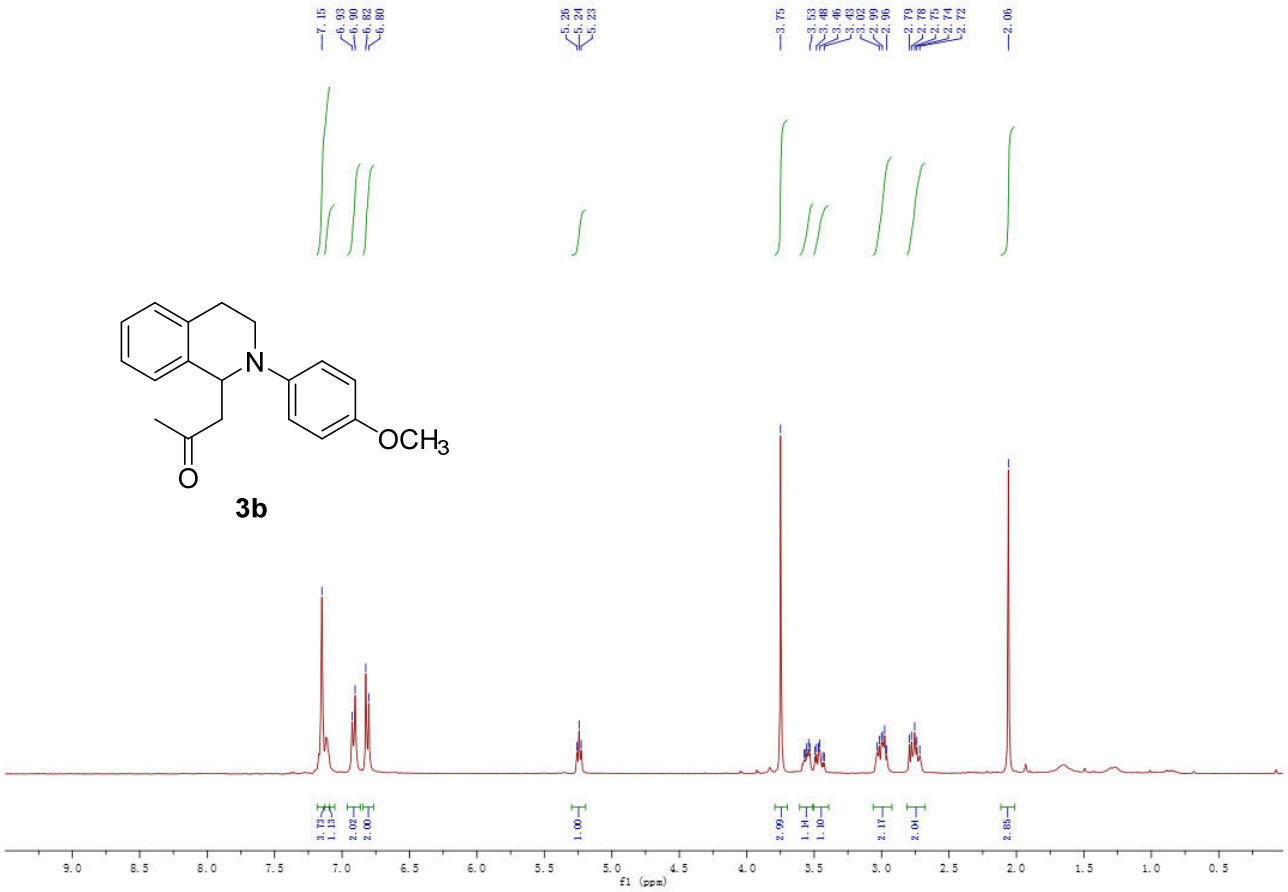
5d

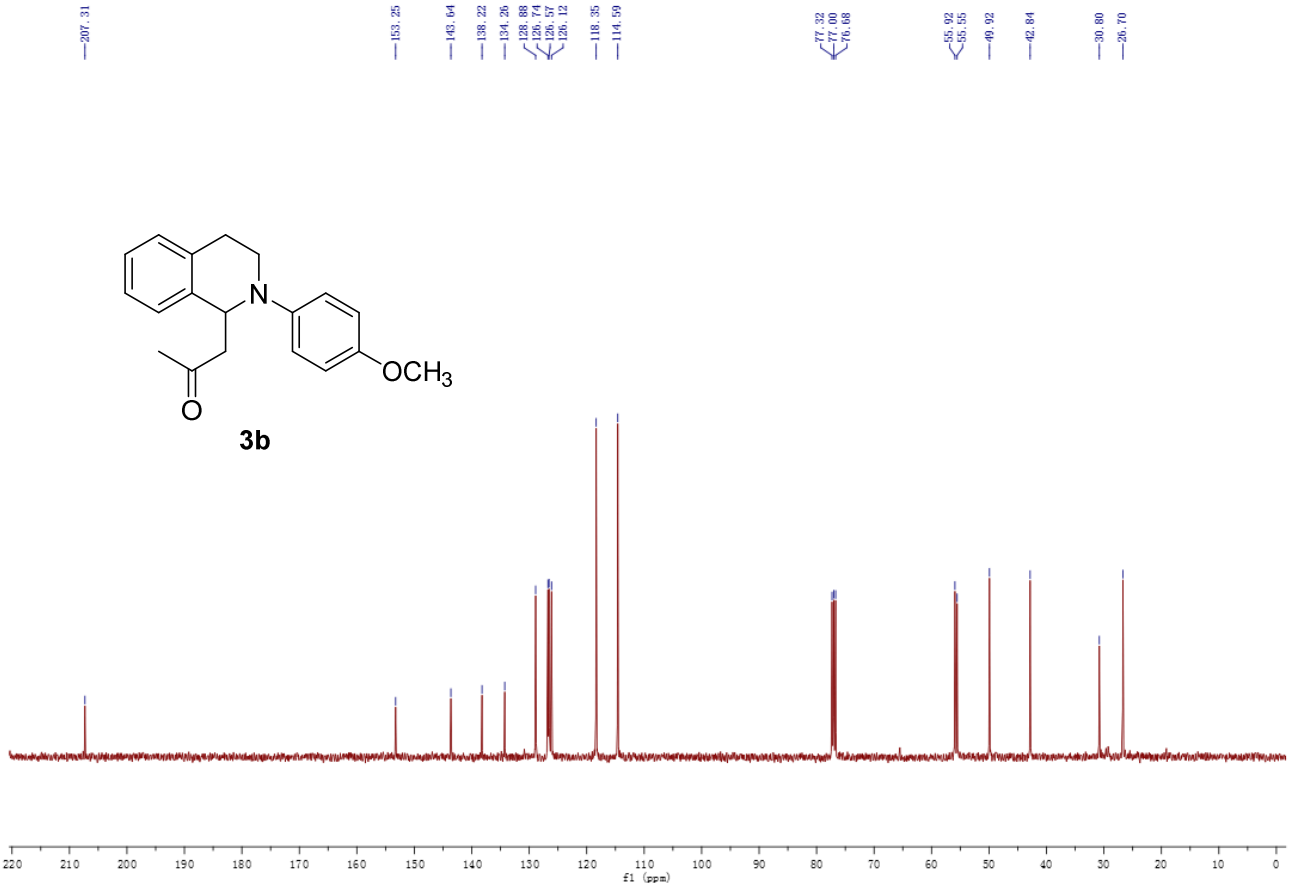
6,7,11b,12-tetrahydro-12-methyl-13*H*-dibenzo[*a*,*f*]quinolizin-13-one (5d), known compound[S7a] **:** Yield 61%. Yellow oil. Isolated major isomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.43 (dd, *J* = 11.3, 4.3 Hz, 1H), 7.29 – 7.16 (m, 3H), 7.12 (d, *J* = 7.4 Hz, 1H), 6.95 (d, *J* = 8.6 Hz, 1H), 6.79 (t, *J* = 7.4 Hz, 1H), 4.79 (s, 1H), 4.07 (dd, *J* = 12.8, 3.4 Hz, 1H), 3.19 – 2.97 (m, 2H), 2.97 – 2.76 (m, 2H), 0.83 (d, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.96, 151.60, 135.31, 134.13, 129.06, 128.47, 126.89, 126.66, 125.48, 118.93, 117.58, 112.64, 60.96, 48.77, 41.25, 29.81, 8.82.

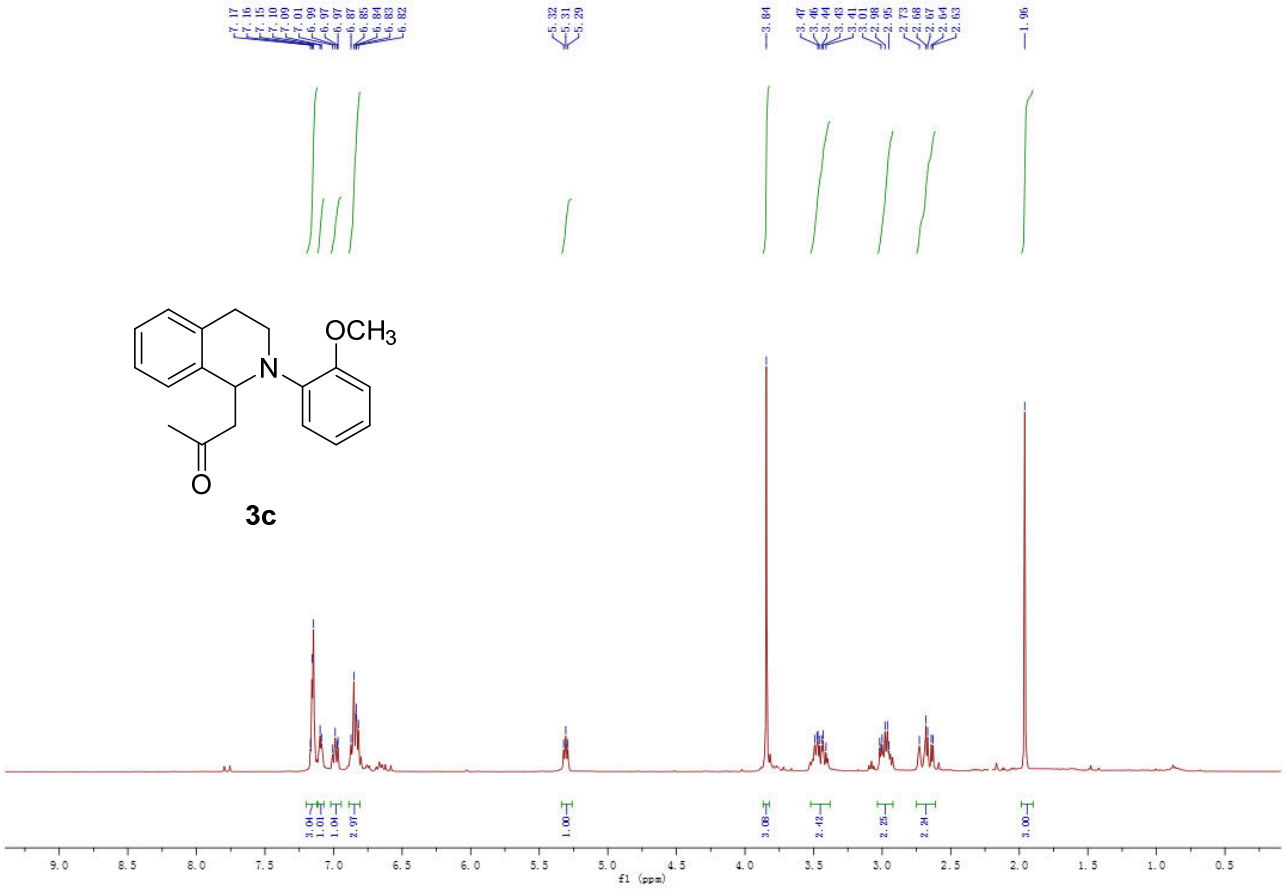
V. ^{1}H NMR and ^{13}C NMR spectra



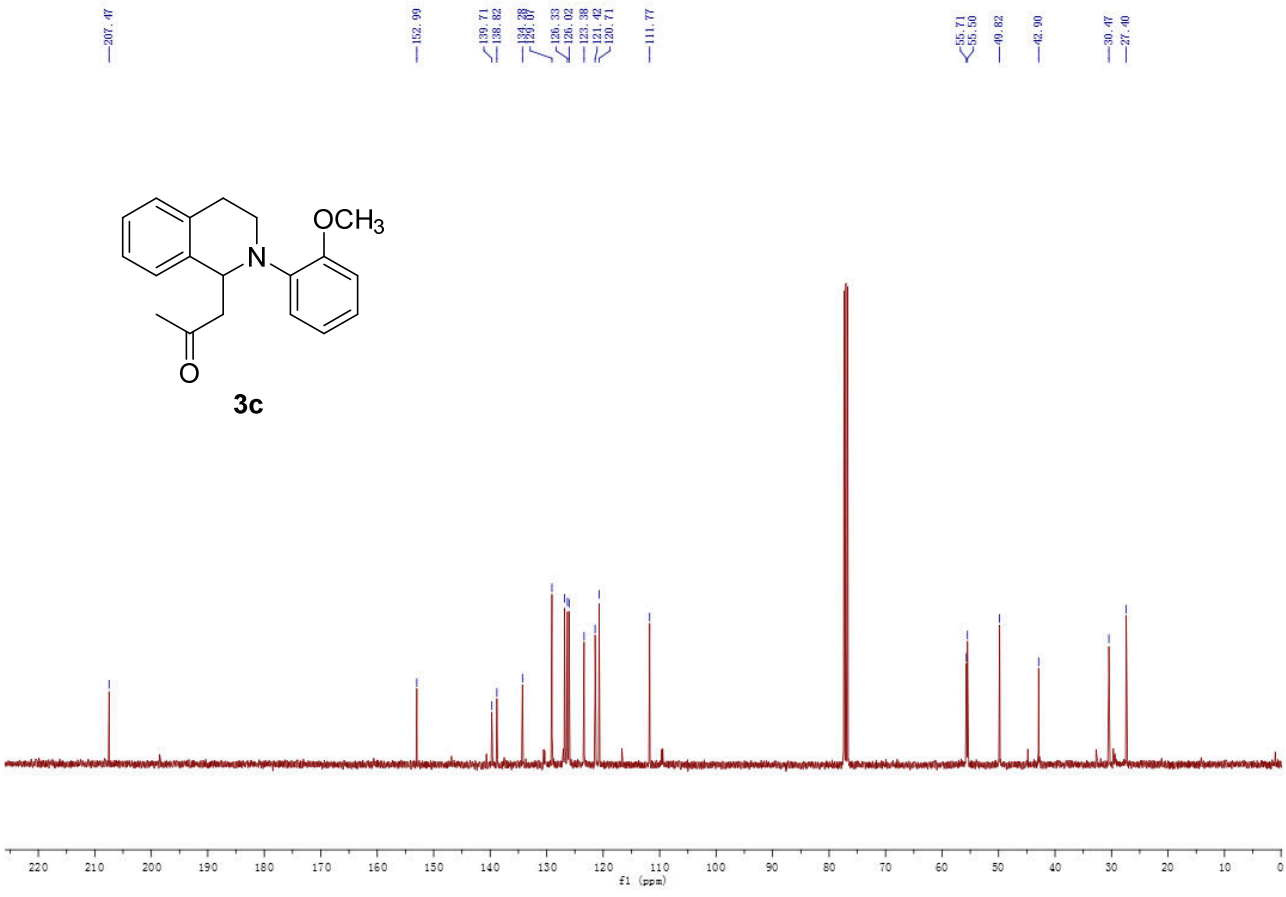



7.15
6.93
6.90
6.82
6.80
5.26
5.24
5.23
3.75
3.53
3.48
3.46
3.43
3.02
2.99
2.96
2.79
2.78
2.75
2.74
2.72
2.06
N
OCH3
O
3b
f1 (ppm)

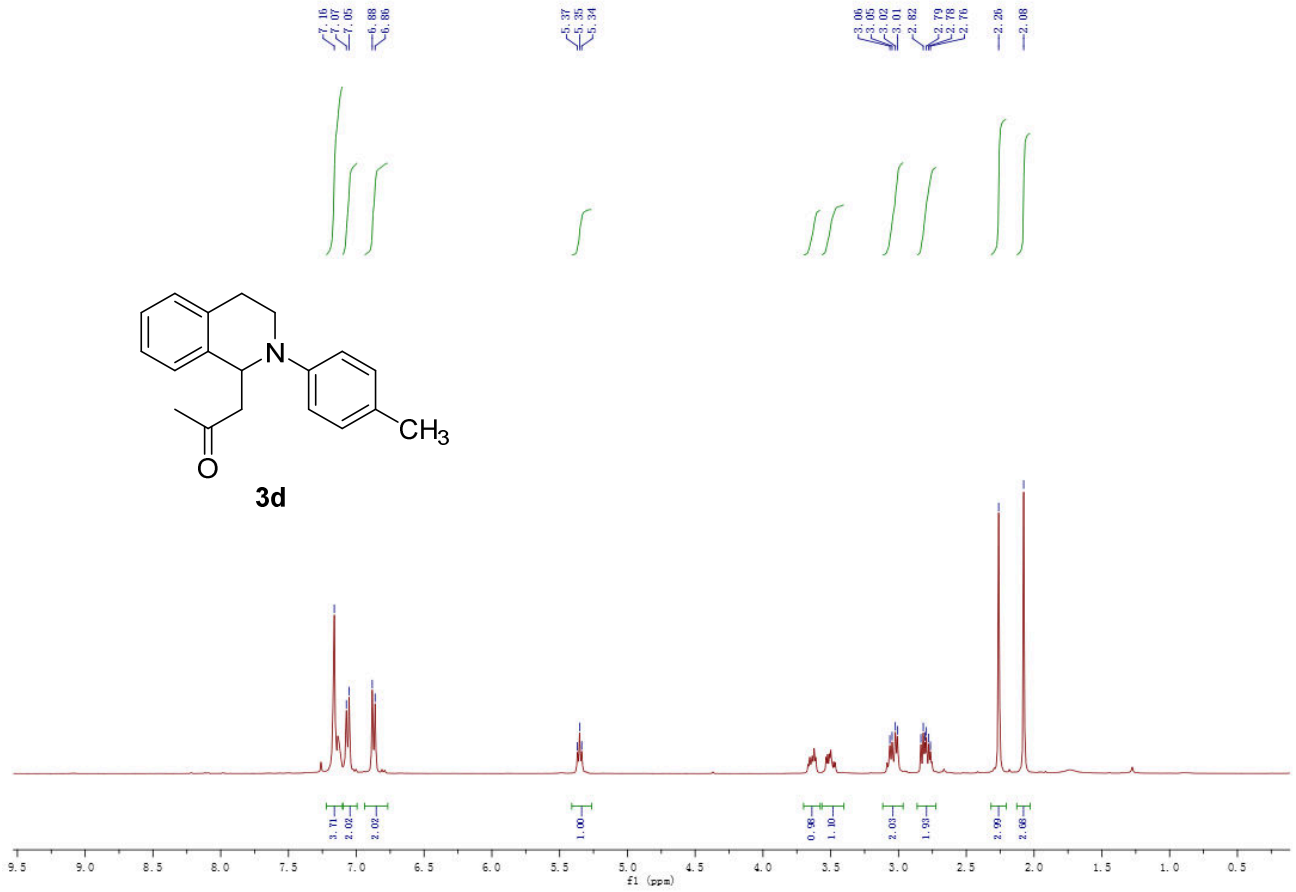

207.31
153.25
143.64
138.22
134.26
128.88
126.74
126.57
126.12
118.35
114.59
77.32
77.00
76.68
55.92
55.55
49.92
42.84
30.80
26.70
N
OCH3
O
3b
f1 (ppm)


7.17
7.16
7.15
7.10
7.09
7.01
7.00
6.99
6.97
6.87
6.85
6.84
6.83
6.82
5.32
5.31
5.29
3.84
3.47
3.46
3.44
3.43
3.41
3.01
2.98
2.95
2.73
2.68
2.67
2.64
2.63
1.96
OCH3
N
O
3.04
1.01
1.04
2.97
1.00
3.06
2.42
2.25
2.24
3.00
f1 (ppm)

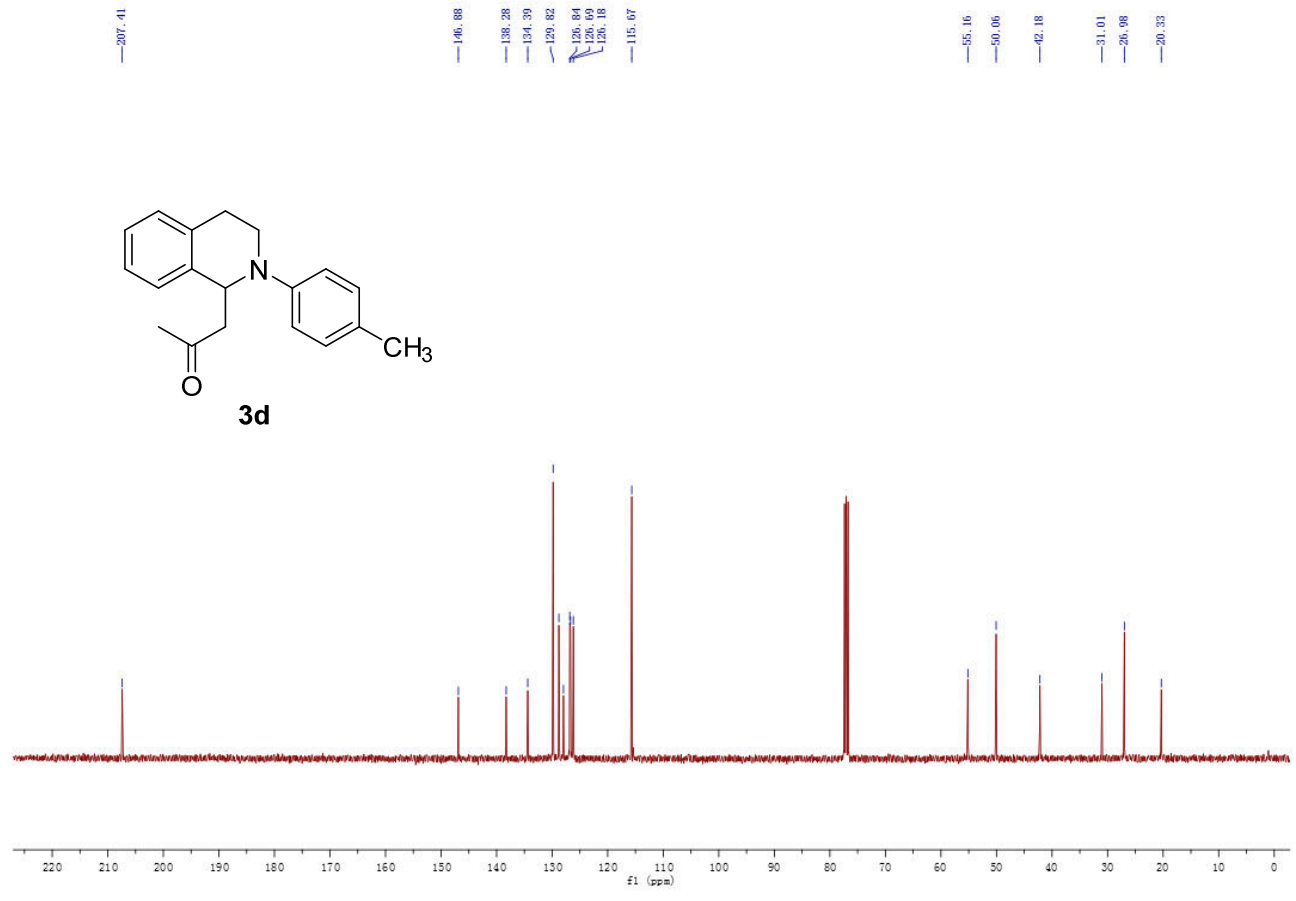
3c


207.47
152.99
139.71
138.82
134.28
129.87
126.33
126.02
123.38
121.42
120.71
111.77
55.71
55.50
49.82
42.90
30.47
27.40
OCH3
N
O
f1 (ppm)

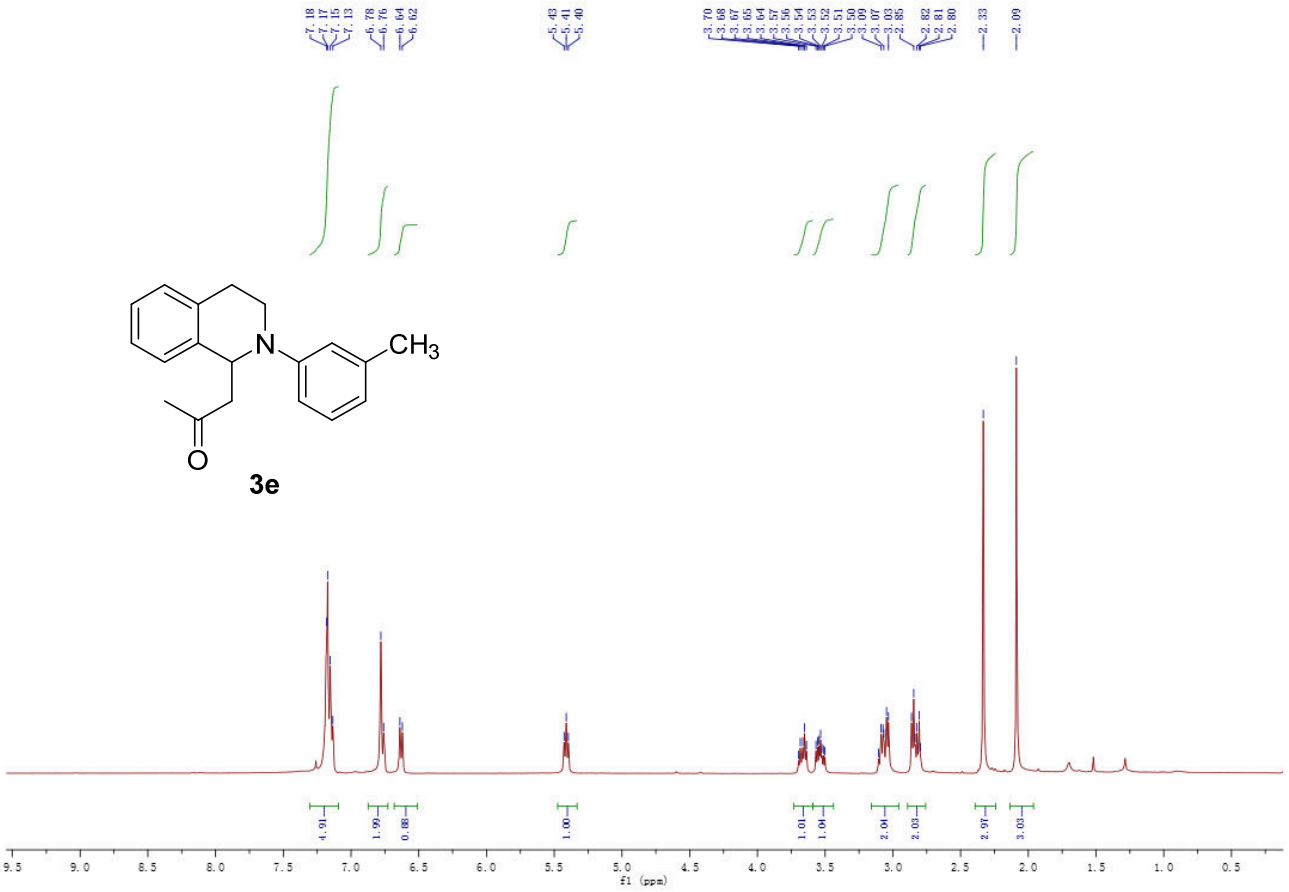
3c

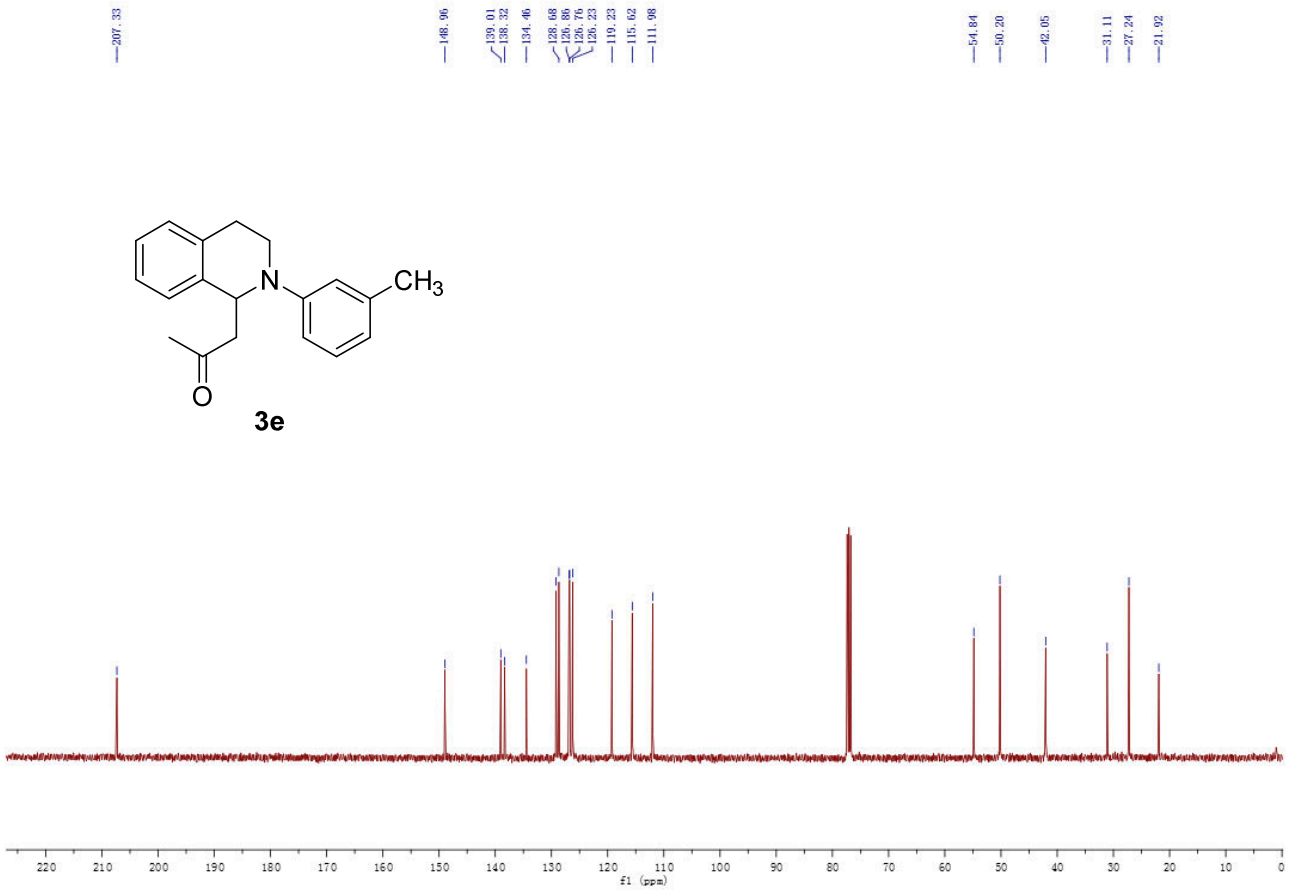

7.16
7.07
7.05
6.88
6.86
5.37
5.35
5.34
3.06
3.05
3.02
3.01
2.82
2.79
2.78
2.76
2.26
2.08
N
CH3
O
3.71
2.02
2.02
1.00
0.98
1.10
2.03
1.93
2.99
2.68
f1 (ppm)

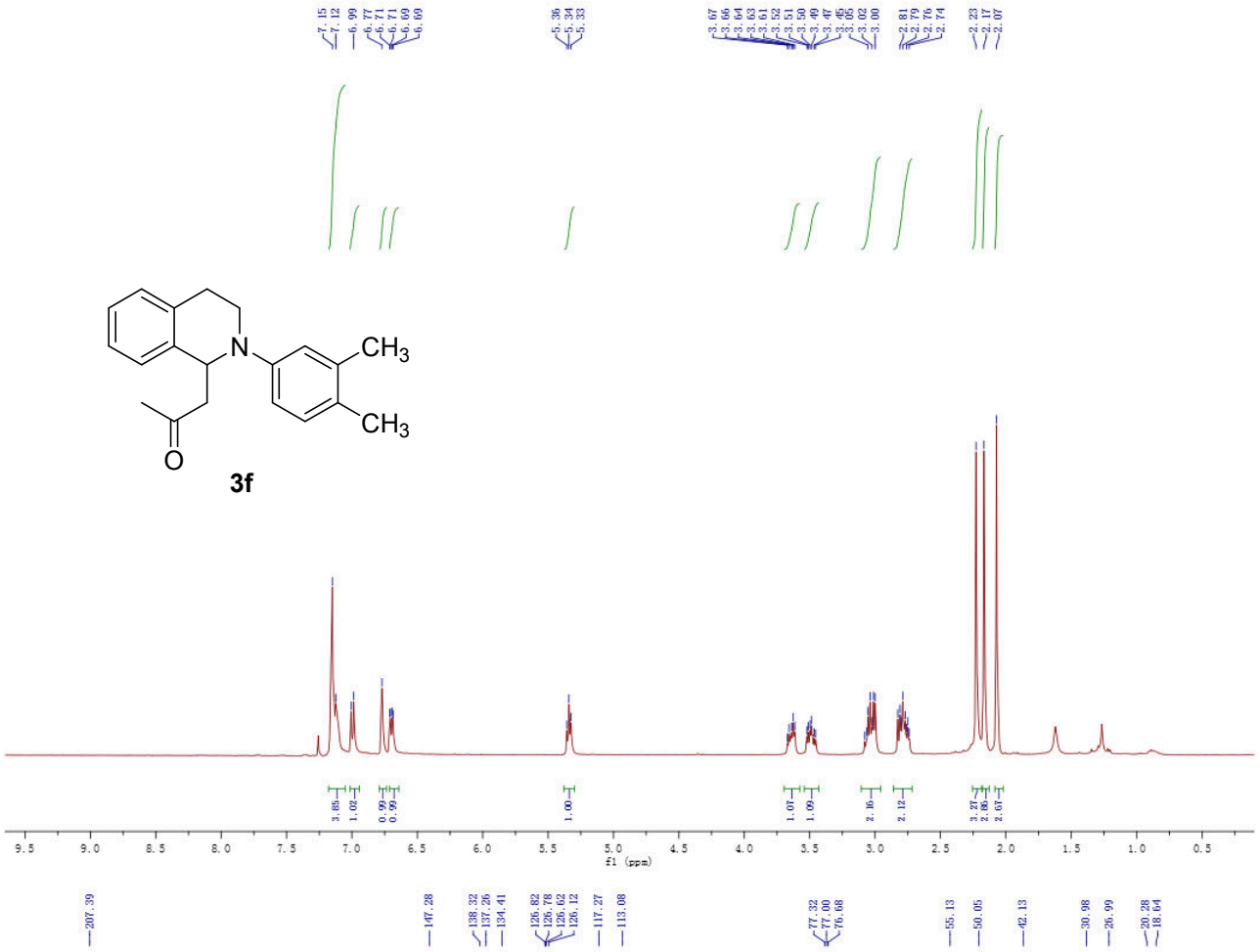
3d


207.41
146.88
138.28
134.39
129.82
126.84
126.69
126.18
115.67
55.16
50.06
42.18
31.01
26.98
20.33
N
CH3
O
f1 (ppm)

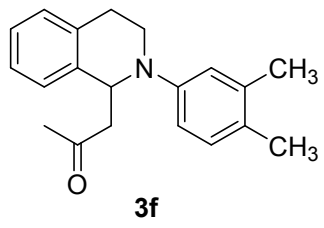
3d

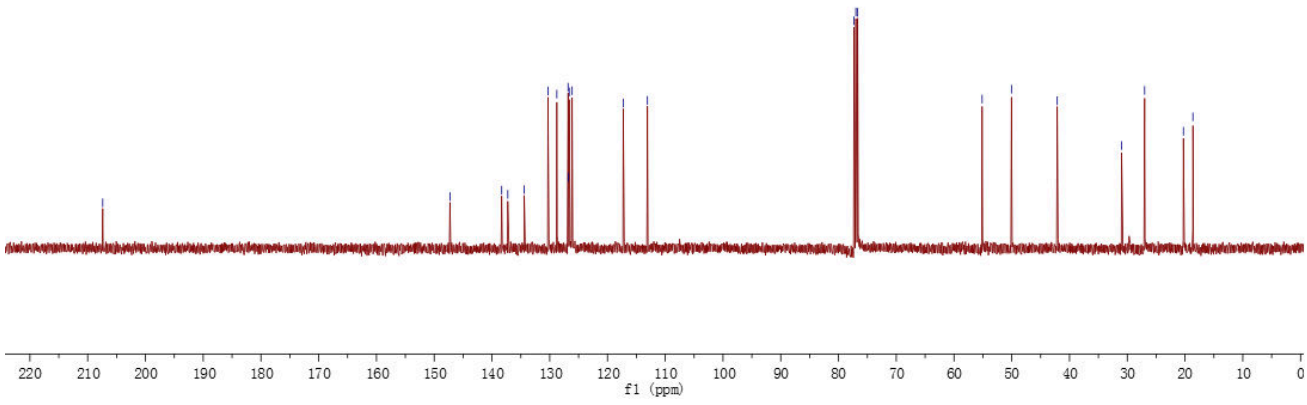

7.18
7.17
7.15
7.13
6.78
6.76
6.64
6.62
5.43
5.41
5.40
3.70
3.68
3.67
3.65
3.64
3.57
3.56
3.54
3.53
3.52
3.51
3.50
3.09
3.07
3.03
2.86
2.82
2.81
2.80
2.33
2.09
N
CH3
O
3e
4.91
1.99
0.88
1.00
1.01
1.04
2.04
2.03
2.97
3.03
f1 (ppm)

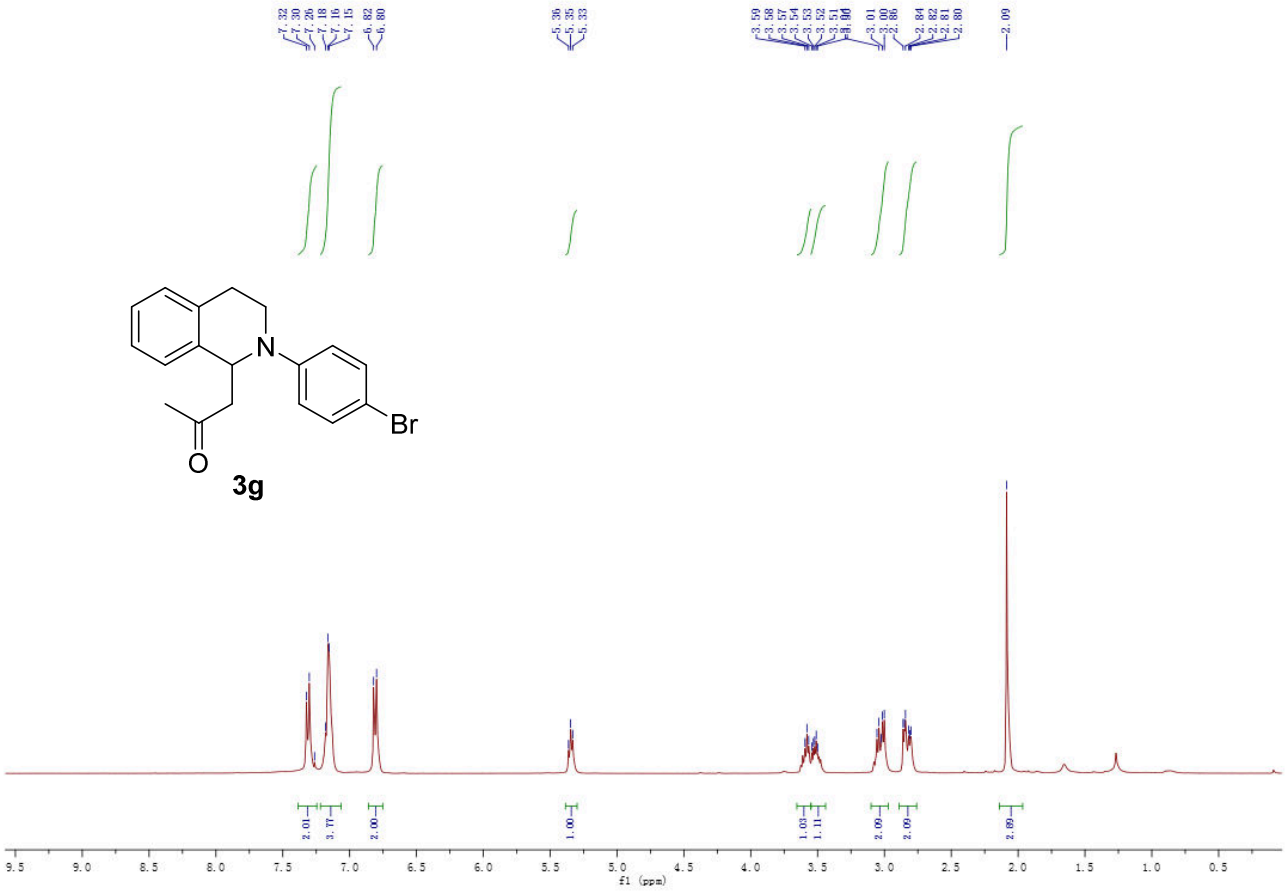

207.33
148.96
139.01
138.32
134.46
128.68
126.86
126.76
126.23
119.23
115.62
111.98
54.84
50.20
42.05
31.11
27.24
21.92
N
CH3
O
3e
f1 (ppm)

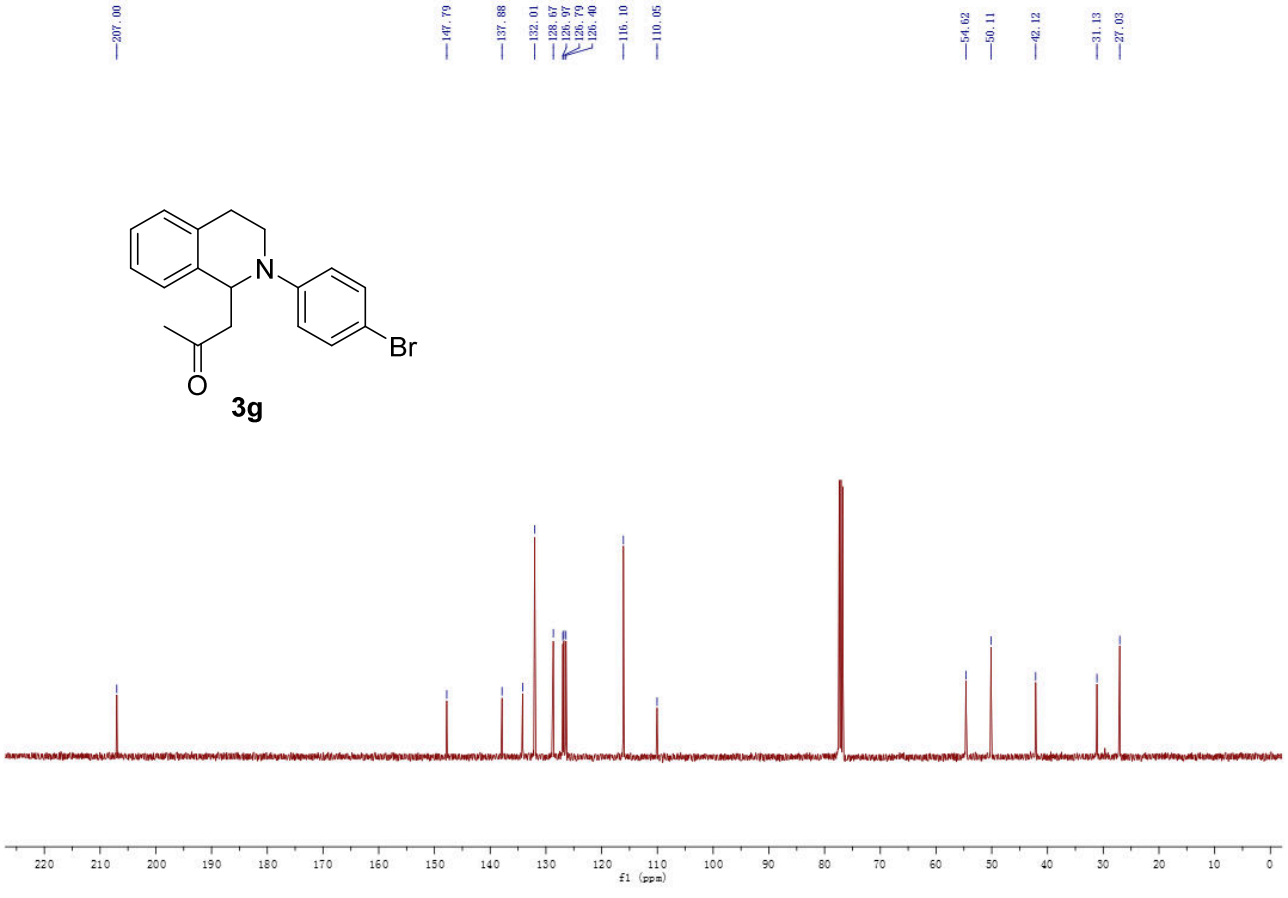

7.15
7.12
6.99
6.77
6.71
6.69
6.69
5.36
5.34
5.33
3.67
3.66
3.64
3.63
3.61
3.52
3.51
3.50
3.49
3.47
3.45
3.02
3.00
2.81
2.79
2.76
2.74
2.23
2.17
2.07
N
CH3
CH3
O
3f
3.85
1.02
0.99
0.99
1.00
1.07
1.09
2.16
2.12
3.27
2.86
2.67
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

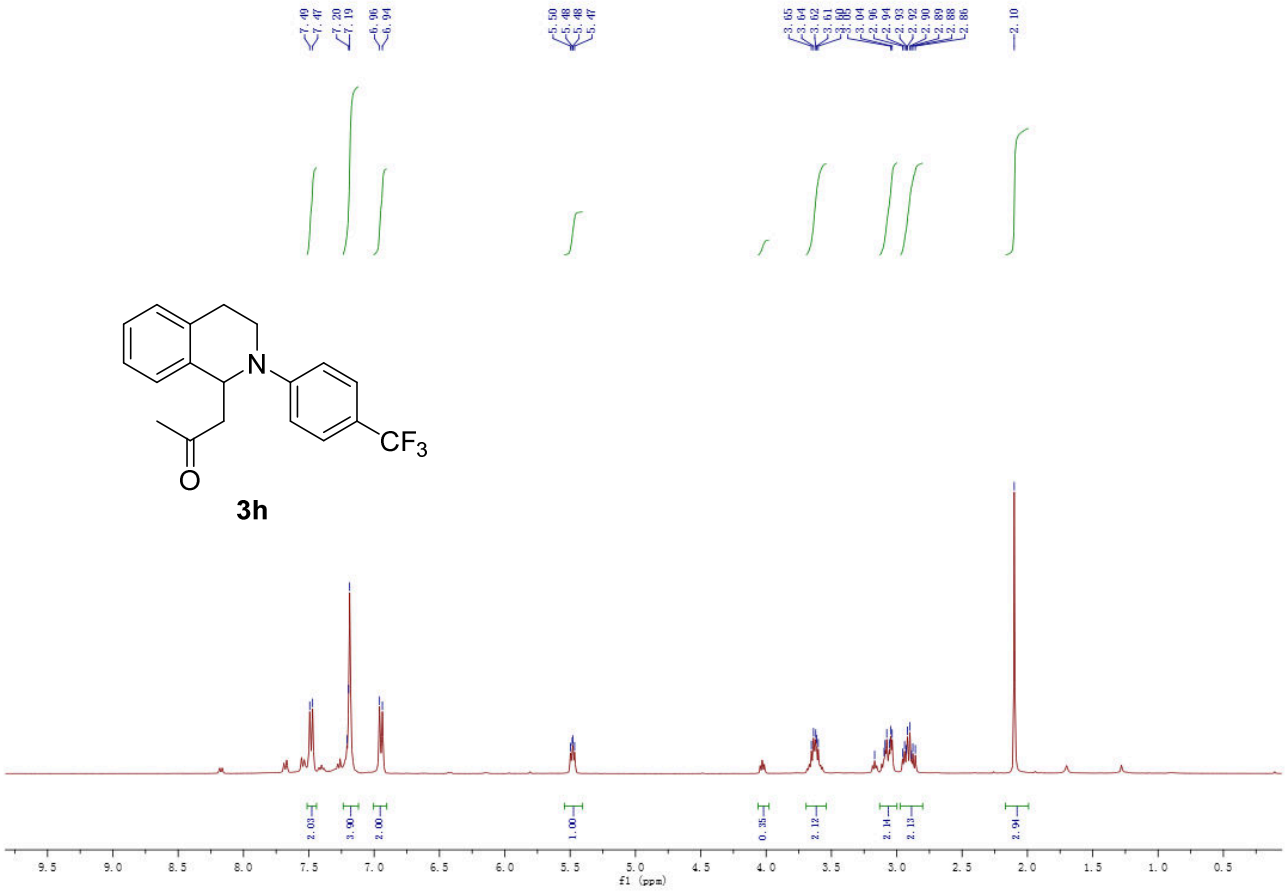
207.39
147.28
138.32
137.26
134.41
126.82
126.78
126.62
126.12
117.27
113.08
77.32
77.00
76.68
55.13
50.05
42.13
30.98
26.99
20.28
18.64


N
CH3
CH3
O
3f

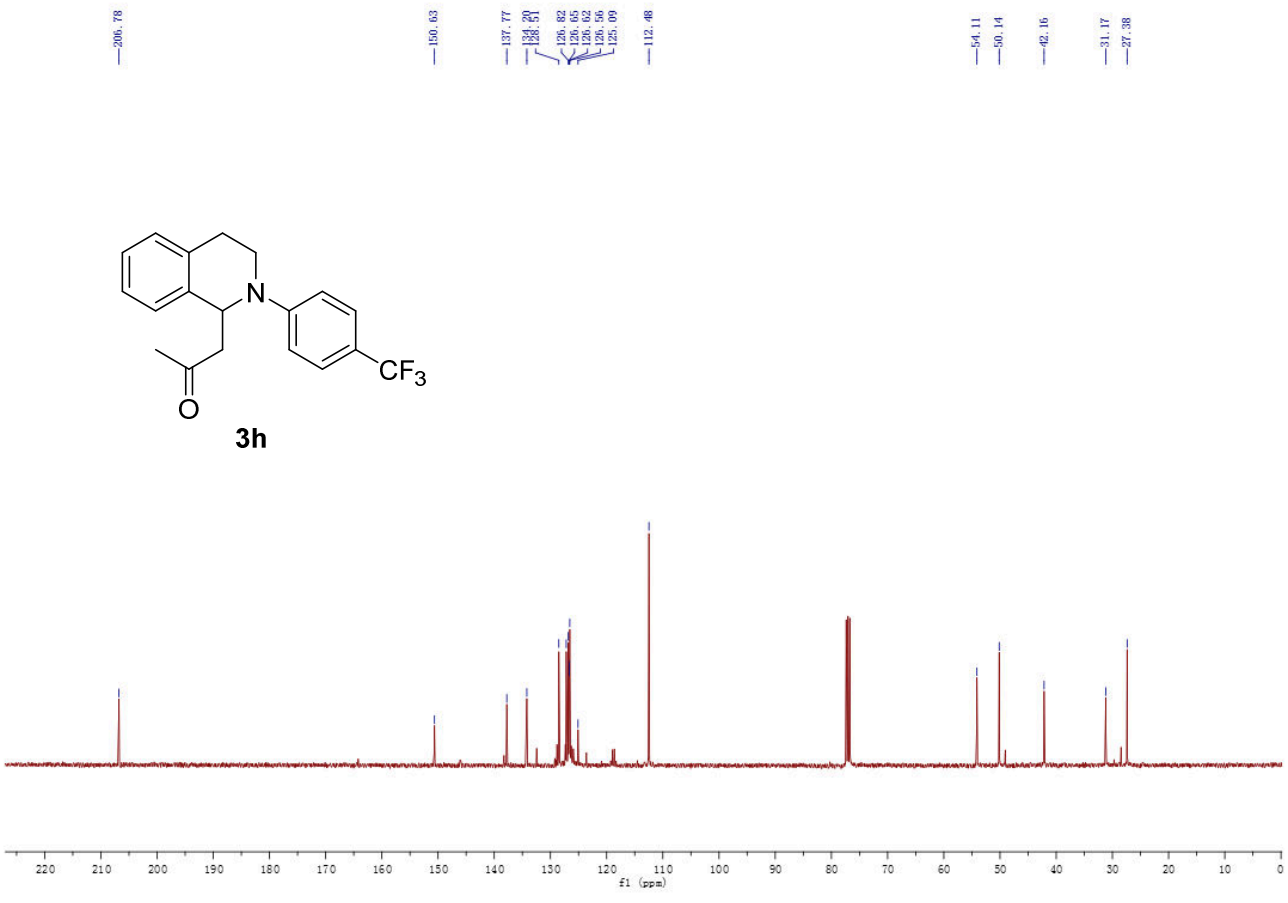

220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.32
7.30
7.26
7.18
7.16
7.15
6.82
6.80
5.36
5.35
5.33
3.59
3.58
3.57
3.54
3.53
3.52
3.01
3.00
2.86
2.84
2.82
2.81
2.80
2.09
N
Br
O
3g
2.01
3.77
2.00
1.00
1.03
1.11
2.09
2.09
2.89
f1 (ppm)

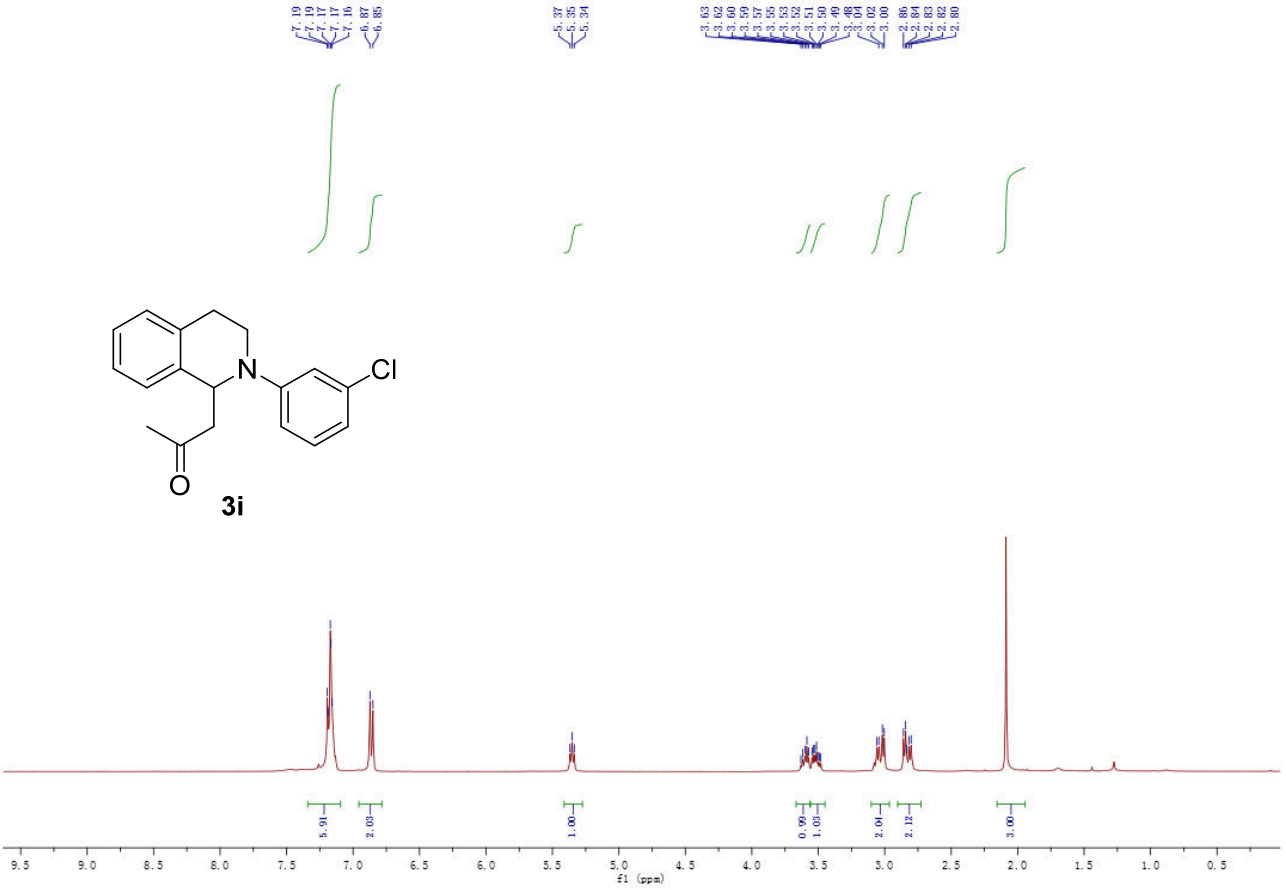

207.00
147.79
137.88
132.01
128.67
126.97
126.79
126.40
116.10
110.05
54.62
50.11
42.12
31.13
27.03
N
Br
O
3g
f1 (ppm)

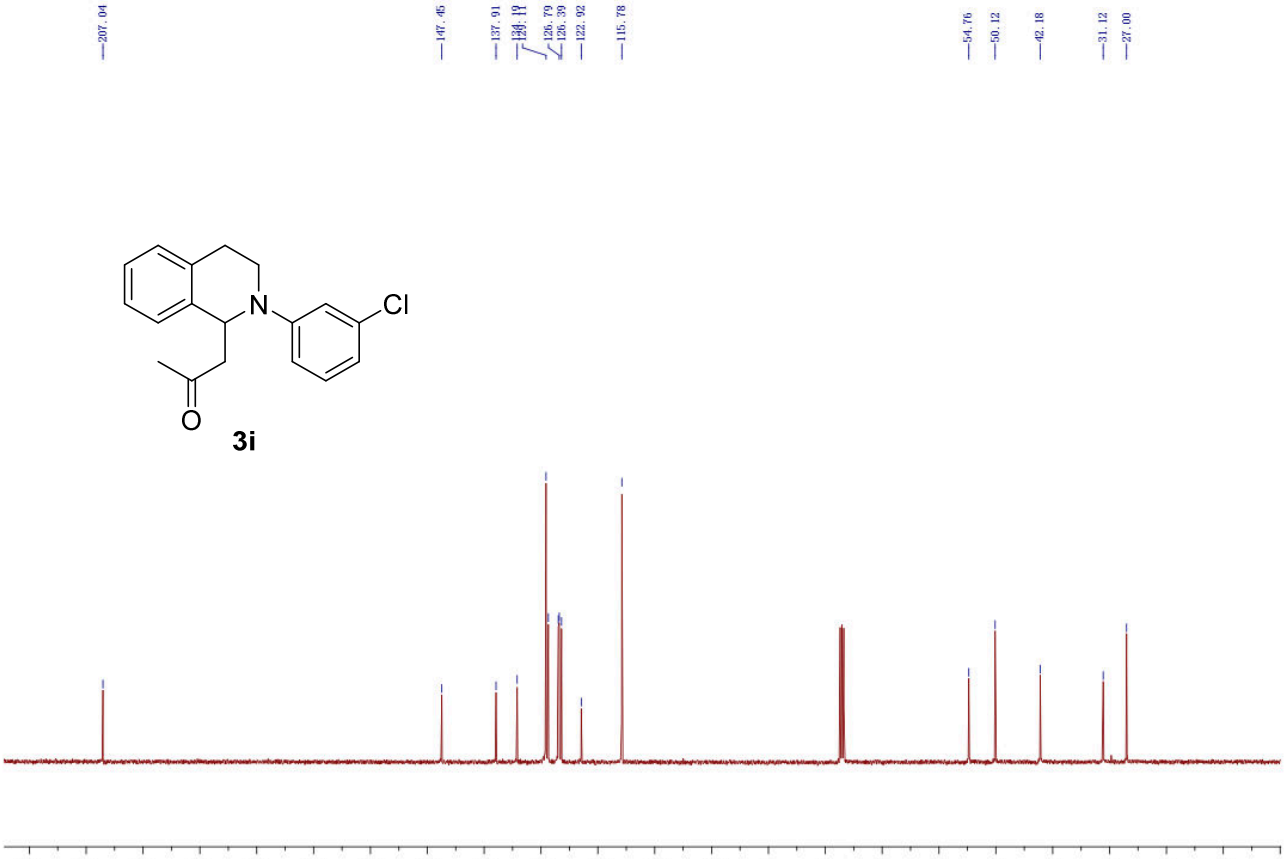

7.49
7.47
7.20
7.19
6.96
6.94
5.50
5.48
5.47
3.65
3.64
3.62
3.61
3.04
2.96
2.94
2.93
2.92
2.90
2.89
2.88
2.86
2.10
N
CF3
O
2.03
3.90
2.00
1.00
0.35
2.12
2.14
2.13
2.94
f1 (ppm)

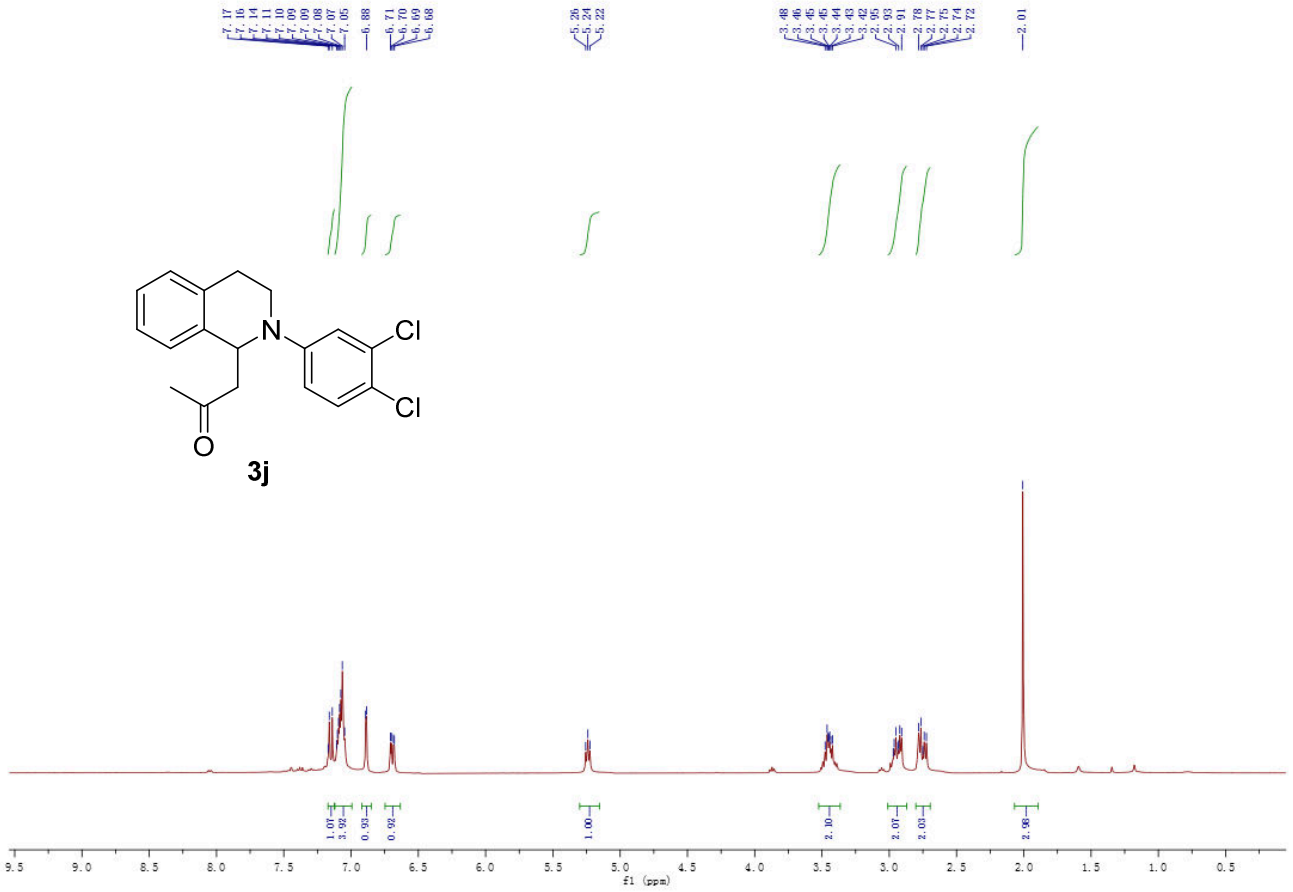
3h


206.78
150.63
137.77
128.51
126.82
126.65
126.62
126.56
125.09
112.48
54.11
50.14
42.16
31.17
27.38
N
CF3
O
f1 (ppm)

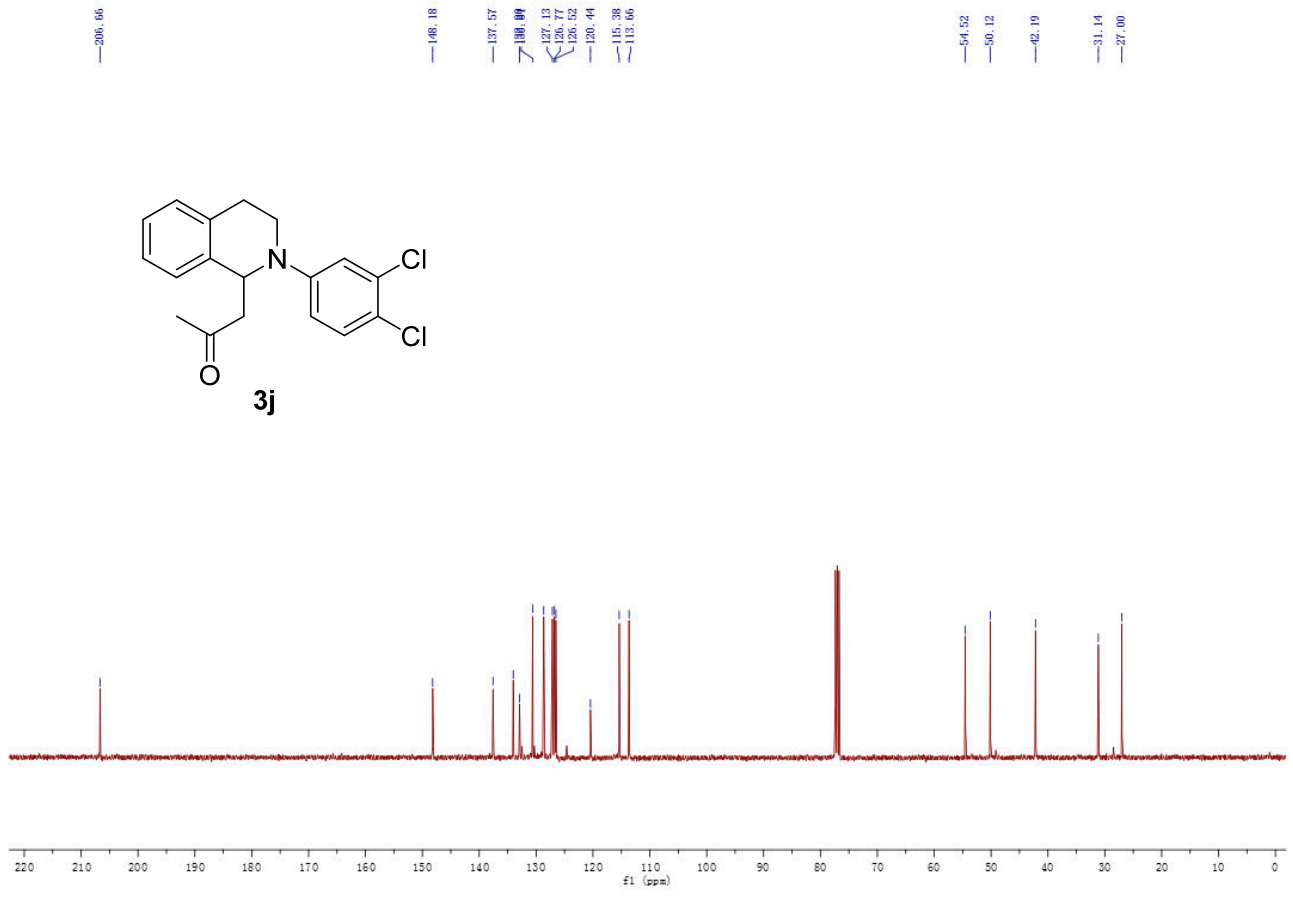
3h


7.19
7.19
7.17
7.17
7.16
6.87
6.85
5.37
5.35
5.34
3.63
3.62
3.60
3.59
3.57
3.55
3.53
3.52
3.51
3.50
3.49
3.48
3.04
3.02
3.00
2.86
2.84
2.83
2.82
2.80
N
Cl
O
3i
5.91
2.03
1.00
0.99
1.03
2.04
2.12
3.00
f1 (ppm)


207.04
147.45
137.91
134.19
129.11
126.79
126.39
122.92
115.78
54.76
50.12
42.18
31.12
27.00
N
Cl
O
3i
f1 (ppm)

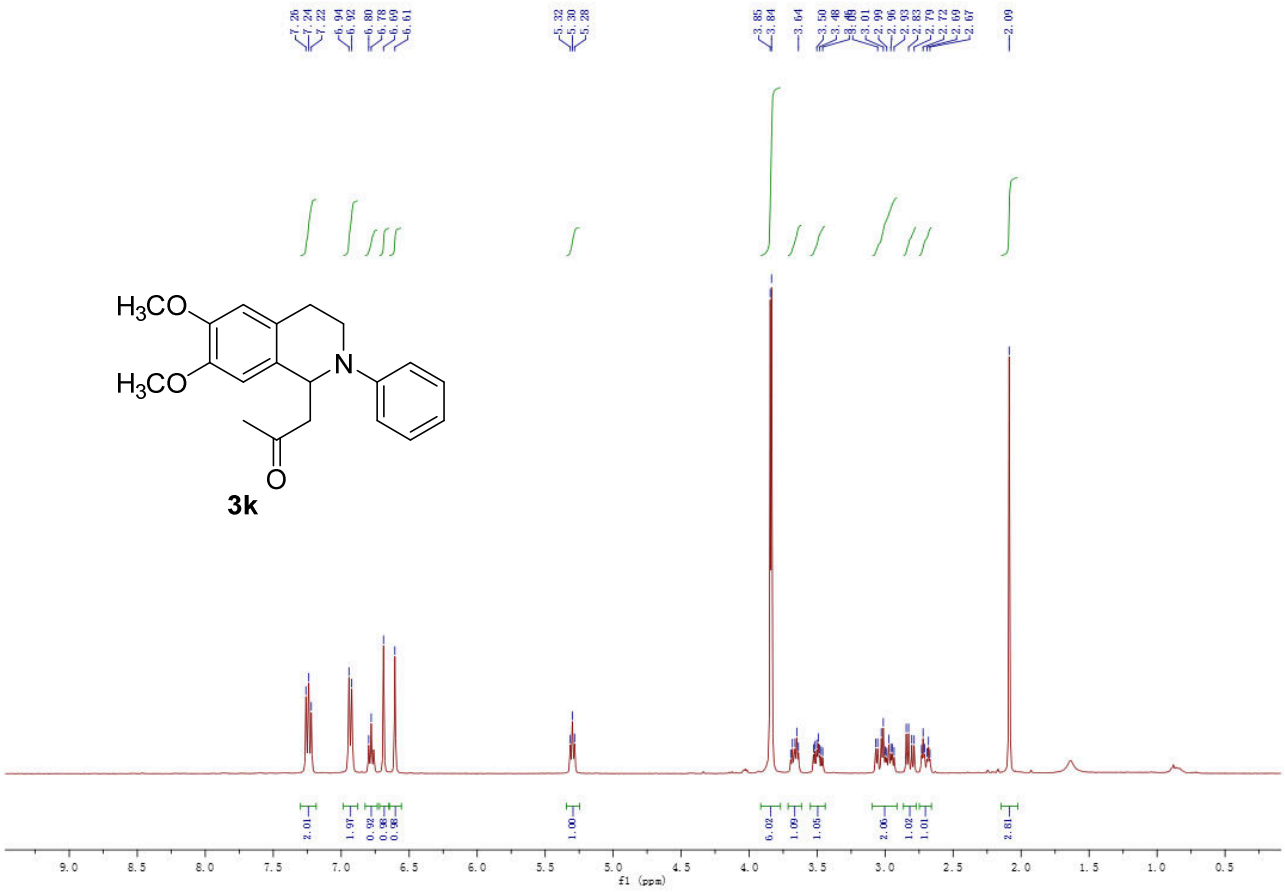

7.17
7.16
7.14
7.11
7.10
7.09
7.09
7.08
7.07
7.05
6.88
6.71
6.70
6.69
6.68
5.26
5.24
5.22
3.48
3.46
3.45
3.45
3.44
3.43
3.42
2.95
2.93
2.91
2.78
2.77
2.75
2.74
2.72
2.01
N
Cl
Cl
O
1.07
3.92
0.93
0.92
1.00
2.10
2.07
2.03
2.98
f1 (ppm)

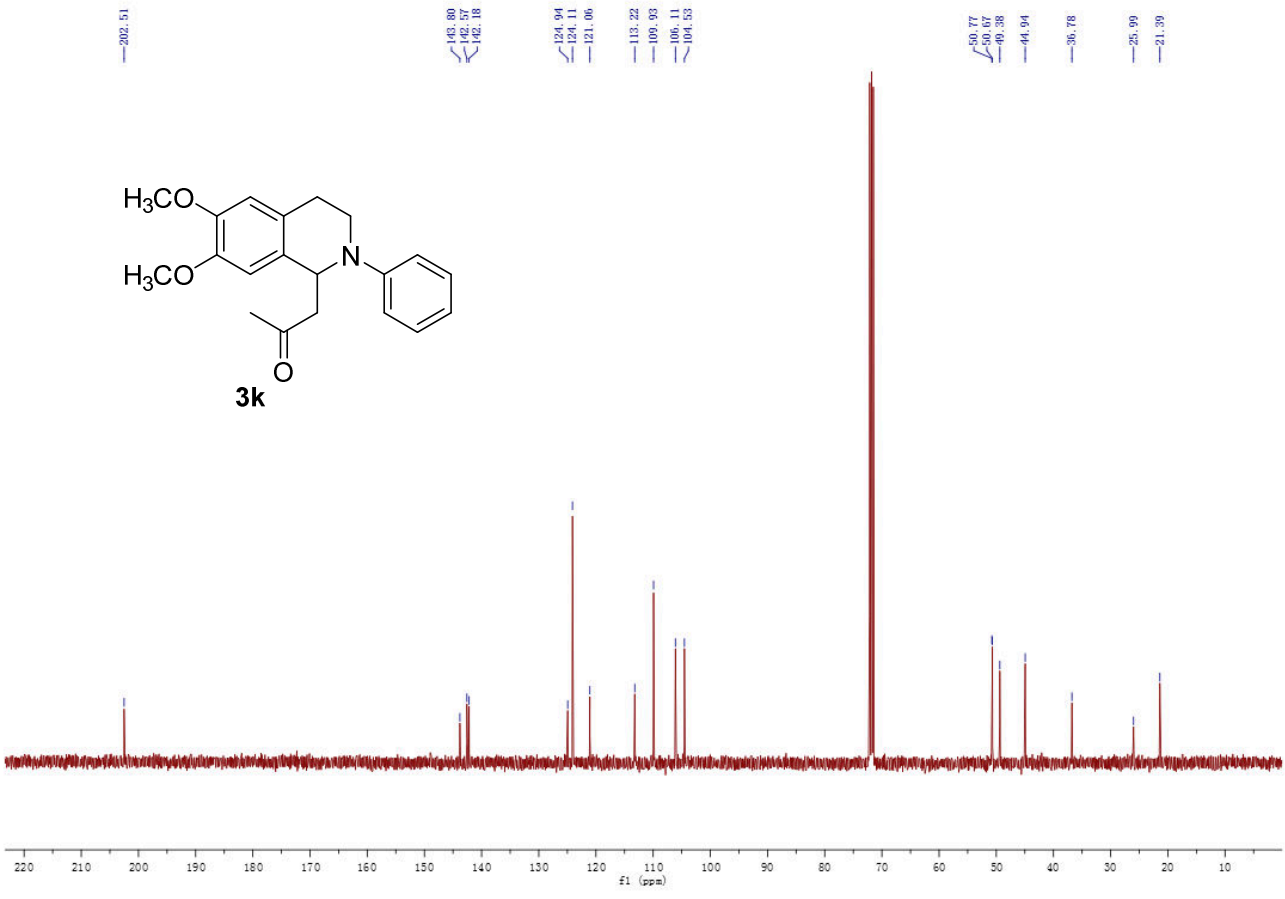
3j

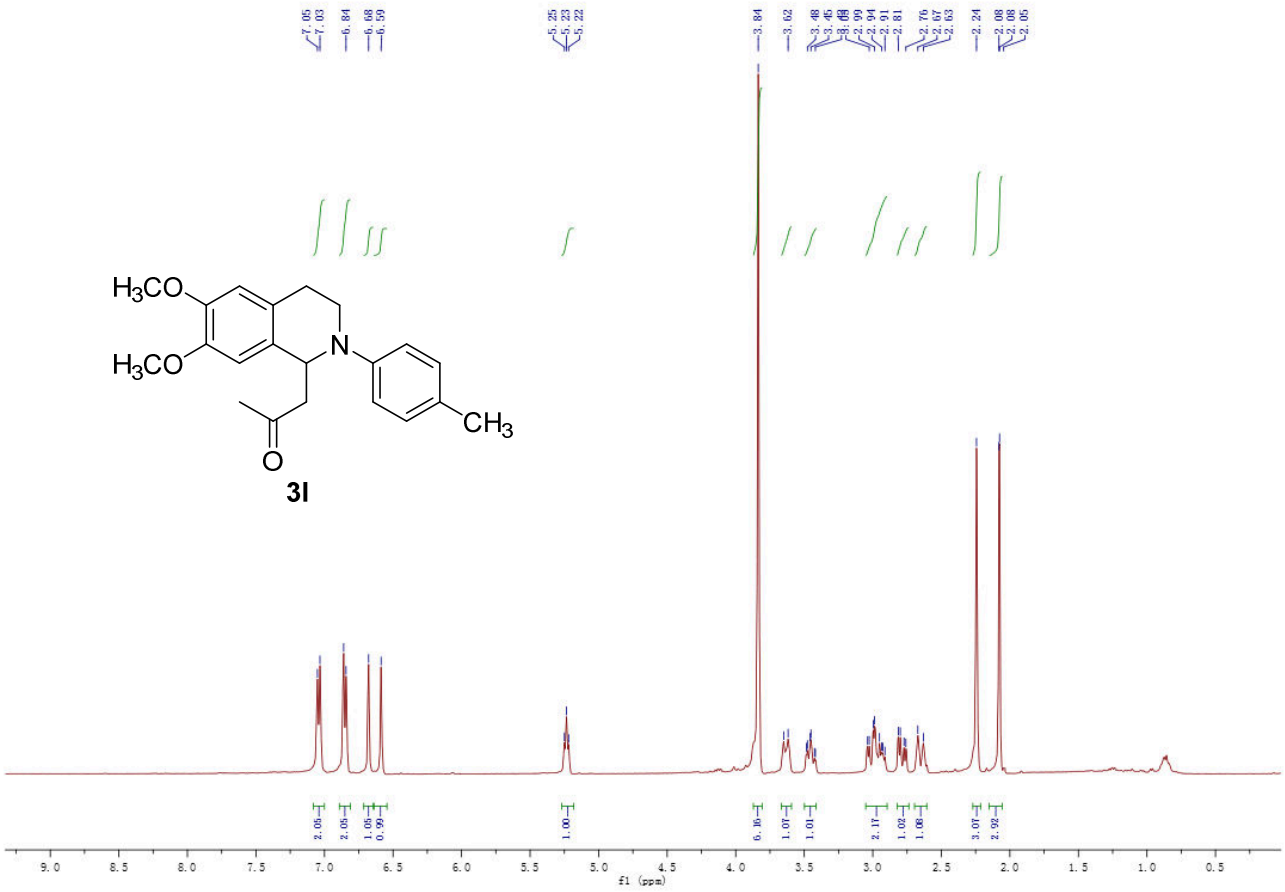

206.66
148.18
137.57
127.13
126.77
126.52
120.44
115.38
113.66
54.52
50.12
42.19
31.14
27.00
f1 (ppm)

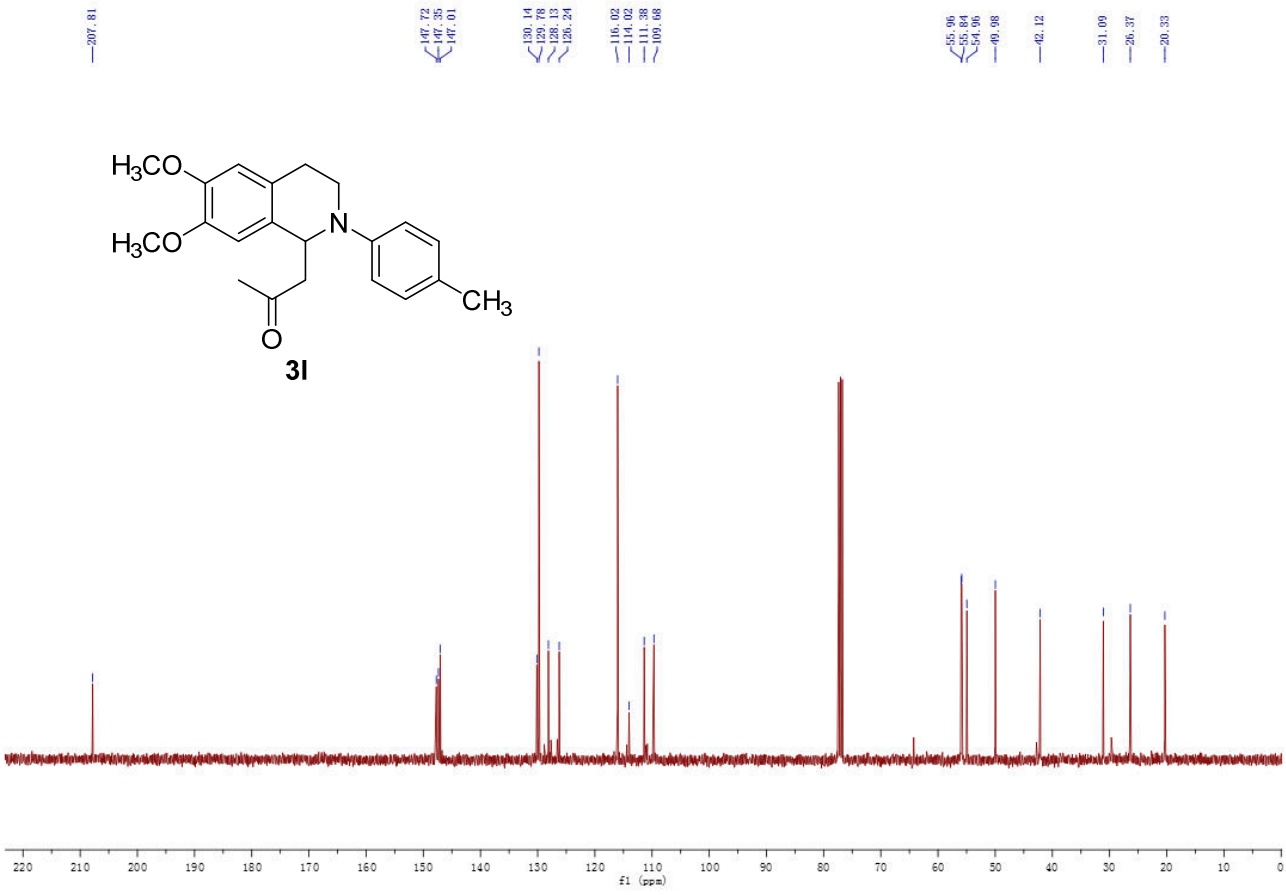
N
Cl
Cl
O

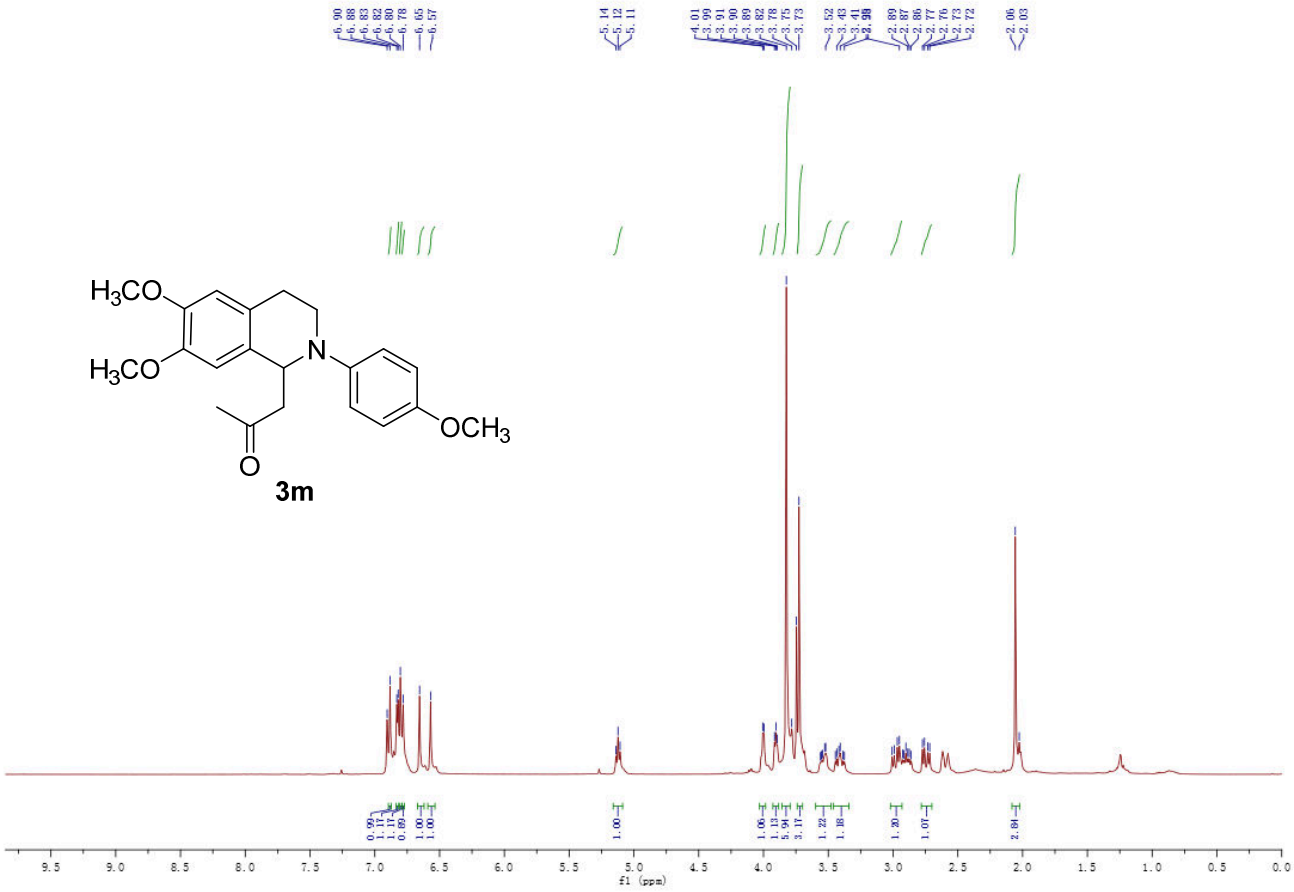
3j

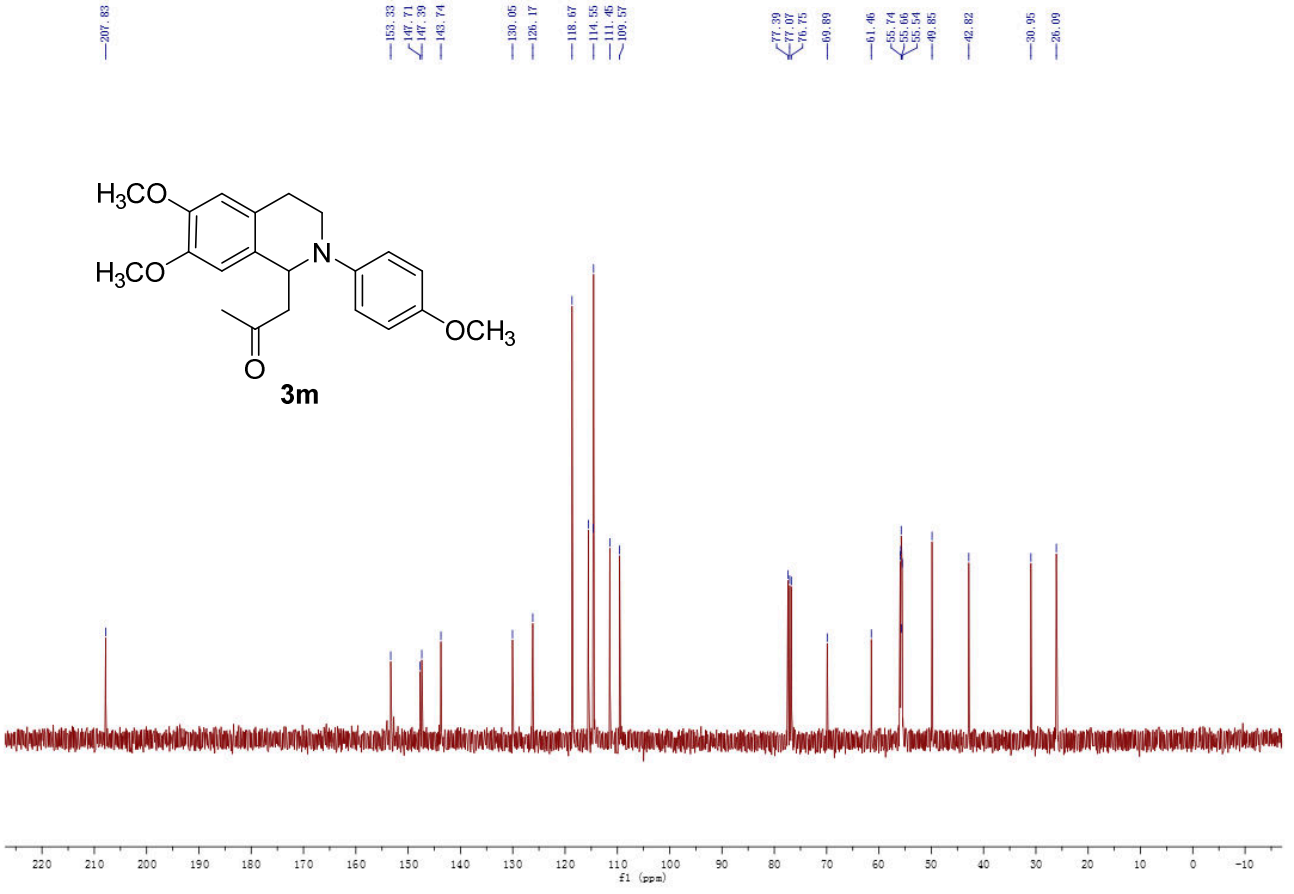

7.26
7.24
7.22
6.94
6.92
6.89
6.78
6.69
6.61
5.32
5.30
5.28
3.85
3.84
3.64
3.50
3.48
3.01
2.99
2.96
2.93
2.83
2.79
2.72
2.69
2.67
2.09
H3CO
H3CO
N
O
3k
2.01
1.97
0.92
0.90
0.88
1.00
6.02
1.09
1.05
2.06
1.02
1.01
2.81
f1 (ppm)

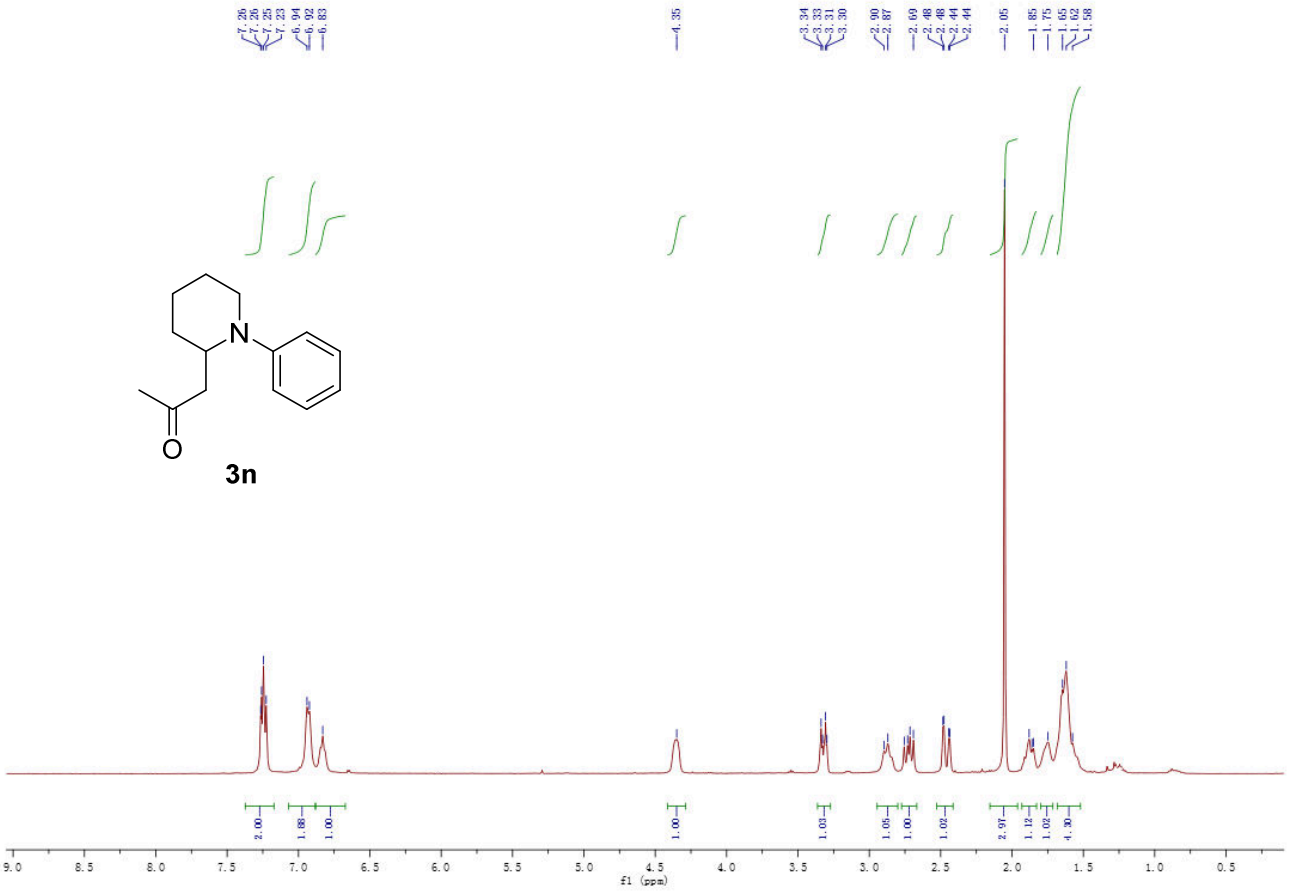

202.51
143.80
142.57
142.18
124.94
124.11
121.06
113.22
109.93
106.11
104.53
50.77
50.67
49.38
44.94
36.78
25.99
21.39
H3CO
H3CO
N
O
3k
f1 (ppm)

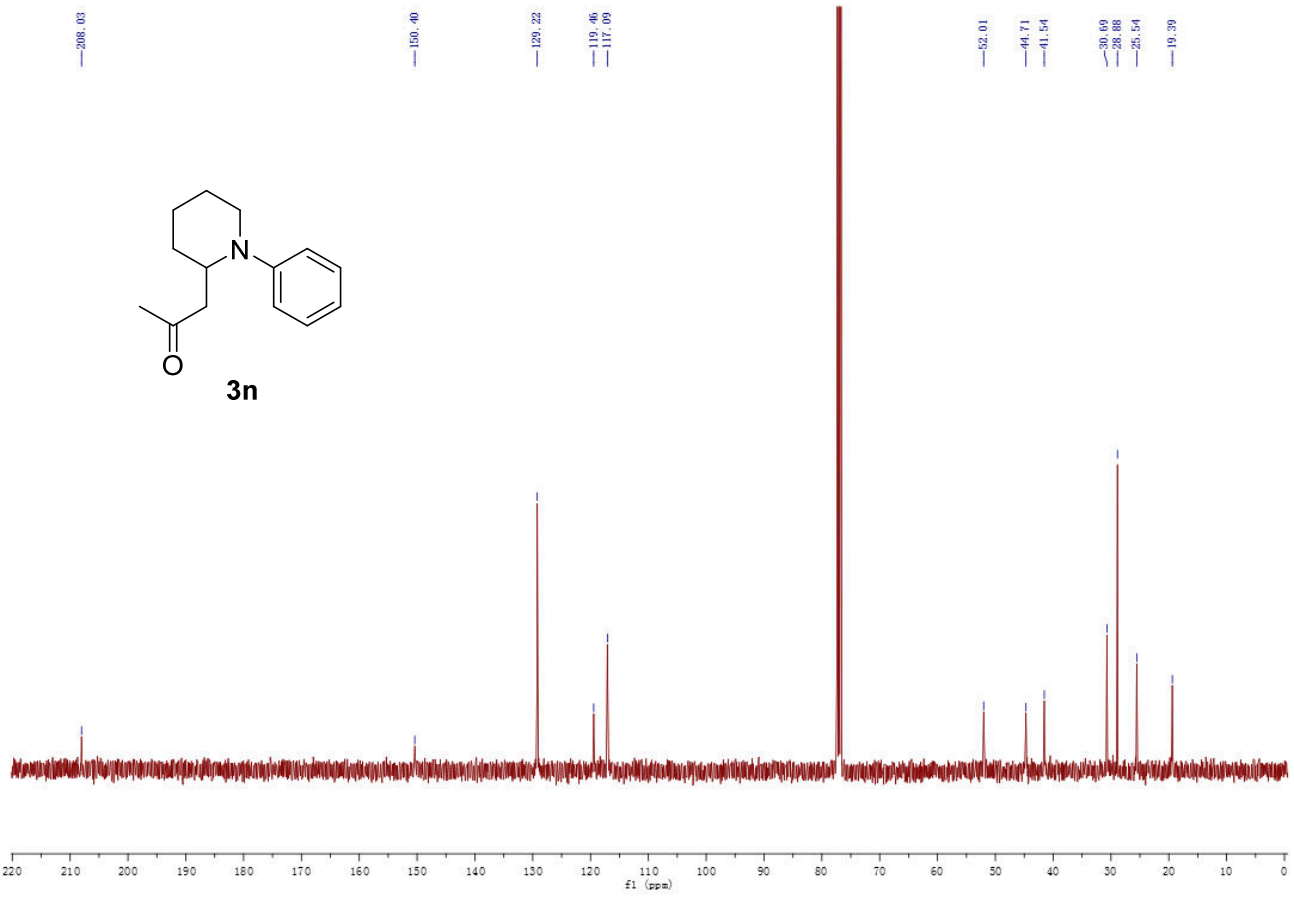

7.05
7.03
6.84
6.68
6.59
5.25
5.23
5.22
3.84
3.62
3.48
3.45
3.09
2.94
2.91
2.81
2.76
2.67
2.63
2.24
2.08
2.06
2.05
H3CO
H3CO
N
CH3
O
3l
2.06
2.09
1.05
0.99
1.00
6.16
1.07
1.01
2.17
1.02
1.08
3.07
2.92
f1 (ppm)

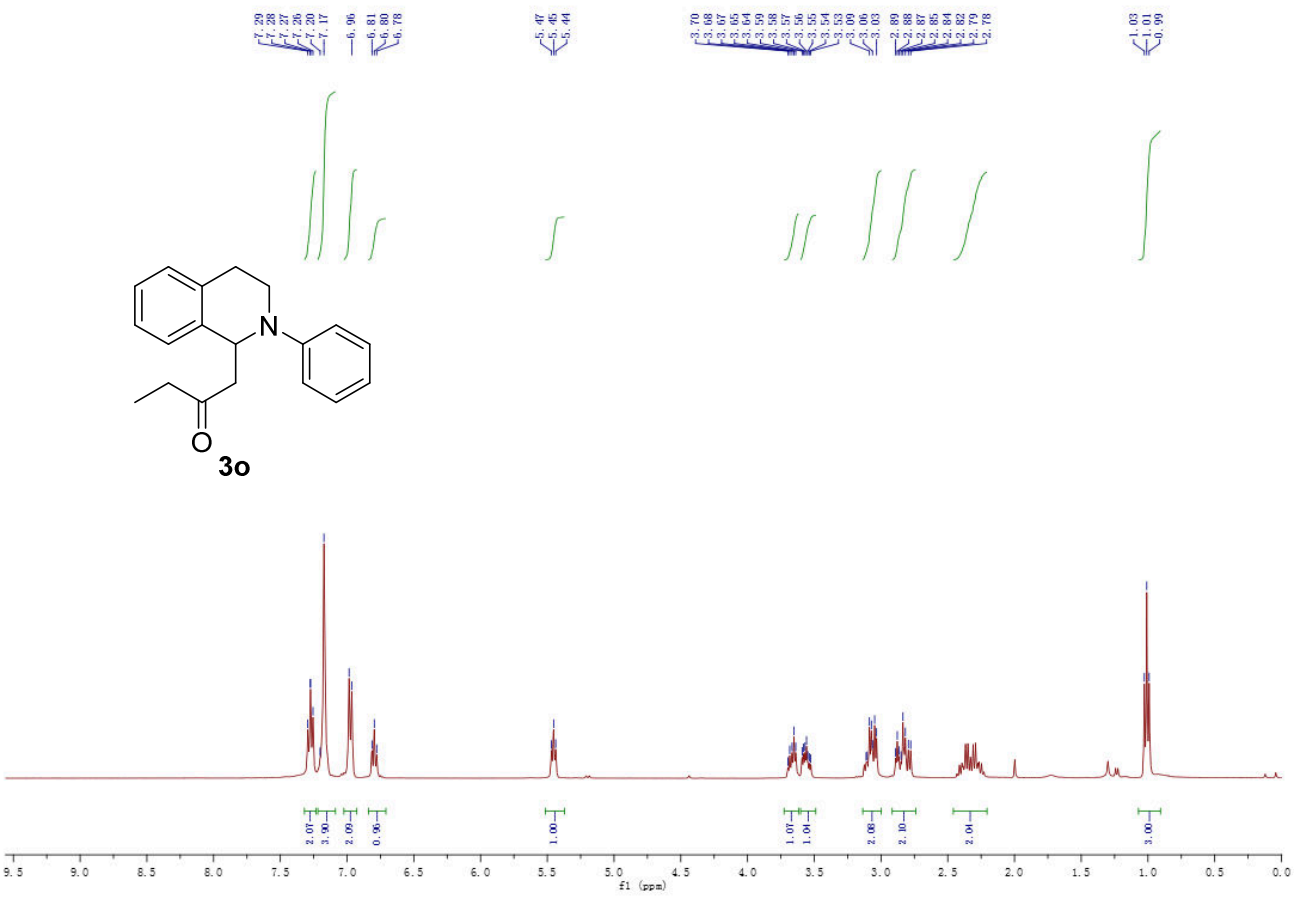

207.81
147.72
147.35
147.01
130.14
129.78
128.13
126.24
116.02
114.02
111.38
109.68
55.96
55.84
54.96
49.98
42.12
31.09
26.37
20.33
H3CO
H3CO
N
CH3
O
3l
f1 (ppm)

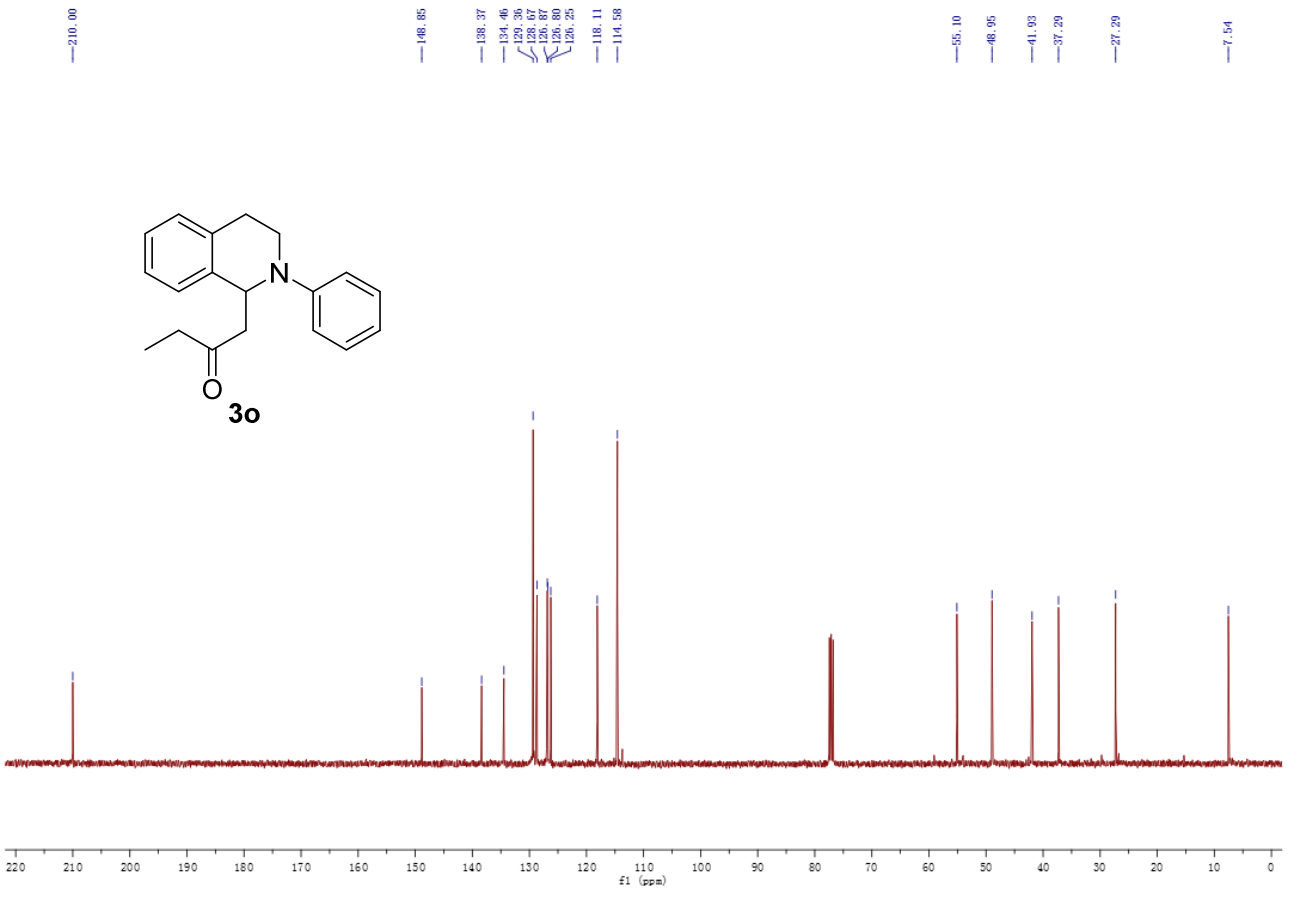

6.90
6.88
6.83
6.82
6.80
6.78
6.65
6.57
5.14
5.12
5.11
4.01
3.99
3.91
3.90
3.89
3.82
3.78
3.75
3.73
3.52
3.43
3.41
2.89
2.87
2.86
2.77
2.76
2.73
2.72
2.06
2.03
H3CO
H3CO
N
OCH3
O
3m
f1 (ppm)

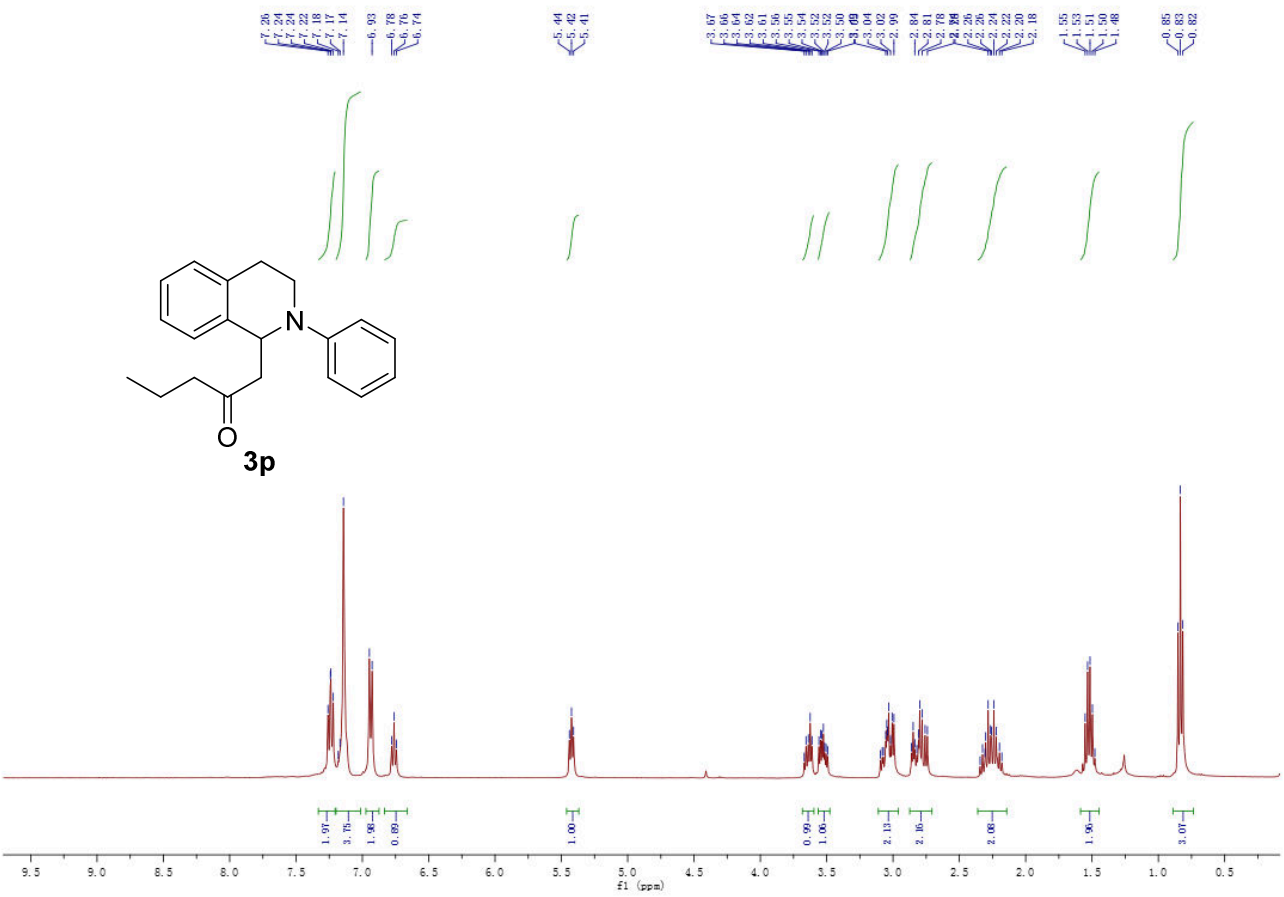

207.83
153.33
147.71
147.39
143.74
130.05
126.17
118.67
114.55
111.46
109.57
77.39
77.07
76.75
69.89
61.46
55.74
55.66
55.54
49.85
42.82
30.95
26.09
H3CO
H3CO
N
OCH3
O
3m
f1 (ppm)

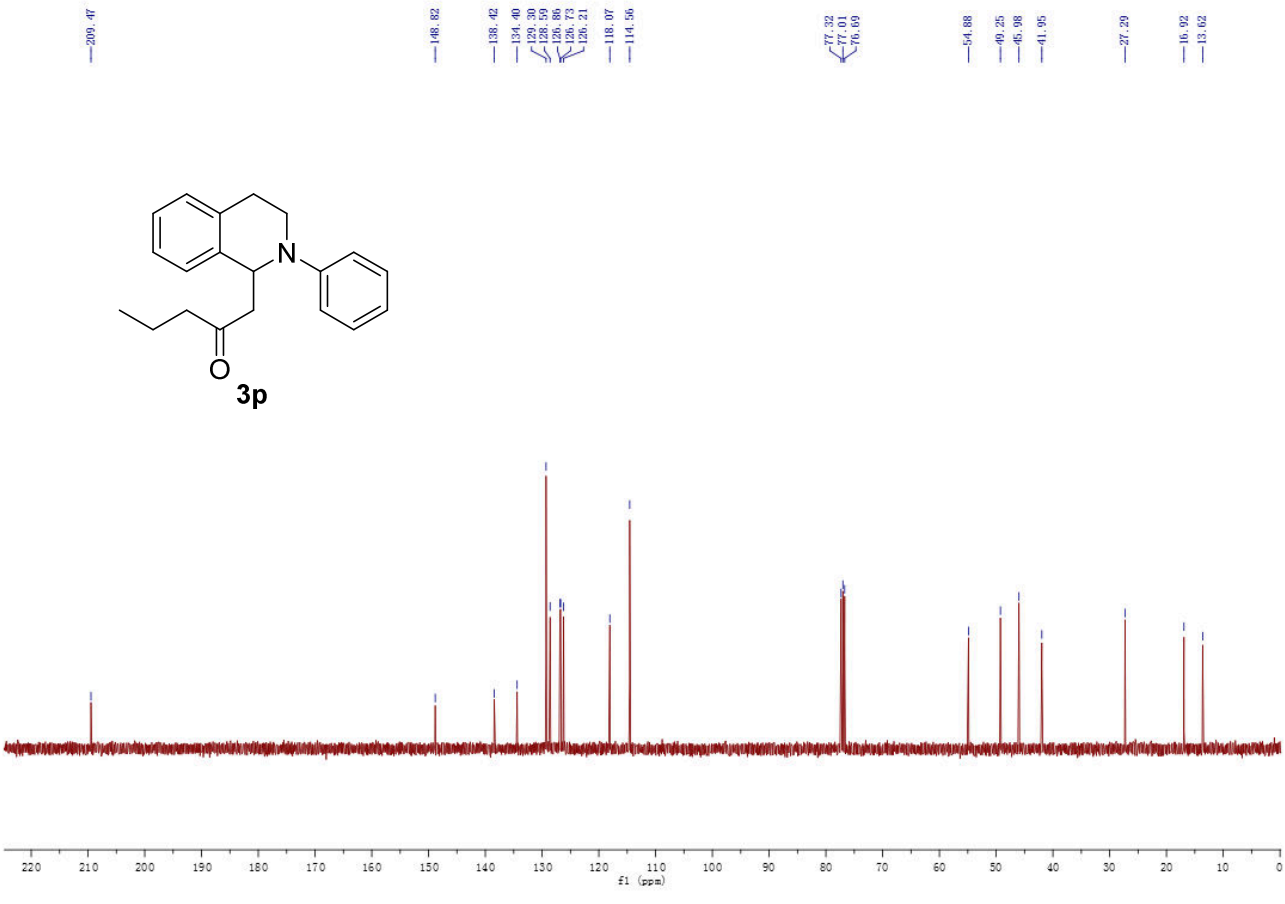

7.26
7.26
7.25
7.23
6.94
6.92
6.83
4.35
3.34
3.33
3.31
3.30
2.90
2.87
2.69
2.48
2.48
2.44
2.44
2.05
1.85
1.75
1.65
1.62
1.58
N
O
3n
2.00
1.88
1.00
1.00
1.03
1.05
1.00
1.02
2.97
1.12
1.02
4.30
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

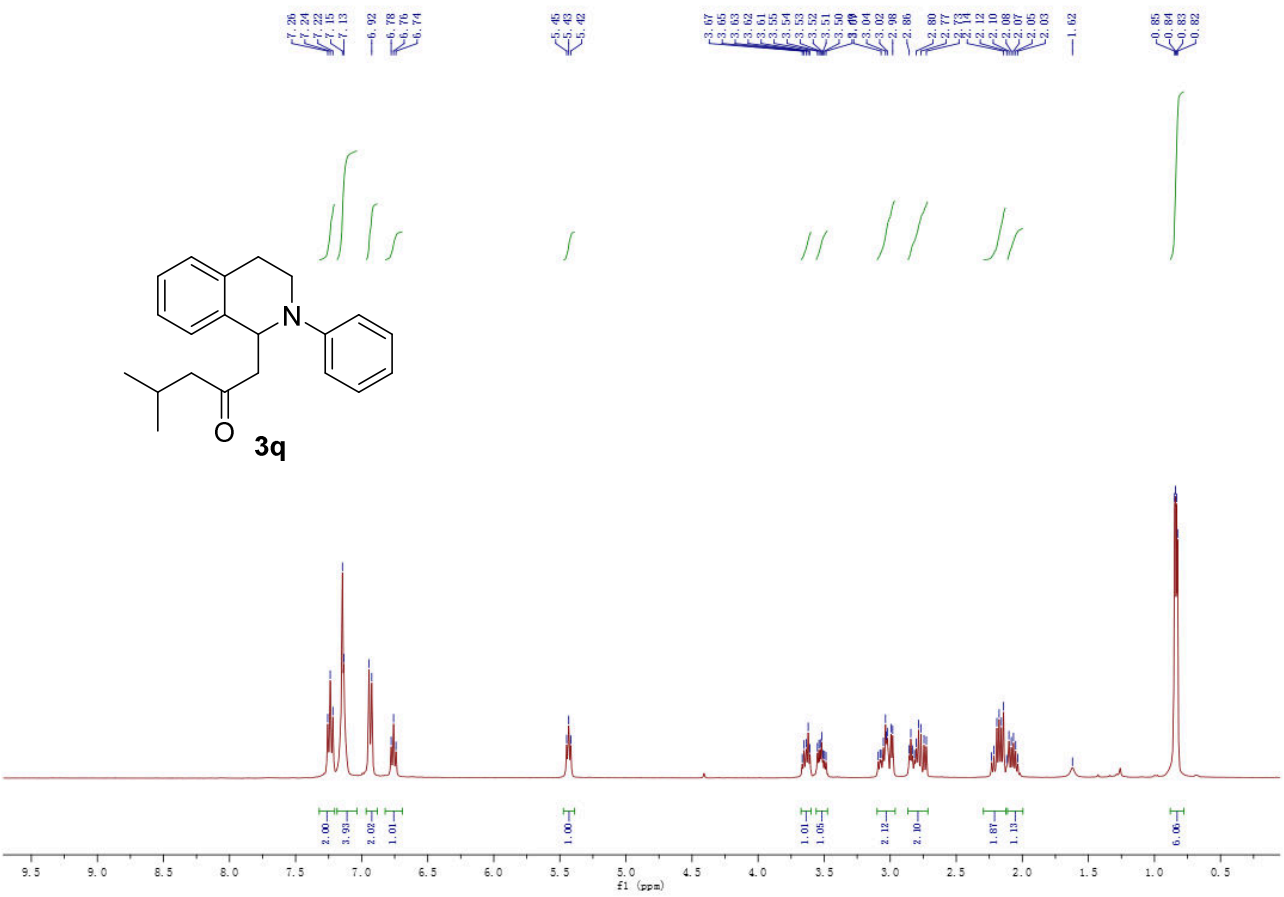

208.03
150.40
129.22
119.46
117.09
52.01
44.71
41.54
30.69
28.88
25.54
19.39
N
O
3n
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

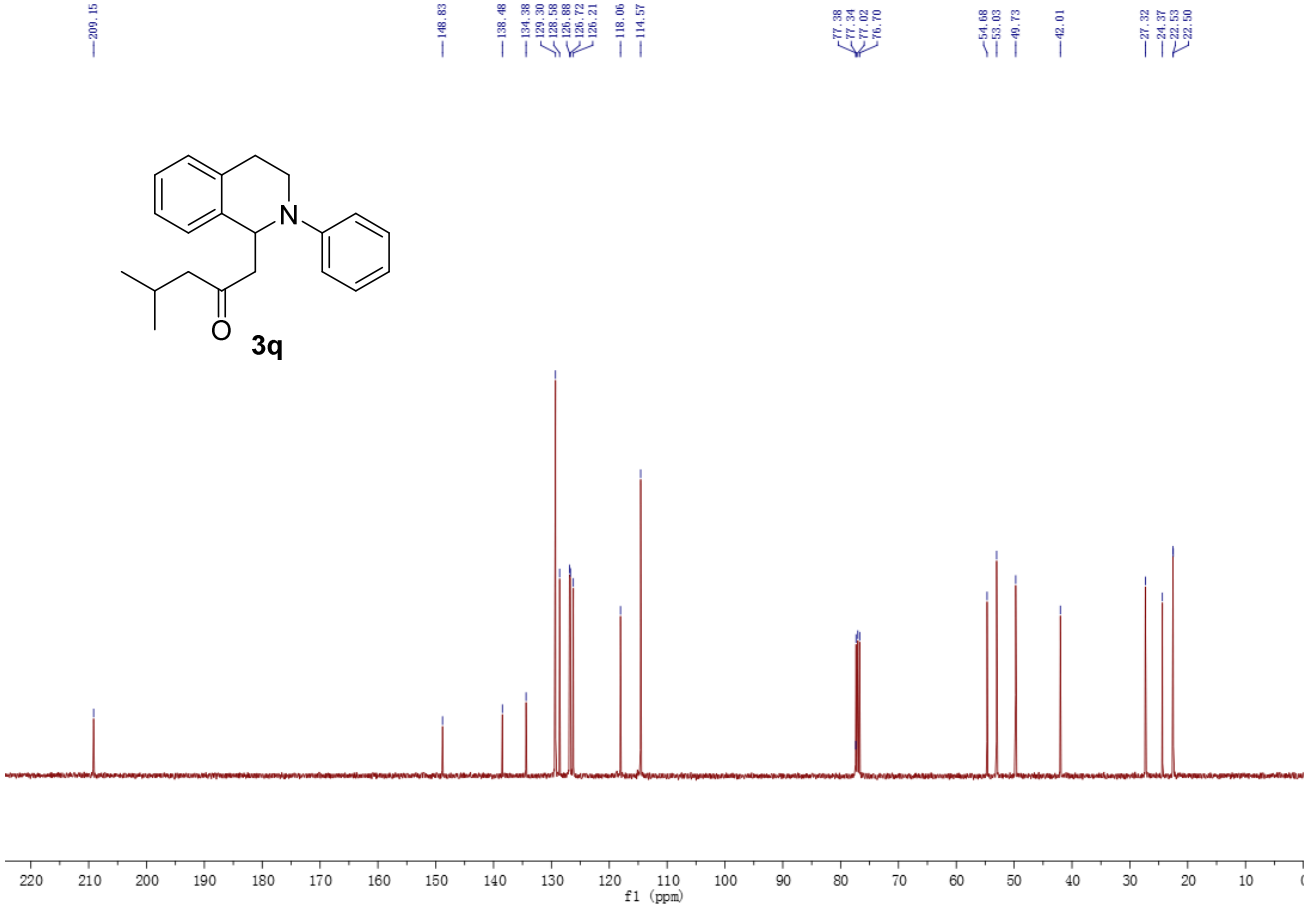

7.29
7.28
7.27
7.26
7.20
7.17
6.96
6.81
6.80
6.78
5.47
5.45
5.44
3.70
3.68
3.67
3.65
3.64
3.59
3.58
3.57
3.56
3.55
3.54
3.53
3.09
3.06
3.03
2.89
2.88
2.87
2.85
2.84
2.82
2.79
2.78
1.03
1.01
0.99
N
O
3o
2.07
3.90
2.09
0.96
1.00
1.07
1.04
2.06
2.10
2.04
3.00
f1 (ppm)

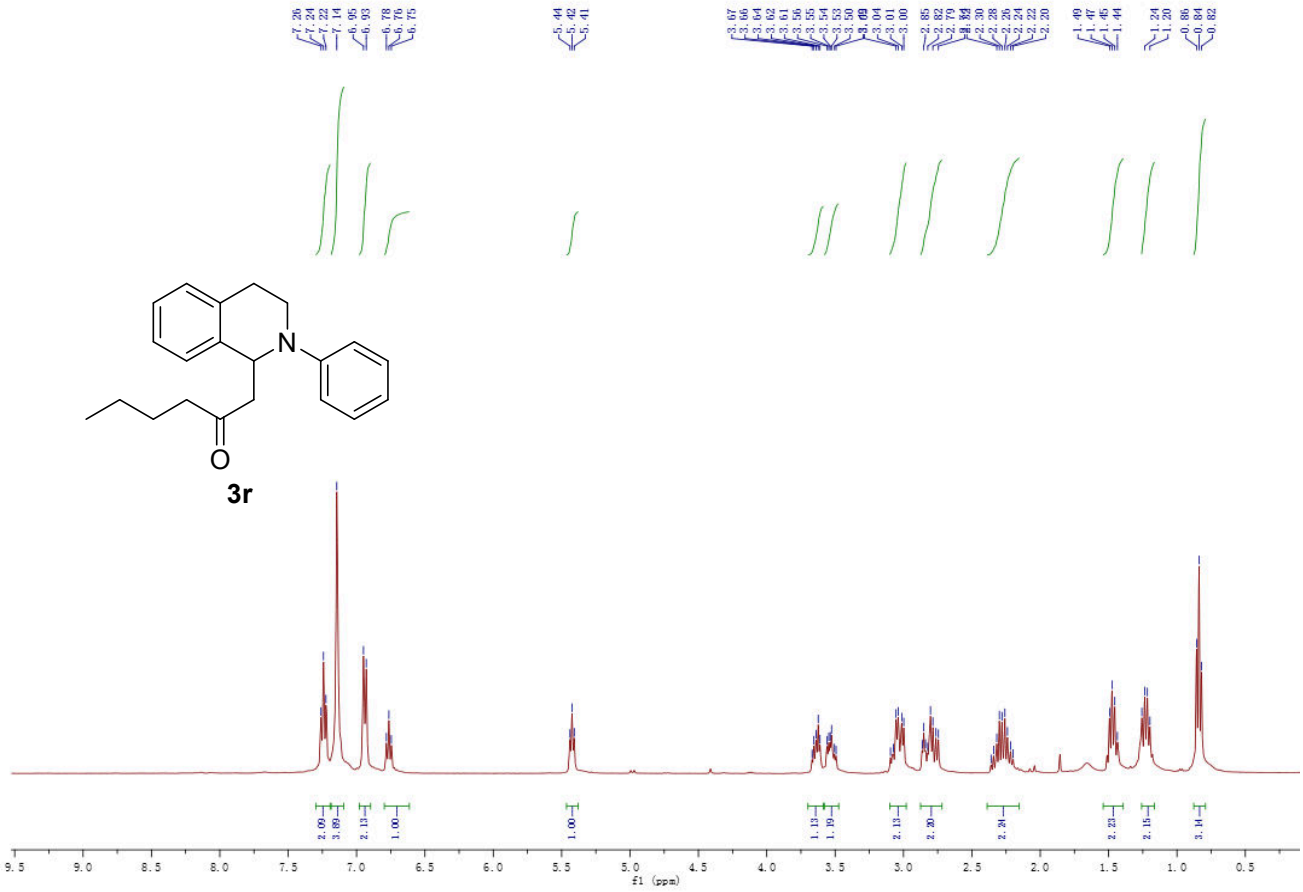

210.00
148.85
138.37
134.46
129.36
128.67
126.87
126.80
126.25
118.11
114.58
55.10
48.95
41.93
37.29
27.29
7.54
N
O
3o
f1 (ppm)

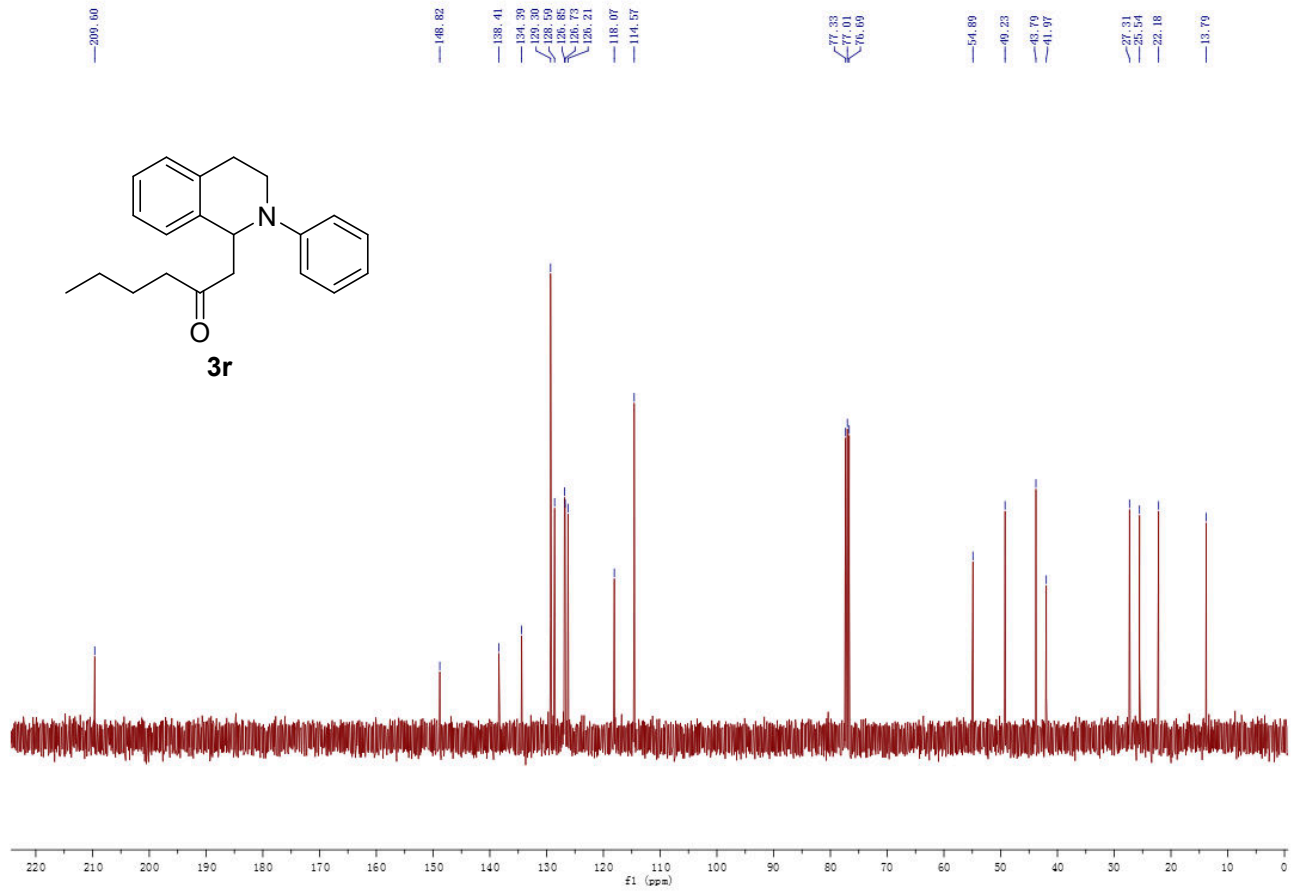

7.26
7.24
7.24
7.22
7.18
7.17
7.14
6.93
6.78
6.76
6.74
5.44
5.42
5.41
3.67
3.66
3.64
3.62
3.61
3.56
3.55
3.54
3.52
3.50
3.04
3.02
2.99
2.84
2.81
2.78
2.26
2.24
2.22
2.20
2.18
1.55
1.53
1.51
1.50
1.48
0.85
0.83
0.82
N
O
3p
1.97
3.75
1.96
0.89
1.00
0.99
1.06
2.13
2.16
2.08
1.96
3.07
f1 (ppm)

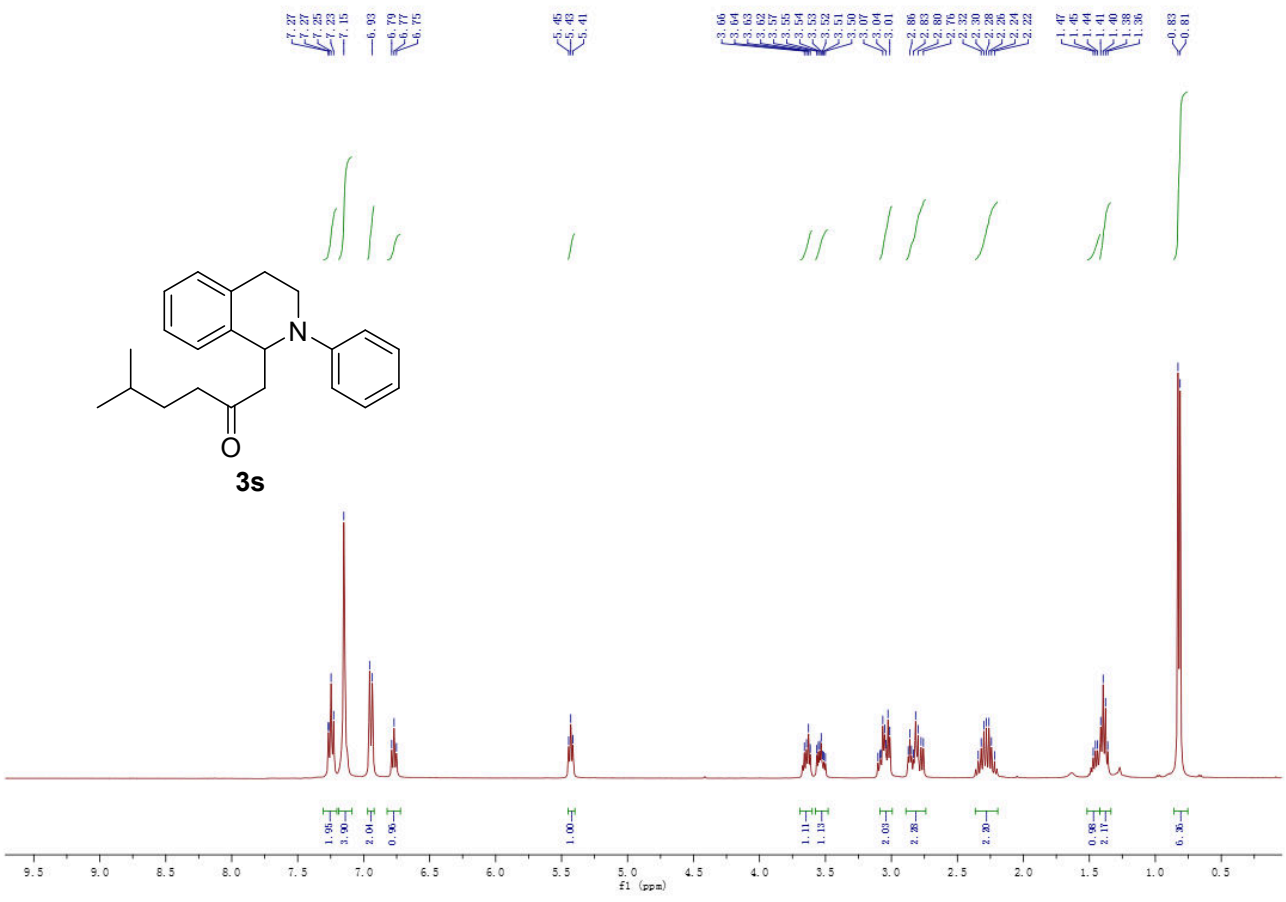

209.47
148.82
138.42
134.40
129.30
128.59
126.86
126.73
126.21
118.07
114.56
77.32
77.01
76.69
54.88
49.25
45.98
41.95
27.29
16.92
13.62
N
O
3p
f1 (ppm)

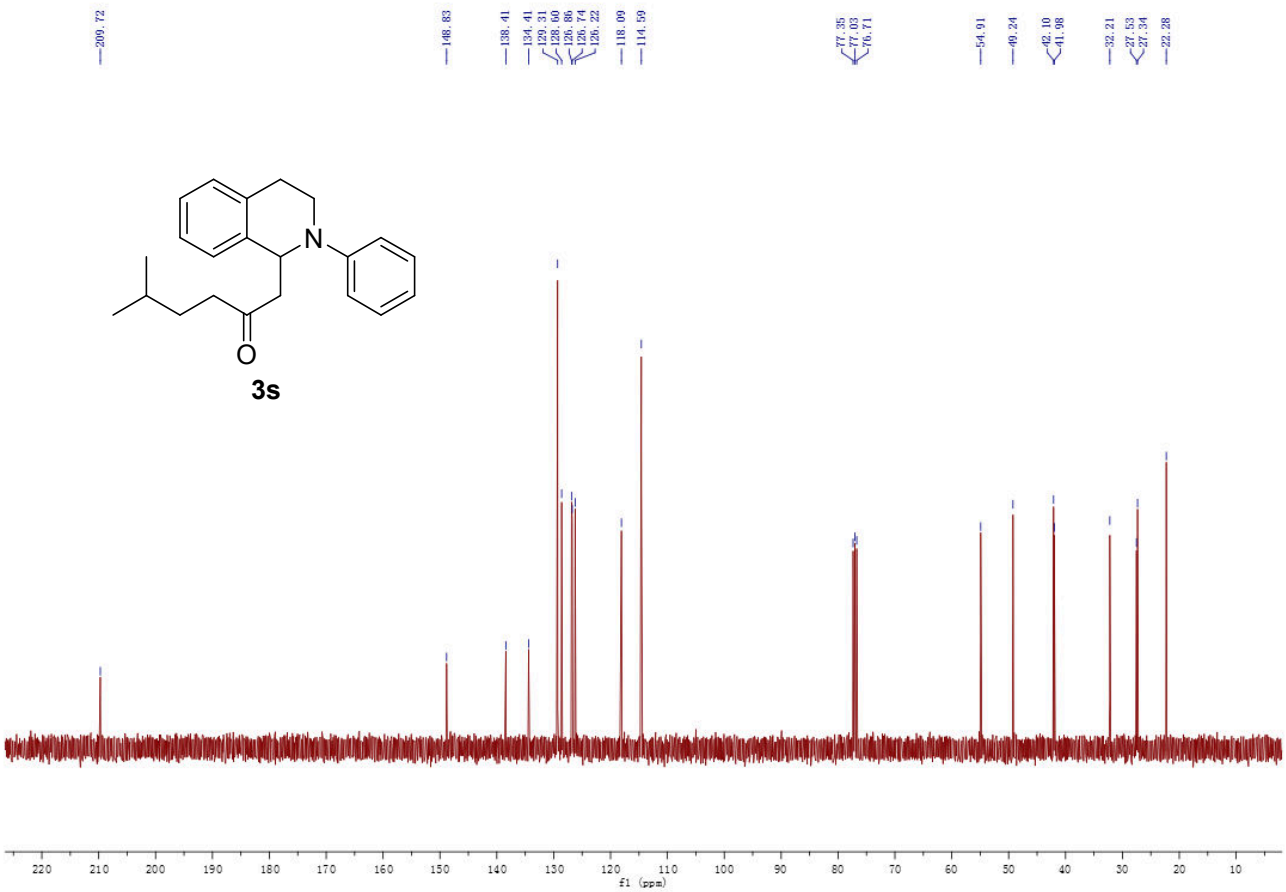

7.26
7.24
7.22
7.15
7.13
6.92
6.78
6.76
6.74
5.45
5.43
5.42
3.67
3.65
3.63
3.62
3.61
3.55
3.54
3.53
3.52
3.51
3.50
3.04
3.02
2.98
2.86
2.80
2.77
2.12
2.10
2.08
2.07
2.05
2.03
1.62
0.85
0.84
0.83
0.82
N
O
3q
2.00
3.93
2.02
1.01
1.00
1.01
1.05
2.12
2.10
1.87
1.13
6.06
f1 (ppm)

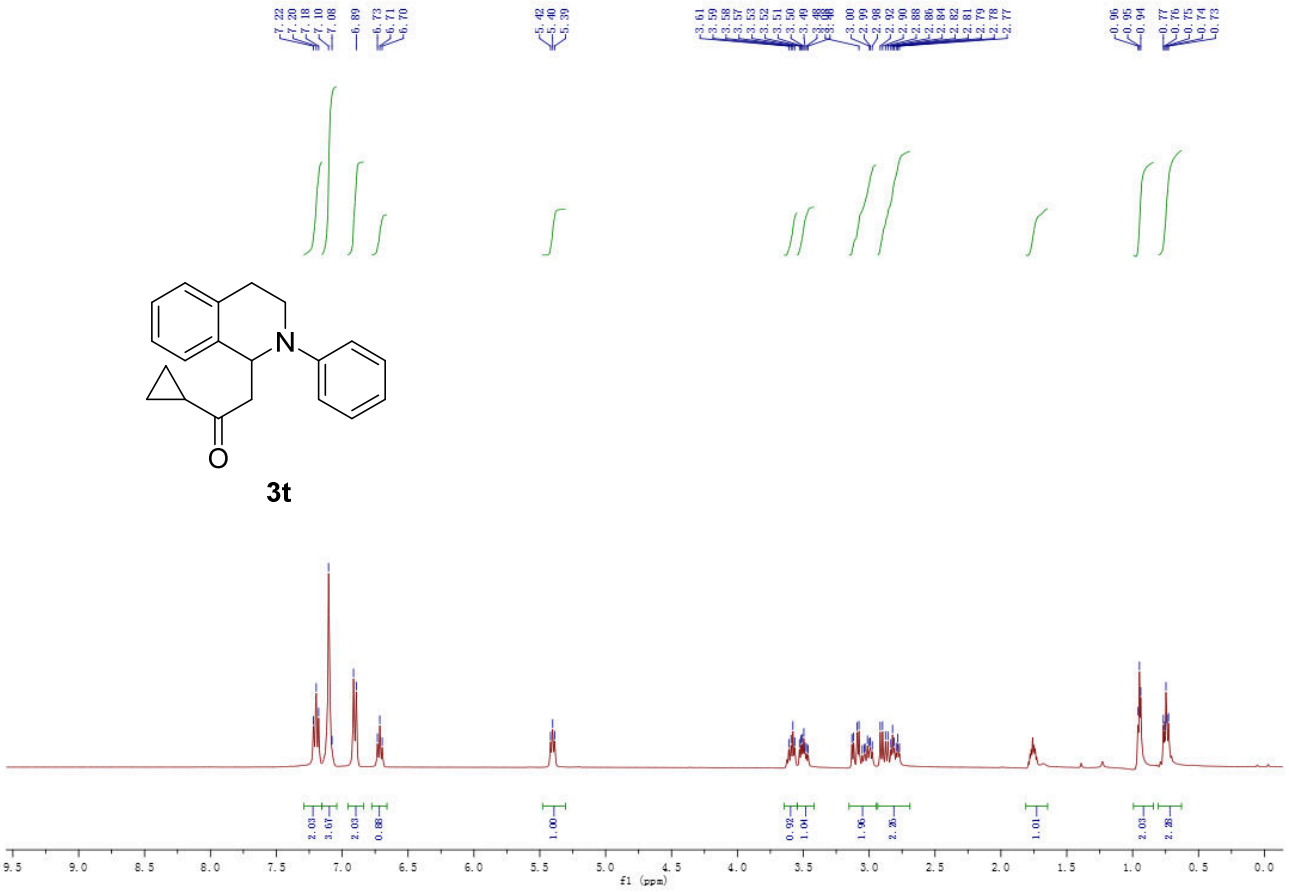

209.15
148.83
138.48
134.38
129.30
128.58
126.88
126.72
126.21
118.06
114.57
77.38
77.34
77.02
76.70
54.68
53.03
49.73
42.01
27.32
24.37
22.53
22.50
N
O
3q
f1 (ppm)

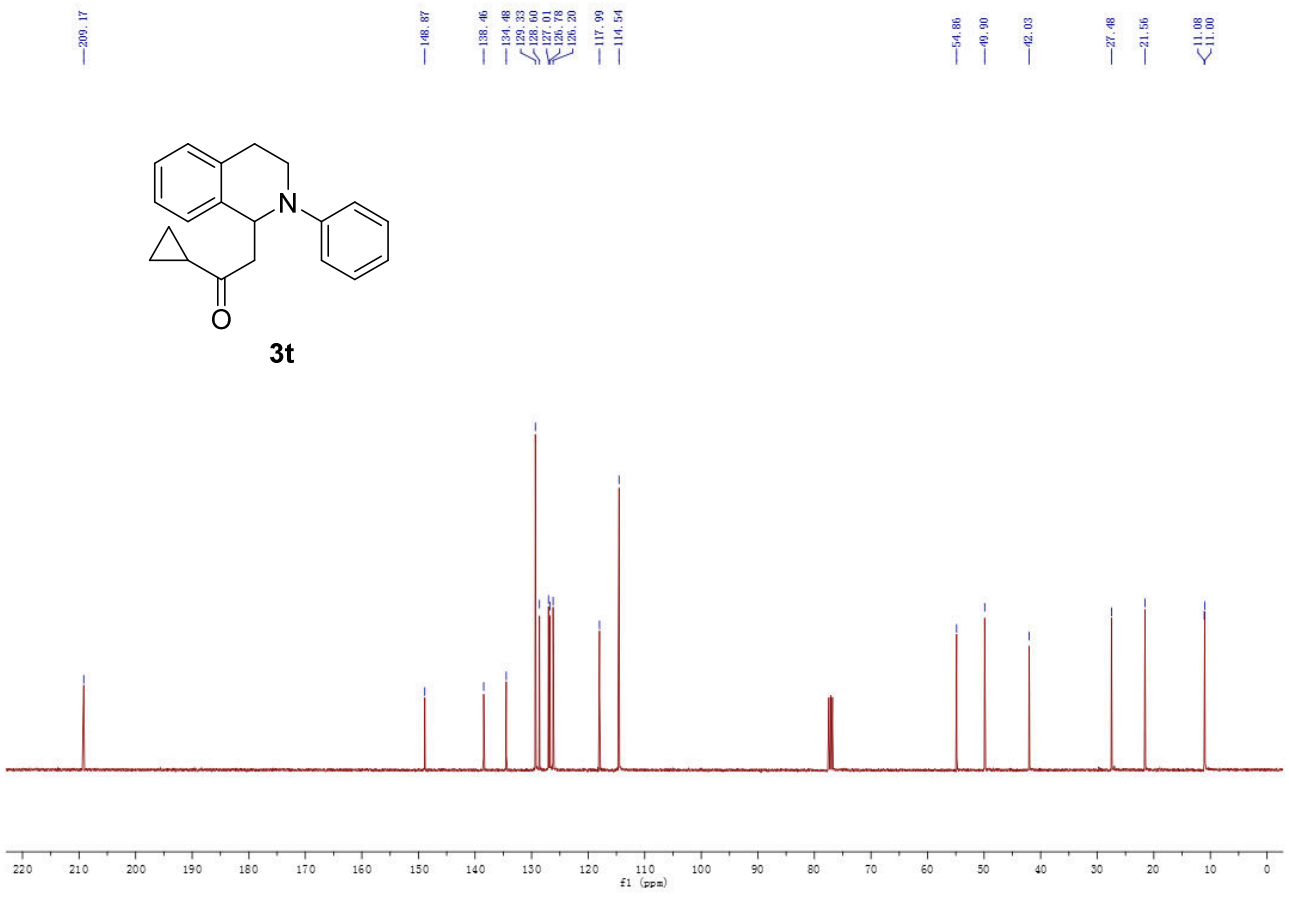

7.26
7.24
7.22
7.14
6.95
6.93
6.78
6.76
6.75
5.44
5.42
5.41
3.67
3.66
3.64
3.62
3.61
3.56
3.55
3.54
3.53
3.01
3.00
2.85
2.82
2.79
2.30
2.28
2.26
2.24
2.22
2.20
1.49
1.47
1.45
1.44
1.24
1.20
0.86
0.84
0.82
N
O
3r
2.09
3.89
2.13
1.00
1.00
1.13
1.19
2.13
2.20
2.24
2.23
2.15
3.14
f1 (ppm)

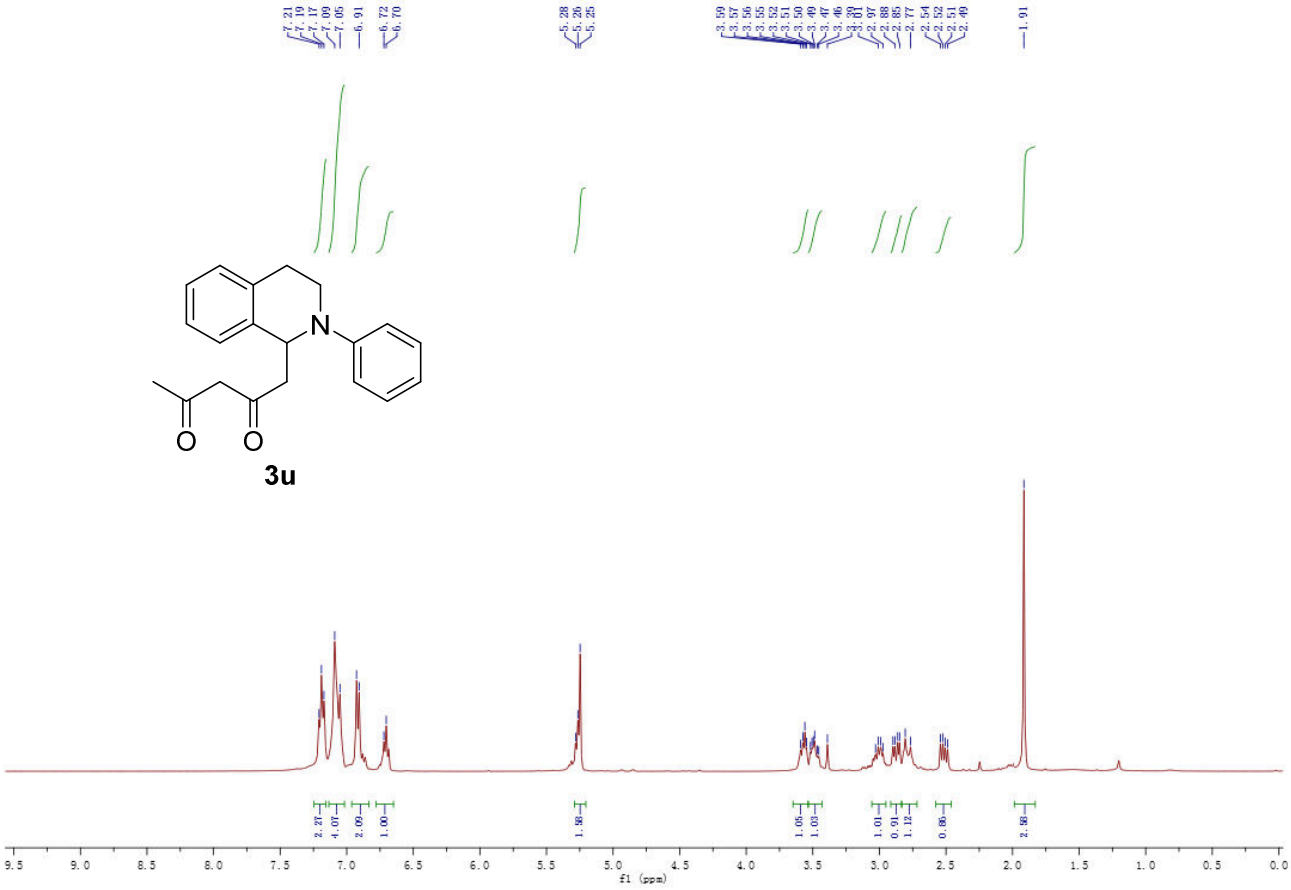

209.60
148.82
138.41
134.39
129.30
128.59
126.85
126.73
126.21
118.07
114.57
77.33
77.01
76.69
54.89
49.23
43.79
41.97
27.31
25.54
22.18
13.79
N
O
3r
f1 (ppm)

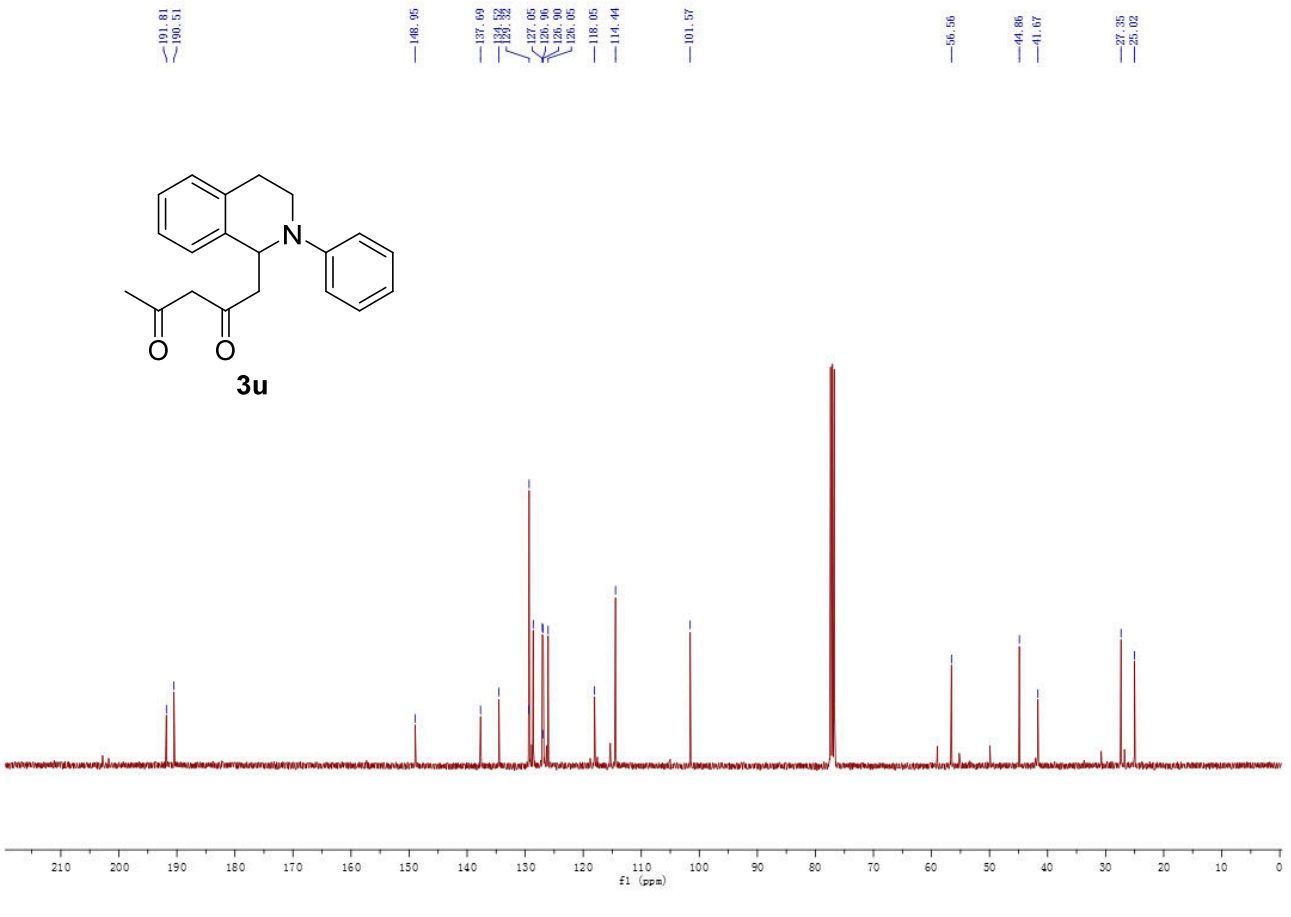

7.27
7.27
7.25
7.23
7.15
6.93
6.79
6.77
6.75
5.45
5.43
5.41
3.66
3.64
3.63
3.62
3.57
3.55
3.54
3.53
3.52
3.51
3.50
3.07
3.04
3.01
2.86
2.83
2.80
2.76
2.32
2.30
2.28
2.26
2.24
2.22
1.47
1.45
1.44
1.41
1.40
1.38
1.36
0.83
0.81
N
O
3s
1.96
3.90
2.04
0.96
1.00
1.11
1.13
2.03
2.28
2.20
0.98
2.17
6.36
f1 (ppm)

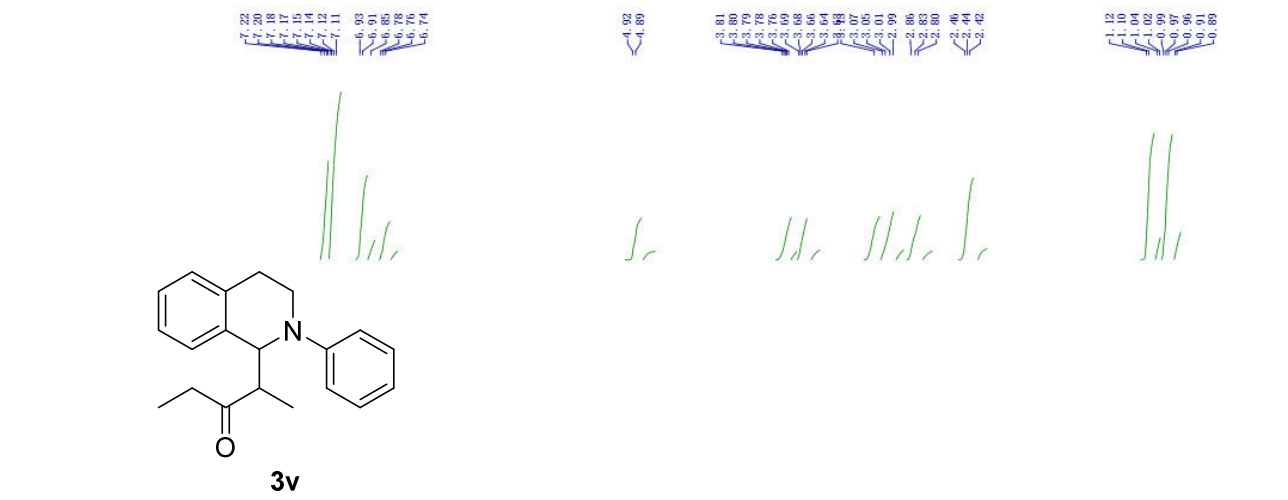

209.72
148.83
138.41
134.41
129.31
128.66
126.86
126.74
126.22
118.09
114.59
77.35
77.03
76.71
54.91
49.24
42.10
41.98
32.21
27.53
27.34
22.28
N
O
3s
f1 (ppm)


7.22
7.20
7.18
7.10
7.08
6.89
6.73
6.71
6.70
5.42
5.40
5.39
3.61
3.59
3.58
3.57
3.53
3.52
3.51
3.50
3.49
3.00
2.99
2.98
2.92
2.90
2.88
2.86
2.84
2.82
2.81
2.79
2.78
2.77
0.96
0.95
0.94
0.77
0.76
0.75
0.74
0.73
N
O
3t
2.03
3.67
2.03
0.88
1.00
0.92
1.04
1.90
2.26
1.01
2.03
2.28
f1 (ppm)

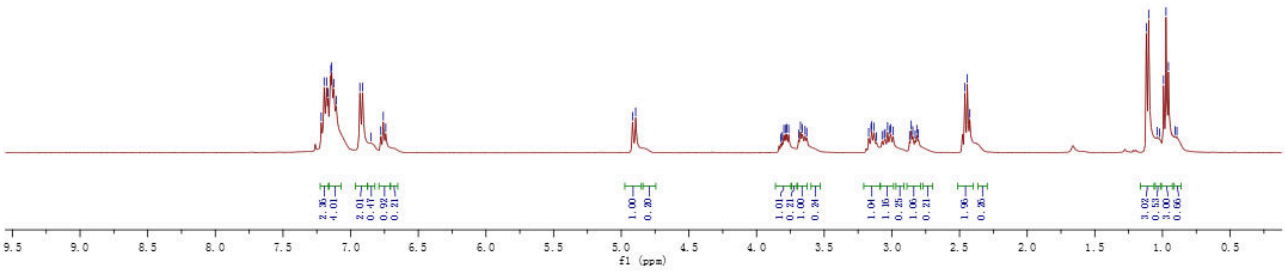

209.17
148.87
138.46
134.48
129.33
128.60
127.01
126.78
126.20
117.99
114.54
54.86
49.90
42.03
27.48
21.56
11.08
11.00
N
O
3t
f1 (ppm)

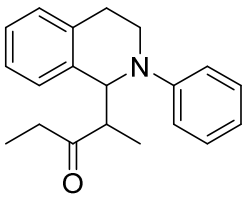

7.21
7.19
7.17
7.09
7.05
6.91
6.72
6.70
5.28
5.26
5.25
3.59
3.57
3.56
3.55
3.52
3.51
3.50
3.49
3.47
3.46
3.30
3.01
2.97
2.88
2.85
2.77
2.54
2.52
2.51
2.49
1.91
N
O
O
3u
2.27
4.07
2.09
1.00
1.98
1.05
1.03
1.01
0.91
1.12
0.86
2.86
f1 (ppm)


191.81
190.51
148.95
137.69
129.32
127.05
126.96
126.90
126.05
118.05
114.44
101.57
56.56
44.86
41.67
27.35
25.02
N
O
O
3u
f1 (ppm)

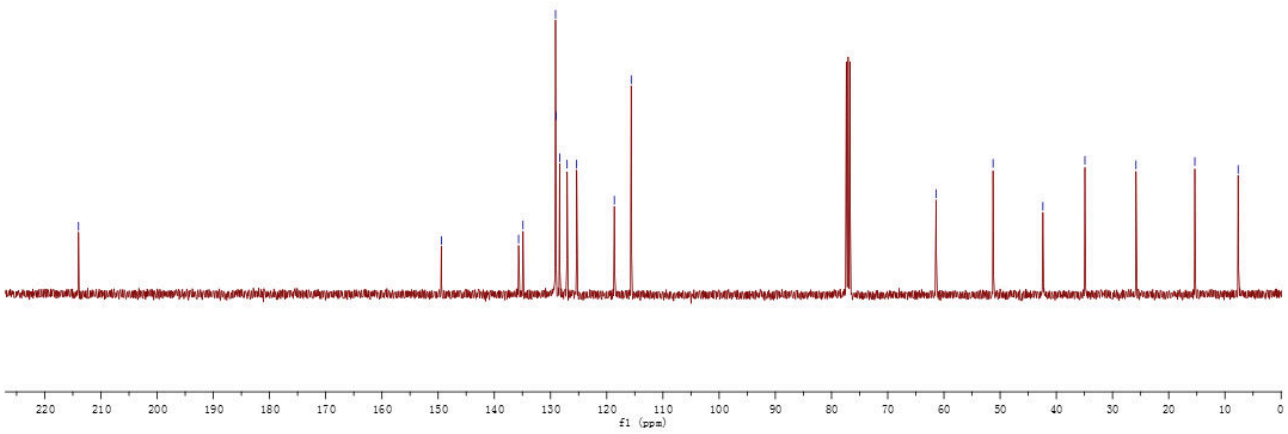


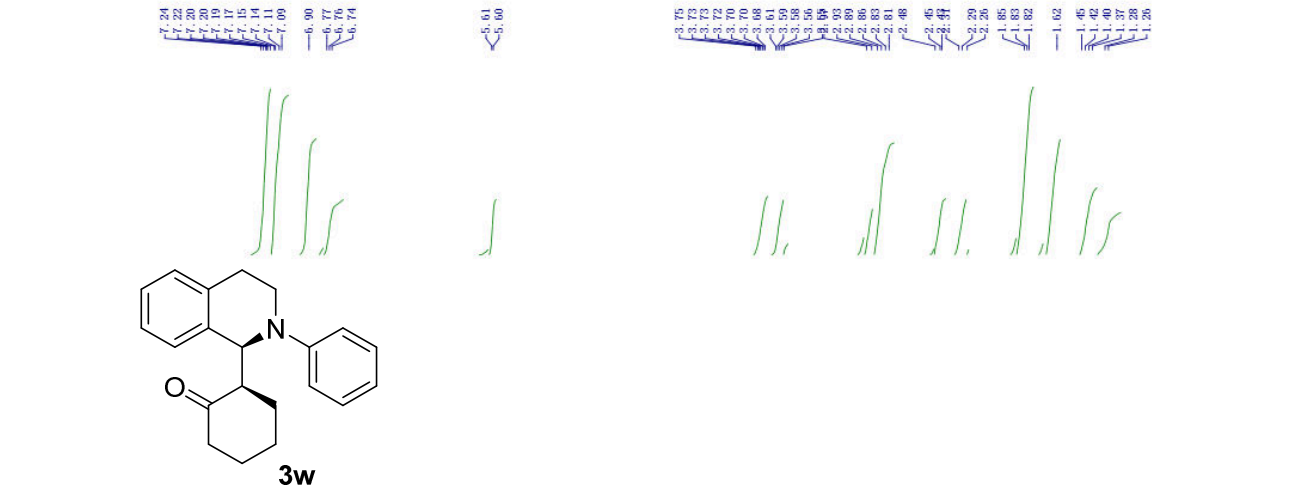
3v

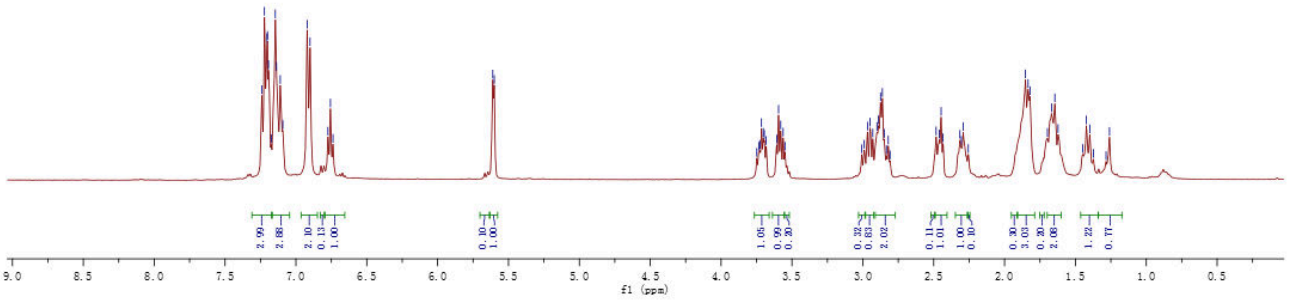




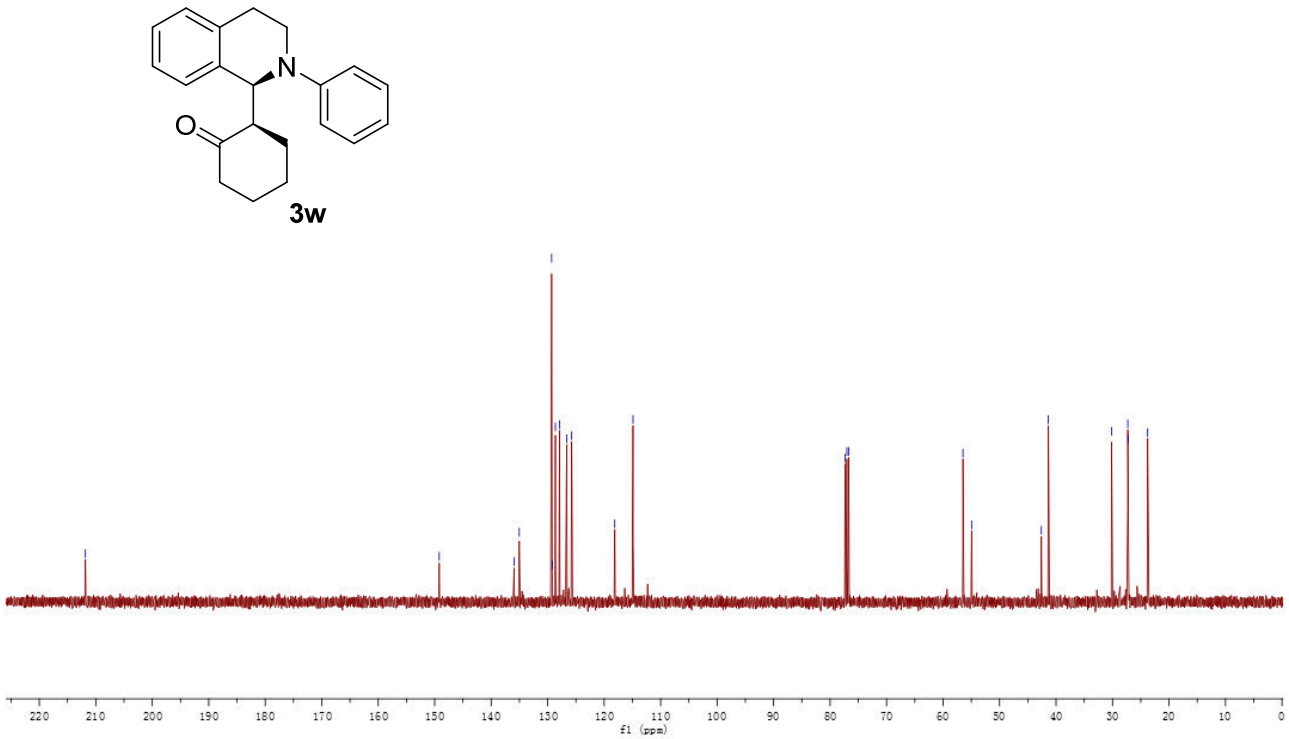
3v

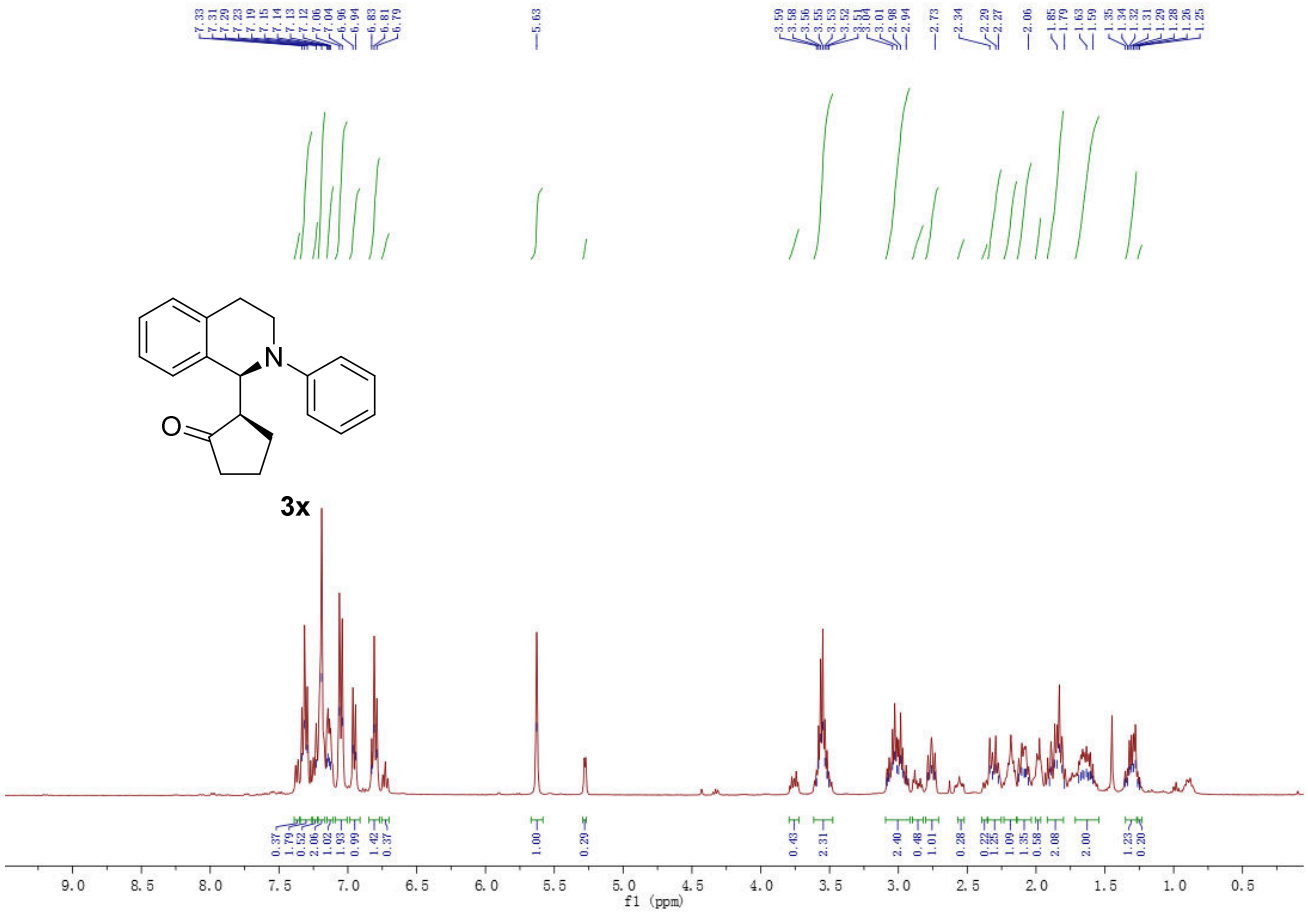



7.24
7.22
7.20
7.20
7.19
7.17
7.15
7.14
7.11
7.09
6.90
6.77
6.76
6.74
5.61
5.60
3.75
3.73
3.73
3.72
3.70
3.70
3.68
3.61
3.59
3.58
3.56
2.93
2.89
2.86
2.83
2.81
2.48
2.45
2.44
2.29
2.26
1.85
1.83
1.82
1.62
1.45
1.42
1.40
1.37
1.28
1.25
N
O
3w

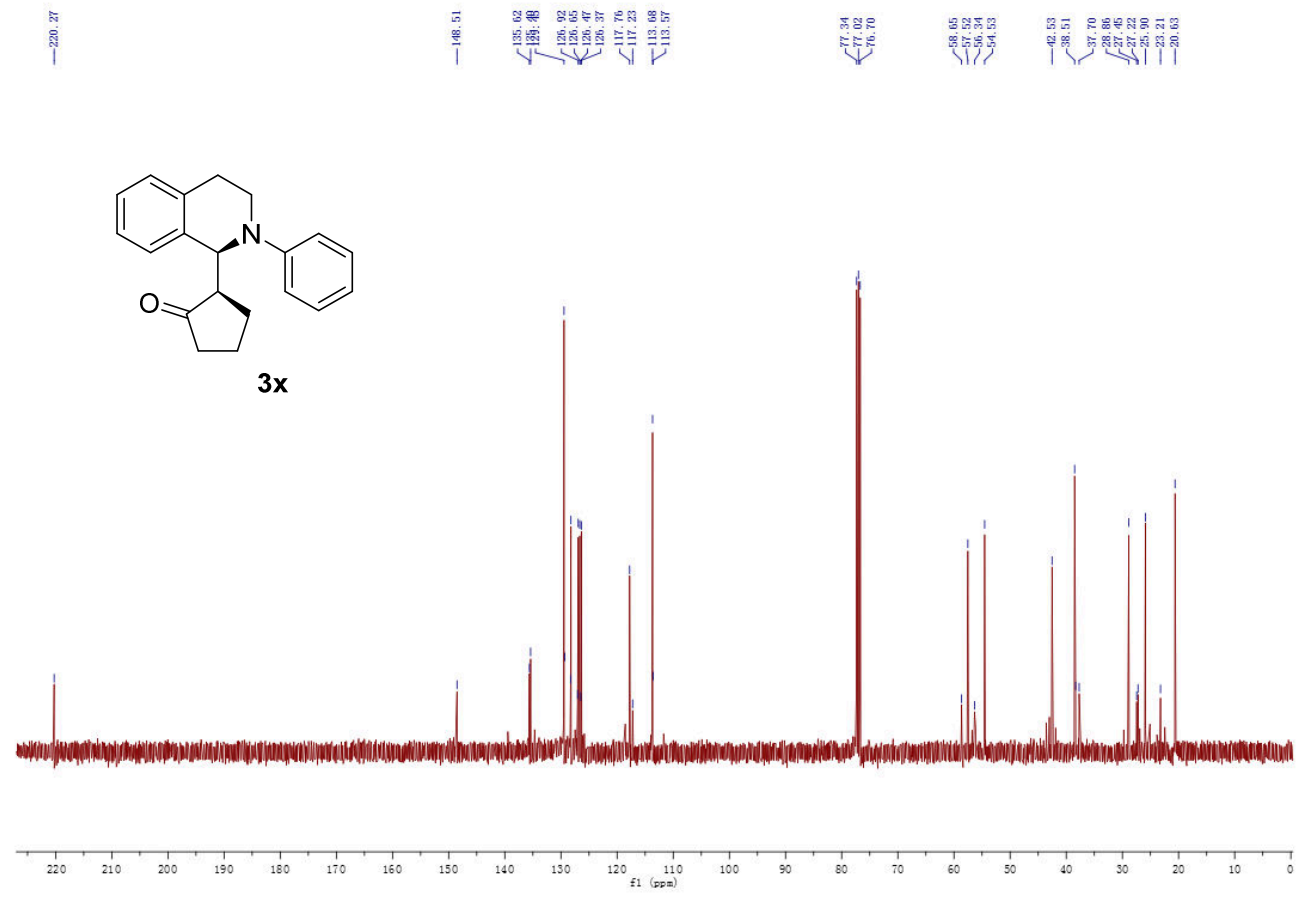

2.99
2.88
2.10
0.13
1.00
0.10
1.00
1.05
0.99
0.20
0.32
0.83
2.02
0.11
1.01
1.00
0.10
0.30
3.03
0.20
2.06
1.22
0.77
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


211.84
149.20
135.94
135.03
129.30
128.63
127.91
126.63
125.75
118.12
114.89
77.35
77.03
76.71
56.48
54.95
42.59
41.35
30.16
27.24
23.79

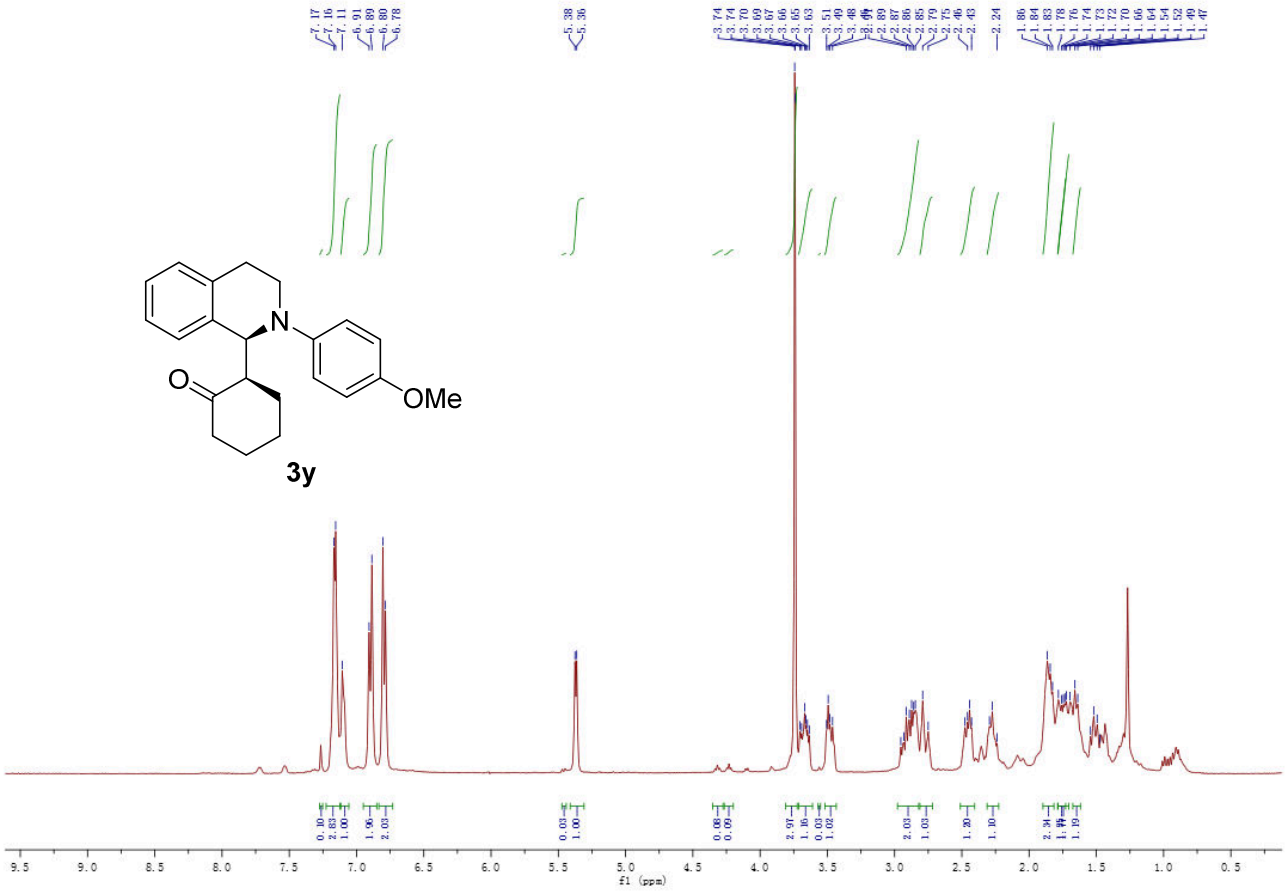

N
O
3w
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



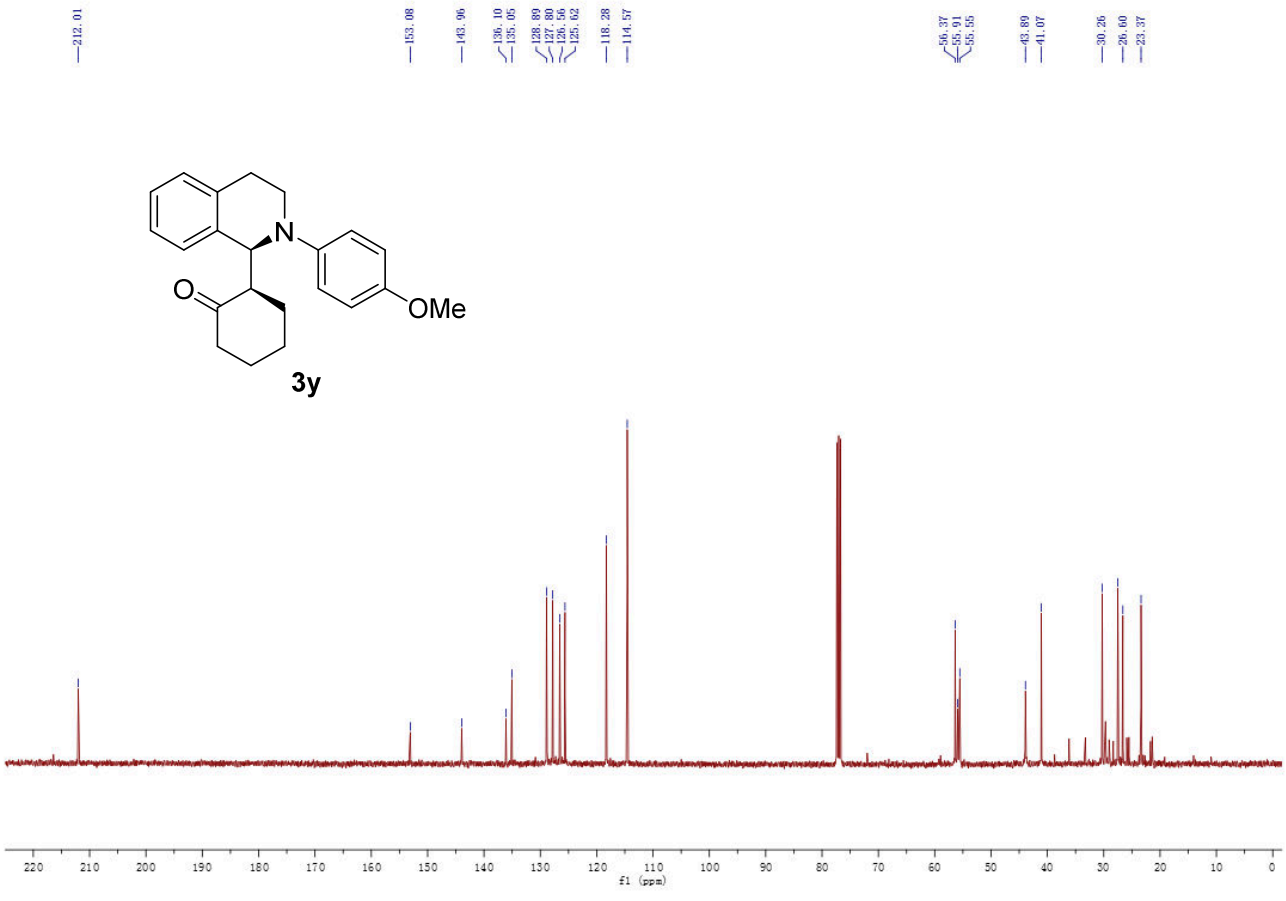
3x



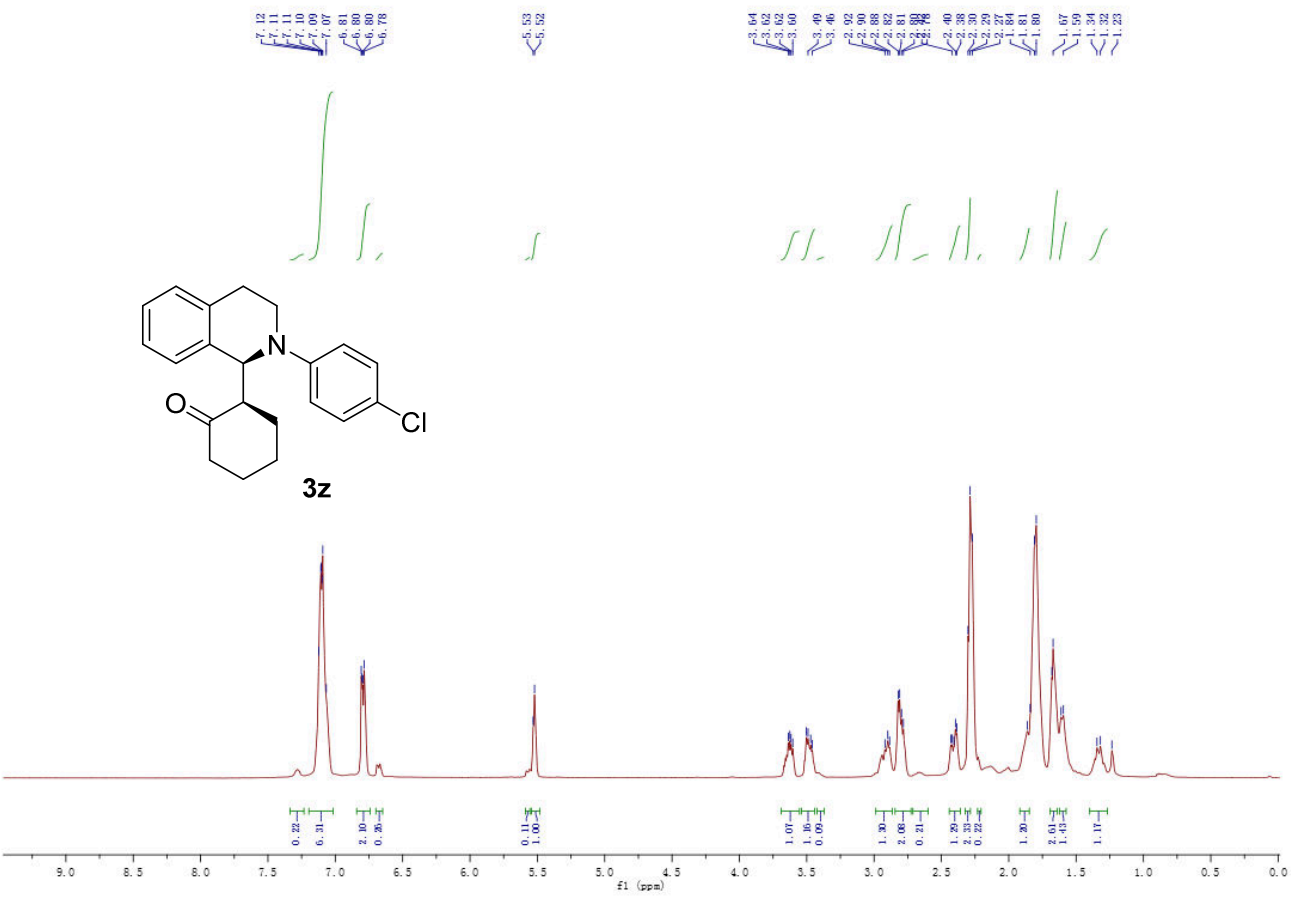
3x

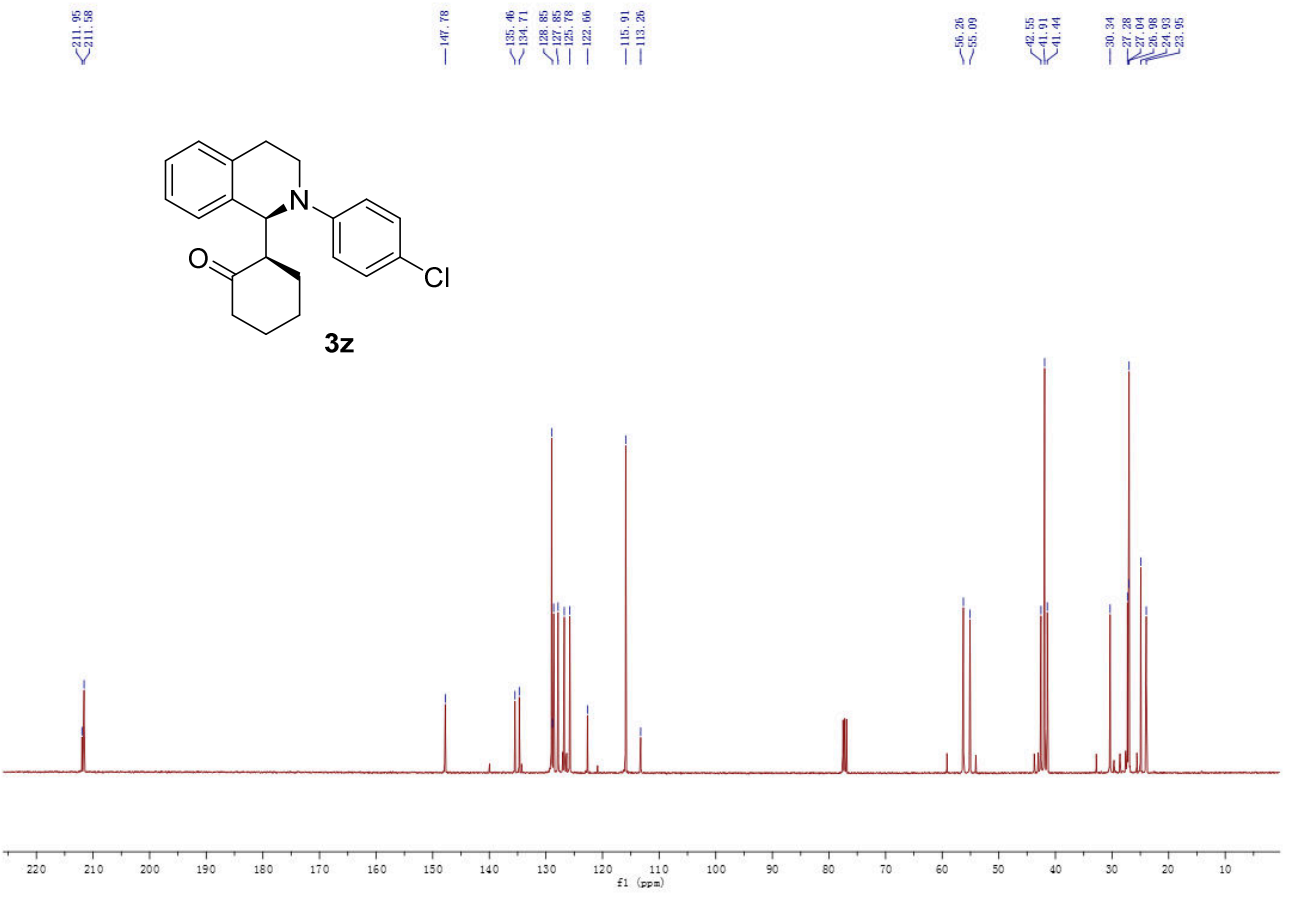


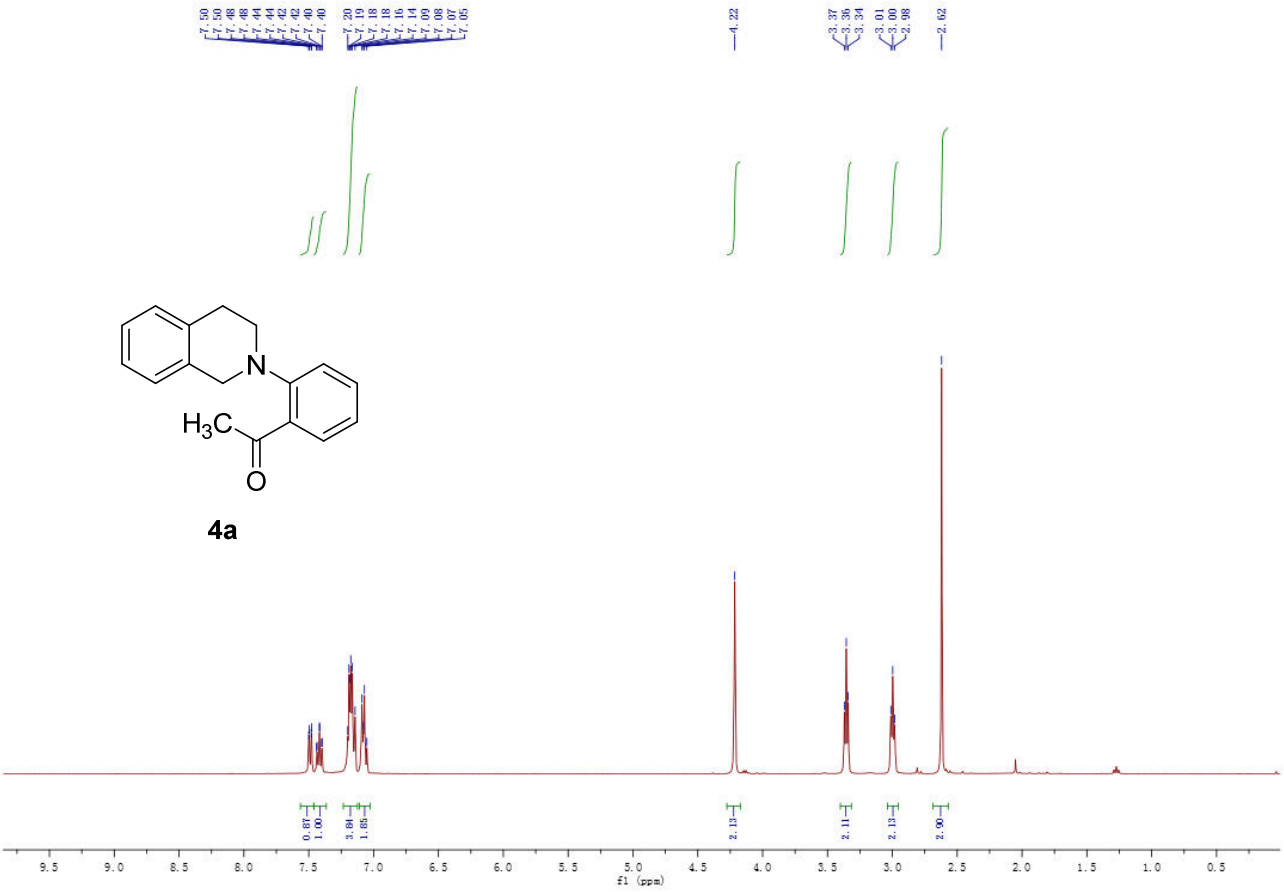
3y



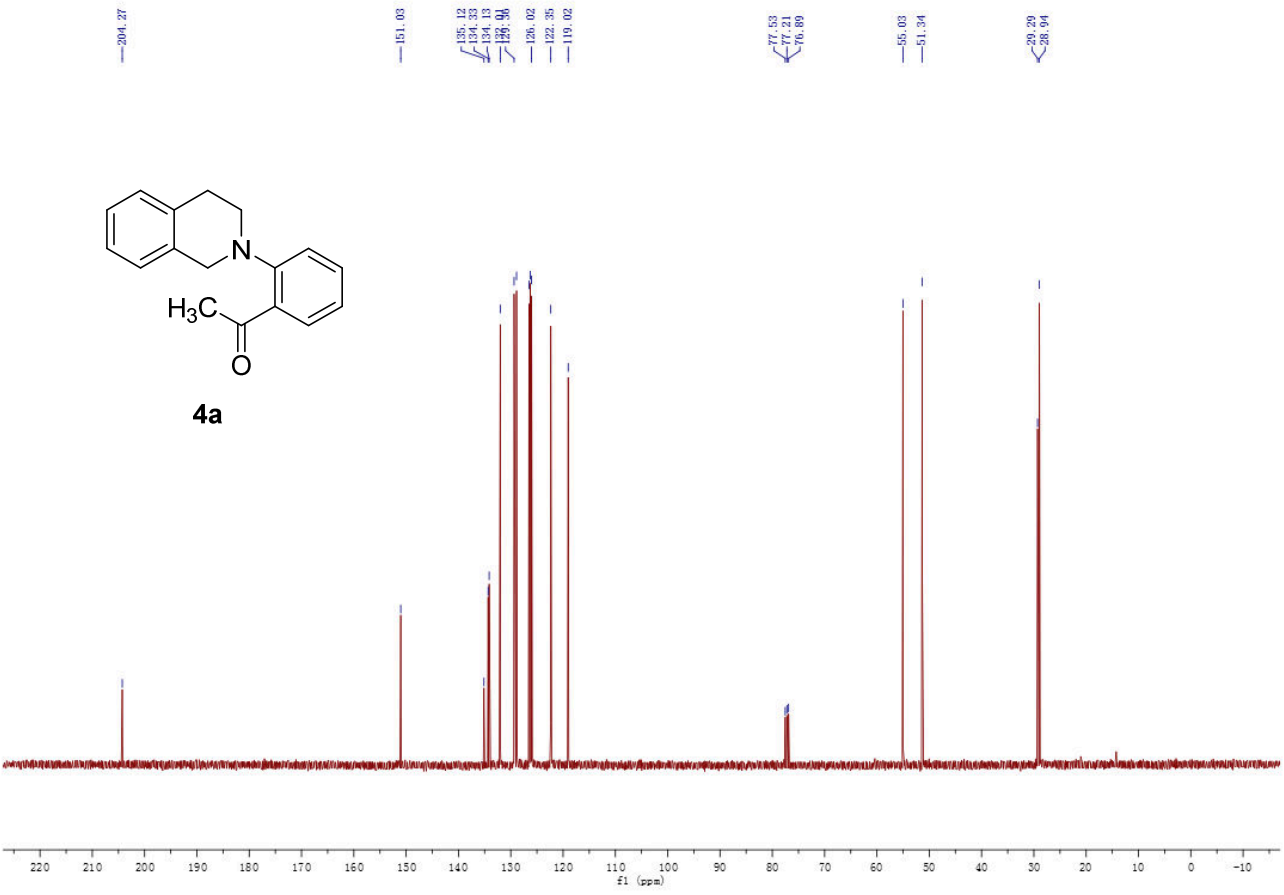
3y


7.12
7.11
7.11
7.10
7.09
7.07
6.81
6.80
6.80
6.78
5.53
5.52
3.64
3.62
3.62
3.60
3.49
3.46
2.92
2.90
2.88
2.82
2.81
2.40
2.38
2.30
2.29
2.27
1.84
1.81
1.80
1.67
1.59
1.34
1.32
1.23
N
O
Cl
3z
0.22
6.31
2.10
0.26
0.11
1.00
1.07
1.16
0.09
1.30
2.08
0.21
1.29
2.33
0.22
1.20
2.61
1.43
1.17
f1 (ppm)

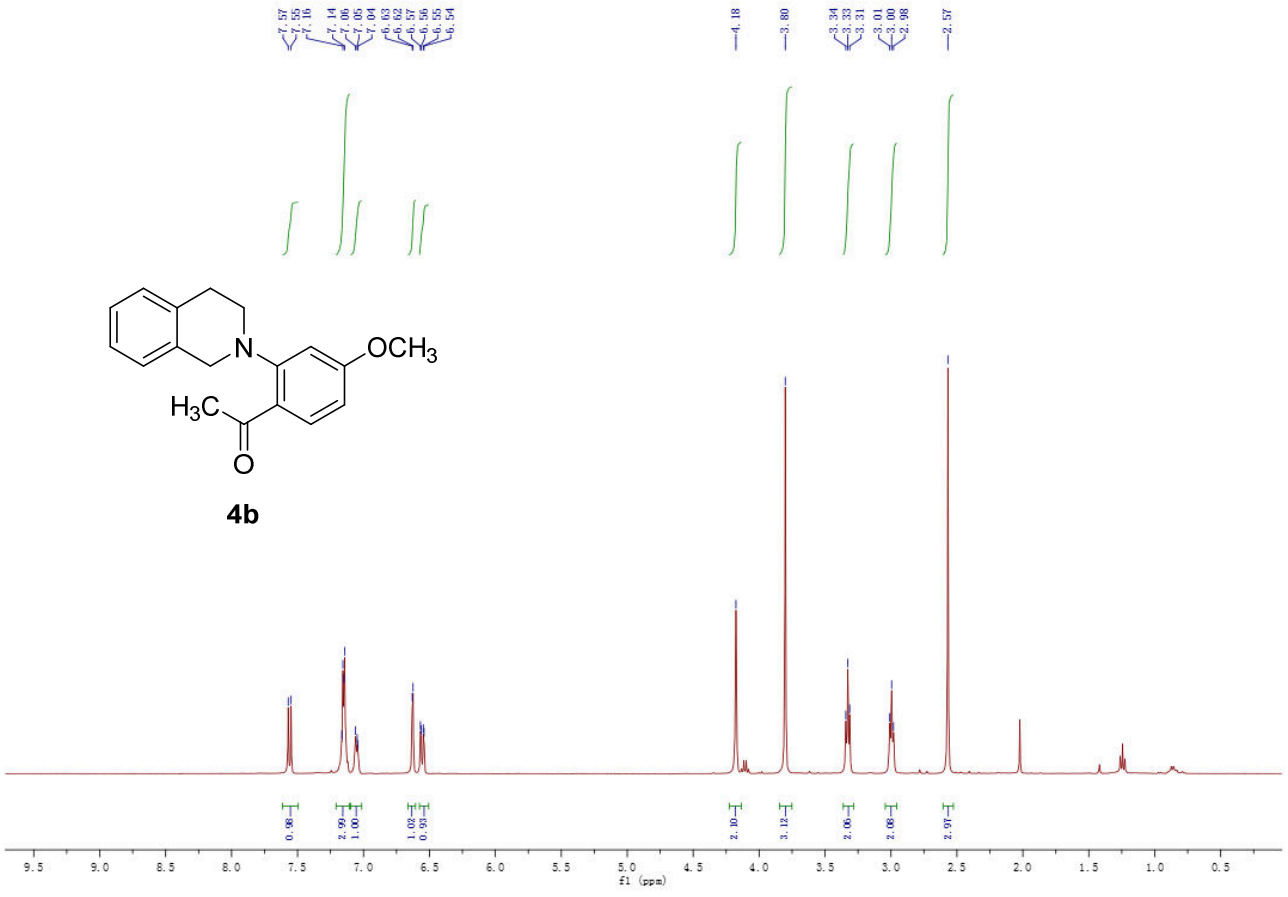

211.95
211.58
147.78
135.46
134.71
128.85
127.85
125.78
122.66
115.91
113.26
56.26
55.09
42.55
41.91
41.44
30.34
27.28
27.04
26.98
24.93
23.95
N
O
Cl
3z
f1 (ppm)


7.50
7.48
7.44
7.42
7.40
7.20
7.19
7.18
7.16
7.14
7.09
7.08
7.07
7.05
4.22
3.37
3.36
3.34
3.01
3.00
2.98
2.62
N
H3C
O
0.87
1.00
3.84
1.85
2.13
2.11
2.13
2.90
f1 (ppm)

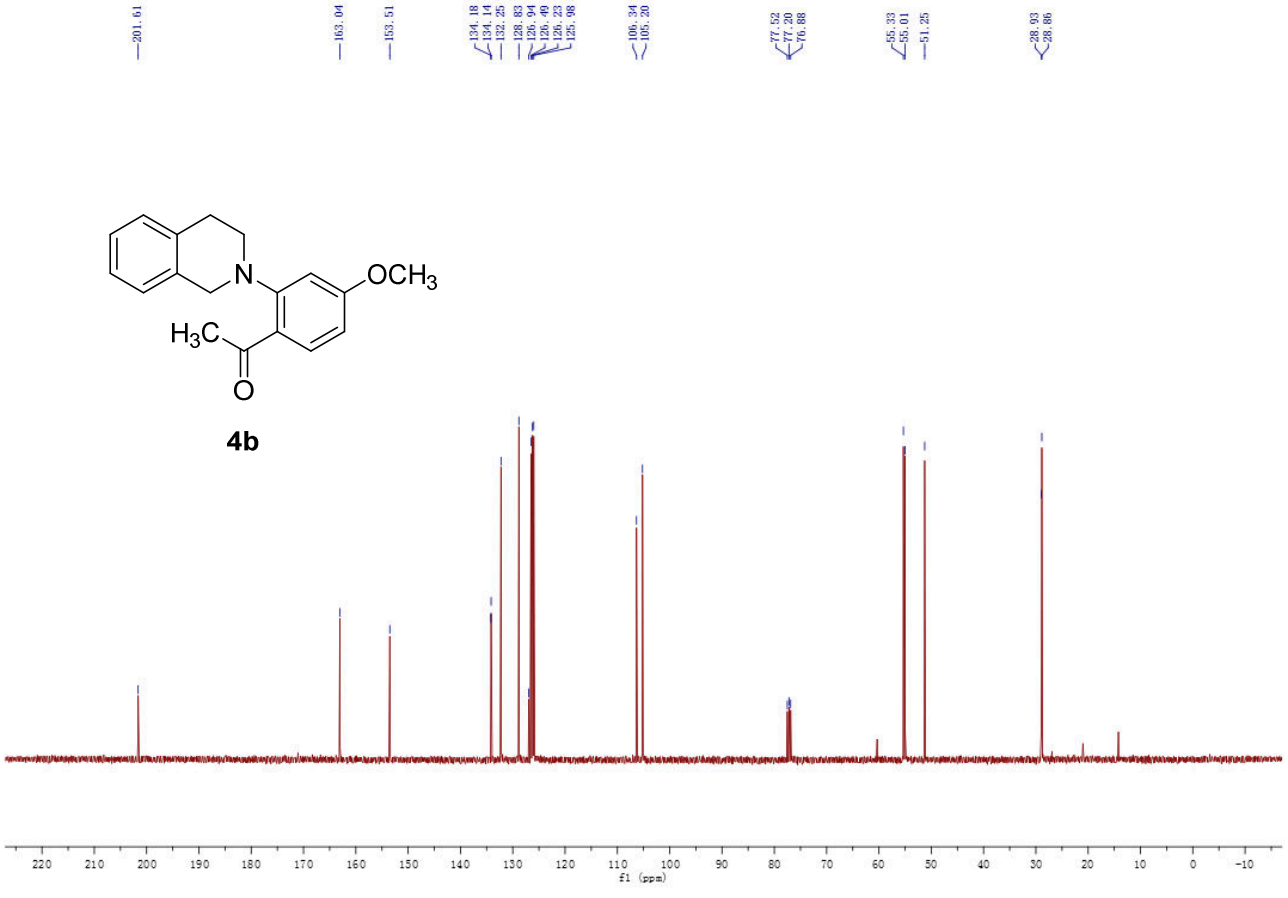
4a


204.27
151.03
135.12
134.33
134.13
126.02
122.35
119.02
77.53
77.21
76.89
55.03
51.34
29.29
28.94
N
H3C
O
f1 (ppm)

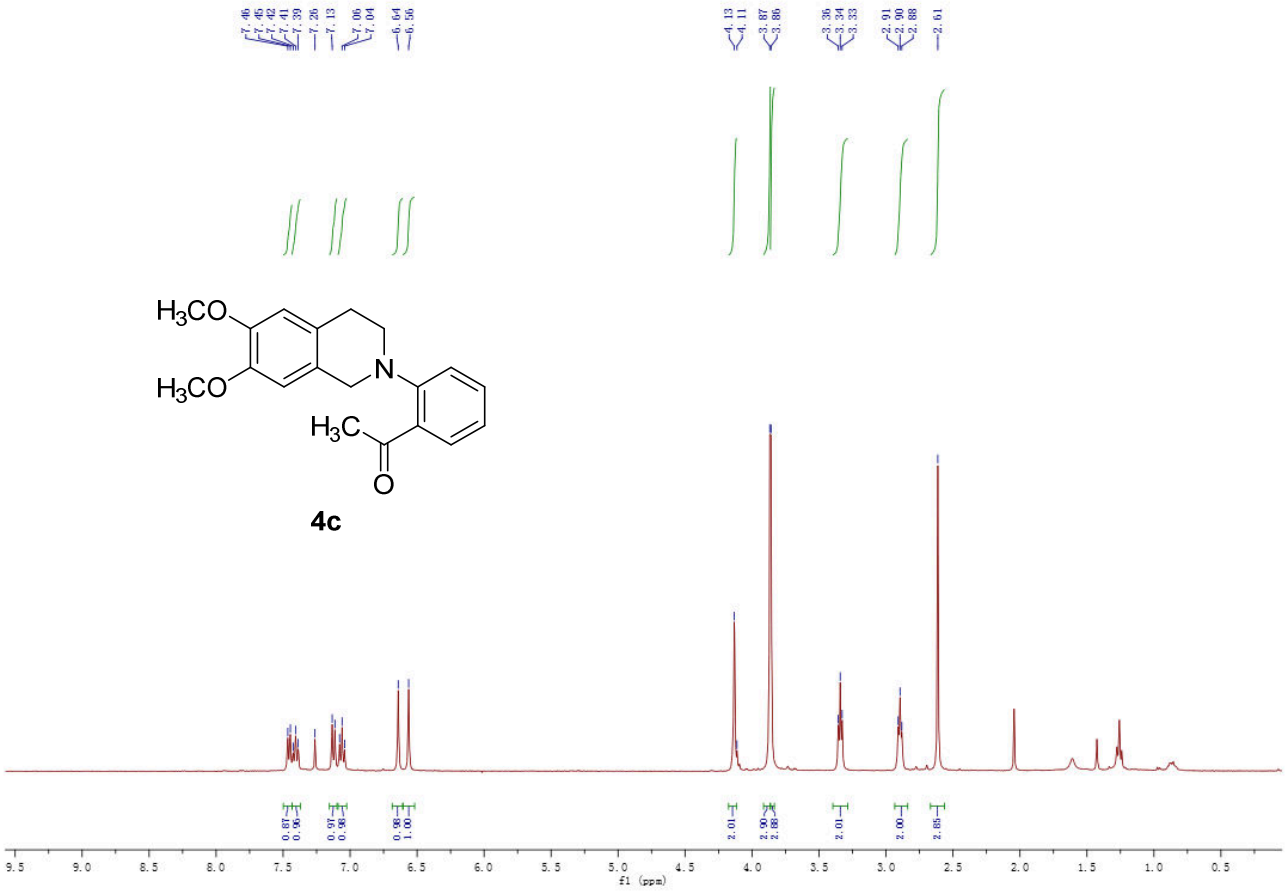
4a


7.57
7.55
7.16
7.14
7.06
7.05
7.04
6.63
6.62
6.57
6.56
6.55
6.54
4.18
3.80
3.34
3.33
3.31
3.01
3.00
2.98
2.57
N
OCH3
H3C
O
0.98
2.99
1.00
1.02
0.98
2.10
3.12
2.06
2.08
2.97
f1 (ppm)

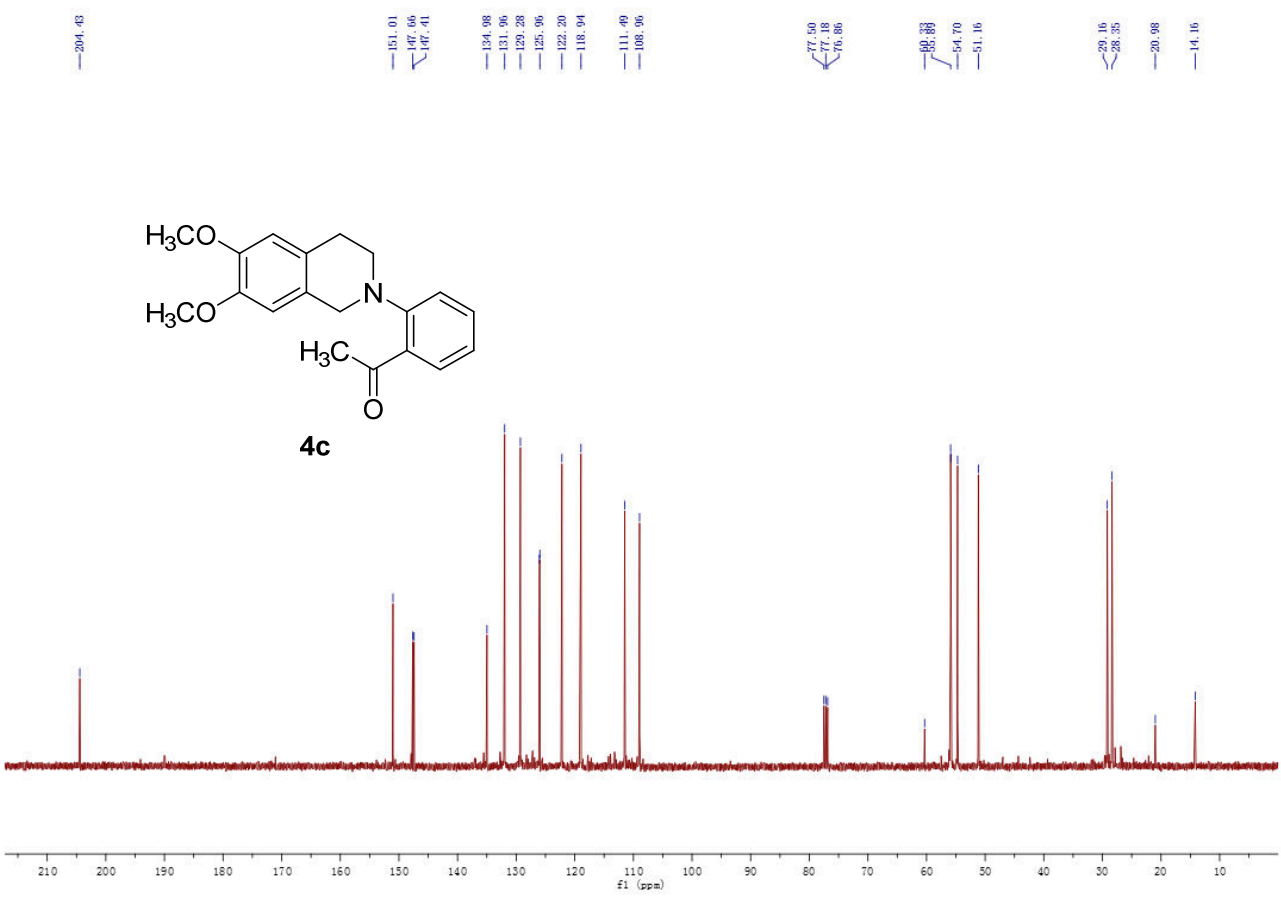
4b


201.61
163.04
153.51
134.18
134.14
132.25
128.83
126.94
126.49
126.23
125.98
106.34
105.20
77.52
77.20
76.88
55.33
55.01
51.25
28.93
28.86
N
OCH3
H3C
O
f1 (ppm)

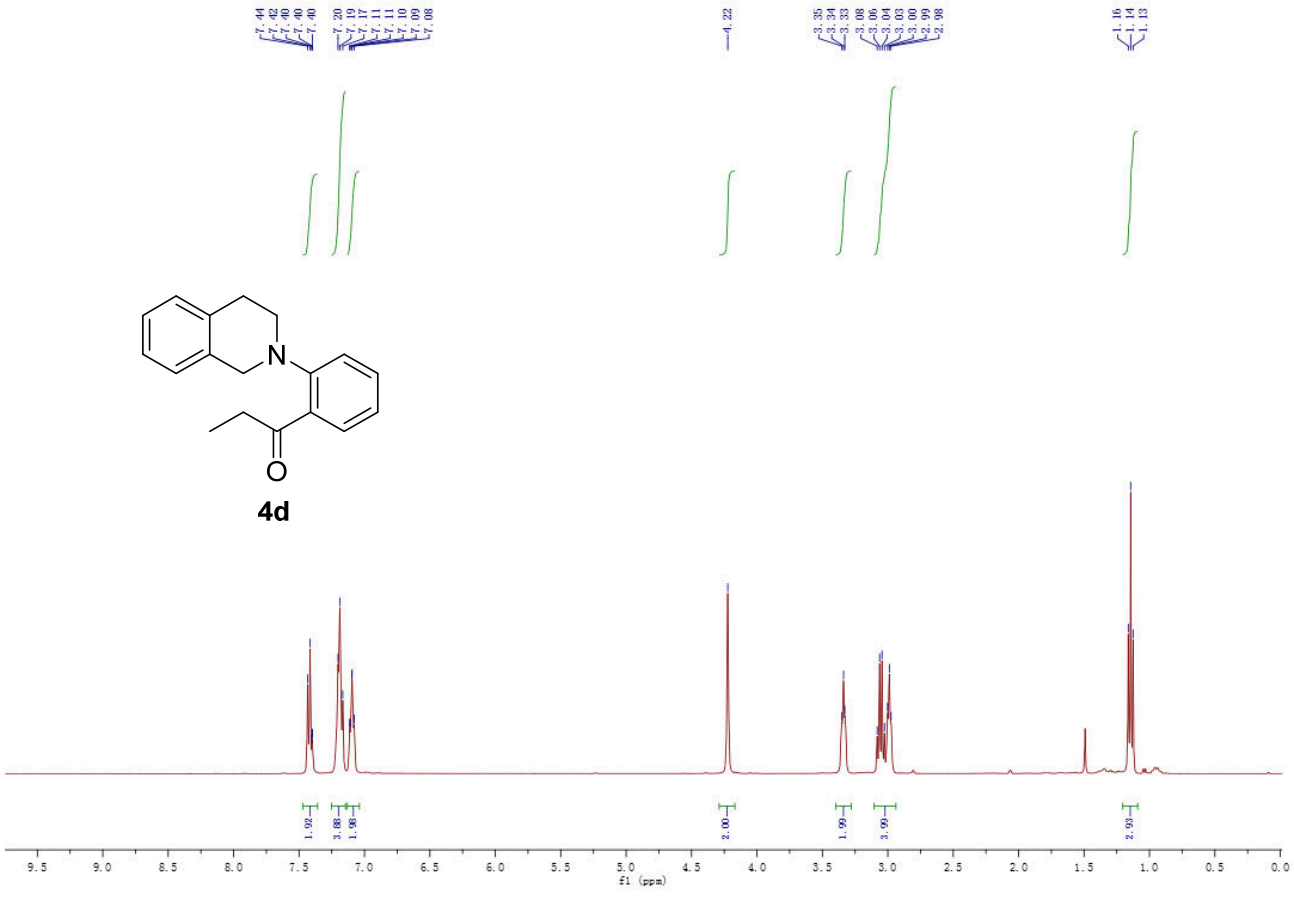
4b


7.46
7.45
7.42
7.41
7.39
7.26
7.13
7.06
7.04
6.64
6.56
4.13
4.11
3.87
3.86
3.36
3.34
3.33
2.91
2.90
2.88
2.61
H3CO
H3CO
N
H3C
O
0.87
0.96
0.97
0.90
0.98
1.00
2.01
2.90
2.86
2.01
2.00
2.85
f1 (ppm)

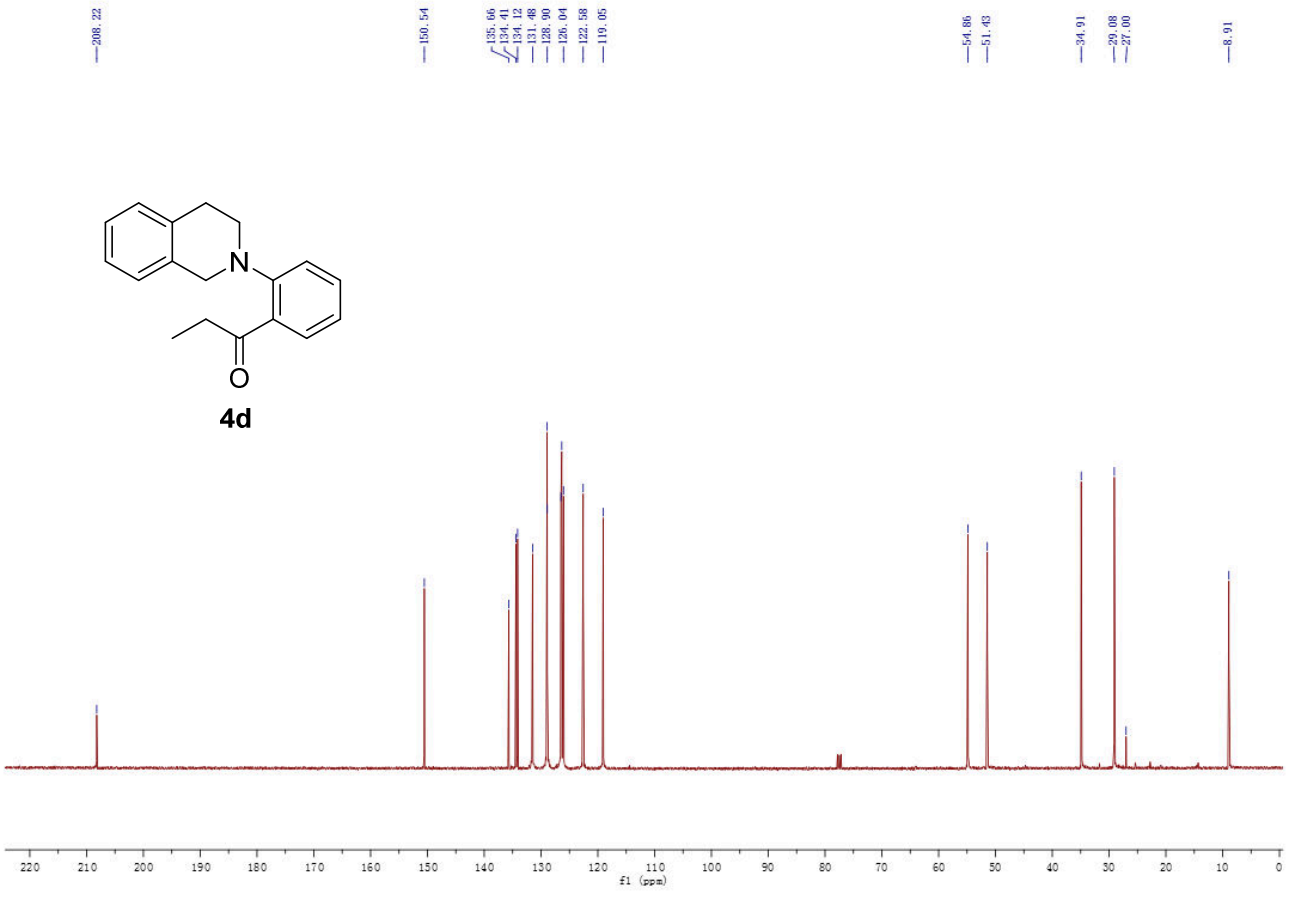
4c


204.43
151.01
147.66
147.41
134.98
131.96
129.28
125.96
122.20
118.94
111.49
108.96
77.50
77.18
76.86
60.33
55.89
54.70
51.16
29.16
28.35
20.98
14.16
H3CO
H3CO
N
H3C
O
f1 (ppm)

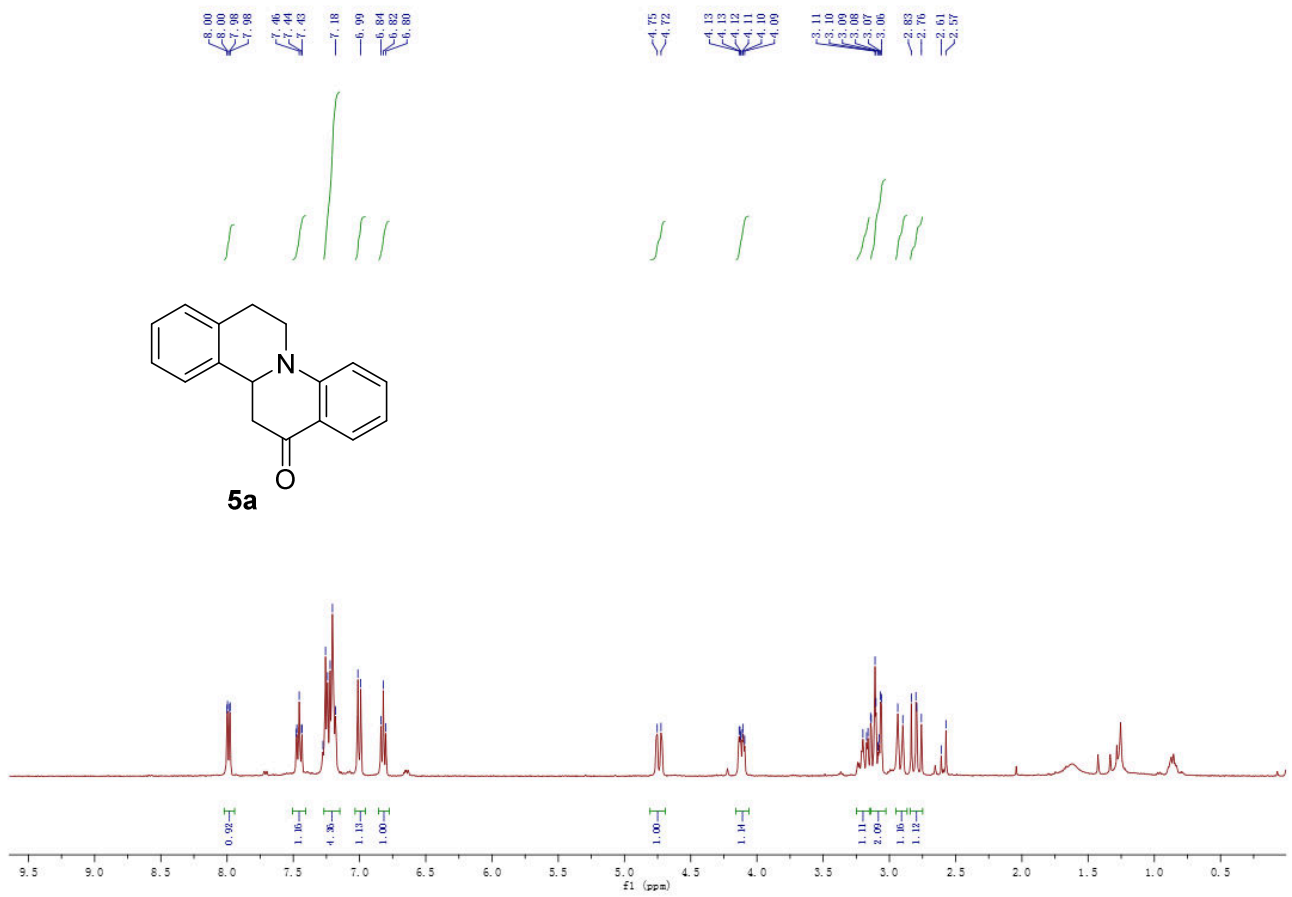
4c

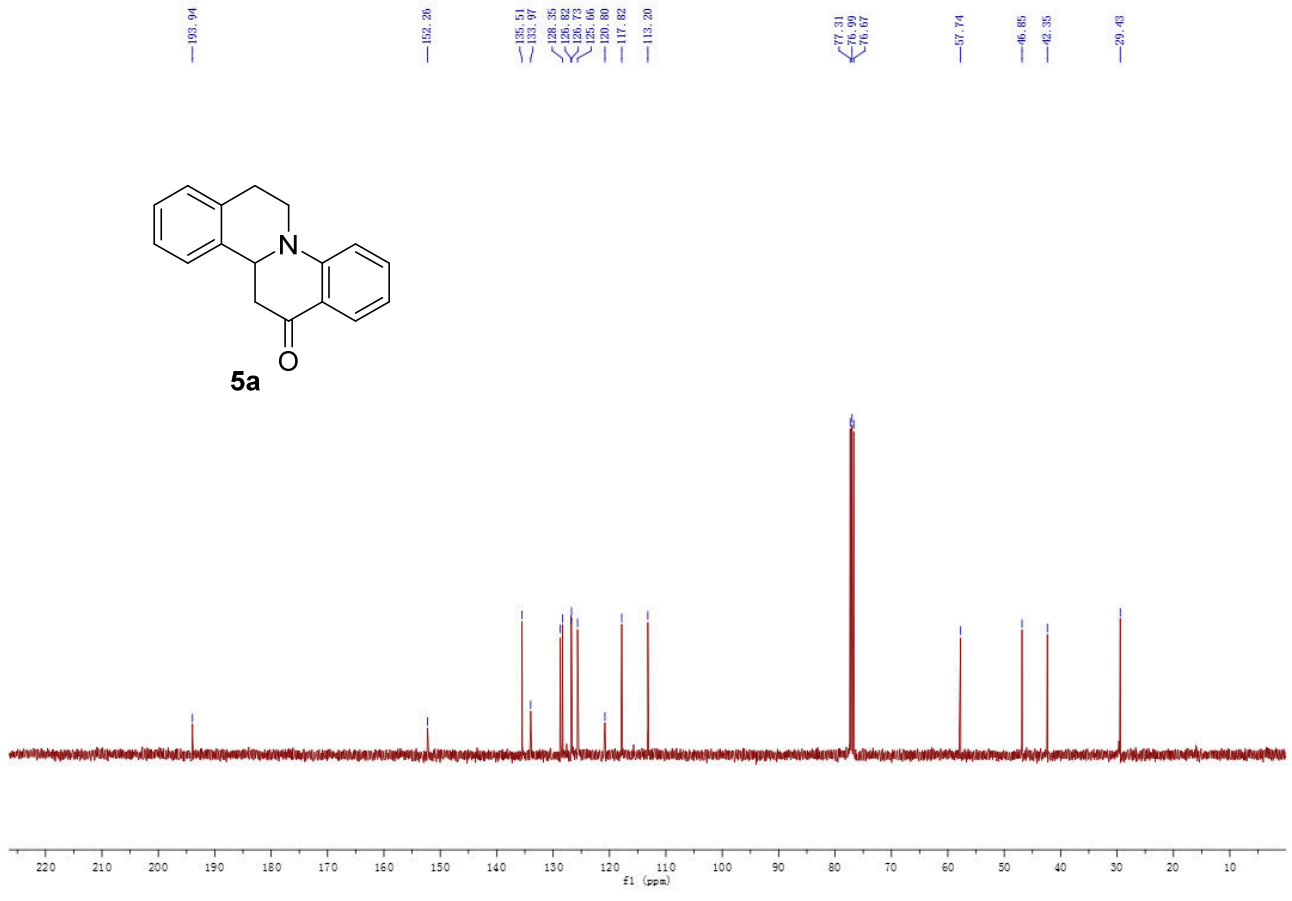

7.44
7.42
7.40
7.40
7.40
7.20
7.19
7.17
7.11
7.10
7.09
7.08
4.22
3.35
3.34
3.33
3.08
3.06
3.04
3.03
3.00
2.99
2.98
1.16
1.14
1.13
1.92
3.88
1.96
2.00
1.99
3.99
2.93
f1 (ppm)

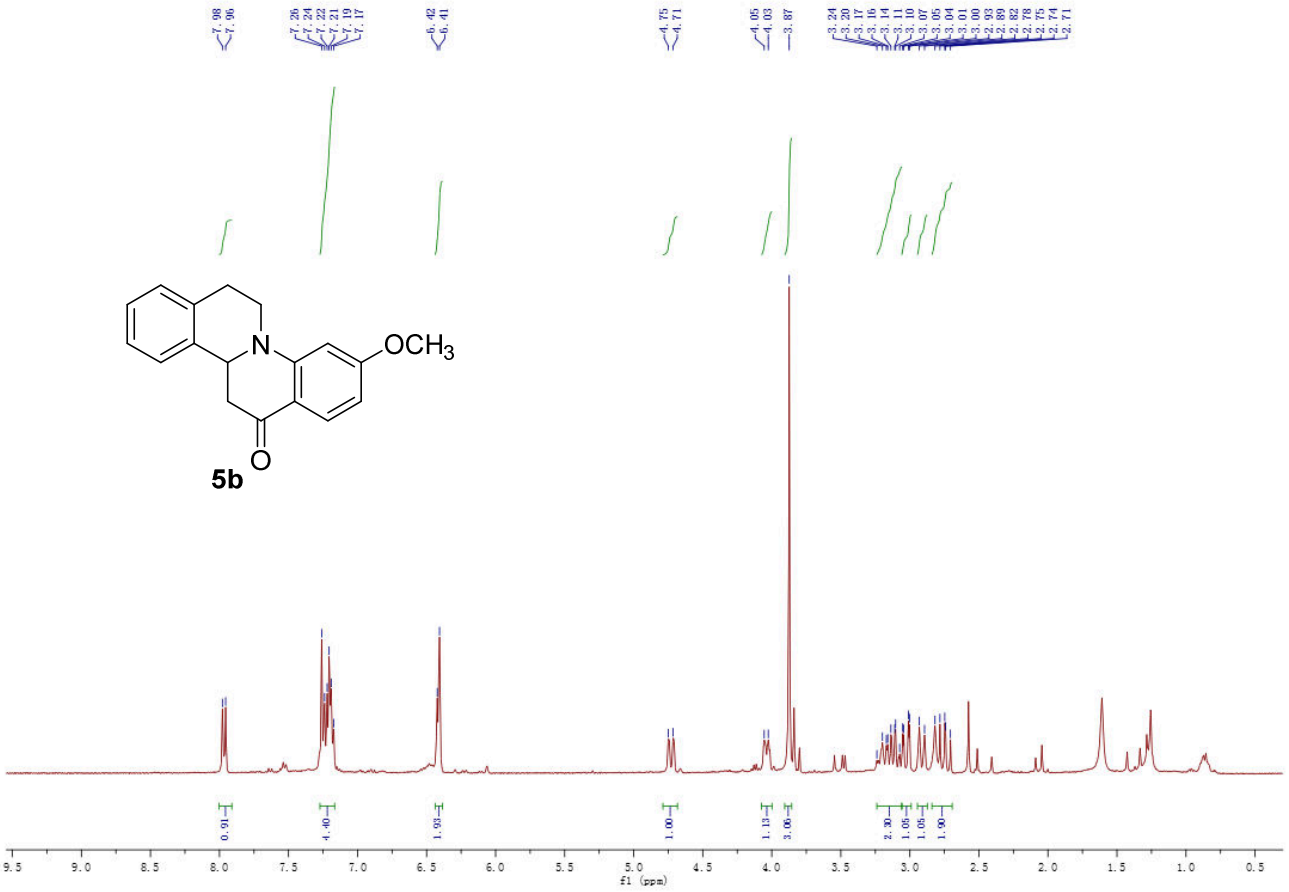
4d

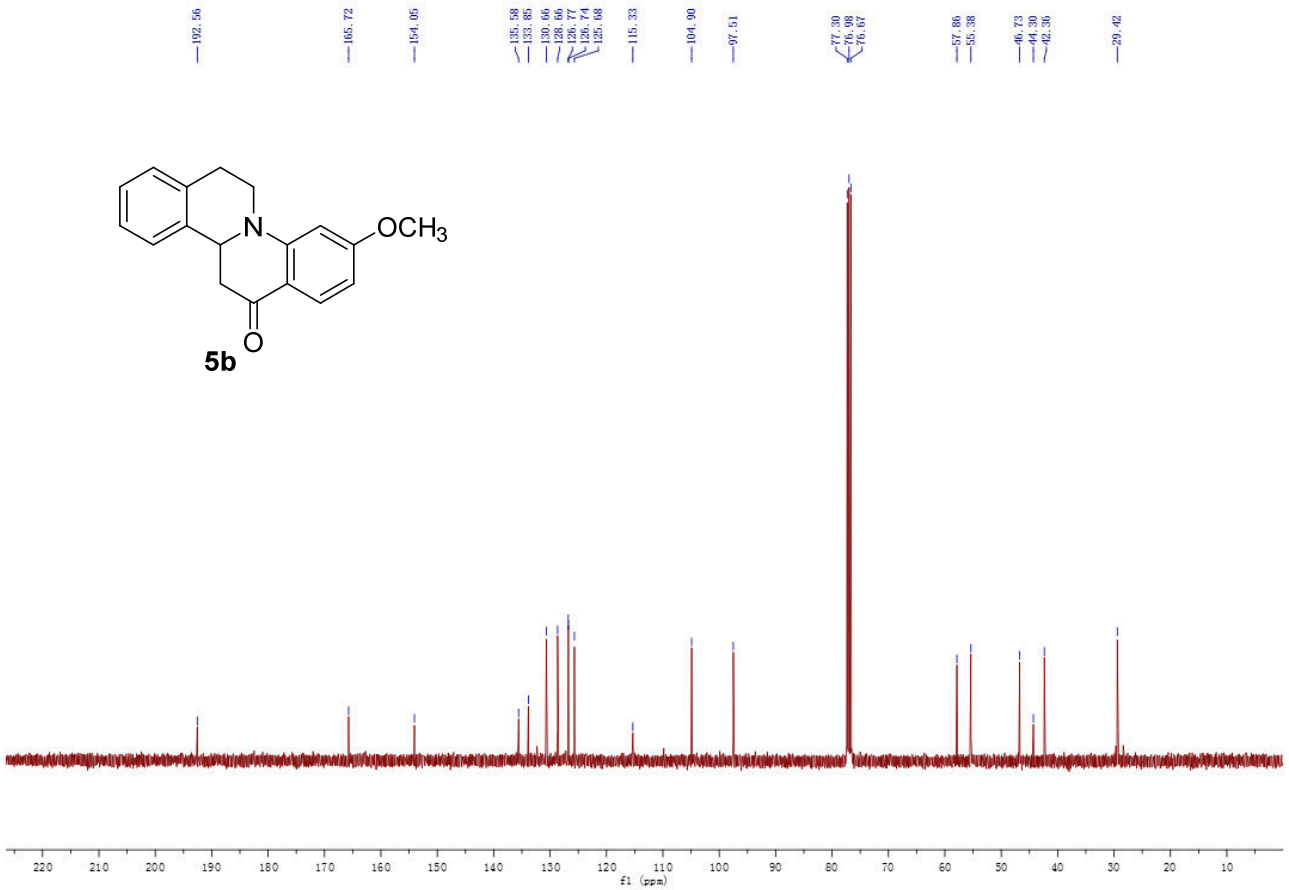

208.22
150.54
135.66
134.41
134.12
131.48
128.90
126.04
122.58
119.05
54.86
51.43
34.91
29.08
27.00
8.91
f1 (ppm)

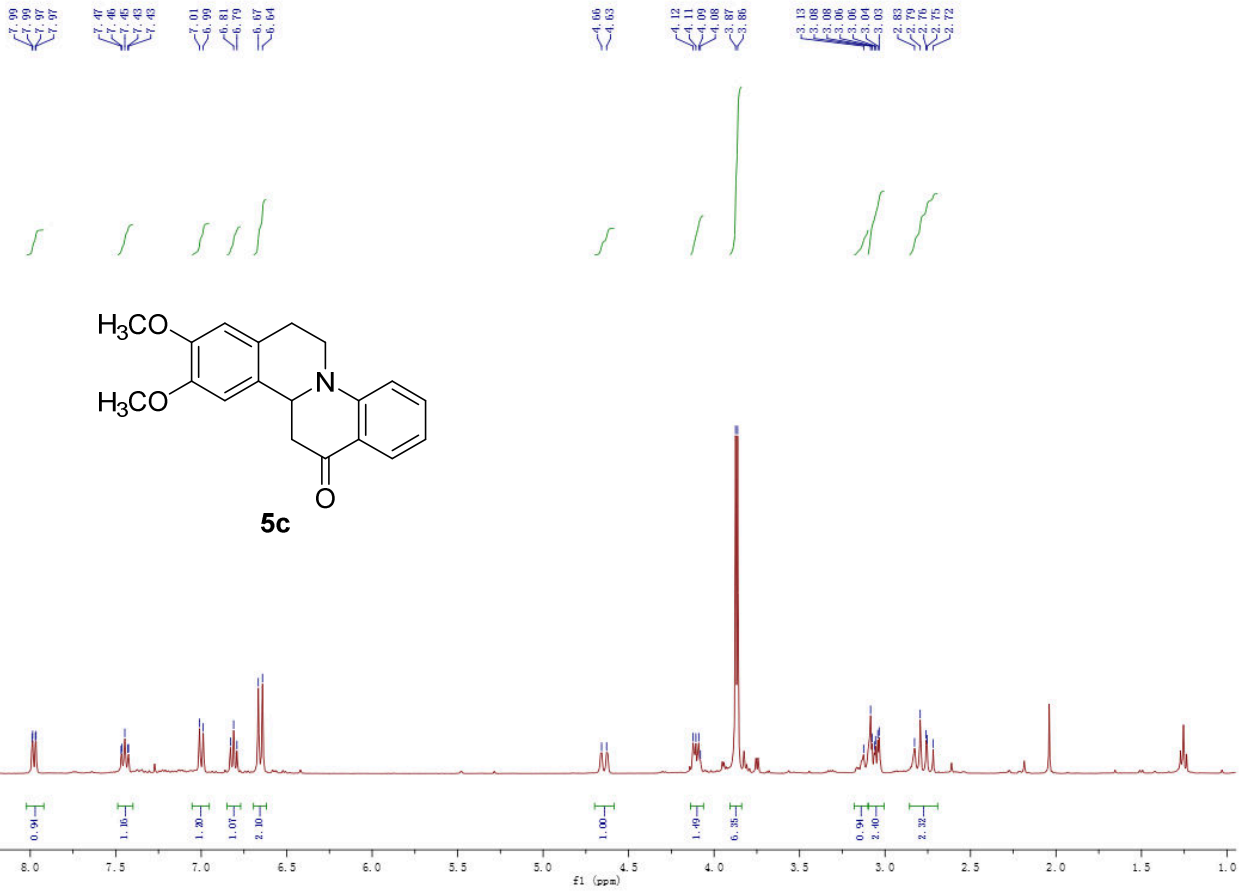
4d

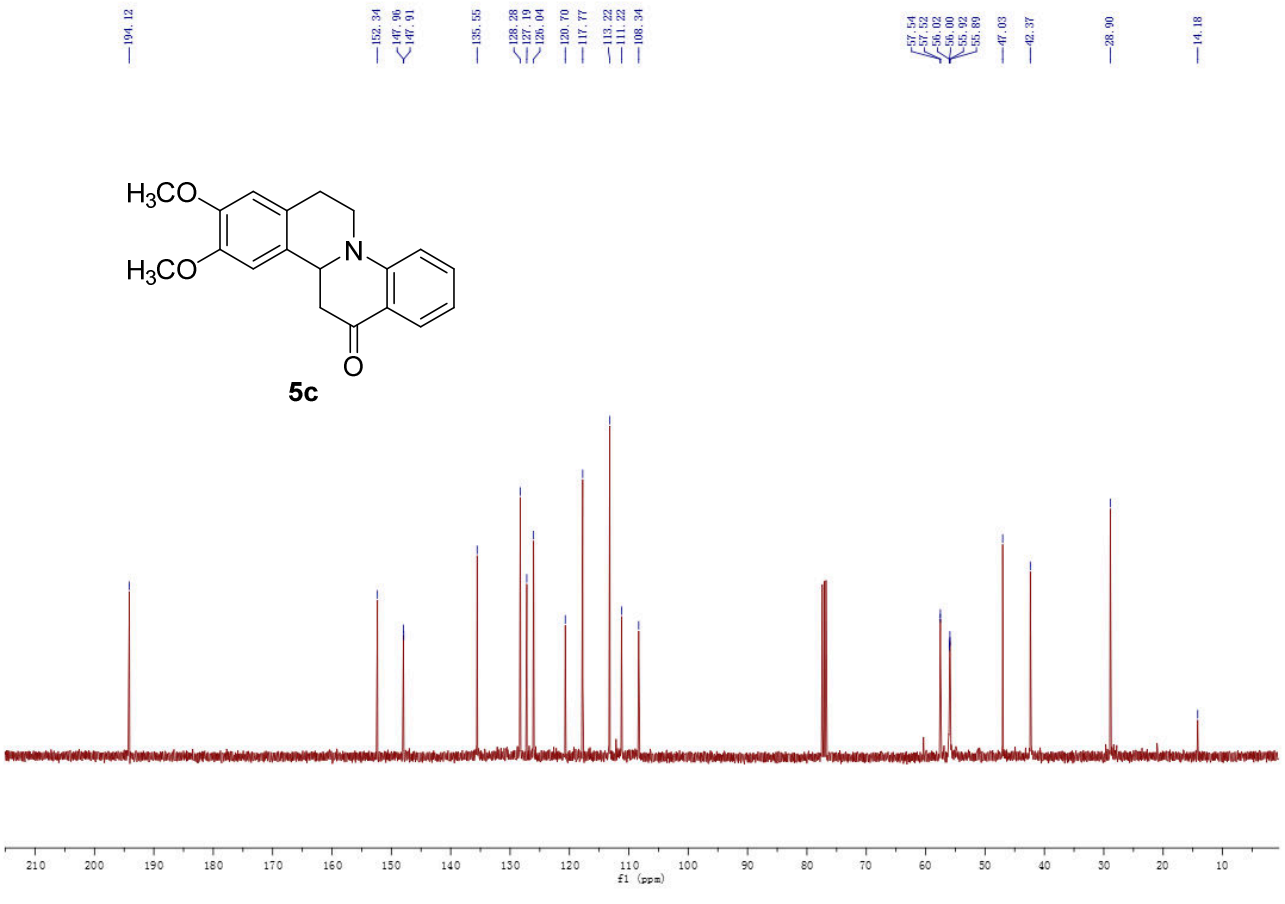

8.00
8.00
7.98
7.98
7.46
7.44
7.43
7.18
6.99
6.84
6.82
6.80
4.75
4.72
4.13
4.12
4.11
4.10
4.09
3.11
3.10
3.09
3.08
3.07
3.06
2.83
2.76
2.61
2.57
N
O
5a
0.92
1.16
4.36
1.13
1.00
1.00
1.14
1.11
2.09
1.16
1.12
f1 (ppm)

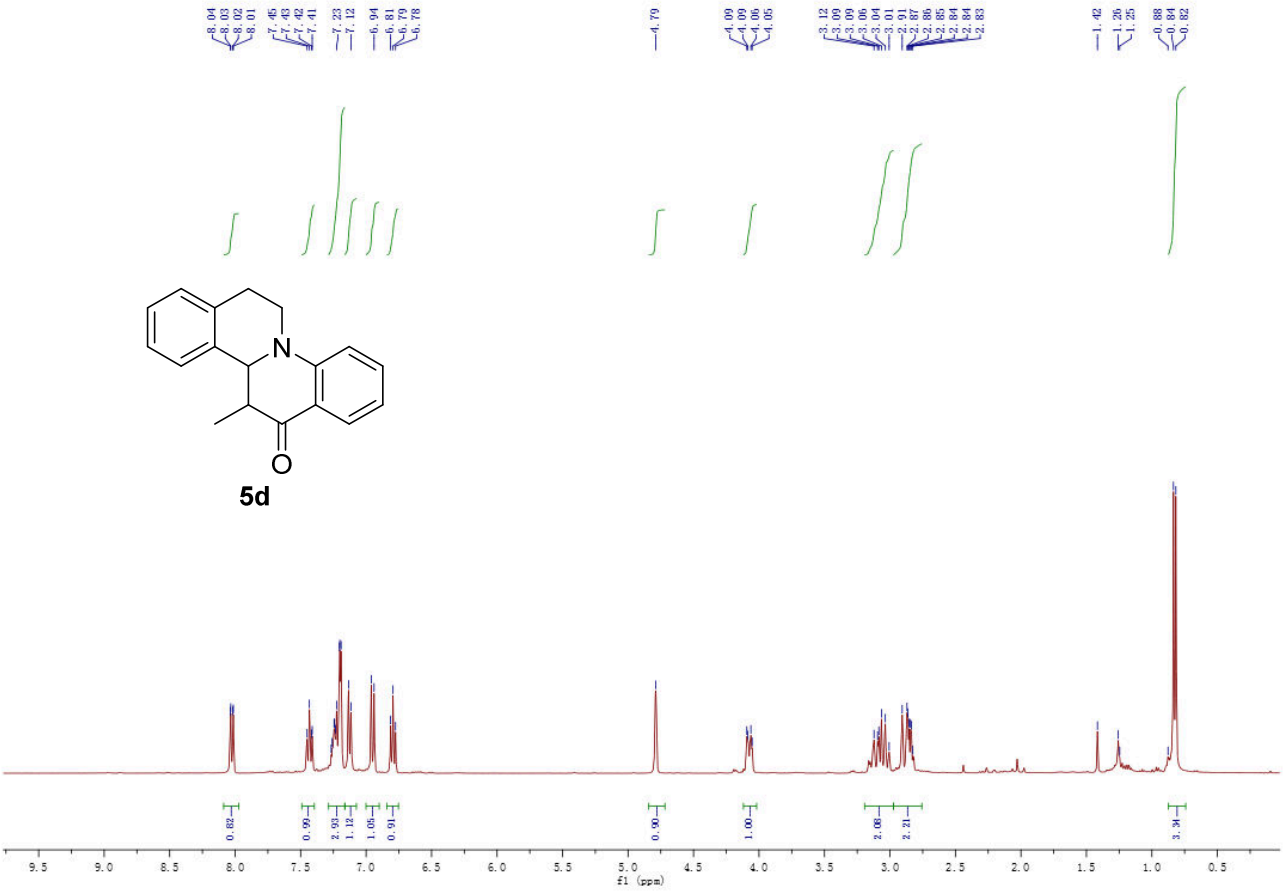

193.94
152.26
135.51
133.97
128.35
126.82
126.73
125.66
120.80
117.82
113.20
77.31
76.99
76.67
57.74
46.85
42.35
29.43
N
O
5a
f1 (ppm)

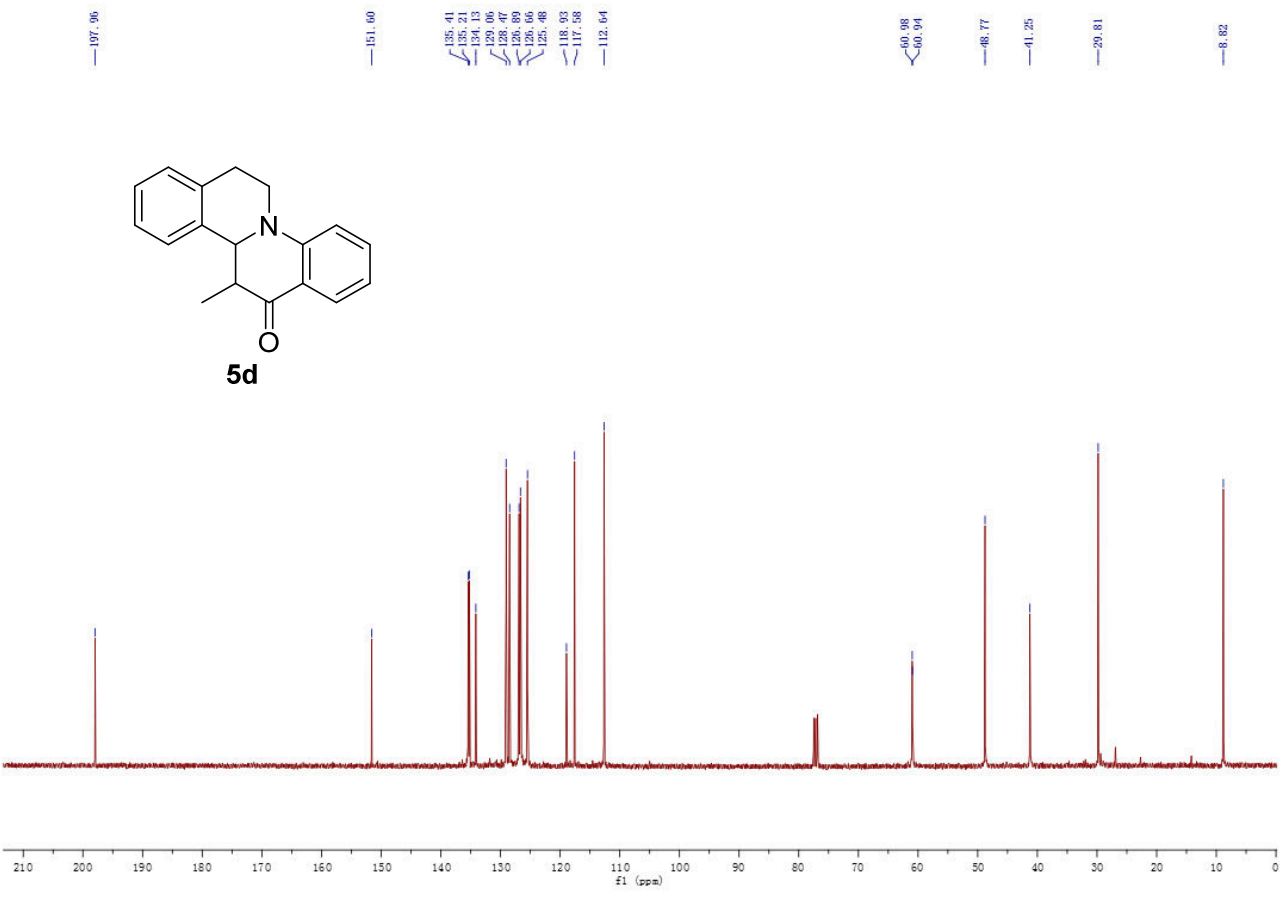

7.98
7.96
7.26
7.24
7.22
7.21
7.19
7.17
6.42
6.41
4.75
4.71
4.05
4.03
3.87
3.24
3.20
3.17
3.16
3.14
3.11
3.10
3.07
3.05
3.04
3.01
3.00
2.93
2.89
2.82
2.78
2.75
2.74
2.71
N
OCH3
O
5b
0.91
4.40
1.93
1.00
1.13
3.06
2.30
1.05
1.05
1.90
f1 (ppm)


192.56
165.72
154.05
135.58
133.85
130.66
128.66
126.77
126.74
125.68
115.33
104.90
97.51
77.30
76.98
76.67
57.86
55.38
46.73
44.30
42.36
29.42
N
OCH3
O
5b
f1 (ppm)


7.99
7.99
7.97
7.97
7.47
7.46
7.45
7.43
7.43
7.01
6.99
6.81
6.79
6.67
6.64
4.66
4.63
4.12
4.11
4.09
4.08
3.87
3.86
3.13
3.08
3.08
3.06
3.06
3.04
3.03
2.83
2.79
2.76
2.75
2.72
H3CO
H3CO
N
O
5c
0.94
1.16
1.20
1.07
2.10
1.00
1.49
6.35
0.91
2.40
2.32
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
f1 (ppm)

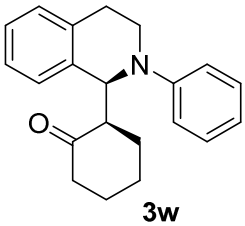

194.12
152.34
147.96
147.91
135.55
128.28
127.19
126.04
120.70
117.77
113.22
111.22
108.34
57.54
57.52
56.02
56.00
55.92
55.89
47.03
42.37
28.90
14.18
H3CO
H3CO
N
O
5c
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


8.04
8.03
8.02
8.01
7.45
7.43
7.42
7.41
7.23
7.12
6.94
6.81
6.79
6.78
4.79
4.09
4.09
4.06
4.05
3.12
3.09
3.09
3.06
3.04
3.01
2.91
2.87
2.86
2.85
2.84
2.84
2.83
1.42
1.26
1.25
0.88
0.84
0.82
N
O
5d
0.82
0.99
2.93
1.12
1.09
0.91
0.90
1.00
2.08
2.21
3.34
f1 (ppm)

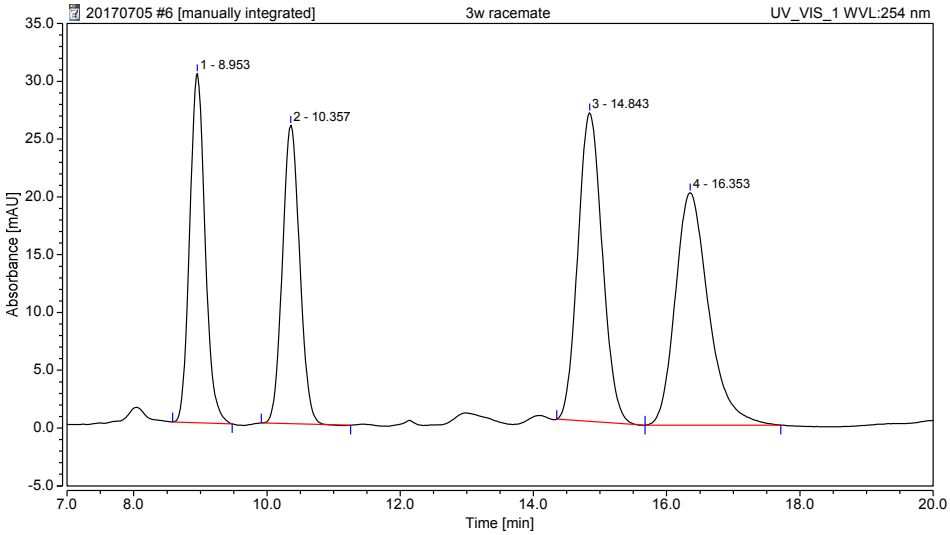

197.96
151.60
135.41
135.21
134.13
129.06
128.47
126.89
126.66
125.48
118.93
117.58
112.64
60.98
60.94
48.77
41.25
29.81
8.82
N
O
5d
f1 (ppm)

VI. HPLC Spectra of Racemic/Chiral Products

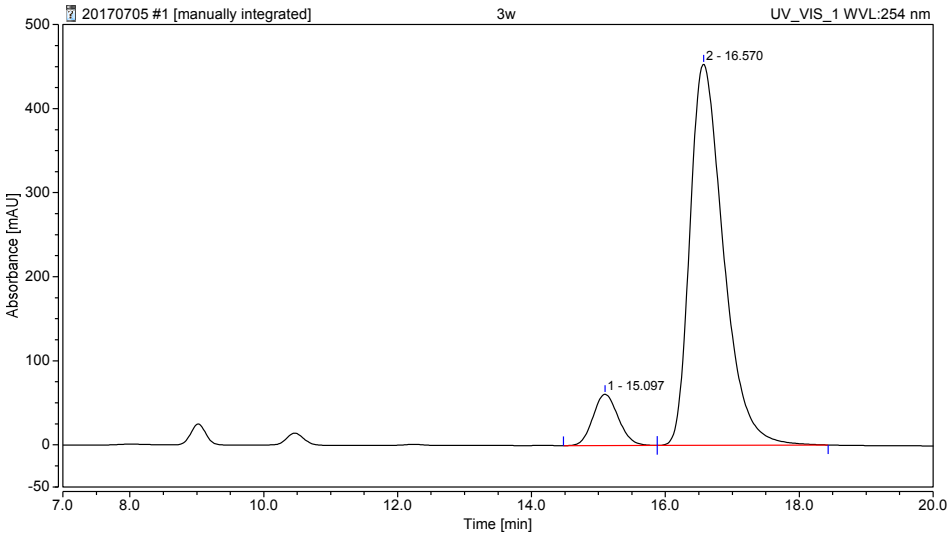
Using an AS-H column (*n*-Hexane/*i*PrOH = 96/4, flow rate 0.8 mL/min, 25 ^{o}C, 254nm)



3w

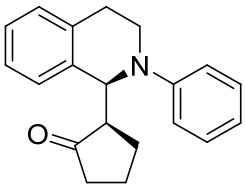


No.	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1	8.953	8.091	30.212	20.81	29.37
2	10.357	7.766	25.829	19.98	25.11
3	14.843	11.357	26.713	29.21	25.97
4	16.353	11.663	20.112	30.00	19.55
Total:		**38.877**	**102.867**	**100.00**	**100.00**

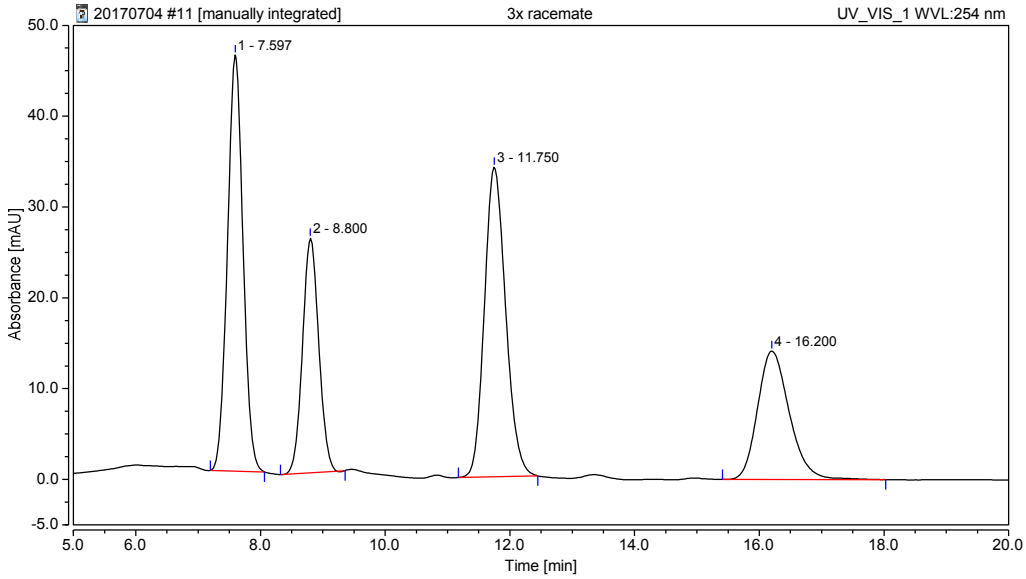


No.	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1	15.097	26.727	60.942	9.23	11.85
2	16.570	262.909	453.554	90.77	88.15
Total:		**289.636**	**514.496**	**100.00**	**100.00**

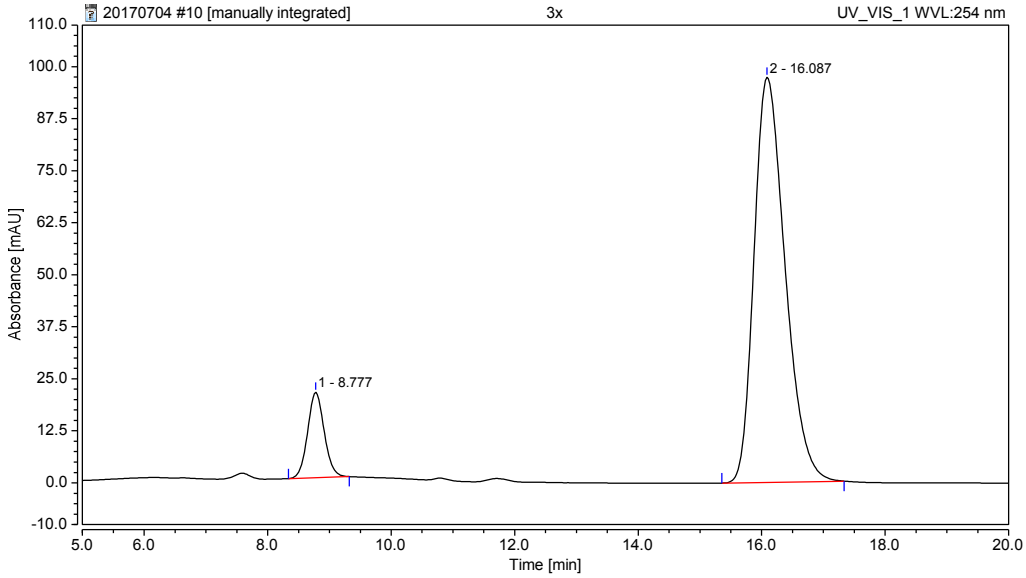
Using an OD-H column (*n*-Hexane/*i*PrOH = 99/1, flow rate 1.0 mL/min, 25 ^{o}C, 254nm)



3x

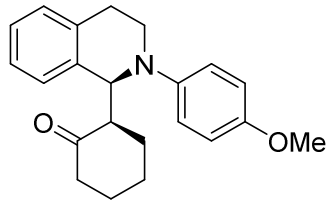


No.	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1	7.597	13.282	45.832	30.99	38.22
2	8.800	7.785	25.828	18.16	21.54
3	11.750	13.467	34.083	31.42	28.43
4	16.200	8.325	14.158	19.42	11.81
Total:		**42.859**	**119.902**	**100.00**	**100.00**

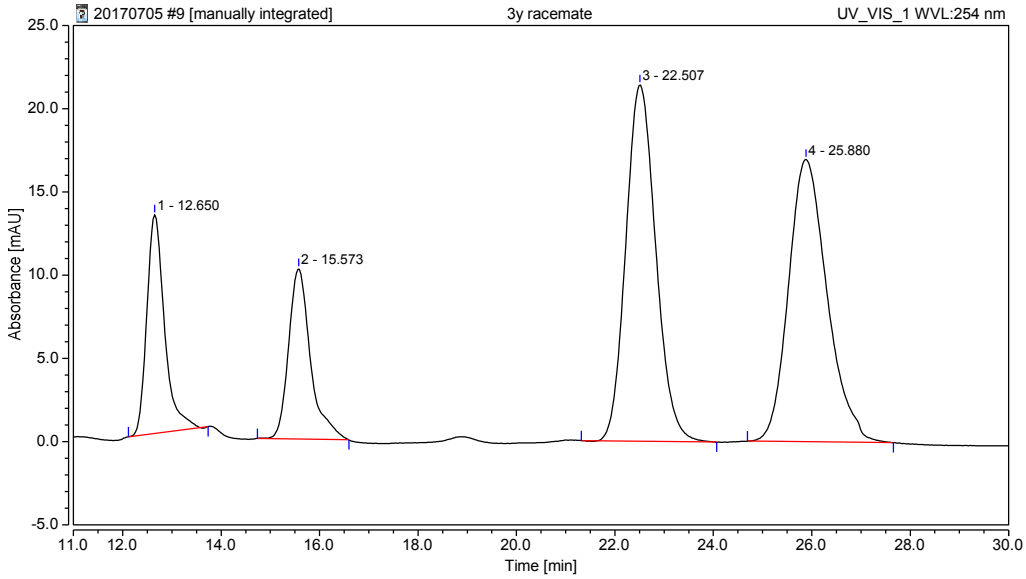


No.	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1	8.777	6.399	20.505	10.15	17.41
2	16.087	56.619	97.306	89.85	82.59
Total:		**63.018**	**117.811**	**100.00**	**100.00**

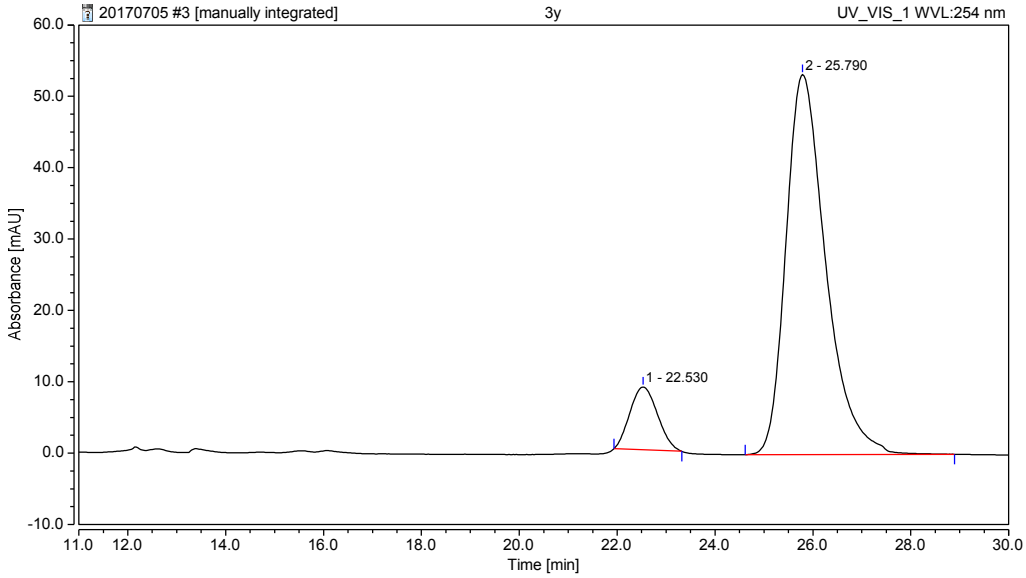
Using an AS-H column (*n*-Hexane/*i*PrOH = 96/4, flow rate 0.8 mL/min, 25 °C, 254nm)



3y

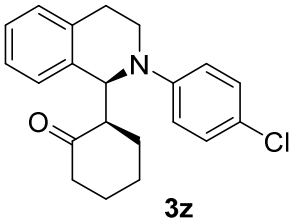


No.	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1	12.650	5.479	13.136	13.29	21.27
2	15.573	5.260	10.234	12.76	16.57
3	22.507	15.090	21.418	36.62	34.68
4	25.880	15.383	16.965	37.33	27.47
Total:		**41.211**	**61.753**	**100.00**	**100.00**

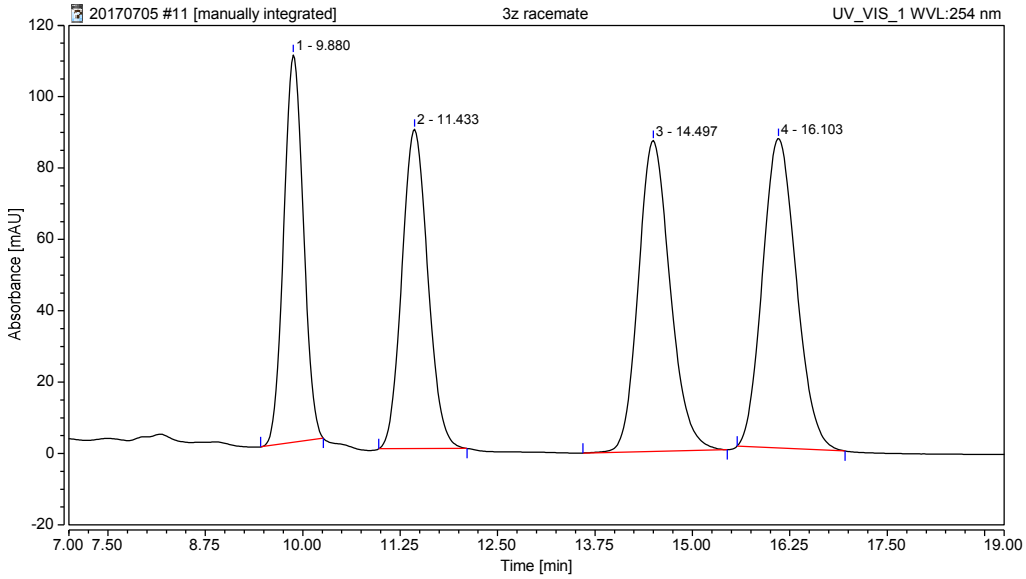


No.	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1	22.530	5.752	8.802	10.29	14.18
2	25.790	50.148	53.260	89.71	85.82
Total:		**55.901**	**62.061**	**100.00**	**100.00**

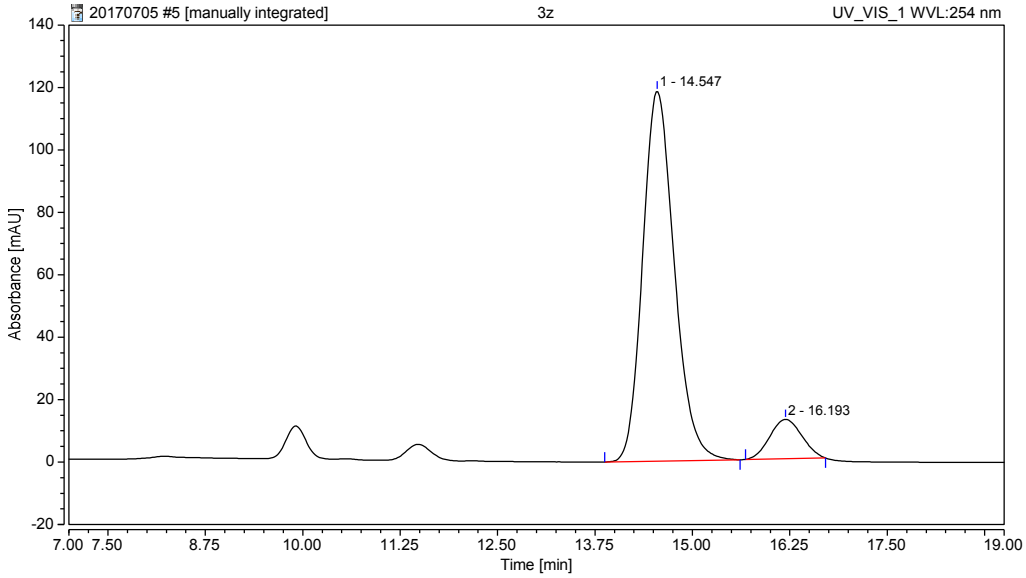
Using an AS-H column (*n*-Hexane/*i*PrOH = 96/4, flow rate 0.8 mL/min, 25 ^{o}C, 254nm)



3z



No.	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1	9.880	31.689	108.642	21.01	29.20
2	11.433	34.441	89.557	22.84	24.07
3	14.497	41.171	87.127	27.30	23.42
4	16.103	43.503	86.758	28.85	23.32
Total:		**150.804**	**372.084**	**100.00**	**100.00**



No.	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %
1	14.547	55.666	118.501	90.30	90.41
2	16.193	5.981	12.571	9.70	9.59
Total:		**61.647**	**131.072**	**100.00**	**100.00**

VII. References (cited in SI)

S1 S. Choi, T. Kwon, H. D. Moon, D. J. Baek, M. Seol, J. P. Duarte and Y. Choi, *ACS Appl. Mater. Interfaces,* 2011, **3**, 4552–4556.

S2 M. Kanaoka, Y. Horikawa, H. Kugo and Y. Nishizawa. *Chem. Pharm. Bull.,* 1985, **33**, 5062-5067.

S3 P. Palladino and D. A. Stetsenko, *Org. Lett.,* 2012, **14**, 6346–6349.

S4 a) A. Zhang and A. D. Schluter, *Chem. Asian. J.,* 2007, **2**, 1540-1548; b) H. Zhang, S. Mitsumori, N. Utsumi, M. Imai, N. Garcia-Delgado, M. Mifsud, K. Albertshofer, P. H. Cheong, K. N. Houk, F. Tanaka and C. F. Barbas, *J. Am. Chem. Soc.,* 2008, **130**, 875-886.

S5 a) F. J. Sayago, M. I. Calaza, I. Jiménez and C. Cativiela, *Tetrahedron: Asymmetry,* 2008, **19**, 2763–2766; b) F. J. Sayago, M. I. Calaza, I. Jiménez and C. Cativiela, *Tetrahedron,* 2009, **65**, 5174–5180; c) F. S. Gibson, S. C. Bergmeier and H. Rapoport, *J.* Org. Chem., 1994, **59**, 3216-3218.

S6 J. Zhang, B. Tiwari, C. Xing, X. Chen and Y. R. Chi, *Angew. Chem. Int. Ed.,* 2012, **51**, 3649-3652.

S7 a) G. Zhang, S. Wang, Y. Ma, W. Kong and R. Wang, *Adv. Synth. Catal.,* 2013, **355**, 874–879; b) W. Wei, X. Dong, S. Nie, Y. Chen, X. Zhang, M. Yan, *Org. Lett.,* 2013, **15**, 6018-6021.

S8 C. Huo, M. Wu, X. Jia, H. Xie, Y. Yuan and J. Tang, *J. Org. Chem.,* 2014, **79**, 9860-9864.

S9 M. Rueping, C. Vila, R. M. Koenigs, K. Poscharny and D. C. Fabry, *Chem. Commun.*, 2011, **47**, 2360-2362.

S10 X. Li, Y. Li, Y. Huang, T. Zhang, Y. Liu, B. Yang, C. He, X. Zhou and J. Zhang, *Green. Chem.,* 2017, **19**, 2925-2930.

S11 J. Johnson, J. Luo, X. Zhang, Y. Chen, M. Morton, E. Echeverría, F. Torres and J. Zhang, ACS Catal., 2015, **5**, 5283-5291.

S12 S. Toshihiro, S. Ikuya, N. Keita and B. Akio, *Org. Lett.,* 1999, **1**, 1579-1581.

S13 a) N. Fu, L. Li, Q. Yang and S. Luo, *Org. Lett.,* 2017, **19**, 2122-2125; b) Q. Yang, L. Zhang, C. Ye, S. Z. Luo, L. Wu and C. H. Tung, *Angew. Chem. Int. Ed.,* 2017, **56**, 3694-3698.

S14 G. Zhang, Y. Ma, S. Wang, W. Kong and R. Wang, *Chem. Sci.*, 2013, **4**, 2645-2651.