Supporting Information

Synthesis of Spiro-Dihydroquinoline and Octahydrophenanthrene Derivatives via Palladium-Catalyzed Intramolecular Oxidative Arylation

Zhong-Lin Zang,[†] Shuklachary Karnakanti,[†] Sheng Zhao, Ping Hu, Zhen Wang, Pan-Lin Shao, and Yun He**

School of Pharmaceutical Sciences and Innovative Drug Research Centre, Chongqing University, 55 Daxuecheng South Road, Shapingba, Chongqing 401331, P.R. China.

E-mail: yun.he@cqu.edu.cn, shaopl@cqu.edu.cn

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1. General Information:

Unless otherwise noted, reactions were carried out in oven-dried glassware or sealed tube under atmosphere of nitrogen. Toluene and acetonitrile (CH_3CN) were distilled from calcium hydride. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were dried and distilled from sodium. Methanol (MeOH) was dried under reflux with magnesium and then distilled. *N*, *N*-Dimethylformamide (DMF) was dried over calcium hydride and distilled under vacuum. Reactions were monitored by analytical thin-layer chromatography (TLC) on Merck silica gel 60 F_{254} plates (0.25 mm), visualized by ultraviolet light (254 nm) or by staining with ceric ammonium molybdate or basic potassium permanganate solutions as appropriate. ^{1}H NMR spectra were obtained on an Agilent 400MR or 600MR DD2 spectrometer at ambient temperature. Data were reported as follows: chemical shift on the δ scale using residual proton solvent as internal standard [δ 7.26 ($CDCl_3$); TMS: 0.00 ppm], multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets), integration, and coupling constant (*J*) in hertz (Hz). ^{13}C NMR spectra were obtained with proton decoupling on an Agilent 400MR DD2 (100 MHz) spectrometer and were reported in ppm with residual solvent for internal standard [δ 77.16 ($CDCl_3$)]. High resolution mass spectra were obtained on a Bruker SolariX 7.0T spectrometer.

2. Synthesis of Starting Materials:

2.1 General Scheme for the Synthesis of Dricted Groups:

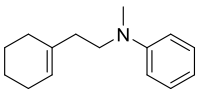
2.1.1 Synthesis of N-(2-(cyclohex-1-en-1-yl)ethyl)-N-methylaniline (Me-1a):

SI-1 **Me-1a**

Procedure SI-A[1]:

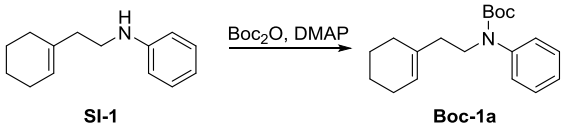
A mixture of iodobenzene (1.50 g, 7.50 mmol), 2-(cyclohex-1-en-1-yl)ethan-1-amine (0.94 g, 7.50 mmol), K_2CO_3 (2.12 g, 2.0 mmol), CuI (0.10 g, 0.50 mmol), and L-proline (115.0 mg, 1.0 mmol) in 3.0 mL of DMSO was heated at 100 ℃ until the start material was consumed as indicated by TLC. The cooled mixture was partitioned between water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residual oil was loaded on a silica gel column and eluted with 1:20 to 1:5 ethyl acetate/petroleum ether to afford the corresponding product **SI-1** (940.0 mg, 63%) as a colorless oil. R_f = 0.50 (silica, hexanes: EtOAc, 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (dd, J = 8.5, 7.2 Hz, 2H), 6.70 (t, J = 7.9, 1H), 6.64 – 6.60 (m, 2H), 5.54 (dt, J = 3.6, 1.9 Hz, 1H), 3.63 (s, 1H), 3.17 (t, J = 6.8 Hz, 2H), 2.27 (t, J = 6.9 Hz, 2H), 2.07 – 2.00 (m, 2H), 1.95 (d, J = 5.5 Hz, 2H), 1.70 – 1.52 (m, 4H).

N-(2-(cyclohex-1-en-1-yl)ethyl)-N-methylaniline



To a stirred solution of **SI-1** (800.0 mg, 1.0 equiv) in dry THF was added NaH (240.0 mg, 1.50 equiv) slowly at 0 °C. After 1 h, MeI (0.40 mL, 1.5 equiv) was added 0 °C. After completion of reaction as monitored by TLC, H_2O was added dropwise and the reaction mixture was stirred for 10 min at 0 °C. The aqueous phase was extracted with EtOAc (20 mL x 3) and the combined organic extracts were dried over Na_2SO_4 and concentrated, then the crude material was purified by flash column chromatography (SiO_2, Hexanes / EtOAc) to afford the title compound **Me-1a** (0.5 g, 58%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (ddd, J = 10.8, 6.0, 2.3 Hz, 2H), 6.78 – 6.62 (m, 3H), 5.45 (s, 1H), 3.39 (t, J = 7.8 Hz, 2H), 2.92 (s, 3H), 2.24 – 2.12 (m, 2H), 1.98 (ddt, J = 6.6, 4.4, 2.0 Hz, 4H), 1.72 – 1.48 (m, 4H).

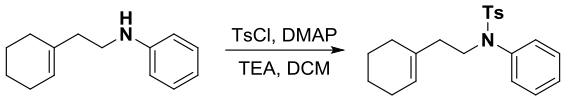
2.1.2 Synthesis of tert-butyl (2-(cyclohex-1-en-1-yl)ethyl)(phenyl)carbamate: [2]



SI-1 **Boc-1a**

Aniline **SI-1** (0.50 g, 2.50 mmol), Di-tert-butyl dicarbonate (0.68 g, 3.00 mmol) and 4-(dimethylamino)pyridine (61.0 mg, 0.5 mmol) were combined and the mixture was stirred at 90 °C for 17 hours. Di-tert-butyl dicarbonate (0.68 g, 3.00 mmol) was added to the mixture. After addition, the mixture was stirred for an additional 5 hours at 90 ℃ and concentrated in vacuo. To the resulting residue was added Di-tert-butyl dicarbonate (0.68 g, 3.00 mmol) and the mixture was stirred overnight at 90 ℃. The mixture was concentrated in vacuo and then the crude product was purified by flash column chromatography to yield **Boc-1a** (430.0 mg, 57%) as a colorless oil. R_f = 0.45 (silica, hexanes: EtOAc, 5:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.7 Hz, 2H), 7.18 (d, *J* = 7.6 Hz, 3H), 5.40 (s, 1H), 3.70 (t, *J* = 7.4 Hz, 2H), 2.16 (t, *J* = 7.5 Hz, 2H), 1.99 – 1.92 (m, 2H), 1.92 – 1.86 (m, 2H), 1.59 – 1.46 (m, 4H), 1.43 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.7, 142.8, 134.9, 128.6, 127.3, 125.9, 123.3, 80.0, 48.8, 37.1, 28.5, 28.2, 25.4, 23.0, 22.4. **HRMS** (ESI): calcd for $C_{19}H_{27}NO_2Na^+$ [M+Na^+]: 324.1934, found 324.1932.

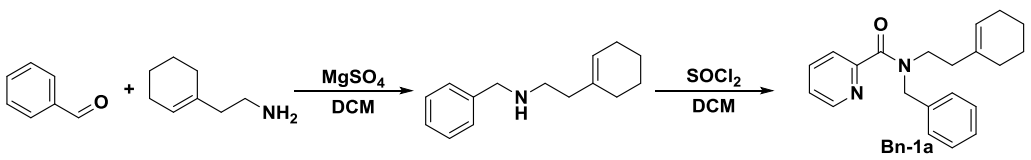
2.1.3 Synthesis of N-(2-(cyclohex-1-en-1-yl)ethyl)-4-methyl-N-phenylbenzenesulfonamide:



SI-1 **Ts-1a**

To a solution of amine **SI-1** (0.29 g, 1.0 equiv) in CH_2Cl_2 (0.3 M) at 0 ℃ was added triethylamine (3 equiv) followed by 4-metylbenzenesulfonyl chloride (0.28 g, 1.0 equiv) and the reaction allowed to room temperature. After stirring overnight, and water was added (equivalent to amount of CH_2Cl_2 solvent in reaction), the layers separated, and the organic layer extracted once with CH_2Cl_2. The combined organics were dried over Na_2SO_4 and concentrated in vacuo. Flash chromatography, using silica gel and Hexane / AcOEt afforded to yield the corresponding *p*-toluenesulfonyl - protected amine **Ts-1a** (260.0 mg, 53%) as a white solid. R_f = 0.40 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.2 Hz, 2H), 7.34 – 7.25 (m, 3H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.03 (dd, *J* = 7.6, 2.1 Hz, 2H), 5.31 (s, 1H), 3.60 (t, *J* = 7.6 Hz, 2H), 2.41 (s, 3H), 2.06 (t, *J* = 7.6 Hz, 2H), 1.95 – 1.91 (m, 2H), 1.87 – 1.82 (m, 2H), 1.60 – 1.47 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.3, 139.4, 135.6, 134.1, 129.4, 129.1, 128.9, 127.8, 123.7, 49.2, 37.1, 28.2, 25.3, 22.9, 22.4, 21.7. **HRMS** (ESI): calcd for $C_{21}H_{26}NO_2SNa^+$ [M+Na^+]: 378.1498, found 378.1495.

2.1.4 Synthesis of N-(2-(cyclohex-1-en-1-yl)ethyl)-N-phenylpicolinamide:



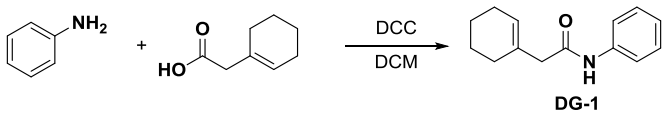
Bn-1a

To a solution of amine (10.0 mmol, 1.0 equiv) in CH_2Cl_2 (0.3 M) at 0 ℃ was added benzaldehyde (11.0 mmol, 1.10

equiv) followed by $MgSO_4$ (10.0g) and the reaction allowed to room temperature. After stirring overnight, the misture was flitted off, and concentrated in vacuo. The mixture was dissolved in EtOH (0.1 M) and added $NaBH_4$ (15.0 mmol, 1.50 equiv). The reaction was stirred at room temperature for 2 hours. Then water was added, the layers separated, and the organic layer extracted once with CH_2Cl_2. The combined organics were dried over Na_2SO_4 and concentrated in vacuo to yield the crude amine which was used in next step without purification.

To a solution of the picolinic acid (10.50 mmol) in DCM (20 mL) at room temperature was added $SOCl_2$ (2 mL) and one drop of dry DMF. The reaction was allowed to stir at 40 ℃ for 4 hours. The solvent was then removed under reduced pressure to afford the corresponding crude acid chloride. Then DCM (20 mL) was added and the solution was cooled to 0 ℃ followed by dropwise addition of NEt_3 (3.5 mL), DMAP (0.25 mmol) and amine (10.0 mmol, 1.0 eq). The reaction mixture was stirred at room temperature overnight, extracted by DCM, the organic layer was dried over Na_2SO_4 and the solvent was evaporated, then purified by flash chromatography(petroleum ether/ EtOAc = 2 : 1) to give **Bn-1a** (2.0 g, 62%) as a white solid. R_f = 0.50 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.8 Hz, 0.5H), 8.55 (d, *J* = 4.9 Hz, 0.5H), 7.79 (td, *J* = 7.7, 1.8 Hz, 0.5H), 7.74 (td, *J* = 7.7, 1.8 Hz, 0.5H), 7.67 (d, *J* = 7.8 Hz, 0.5H), 7.61 (d, *J* = 7.8 Hz, 0.5H), 7.42 – 7.24 (m, 6H), 5.47 (s, 0.5H), 5.27 (s, 0.5H), 4.80 (s, 1H), 4.67 (s, 1H), 3.51 (dd, *J* = 8.8, 6.5 Hz, 1H), 3.46 – 3.39 (m, 1H), 2.27 (t, *J* = 7.7 Hz, 1H), 2.16 (t, *J* = 7.8 Hz, 1H), 2.01 – 1.93 (m, 2H), 1.91 – 1.85 (m, 1H), 1.69 – 1.58 (m, 2H), 1.57 – 1.51 (m, 1H), 1.45 (p, *J* = 3.9 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.3, 169.0, 155.0, 155.0, 148.4, 148.3, 137.5, 137.4, 137.0, 136.9, 135.1, 134.3, 128.7, 128.7, 128.2, 127.7, 127.6, 127.4, 124.4, 124.3, 123.8, 123.6, 123.1, 52.4, 48.6, 47.2, 44.2, 37.1, 35.4, 28.4, 28.2, 25.4, 25.3, 23.1, 22.8, 22.5, 22.2. **HRMS** (ESI): calcd for $C_{21}H_{24}N_2ONa^+$ [M+Na$^+$]: 343.1781, found 343.1778.

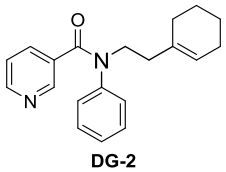
2.1.5 General Scheme for the Synthesis of N-(2-(cyclohex-1-en-1-yl)acetyl)-N-phenylpicolinamide:



DG-1

To a stirred solution of (Z)- 2-cyclohexenylacetic acid (0.50 g, 3.6 mmol) in CH_2Cl_2 (14 mL) was added DCC (1.11 g, 5.4 mmol) and DMAP (0.058 g, 0.72 mmol) at 0 ℃, 10 minutes later, aniline (0.66 mL, 7.2 mmol) was added and the reaction was warmed up to 23 ℃. After overnight, the reaction was quenched with HCl (1.0 N aqueous, 3 mL) and extracted three times with CH_2Cl_2 (5 mL x 3). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified by silica gel chromatography (EA/PE = 15/85) to give **DG-1** (0.45 g), yield 59%. White solid. mp: 117-118 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (brs, 1H), 7.06-7.57 (m, 5H), 5.76 (s, 1H), 3.04 (s, 2H), 2.04-2.17 (m, 4H), 1.54-1.74 (m, 4H).

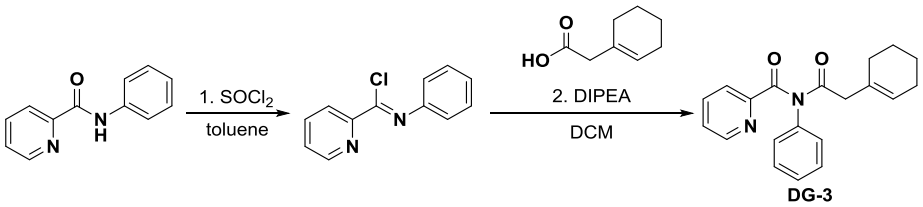
2.1.6 N-(2-(cyclohex-1-en-1-yl)ethyl)-N-phenylnicotinamide (DG-2):



DG-2

Prepared according to general procedure **SI-B**. from **SI-1** (290.0 mg, 1.45 mmol, 1.00 equiv) to yield **DG-2** (400.0 mg, 90%) as a colorless oil. R_f = 0.50 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 2.2 Hz, 1H), 8.41 (dd, *J* = 4.9, 1.6 Hz, 1H), 7.55 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 2H), 7.15 (t, *J* = 7.3 Hz, 1H), 7.08 (dd, *J* = 7.9, 4.9 Hz, 1H), 7.01 (d, *J* = 7.6 Hz, 2H), 5.44 (s, 1H), 4.01 (t, *J* = 7.5 Hz, 2H), 2.27 (t, *J* = 7.5 Hz, 2H), 2.09 – 1.81 (m, 5H), 1.68 – 1.41 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.8, 150.2, 149.6, 143.0, 136.1, 134.7, 132.4, 129.4, 128.2, 127.3, 123.5, 122.7, 49.1, 36.0, 28.3, 25.4, 22.9, 22.4. **HRMS** (ESI): calcd for $C_{20}H_{22}N_2ONa^+$ [M+Na^+]: 329.1624, found 329.1620.

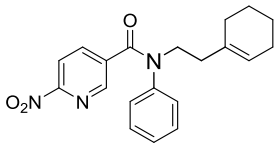
2.1.7 General Scheme for the Synthesis of N-(2-(cyclohex-1-en-1-yl)acetyl)-N-phenylpicolinamide[5]:



DG-3

A mixture of **N-phenylpicolinamide** (0.5 g, 2.50 mmol), toluene (5 mL), thionyl chloride (2.0 mL) and DMF (20 μL) was refluxed for 2.5 h. The resulting solution was concentrated under reduced pressure at 45 ℃ to afford crude 10a as a yellow air-sensitive oil; This material was dissolved in CH_2Cl_2 (4.0 mL) and added to a solution of 2-(cyclohex-1-en-1-yl)acetic acid (268.0 mg, 1.91 mmol) and N,N-diisopropylethylamine (1.5 mL, 1.1 g, 8.5 mmol) in CH_2Cl_2 (6 mL) at 0-5 ℃. The reaction mixture was stirred for 1 h at this temperature and then warmed to room temperature overnight. The resulting solution was washed with 10% aqueous citric acid (2 × 15 mL) followed by saturated aqueous $NaHCO_3$ (10 mL), dried over sodium sulfate and concentrated in vacuo. Purification by flash chromatography on silica gel eluting with 20% ethyl acetate in hexanes afforded **DG-3** (0.20 g, 25%) as a light brown foam. R_f = 0.50 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.8 Hz, 1H), 7.82 – 7.70 (m, 2H), 7.43 (dd, *J* = 8.3, 6.5 Hz, 2H), 7.39 – 7.31 (m, 2H), 7.31 – 7.25 (m, 2H), 5.41 (s, 1H), 3.11 (s, 2H), 2.02 – 1.91 (m, 4H), 1.60 (tdd, *J* = 7.9, 4.7, 2.4 Hz, 2H), 1.56 – 1.44 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.8, 172.2, 153.1, 148.5, 138.7, 136.9, 131.0, 129.5, 129.0, 128.6, 126.7, 125.7, 123.7, 46.1, 28.4, 25.4, 22.8, 22.0. **HRMS** (ESI): calcd for $C_{20}H_{20}NO_2Na^+$ [M+Na^+]: 343.1417, found 343.1415.

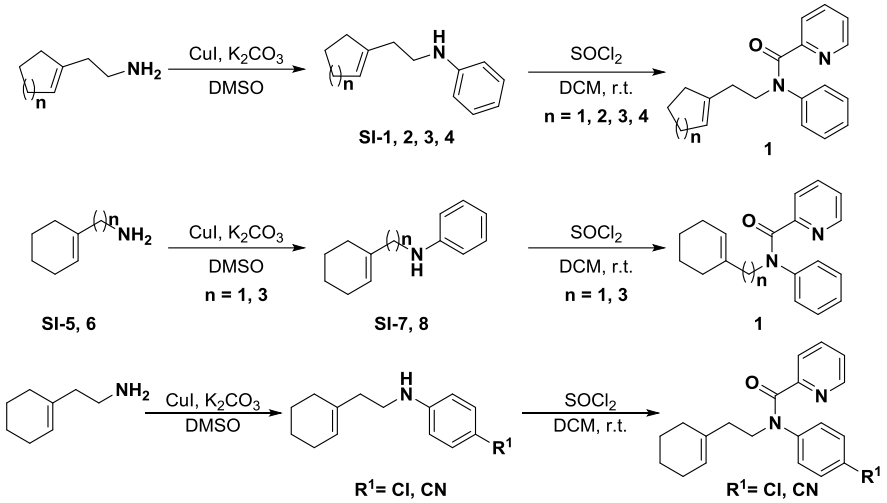
2.1.8 N-(2-(cyclohex-1-en-1-yl)ethyl)-6-nitro-N-phenylnicotinamide (DG-4):



DG-4

Prepared according to general procedure **SI-B**. from **SI-1** (290.0 mg, 1.45 mmol, 1.00 equiv) to yield DG-**4** (400.0 mg, 90%) as a colorless oil. R_f = 0.50 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.09 (d, *J* = 2.5 Hz, 1H), 8.33 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.56 (d, *J* = 8.5 Hz, 1H), 7.21 – 7.12 (m, 3H), 7.02 (d, *J* = 7.4 Hz, 2H), 5.45 (s, 1H), 4.04 (t, *J* = 7.5 Hz, 2H), 2.30 (t, *J* = 7.6 Hz, 2H), 2.01 – 1.87 (m, 4H), 1.61 – 1.45 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.4, 159.8, 143.8, 143.2, 141.9, 134.4, 131.4, 129.1, 128.0, 127.3, 123.7, 123.5, 48.7, 35.8, 28.2, 25.3, 22.8, 22.3. **HRMS** (ESI): calcd for $C_{20}H_{21}N_3O_3Na^+$ [M+Na^+]: 374.1475, found 374.1478.

2.2 General Scheme for the Synthesis of SI-9, 10, 11, 12:



Procedure SI-A[1]:

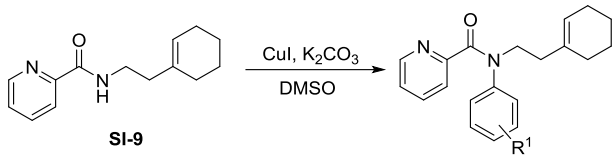
A mixture of **aryl bromide** (1.0 mmol), **Amine [4]** (2 mmol), K_2CO_3 (2.0 mmol), CuI (0.10 mmol), and L-proline (0.20 mmol) in 1 mL of DMSO was heated at 80 to 100 ℃ until the start material was consumed as indicated by TLC. The cooled mixture was partitioned between water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residual oil was loaded on a silica gel column and eluted with 1:20 to 1:5 ethyl acetate/petroleum ether to afford the corresponding product (SI-5, 6, 7, 8).

Procedure SI-B[3]:

To a solution of the picolinic acid (2.50 mmol) in DCM (20 mL) at room temperature was added $SOCl_2$ (2 mL) and one drop of dry DMF. The reaction was allowed to stir at 40 ℃ for 4 hours. The solvent was then removed under reduced pressure to afford the corresponding crude acid chloride. Then DCM (20 mL) was added and the solution was cooled to 0 ℃ followed by dropwise addition of NEt_3 (1.5 mL), DMAP (0.25 mmol) and amine (2.50 mmol, 1.0 eq). The reaction mixture was stirred at room temperature overnight, extracted by DCM, the organic layer was dried

over Na_2SO_4 and the solvent was evaporated, then purified by flash chromatography(petroleum ether/ EtOAc = 2 : 1).

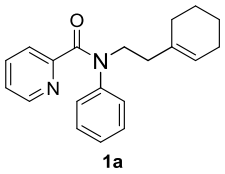
2.2.2 General Scheme for the Synthesis of 1b, 10, 11, 12:



Procedure SI-C[3]:

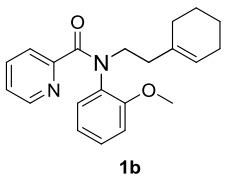
A mixture of **aryl bromide** (1.10 mmol), **Amine**(**SI-9**, 1.0 mmol), K_2CO_3 (2.0 mmol), CuI (0.10 mmol), and L-proline (0.20 mmol) in 1 mL of DMSO was heated at 80 to 100 ℃ until the start material was consumed as indicated by TLC. The cooled mixture was partitioned between water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residual oil was loaded on a silica gel column and eluted with 1:20 to 1:5 ethyl acetate/petroleum ether to afford the corresponding product (SI-5, 6, 7, 8)

N-(2-(cyclohex-1-en-1-yl)ethyl)-N-phenylpicolinamide (1a):


1a

Prepared according to general procedure **SI-B**. from **SI-1** (290.0 mg, 1.45 mmol, 1.00 equiv) to yield **1a** (400.0 mg, 90%) as a colorless oil. R_f = 0.50 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.53 (d, *J* = 9.8 Hz, 1H), 7.36 (s, 1H), 7.24 – 6.96 (m, 6H), 5.43 (s, 1H), 4.03 (t, *J* = 7.7 Hz, 2H), 2.29 (t, *J* = 7.7 Hz, 2H), 2.05 – 1.85 (m, 4H), 1.57 – 1.43 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.5, 154.8, 148.5, 143.0, 136.1, 134.8, 128.9, 127.9, 126.6, 123.7, 123.6, 123.2, 48.7, 36.0, 28.3, 25.3, 22.9, 22.4. **^{1}H NMR** (600 MHz, $CDCl_3$, 25 ℃) δ 8.31 (s, 1H), 7.54 (s, 1H), 7.36 (s, 1H), 7.13 (s, 2H), 7.09 (s, 2H), 7.02 (s, 2H), 5.44 (s, 1H), 4.03 (s, 2H), 2.29 (s, 2H), 1.93 (s, 4H), 1.54 (s, 2H), 1.49 (d, *J* = 3.6 Hz, 2H). **^{1}H NMR** (600 MHz, $CDCl_3$, 55 ℃) δ 8.33 (s, 1H), 7.55 (t, *J* = 7.8 Hz, 1H), 7.40 (s, 1H), 7.18 (t, *J* = 7.7 Hz, 2H), 7.15 – 7.02 (m, 4H), 5.44 (s, 1H), 4.02 (t, *J* = 7.6 Hz, 2H), 2.31 (t, *J* = 7.7 Hz, 2H), 1.96 (s, 2H), 1.91 (s, 2H), 1.58 – 1.57 (m, 2H), 1.52 – 1.50 (m, 2H). **^{1}H NMR** (400 MHz, Benzene-d_6) δ 8.02 (s, 1H), 7.57 (d, J = 7.8 Hz, 1H), 7.08 – 6.88 (m, 5H), 6.81 (t, J = 7.2 Hz, 1H), 6.35 (t, J = 5.9 Hz, 1H), 5.43 (s, 1H), 4.08 (t, J = 7.5 Hz, 2H), 2.39 (t, J = 7.5 Hz, 2H), 1.96 – 1.81 (m, 4H), 1.55 – 1.39 (m, 4H). **^{13}C NMR** (101 MHz, Benzene-d_6) δ 168.3, 155.7, 148.1, 144.2, 135.9, 135.2, 128.8, 128.3, 126.2, 124.1, 123.5, 123.3, 49.2, 36.6, 28.5, 25.7, 23.3, 22.8. **HRMS** (ESI): calcd for $C_{20}H_{22}N_2ONa^+$ [M+Na^+]: 329.1624, found 329.1624.

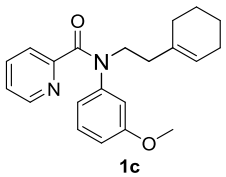
N-(2-(cyclohex-1-en-1-yl)ethyl)-N-(2-methoxyphenyl)picolinamide (1b):



1b

Prepared according to general procedure **SI-C**. from **SI-9** (500.0 mg, 2.17 mmol, 1.00 equiv) and **1-bromo-2-methoxybenzene** (450.0 mg, 2.39 mmol, 1.10 equiv) to yield **1b** (437.0 mg, 60%) as a colorless oil. R_f = 0.30 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 4.8 Hz, 1H), 7.49 (td, *J* = 7.7, 1.7 Hz, 1H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.14 – 7.00 (m, 3H), 6.76 (td, *J* = 7.6, 1.3 Hz, 1H), 6.72 – 6.65 (m, 1H), 5.42 (s, 1H), 4.07 (ddd, *J* = 13.2, 9.7, 6.1 Hz, 1H), 3.75 (ddd, *J* = 13.2, 9.8, 6.0 Hz, 1H), 3.67 (s, 3H), 2.25 (qd, *J* = 14.0, 11.7, 6.0 Hz, 2H), 1.98 – 1.83 (m, 4H), 1.60 – 1.42 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.2, 154.9, 154.7, 148.2, 135.7, 135.1, 131.7, 130.2, 128.5, 123.7, 122.7, 122.6, 120.5, 111.4, 55.4, 47.8, 35.7, 28.4, 25.4, 23.0, 22.5. **HRMS** (ESI): calcd for $C_{21}H_{24}N_2O_2Na^+$ [M+Na^+]: 359.1730, found 359.1728.

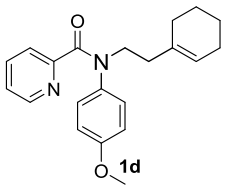
N-(2-(cyclohex-1-en-1-yl)ethyl)-N-(3-methoxyphenyl)picolinamide (1c):



1c

Prepared according to general procedure **SI-C**. from **SI-9** (500.0 mg, 2.17 mmol, 1.00 equiv) and **1-bromo-3-methoxybenzene** (450.0 mg, 2.39 mmol, 1.10 equiv) to yield **1c** (495.0 mg, 68%) as a colorless oil. R_f = 0.30 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, Benzene-d_6) δ 8.06 (d, *J* = 4.7 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 6.91 (dt, *J* = 9.6, 4.8 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.77 (s, 1H), 6.62 (d, *J* = 7.8 Hz, 1H), 6.54 – 6.44 (m, 1H), 6.38 (t, *J* = 6.3 Hz, 1H), 5.45 (s, 1H), 4.10 (t, *J* = 7.5 Hz, 2H), 3.17 (s, 3H), 2.43 (t, *J* = 7.6 Hz, 2H), 1.90 (s, 4H), 1.55 – 1.41 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.5, 159.9, 154.9, 148.7, 144.1, 136.2, 134.8, 129.5, 123.8, 123.4, 123.3, 120.1, 113.7, 112.4, 55.4, 48.8, 36.0, 28.4, 25.4, 22.9, 22.4. **HRMS** (ESI): calcd for $C_{21}H_{24}N_2O_2Na^+$ [M+Na^+]: 359.1730, found 359.1728.

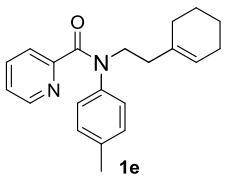
N-(2-(cyclohex-1-en-1-yl)ethyl)-N-(4-methoxyphenyl)picolinamide (1d):



1d

Prepared according to general procedure **SI-C**. from **SI-9** (500.0 mg, 2.17 mmol, 1.00 equiv) and **1-bromo-4-methoxybenzene** (450.0 mg, 2.39 mmol, 1.10 equiv) to yield **1d** (460.0 mg, 63%) as a colorless oil. R_f = 0.30 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 4.9 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 7.7 Hz, 1H), 7.07 (t, *J* = 6.1 Hz, 1H), 6.95 (d, *J* = 8.3 Hz, 2H), 6.68 (d, *J* = 8.3 Hz, 2H), 5.45 (s, 1H), 3.99 (t, *J* = 7.6 Hz, 2H), 3.71 (s, 3H), 2.28 (d, *J* = 7.8 Hz, 2H), 2.04 – 1.86 (m, 4H), 1.58 – 1.50 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.5, 157.9, 154.9, 148.6, 136.0, 135.6, 134.8, 129.1, 123.4, 123.2, 123.0, 113.9, 55.3, 48.6, 35.8, 28.3, 25.3, 22.9, 22.3. **HRMS** (ESI): calcd for $C_{21}H_{24}N_2O_2Na^+$ [M+Na^+]: 359.1730, found 359.1728.

N-(2-(cyclohex-1-en-1-yl)ethyl)-N-(p-tolyl)picolinamide (1e):



1e

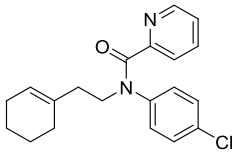
Prepared according to general procedure **SI-C**. from **SI-9** (500.0 mg, 2.17 mmol, 1.00 equiv) and **1-bromo-4-methylbenzene** (410.0 mg, 2.39 mmol, 1.10 equiv) to yield **1e** (450.0 mg, 65%) as a colorless oil. R_f = 0.40 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, Benzene-d_6) δ 8.06 (s, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 6.93 (t, *J* = 7.8 Hz, 3H), 6.74 (d, *J* = 7.7 Hz, 2H), 6.38 (t, *J* = 6.0 Hz, 1H), 5.45 (s, 1H), 4.10 (t, *J* = 7.5 Hz, 2H), 2.41 (t, *J* = 7.6 Hz, 2H), 1.92 (d, *J* = 11.5 Hz, 7H), 1.58 – 1.40 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.5, 154.9, 148.6, 140.3, 136.3, 136.0, 134.8, 129.5, 127.6, 123.5, 123.4, 123.1, 48.7, 35.8, 28.3, 25.3, 22.9, 22.4, 21.0. **HRMS** (ESI): calcd for $C_{21}H_{24}N_2ONa^+$ [M+Na^+]: 343.1781, found 343.1778.

4-chloro-N-(2-(cyclohex-1-en-1-yl)ethyl)aniline (SI-1f).

SI-1f

Prepared according to General Procedure **SI-A**: from 2-(cyclohex-1-en-1-yl)ethan-1-amine (0.78 g, 6.28 mmol, 1.5 equiv) and 4-chlorobenzonitrile (1.0 g, 4.19 mmol, 1.0 equiv) to yield **SI-1f** (0.86 g, 87.9%) as pale yellow liquid. R_f = 0.80 (silica, EtOAc:hexanes, 1:9); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.11 (d, *J* = 12.0 Hz, 2H), 6.51 (d, *J* = 8.0 Hz, 2H), 5.52 (s, 1H), 3.63 (s, 1H), 3.12 (t, *J* = 6.8 Hz, 2H), 2.25 (t, *J* = 6.8 Hz, 2H), 2.04 - 2.00 (m, 2H), 1.95 -1.91 (m, 2H), 1.66 - 1.54 (m, 4H).

***N*-(4-chlorophenyl)-*N*-(2-(cyclohex-1-en-1-yl)ethyl)picolinamide** (**1f**).



1f

Prepared according to General Procedure **SI-B**: from 4-chloro-*N*-(2-(cyclohex-1-en-1-yl)ethyl)aniline (0.7 g, 2.97 mmol, 1.00 equiv) and picolinoyl chloride (0.5 g, 3.57 mmol, 1.2 equiv) to yield **1f** (0.91 g, 91.0%) as brown liquid. R_f = 0.70 (silica, EtOAc:hexanes, 1:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.31 (s, 1H), 7.61 (s, 1H), 7.45 (s, 1H), 7.14 (s, 3H), 6.96 (s, 2H), 5.42 (s, 1H), 3.99 (s, 2H), 2.27 (t, *J* = 6.8 Hz, 2H), 1.94 (s, 4H), 1.55 - 1.49 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 168.17, 154.17, 148.32, 141.60, 136.26, 134.44, 132.00, 128.92, 123.88, 123.61, 123.31, 48.65, 35.80, 28.10, 25.16, 22.70, 22.17; **HRMS (ESI)**: calcd for $C_{20}H_{21}ClN_2NaO^+$ [M+Na^+]: 363.1231, found 363.1234.

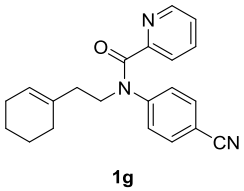
4-((2-(cyclohex-1-en-1-yl)ethyl)amino)benzonitrile (**SI-1g**).

SI-1g

Prepared according to General Procedure **SI-A**: from 2-(cyclohex-1-en-1-yl)ethan-1-amine (0.81 g, 6.55 mmol, 1.5 equiv) and 4-iodobenzonitrile (1.0 g, 4.36 mmol, 1.0 equiv) to yield **SI-1g** (0.82 g, 83.8%) as pale yellow liquid. R_f = 0.70 (silica, EtOAc:hexanes, 1:9); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.41 (d, *J* = 8.0 Hz, 2H), 6.54 (d, *J* = 8.0 Hz, 2H), 5.53 (s,

1H), 4.16 (s, 1H), 3.19 (q, *J* = 8.0, 4.0 Hz, 2H), 2.27 (t, *J* = 6.9 Hz, 2H), 2.04 - 2.00 (m, 2H), 1.95 - 1.92 (m, 2H), 1.67 - 1.53 (m, 4H).

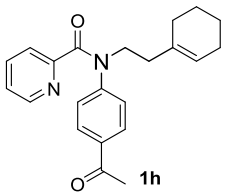
***N*-(4-cyanophenyl)-*N*-(2-(cyclohex-1-en-1-yl)ethyl)picolinamide** (**1g**).



1g

Prepared according to General Procedure **SI-B**: from 4-((2-(cyclohex-1-en-1-yl)ethyl)amino)-benzonitrile (0.7 g, 3.09 mmol, 1.00 equiv) and picolinoyl chloride (0.52 g, 3.71 mmol, 1.2 equiv) to yield **1g** (0.89 g, 87.2%) as brown liquid. R_f = 0.70 (silica, EtOAc:hexanes, 1:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.27 (d, *J* = 4.4 Hz, 1H), 7.71 - 7.67 (m, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.19 (t, *J* = 6.0 Hz, 1H), 7.12 (d, *J* = 8.4 Hz, 2H), 5.40 (s, 1H), 4.05 (t, *J* = 7.6 Hz, 2H), 2.28 (t, *J* = 7.6 Hz, 2H), 1.92 1.87 (m, 4H), 1.52 - 1.46 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 167.99, 153.36, 148.11, 136.63, 134.16, 132.61, 127.81, 124.51, 124.17, 123.74, 118.23, 109.60, 48.86, 36.19, 28.03, 25.14, 22.64, 22.11; **HRMS (ESI)**: calcd for $C_{21}H_{22}N_3O^+$ [M+H$^+$]: 332.1754, found 332.1757.

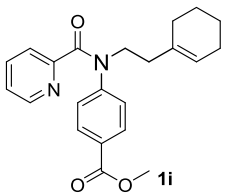
N-(4-acetylphenyl)-N-(2-(cyclohex-1-en-1-yl)ethyl)picolinamide (1h):



1h

Prepared according to general procedure **SI-C**. from **SI-9** (500.0 mg, 2.17 mmol, 1.00 equiv) and **1-(4-bromophenyl)ethan-1-one** (480.0 mg, 2.39 mmol, 1.10 equiv) to yield **1h** (450.0 mg, 59%) as a colorless oil. R_f = 0.25 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 4.8 Hz, 1H), 7.78 (d, *J* = 8.5 Hz, 2H), 7.62 (td, *J* = 7.7, 1.7 Hz, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.17 – 7.12 (m, 1H), 7.09 (d, *J* = 8.1 Hz, 2H), 5.40 (s, 1H), 4.04 (t, *J* = 7.6 Hz, 2H), 2.52 (s, 3H), 2.27 (t, *J* = 7.6 Hz, 2H), 1.96 – 1.83 (m, 4H), 1.55 – 1.40 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.1, 168.4, 154.0, 148.4, 147.6, 136.6, 134.7, 134.5, 129.1, 127.3, 124.4, 124.0, 123.7, 48.9, 36.2, 28.2, 26.6, 25.3, 22.8, 22.3. **HRMS** (ESI): calcd for $C_{22}H_{24}N_2O_2Na^+$ [M+Na$^+$]: 371.1730, found 371.1727.

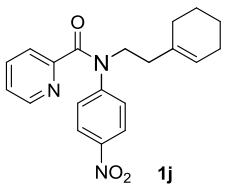
Methyl 4-(N-(2-(cyclohex-1-en-1-yl)ethyl)picolinamido)benzoate (1i):



1i

Prepared according to general procedure **SI-C**. from **SI-9** (500.0 mg, 2.17 mmol, 1.00 equiv) and **methyl 4-bromobenzoate** (510.0 mg, 2.39 mmol, 1.10 equiv) to yield **1i** (420.0 mg, 53%) as a colorless oil. R_f = 0.20 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 4.8 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 2H), 7.61 (td, *J* = 7.7, 1.7 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.17 – 7.10 (m, 1H), 7.07 (d, *J* = 8.1 Hz, 2H), 5.40 (s, 1H), 4.04 (t, *J* = 7.5 Hz, 2H), 3.85 (s, 3H), 2.27 (t, *J* = 7.5 Hz, 2H), 1.95 – 1.84 (m, 4H), 1.55 – 1.41 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.3, 166.4, 154.1, 148.4, 147.5, 136.5, 134.5, 130.3, 127.8, 127.3, 124.3, 124.0, 123.6, 52.2, 48.9, 36.2, 28.2, 25.3, 22.8, 22.3. **HRMS** (ESI): calcd for $C_{22}H_{24}N_2O_3Na^+$ [M+Na$^+$]: 387.1679, found 387.1676.

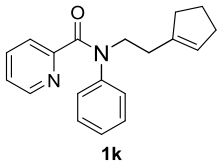
N-(2-(cyclohex-1-en-1-yl)ethyl)-N-(4-nitrophenyl)picolinamide (1j):



1j

Prepared according to general procedure **SI-C**. from **SI-9** (500.0 mg, 2.17 mmol, 1.00 equiv) and **1-bromo-4-nitrobenzene** (540.0 mg, 2.39 mmol, 1.10 equiv) to yield **1j** (460.0 mg, 60%) as a colorless oil. R_f = 0.30 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 4.8 Hz, 1H), 8.09 – 8.03 (m, 2H), 7.74 – 7.64 (m, 2H), 7.20 (ddd, *J* = 6.9, 4.8, 1.6 Hz, 1H), 7.18 – 7.13 (m, 2H), 5.40 (s, 1H), 4.08 ((t, *J* = 7.5 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.00 – 1.83 (m, 4H), 1.59 – 1.43 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.2, 153.4, 149.6, 148.3, 145.3, 136.9, 134.3, 127.7, 124.9, 124.5, 124.3, 124.0, 49.2, 36.4, 28.2, 25.3, 22.8, 22.3. **HRMS** (ESI): calcd for $C_{20}H_{22}N_3O_3Na^+$ [M+Na^+]: 352.1656, found 352.1654.

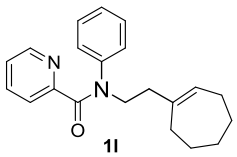
N-(2-(cyclopent-1-en-1-yl)ethyl)-N-phenylpicolinamide (1k):



1k

Prepared according to general procedure **SI-B**. from **SI-2** (930.0 mg, 5.0 mmol, 1.00 equiv) to yield **1k** (880.0 mg, 60%) as a colorless oil. R_f = 0.40 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.54 (t, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.23 – 6.89 (m, 6H), 5.39 (s, 1H), 4.08 (t, *J* = 7.8 Hz, 2H), 2.43 (t, *J* = 7.8 Hz, 2H), 2.32 – 2.15 (m, 4H), 1.86 – 1.71 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.6, 154.8, 148.6, 142.9, 141.4, 136.2, 129.0, 127.9, 126.7, 125.3, 123.8, 123.6, 48.6, 35.2, 32.7, 29.3, 23.4. **HRMS** (ESI): calcd for $C_{19}H_{20}N_2ONa^+$ [M+Na^+]: 315.1468, found 315.1466.

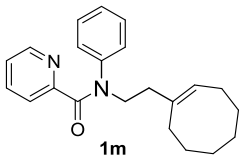
N-(2-(cyclohept-1-en-1-yl)ethyl)-N-phenylpicolinamide (1l):



1l

Prepared according to general procedure **SI-B**. from **SI-3** (930.0 mg, 5.0 mmol, 1.00 equiv) to yield **1l** (800.0 mg, 50%) as a colorless oil. R_f = 0.45 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.32 (d, *J* = 7.8 Hz, 1H), 7.19 – 6.92 (m, 6H), 5.54 (s, 1H), 3.96 (t, *J* = 7.9 Hz, 2H), 2.30 (t, *J* = 7.8 Hz, 2H), 2.12 – 2.03 (m, 2H), 2.01 – 1.97 (m, 2H), 1.674 – 1.615 (m, 2H), 1.412 – 1.356 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.5, 154.8, 148.5, 143.0, 141.5, 136.1, 128.9, 128.3, 127.9, 126.6, 123.7, 123.6, 49.1, 38.3, 32.8, 32.6, 28.5, 27.2, 26.8. **HRMS** (ESI): calcd for $C_{21}H_{24}N_2ONa^+$ [M+Na^+]: 343.1781, found 343.1778.

(E)-N-(2-(cyclooct-1-en-1-yl)ethyl)-N-phenylpicolinamide (1m):

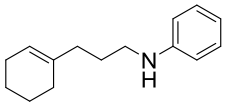


1m

Prepared according to general procedure **SI-B**. from **SI-4** (930.0 mg, 5.0 mmol, 1.00 equiv) to yield **1m** (868.0 mg, 52%) as a colorless oil. R_f = 0.45 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.54 (s, 1H), 7.44 – 7.30 (m, 1H), 7.21 – 6.94 (m, 6H), 5.37 (d, *J* = 8.5 Hz, 1H), 4.02 (t, *J* = 8.1 Hz, 2H), 2.33 (t, *J* = 8.0 Hz, 2H), 2.14 (s, 2H), 2.05 (s,

2H), 1.43 (s, 8H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.5, 154.7, 148.5, 142.9, 137.7, 136.1, 128.9, 127.8, 126.6, 126.1, 123.6, 49.3, 35.3, 29.8, 28.9, 28.8, 26.5, 26.4, 26.2. **HRMS** (ESI): calcd for $C_{22}H_{26}N_2ONa^+$ [M+Na^+]: 357.1937, found 357.1934.

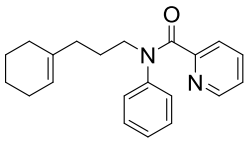
***N*-(3-(cyclohex-1-en-1-yl)propyl)aniline** (**SI-1n**).



SI-1n

Prepared according to General Procedure **SI-A**: from 3-(cyclohex-1-en-1-yl)propan-1-amine (0.51 g, 3.67 mmol, 1.5 equiv) and iodobenzene (0.5 g, 2.45 mmol, 1.0 equiv) to yield **SI-1n** (0.41 g, 77.9%) as brown liquid. R_f = 0.80 (silica, EtOAc:hexanes, 1:9); Crude compound carried to next step.

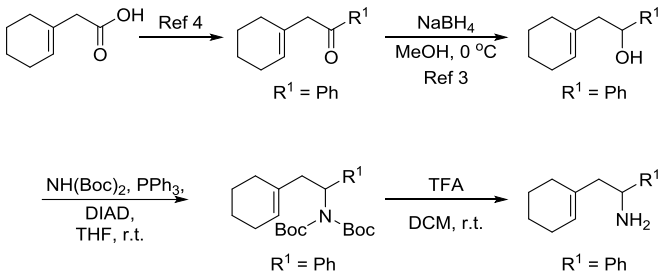
***N*-(3-(cyclohex-1-en-1-yl)propyl)-*N*-phenylpicolinamide** (**1n**).



1n

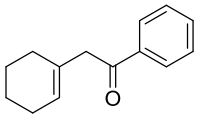
Prepared according to General Procedure **SI-B**: from *N*-(3-(cyclohex-1-en-1-yl)propyl)aniline (0.45 g, 2.09 mmol, 1.0 equiv) and picolinoyl chloride (0.35 g, 2.51 mmol, 1.2 equiv) to yield **1n** (0.66 g, 77.7%) as brown liquid. R_f = 0.50 (silica, EtOAc:hexanes, 1:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.32 (s, 1H), 7.54 (s, 1H), 7.36 (s, 1H), 7.18 - 7.04 (m, 6H), 5.35 (s, 1H), 3.91 (s, 2H), 1.94 - 1.74 (m, 8H), 1.62 - 1.51 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 168.40, 154.58, 148.39, 136.64, 135.97, 128.82, 127.65, 127.60, 126.50, 123.57, 123.40, 121.25, 49.80, 35.12, 33.20, 28.04, 25.11, 22.85, 22.41; **HRMS (ESI)**: calcd for $C_{21}H_{24}N_2NaO^+$ [M+Na^+]: 343.1778, found 343.1780.

2.3 General Scheme for the Synthesis of SI-31 and SI-32:



2.3.1 Procedure SI-D[3]:

2-(cyclohex-1-en-1-yl)-1-phenylethan-1-one (SI-10) [4]:



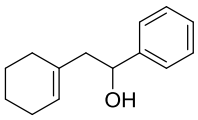
SI-10

To a stirred solution of 2-(cyclohex-1-en-1-yl)acetic acid (560 mg, 1.0 equiv), CH_3NOCH_3·HCl (546 mg, 1.3 equiv), and HATU (1.672 g, 1.1 equiv) in DCM (20 mL) was added DIPEA (1.65 mL, 2.5 equiv) at 0 °C. The reaction mixture was stirred at 25 °C for 2 h. After completion of reaction as monitored by TLC (R_f = 0.70, silica, EtOAc : hexanes, 1:2), $NaHSO_4$

(1M, 5 mL) was added dropwise and the reaction mixture was stirred for 5 min at 0 °C. The aqueous phase was extracted with EtOAc (20 mL x 3) and the combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using hexanes/EtOAc as eluent to afford the weinreb amide product (80%). To the solution of above amide product was added the solution of PhLi (1.2 equiv) in dry THF at -78 °C. After 1 h, the reaction mixture was stirred at -20 °C for 2 h. After completion of reaction as monitored by TLC (R_f = 0.90, silica, EtOAc:hexanes, 1:10), saturated $NaHPO_4$ was added dropwise and the reaction mixture was stirred for 5 min at 0 °C. The aqueous phase was extracted with EtOAc (20 mL x 3) and the combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using hexanes/EtOAc as eluent to afford the desired product (**SI-10**, 91%). NMR of **SI-26** is consistent with the previous report [8]. **SI-26** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.95 (m, 2H), 7.54 (*t*, J = 7.4 Hz, 1H), 7.44 (*t*, J = 7.6 Hz, 2H), 5.57 (s, 1H), 3.58 (s, 2H), 2.08-1.94 (m, 6H), 1.67-1.51 (m, 6H).

2.3.2 Procedure SI-E[3]:

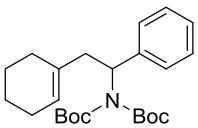
2-(cyclohex-1-en-1-yl)-1-phenylethan-1-ol (SI-11):



SI-11

To a stirred solution of aldehyde **SI-10** (1.17 g, 1.0 equiv) in MeOH (30 mL) was added $NaBH_4$ (640 mg, 2.0 equiv) at 0 °C. After completion of reaction as monitored by TLC (R_f = 0.60, silica, EtOAc:hexanes, 1:10), H_2O was added dropwise and the reaction mixture was stirred for 10 min at 0 °C. The aqueous phase was extracted with EtOAc (10 mL x 3) and the combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using hexanes / EtOAc as eluent to afford the desired product (**SI-11**, 98%).

2.3.3 Procedure SI-F[3], Synthesis of SI-12:

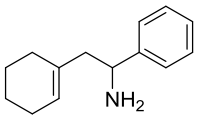


SI-12

A mixture of $HN(Boc)_2$ (478 mg, 1.0 equiv), Ph_3P (576 mg, 1.0 equiv), and alcohol **SI-11** (280 mg, 1.0 equiv) in THF (30 mL) was added DIAD (444 mg, 1.0 equiv) in THF dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. After completion of reaction as monitored by TLC (R_f = 0.75, silica, EtOAc : hexanes, 1:5), the solvent was evaporated and the residue suspended in Et_2O. After the precipitate was filtered, the organic extracts were concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using

hexanes/EtOAc as eluent to afford the desired product (**SI-12**, 75%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.7 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 7.2 Hz, 1H), 5.59-5.49 (m, 2H), 2.97 (dd, *J* = 13.3, 11.0 Hz, 1H), 2.61 (dd, *J* = 13.6, 4.6 Hz, 1H), 2.18-2.06(s, 1H), 2.02-1.96(s, 2H), 1.96-1.85 (m, 1H), 1.66-1.51 (m, 4H), 1.38 (s, 18H).

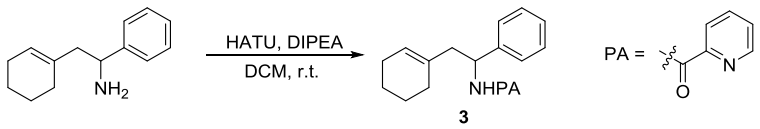
2.3.4 Procedure SI-G[3], Synthesis of SI-13:



SI-13

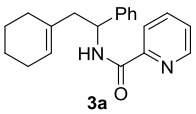
To the solution of **SI-12** (1.115 g, 1.0 equiv) in DCM (30 mL) was added TFA (3 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. After completion of reaction as monitored by TLC (R_f = 0.10, silica, EtOAc : hexanes, 1:2), H_2O was added dropwise and the reaction mixture was stirred for 10 min at 0 °C. The aqueous phase was extracted with EtOAc (10 mL x 3) and the combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure to get the crude product which was used to the next step without further purification (**SI-13**, 99%).

2.3.5 General Procedure SI-H: preparation of PA substrates:



A mixture of amine (1.0 equiv), picolimic acid (1.1 equiv), HATU (1.1 equiv) and DIPEA (845 mg, 3.0 equiv) in DCM (30 mL) was stirred overnight at room temperature. After completion of reaction as monitored by TLC, H_2O was added dropwise and the reaction mixture was stirred for 10 min at 0 °C. The aqueous phase was extracted with DCM (20 mL x 3) and the combined organic extracts were dried over Na_2SO_4, concentrated under reduced pressure and purification by flash column chromatography (SiO2, hexanes/EtOAc) to afford the compound 1

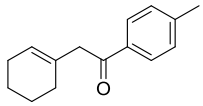
N-(2-(cyclohex-1-en-1-yl)-1-phenylethyl)picolinamide(3a)[4a]:



3a

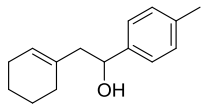
Prepared according to general procedure **SI-H**, White solid (84% Yield); **m.p.** = 94.5-96.0 °C; R_f = 0.65 (silica, EtOAc:hexanes, 1:2); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.7 Hz, 1H), 8.37 (d, *J* = 8.1 Hz, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.80 (td, *J* = 7.7, 1.7 Hz, 1H), 7.39 (dd, *J* = 7.5, 4.9 Hz, 1H), 7.36 (d, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 5.50 (d, *J* = 4.2 Hz, 1H), 5.24 (q, *J* = 7.8 Hz, 1H), 2.51 (d, *J* = 7.7 Hz, 2H), 2.00 – 1.98 (m, 1H), 1.90 – 1.87 (m, 3H), 1.54 (p, *J* = 5.9 Hz, 2H), 1.45 (qp, *J* = 12.4, 6.0 Hz, 2H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.6, 149.0, 148.0, 142.7, 137.2, 133.9, 128.5, 127.1, 126.4, 126.0, 125.1, 122.2, 51.7, 45.8, 28.2, 25.3, 22.8, 22.2; **HRMS** (ESI): calcd for $C_{20}H_{22}N_2NaO^+$ [M+Na^+]: 329.1615, found 329.1624.

2-(cyclohex-1-en-1-yl)-1-(*p*-tolyl)ethan-1-one (**SI-14**).


SI-14

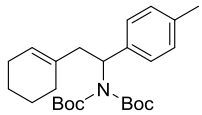
Prepared according to General Procedure **SI-D**: from 2-(cyclohex-1-en-1-yl)-*N*-methoxy-*N*-methylacetamide (5.6 g, 30.60 mmol, 1.0 equiv) and *p*-tolylmagnesium bromide (33.6 mL, 33.6 mmol, 1.0 M in toluene) to yield **SI-14** (4.5 g, 69%) as brown liquid. Rf = 0.70 (silica, EtOAc:hexanes, 1:9); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 5.57 (s, 1H), 3.56 (s, 2H), 2.41 (s, 3H), 2.05-1.98 (m, 4H), 1.66 - 1.52 (m, 4H).

2-(cyclohex-1-en-1-yl)-1-(*p*-tolyl)ethan-1-ol (**SI-15**).


SI-15

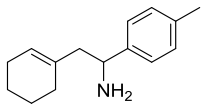
Prepared according to General Procedure **SI-E**: from 2-(cyclohex-1-en-1-yl)-1-(*p*-tolyl)ethan-1-one (2.8 g, 13.27 mmol, 1.0 equiv) and $NaBH_4$ (1.51 g, 39.25 mmol, 3.0 equiv) to yield **SI-15** (1.9 g, 67%) as colorless liquid. R_f = 0.50 (silica, EtOAc:hexanes, 1:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.27-7.24 (m, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 5.59 (s, 1H), 4.74-4.71 (m, 1H), 2.34 - 2.29 (m, 5H), 2.10 - 2.03 (m, 4H), 1.68 - 1.56 (m, 4H).

***N*-(3-(cyclohex-1-en-1-yl)propyl)-*N*-phenylpicolinamide** (**SI-16**).


SI-16

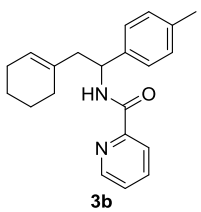
Prepared according to General Procedure **SI-F**: from 2-(cyclohex-1-en-1-yl)-1-(*p*-tolyl)ethan-1-ol (1.6 g, 7.40 mmol, 1.0 equiv) and **16** (1.60 g, 7.40 mmol, 1.0 equiv) to yield **SI-16** (1.5 g, 48%) as colorless liquid. R_f = 0.70 (silica, EtOAc:hexanes, 1:9); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.27 - 7.23 (m, 3H), 7.10 (d, *J* = 7.8 Hz, 2H), 5.50 (q, *J* = 5.5 Hz, 2H), 2.96 (dd, *J* = 13.6, 10.7 Hz, 1H), 2.58 (dd, *J* = 13.5, 5.1 Hz, 1H), 2.32 (d, *J* = 5.1 Hz, 4H), 2.21 - 1.82 (m, 5H), 1.64 - 1.46 (m, 6H), 1.38 (s, 18H).

2-(cyclohex-1-en-1-yl)-1-(*p*-tolyl)ethan-1-amine (**SI-17**).


SI-17

Prepared according to General Procedure **SI-G**: from **12** (1.5 g, 3.61 mmol, 1.0 equiv) and trifluoroacetic acid (2.06 g, 18.07 mmol, 5.0 equiv) to yield **SI-17** (0.62 g, 80%) as pale brown liquid. Rf = 0.40 (silica, MeOH:DCM, 1:9); Crude compound carried to next step.

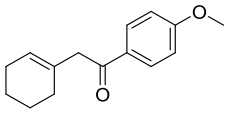
N-(2-(cyclohex-1-en-1-yl)-1-(*p*-tolyl)ethyl)picolinamide (**3b**).


3b

Prepared according to General Procedure **SI-H**: from 2-(cyclohex-1-en-1-yl)-1-(*p*-tolyl)ethan-1-amine (0.5 g, 2.32 mmol, 1.0 equiv) and picolinic acid (0.31 g, 2.55 mmol, 1.1 equiv) to yield **3b** (0.51 g, 68%) as pale brown liquid. R_f = 0.50 (silica, EtOAc:hexanes, 1:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.55 - 8.53 (m, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.83 - 7.79 (m, 1H), 7.41 - 7.38 (m, 1H), 7.27 - 7.25 (m, 2H), 7.12 (d, *J* = 8.0 Hz, 1H), 5.51 (s, 1H), 5.21 (q, *J* = 8.0 Hz, 2H), 2.51 (d, *J* = 7.6 Hz, 2H), 2.31 (s, 3H), 2.03 -1.88 (m, 4H), 1.64 - 1.42 (m, 4H); **^{13}C**

NMR (100 MHz, $CDCl_3$): δ = 163.49, 150.03, 148.00, 139.77, 137.20, 136.61, 134.01, 129.14, 126.31, 125.98, 124.92, 122.18, 51.47, 45.72, 28.15, 25.29, 22.80, 22.22, 21.06; **HRMS (ESI)**: calcd for $C_{21}H_{24}N_2NaO^+$ [M+Na^+]: 343.1778, found 343.1780.

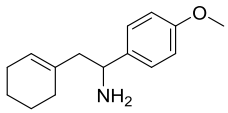
2-(cyclohex-1-en-1-yl)-1-(4-methoxyphenyl)ethan-1-one (**SI-18**).



SI-18

Prepared according to General Procedure **SI-D**: from 2-(cyclohex-1-en-1-yl)-*N*-methoxy-*N*-methylacetamide (3.0 g, 16.39 mmol, 1.0 equiv) and (4-methoxyphenyl)magnesium bromide (18.0 mL, 18.03 mmol, 1.0 M in THF) to yield **SI-18** (2.79 g, 74%) as colorless liquid. R_f = 0.80 (silica, EtOAc:hexanes, 1:9); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 12.0 Hz, 2H), 6.92 (d, *J* = 12.0 Hz, 2H), 5.56 (s, 1H), 3.87 (s, 3H), 3.54 (s, 2H), 2.05 - 1.94 (m, 4H), 1.66 - 1.52 (m, 4H).

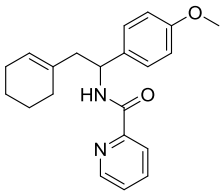
2-(cyclohex-1-en-1-yl)-1-(4-methoxyphenyl)ethan-1-amine (**SI-19**).



SI-19

To a solution of 2-(cyclohex-1-en-1-yl)-1-(4-methoxyphenyl) ethan-1-one (2.5 g, 10.86 mmol, 1.0 equiv) and ammonium acetate (8.36 g, 108.6 mmol, 10.0 equiv) in abs. methanol (50 mL) was added $NaBH_3CN$ (0.47 g, 7.60 mmol, 1.0 equiv) in one portion at room temperature. The mixture was stirred at room temperature for 48 h. Concentrated HCl was added until pH < 2, and the solvent was removed in vacuo. The residue was taken up in 30 mL of water and extracted once with ether (30 mL). The aqueous solution was brought to pH > 12 with solid KOH and extracted with ether (3 × 50 mL). The combined extracts were dried over Na_2SO_4 and evaporated in vacuo to afford 1.1 g of crude product **SI-19** as pale yellow liquid.

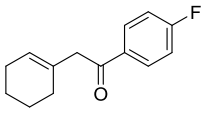
***N*-(2-(cyclohex-1-en-1-yl)-1-(4-methoxyphenyl)ethyl)picolinamide** (**3c**).



3c

Prepared according to General Procedure **SI-H**: from 2-(cyclohex-1-en-1-yl)-1-(4-methoxyphenyl)ethan-1-amine (0.37 g, 1.60 mmol, 1.0 equiv) and picolinic acid (0.21 g, 1.76 mmol, 1.1 equiv) to yield **3c** (0.41 g, 76%) as brown liquid. R_f = 0.50 (silica, EtOAc:hexanes, 1:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.52 (d, *J* = 7.2 Hz, 1H), 8.31 (d, *J* = 7.6 Hz, 1H), 7.82 - 7.78 (m, 1H), 7.40 - 7.37 (m, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 5.48 (s, 1H), 5.18 (q, *J* = 7.6 Hz, 1H), 3.76 (s, 3H), 2.49 (d, *J* = 7.6 Hz, 2H), 2.00 -1.86 (m, 4H), 1.57 - 1.42 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 163.41, 158.53, 149.96, 147.95, 137.17, 134.82, 133.92, 127.50, 125.94, 124.89, 122.13, 113.77, 55.17, 51.12, 45.56, 28.12, 25.24, 22.75, 22.16; **HRMS (ESI)**: calcd for $C_{21}H_{24}N_2NaO_2^+$ [M+Na^+]: 359.1726, found 359.1730.

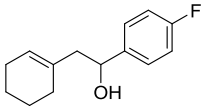
2-(cyclohex-1-en-1-yl)-1-(4-fluorophenyl)ethan-1-one (**SI-20**).



SI-20

Prepared according to General Procedure **SI-D**: from 2-(cyclohex-1-en-1-yl)-*N*-methoxy-*N*-methylacetamide (5.0 g, 27.32 mmol, 1.0 equiv) and (4-fluorophenyl)magnesium bromide (30.0 mL, 30.0 mmol, 1.0 M in THF) to yield **SI-20** (3.9 g, 65%) as brown liquid. R_f = 0.70 (silica, EtOAc:hexanes, 1:9); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.02 - 7.97 (m, 2H), 7.12 (t, *J* = 8.6 Hz, 2H), 5.57 (s, 1H), 3.56 (s, 2H), 2.05-1.97 (m, 4H), 1.68 - 1.53 (m, 4H).

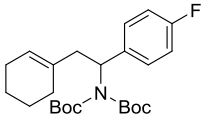
2-(cyclohex-1-en-1-yl)-1-(4-fluorophenyl)ethan-1-ol (**SI-21**).



SI-21

Prepared according to General Procedure **SI-E**: from 2-(cyclohex-1-en-1-yl)-1-(4-fluorophenyl)ethan-1-one (2.7 g, 12.66 mmol, 1.0 equiv) and $NaBH_4$ (1.44 g, 37.98 mmol, 3.0 equiv) to yield **SI-21** (2.46 g, 88%) as colorless liquid. R_f = 0.50 (silica, EtOAc:hexanes, 1:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.33 - 7.29 (m, 2H), 7.01 (t, *J* = 8.0 Hz, 2H), 5.57 (s, 1H), 4.72 (dd, *J* = 9.0, 4.8 Hz, 1H), 2.30-2.23 (m, 2H), 2.08 - 1.86 (m, 4H), 1.67 - 1.54 (m, 4H).

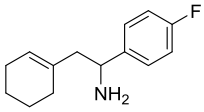
***N*-(3-(cyclohex-1-en-1-yl)propyl)-*N*-phenylpicolinamide** (**SI-22**).



SI-22

Prepared according to General Procedure **SI-F**: from 2-(cyclohex-1-en-1-yl)-1-(4-fluorophenyl)ethan-1-ol (2.26 g, 10.27 mmol, 1.0 equiv) and **16** (2.22 g, 10.27 mmol, 1.0 equiv) to yield **SI-22** (1.9 g, 43%) as colorless liquid. R_f = 0.70 (silica, EtOAc:hexanes, 1:9); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.35 (dd, *J* = 8.6, 5.5 Hz, 2H), 6.98 (t, *J* = 8.0 Hz, 2H), 5.52 - 5.47 (m, 2H), 2.95 (dd, *J* = 13.6, 10.5 Hz, 1H), 2.57 (dd, *J* = 13.7, 5.3 Hz, 1H), 2.29 - 1.83 (m, 4H), 1.68 - 1.50 (m, 4H), 1.39 (s, 18H).

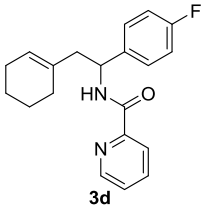
2-(cyclohex-1-en-1-yl)-1-(4-fluorophenyl)ethan-1-amine (SI-23).



SI-23

Prepared according to General Procedure **SI-G**: from **12** (1.37 g, 3.26 mmol, 1.0 equiv) and trifluoroacetic acid (5.59 g, 49.0 mmol, 15.0 equiv) to yield **SI-23** (0.71 g, 92%) as pale brown liquid. R_f = 0.40 (silica, MeOH:DCM, 1:9); Crude compound carried to next step.

***N*-(2-(cyclohex-1-en-1-yl)-1-(4-fluorophenyl)ethyl)picolinamide** (**3d**).

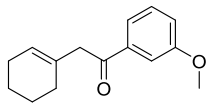


3d

Prepared according to General Procedure **SI-H**: from 2-(cyclohex-1-en-1-yl)-1-(4-fluorophenyl)ethan-1-amine (0.62 g, 2.83 mmol, 1.0 equiv) and picolinic acid (0.38 g, 3.11 mmol, 1.1 equiv) to yield **3d** (0.62 g, 67%) as brown liquid. R_f = 0.50 (silica, EtOAc:hexanes, 1:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.56 (d, *J* = 4.4 Hz, 1H), 8.36 (d, *J* = 7.6 Hz, 1H), 8.14 (d, *J* = 7.6 Hz, 1H), 7.84 - 7.80 (m, 1H), 7.43 - 7.40 (m, 1H), 7.34 - 7.31 (m, 2H), 7.00 (t, *J* = 8.8 Hz, 2H), 5.50 (s, 1H), 5.20 (q, *J* = 7.6 Hz, 2H), 2.49 (d, *J* = 7.6 Hz, 2H), 2.00 -1.85 (m, 4H), 1.58 - 1.44 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 163.58, 163.00, 160.57, 149.76, 148.01, 138.48, 138.44, 137.24, 133.58, 127.95, 127.87, 126.08, 125.28, 122.14, 115.29, 115.08, 51.09, 45.64, 28.09, 25.22, 22.70, 22.11; **HRMS (ESI)**: calcd for $C_{20}H_{22}FN_2O^+$

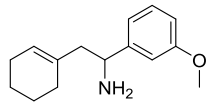
[M+H$^+$]: 325.1708, found 325.1710.

2-(cyclohex-1-en-1-yl)-1-(3-methoxyphenyl)ethan-1-one (**SI-24**).


SI-24

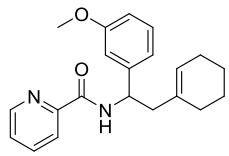
Prepared according to General Procedure **SI-D**: from 2-(cyclohex-1-en-1-yl)-*N*-methoxy-*N*-methylacetamide (3.0 g, 16.39 mmol, 1.0 equiv) and (3-methoxyphenyl)magnesium bromide (18.0 mL, 18.03 mmol, 1.0 M in THF) to yield **SI-24** (2.70 g, 71%) as colorless liquid. Rf = 0.80 (silica, EtOAc:hexanes, 1:9); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 - 7.46 (m, 2H), 7.38 - 7.33 (m, 1H), 7.10 (dd, *J* = 8.0, 4.0 Hz, 1H), 5.57 (s, 1H), 3.85 (s, 3H), 3.57 (s, 2H), 2.07 - 1.96 (m, 4H), 1.67 - 1.52 (m, 4H).

2-(cyclohex-1-en-1-yl)-1-(3-methoxyphenyl)ethan-1-amine (**SI-25**).


SI-25

Prepared according to General Procedure **SI-G**: from 2-(cyclohex-1-en-1-yl)-1-(3-methoxyphenyl)ethan-1-one (1.8 g, 7.78 mmol, 1.0 equiv) and ammonium acetate (5.99 g, 77.8 mmol, 10.0 equiv) to yield **SI-25** (0.8 g, 44%) as colorless liquid. Rf = 0.40 (silica, MeOH:DCM, 1:9); Crude compound carried to next step.

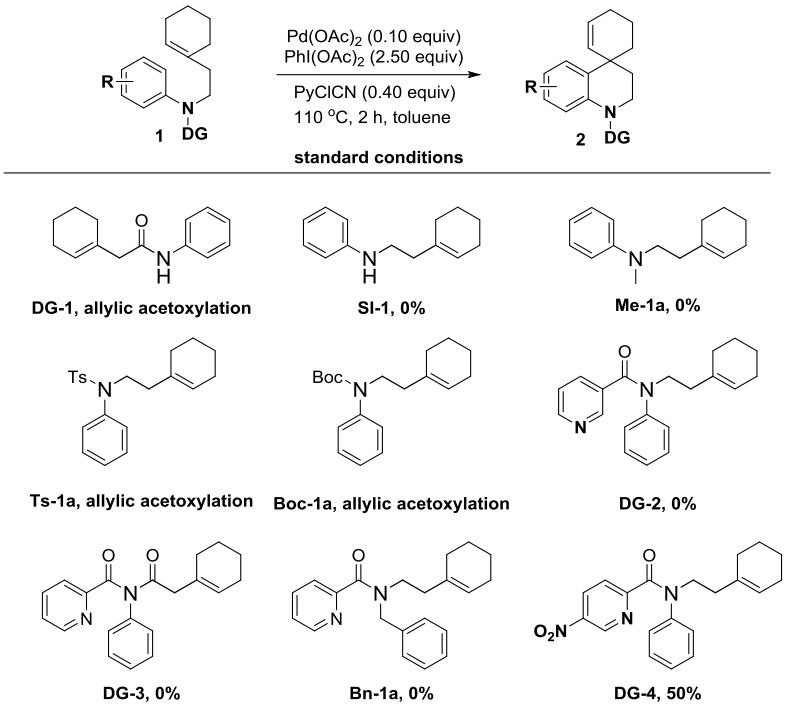
***N*-(2-(cyclohex-1-en-1-yl)-1-(3-methoxyphenyl)ethyl)picolinamide** (**3e**).


3e

Prepared according to General Procedure **SI-H**: from 2-(cyclohex-1-en-1-yl)-1-(3-methoxyphenyl)ethan-1-amine (0.35 g, 1.51 mmol, 1.0 equiv) and picolinic acid (0.20 g, 1.66 mmol, 1.1 equiv) to yield **3e** (0.42 g, 82%) as pale yellow liquid. R_f = 0.50 (silica, EtOAc:hexanes, 1:3); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.55 (d, *J* = 4.8 Hz, 1H), 8.36 (d, *J* = 8.0 Hz, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.83 - 7.79 (m, 1H), 7.42 - 7.39 (m, 1H), 7.22 (d, *J* = 8.0 Hz, 1H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.90 (s, 1H), 6.78 - 6.75 (m, 1H), 5.51 (s, 1H), 5.21 (q, *J* = 8.0, 6.8 Hz, 1H), 3.79 (s, 3H), 2.50 (m, 2H), 2.04 - 1.88 (m, 4H), 1.57 - 1.42 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 163.51, 159.62, 149.89, 147.97, 144.42, 137.16, 133.83, 129.42, 125.97, 125.00, 122.13, 118.66, 112.27, 112.21, 55.12, 51.66, 45.67, 28.10, 25.24, 22.74, 22.15; **HRMS (ESI)**: calcd for $C_{21}H_{24}N_2NaO_2^+$ [M+Na$^+$]: 359.1726, found 359.1730.

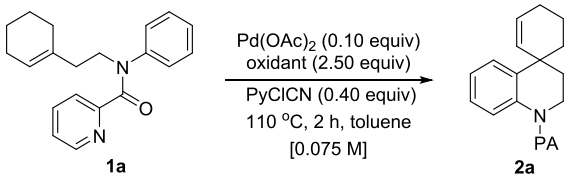
3. Optimization and Substrate Scope of Alkenyl Aniline Compounds.

Table 1. Optimization of other DGs of arylation reactions[a]



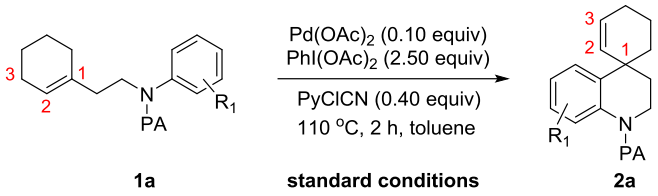
[a]Reactions conditions: **1** (0.3 mmol), $Pd(OAc)_2$ (0.03 mmol), $PhI(OAc)_2$ (0.75 mmol), 2-Chloro-4-cyanopyridine (0.12 mmol), toluene (5 mL), N_2, 2 h. [b]Yield is that of the isolated product.

Table 2. Optimization using other oxidants of the arylation reaction[a,b]



entry	oxidant	temp (°C)	solvent	time (h)	result
1	Dess-Martin reagent (2.50 equiv)	110	Toluene	2	71%, some SM remained
2	iodoso-benzen (2.50 equiv)	110	Toluene	2	2.6%, some SM remained
3	$NaIO_4$ (2.50 equiv)	110	Toluene	2	7.4%, some SM remained
4	NFSI (2.50 equiv)	110	Toluene	2	no product, no SM left
5	Oxone (2.50 equiv)	110	Toluene	2	16%, some SM remained
6	TBHP (2.50 equiv)	110	Toluene	2	60%, some SM remained
7	benzoquinone (2.50 equiv)	110	Toluene	2	11%, some SM remained
8	$Cu(OAc)_2$ (2.50 equiv)	110	Toluene	2	16%, some SM remained

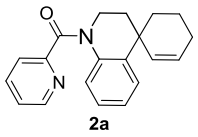
[a]Reactions conditions: **1** (0.3 mmol), $Pd(OAc)_2$ (0.03 mmol), oxidant (0.75 mmol), 2-Chloro-4-cyanopyridine (0.12 mmol), toluene (4 mL), N_2, 2 h. [b]Yield is that of the isolated product.



Scheme 1. Synthesis of arylation reactions 1.

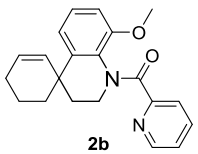
General Procedure A: To a solution of **1** (0.3 mmol, 1.0 equiv) and $Pd(OAc)_2$ (0.015 mmol, 0.05 equiv) in anhydrous toluene (4 mL) at r.t. was added $PhI(OAc)_2$ (0.75 mmol, 2.5 equiv), 2-chloroisonicotinonitrile (16.6mg, 0.12 mmol, 0.4 equiv) in a 15 mL flame-dried sealed tube (purged with N_2, sealed with PTFE cap). The mixture was heated at 110 °C for 2 hours. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by silica gel flash chromatography (petroleum ether / EtOAc) to give the product.

(2', 3'-dihydro-1'H-spiro[cyclohexane-1,4'-quinolin]-2-en-1'-yl)(pyridin-2-yl)methanone (2a):



Prepared according to general procedure **A**. from **1a** (46.0 mg, 0.15 mmol, 1.00 equiv) and $Pd(OAc)_2$ (3.4 mg, 0.10 equiv) at 110 °C for 2 hours to yield **2a** (37.0 mg, 80%) as a colorless oil. When scale up of the reaction from **1a** (500.0 mg, 1.63 mmol, 1.00 equiv) and $Pd(OAc)_2$ (34.0 mg, 0.10 equiv) at 110 °C for 2 hours afforded **2a** (332.0 mg, 67%) as a colorless oil. R_f = 0.45 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.8 Hz, 1H), 7.66 (t, *J* = 7.7 Hz, 1H), 7.37 (d, *J* = 7.5 Hz, 1H), 7.26 (q, *J* = 4.2 Hz, 2.5H), 7.12 – 6.63 (m, 2.5H), 5.96 (dt, *J* = 10.0, 3.8 Hz, 1H), 5.53 (d, *J* = 10.0 Hz, 1H), 3.97 (dt, *J* = 9.4, 4.8 Hz, 2H), 2.19 – 2.07 (m, 2H), 2.10 – 1.96 (m, 2H), 1.95 – 1.77 (m, 2H), 1.77 – 1.56 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.3, 154.7, 149.0, 137.7, 137.0, 136.5, 133.3, 128.3, 127.9, 125.8, 124.9, 124.3, 124.2, 123.3, 42.3, 38.4, 35.9, 33.6, 25.1, 18.8. **HRMS** (ESI): calcd for $C_{20}H_{20}N2ONa^+$ [M+Na^+]: 327.1468, found 327.1466.

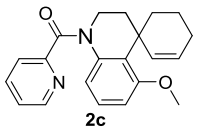
(8'-methoxy-2',3'-dihydro-1'H-spiro[cyclohexane-1,4'-quinolin]-2-en-1'-yl)(pyridin-2-yl)methanone (2b):



Prepared according to general procedure **A**. from **1d** (51.0 mg, 0.15 mmol, 1.00 equiv) and $Pd(OAc)_2$ (3.4 mg, 0.10 equiv) at 100 °C for 2 hours to yield **2b** (48.0 mg, **2b** : **2b**'=2.86 : 1 94%) as a colorless oil. R_f = 0.40 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.46 (s, 0.35H), 8.29 (s, 1H), 7.76 – 7.66 (m, 0.35H), 7.60 (t, *J* = 7.9 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 10.8 Hz, 0.35H), 7.15 (t, *J* = 6.2 Hz, 1H), 7.09 – 6.98 (m, 1.3H), 6.91 (d, *J* = 7.8 Hz, 1.3H), 6.57 (d, *J* = 7.9 Hz, 0.35H), 6.43 (d, *J* = 8.1 Hz, 1H), 5.99 (d, *J* = 10.1 Hz, 1H), 5.88 (d, *J* = 10.0 Hz, 0.35H), 5.75 (d, *J* = 9.9 Hz, 0.35H), 5.51 (d, *J* = 10.0 Hz, 1H), 4.55 – 4.20 (m, 1.35H), 3.69 (t, *J* = 10.6 Hz, 1H), 3.55 (s, 0.35H), 3.42 (s, 1H), 3.17 (s, 3H), 2.29 (t, *J* = 9.4 Hz, 1H), 2.17 – 1.98 (m, 4H), 1.89 – 1.57 (m, 6H). **^{1}H NMR** (600 MHz, $CDCl_3$, 55 °C) δ 8.22

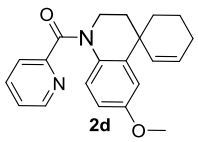
(s, 1H), 7.58 (d, *J* = 29.1 Hz, 2H), 7.13 (s, 1H), 6.99 (t, *J* = 8.1 Hz, 1H), 6.91 (d, *J* = 7.7 Hz, 1H), 6.43 (s, 1H), 5.97 (s, 1H), 5.52 (s, 1H), 4.34 (s, 1H), 3.78 – 3.54 (m, 1H), 3.38 (d, *J* = 21.6 Hz, 0H), 3.19 (s, 2H), 2.55 – 2.26 (m, 1H), 2.19 – 1.99 (m, 3H), 1.87 – 1.58 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.9, 154.6, 151.3, 148.2, 148.0, 140.2, 136.2, 135.7, 133.3, 133.0, 128.8, 128.0, 127.7, 125.7, 125.1, 124.5, 124.2, 123.4, 122.5, 119.9, 119.3, 109.4, 55.1, 54.6, 43.2, 41.9, 39.3, 37.4, 36.7, 31.4, 25.4, 25.2, 19.3. **HRMS** (ESI): calcd for $C_{21}H_{22}N_2O_2Na^+$ [M+Na^+]: 357.1574, found 357.1571.

(5'-methoxy-2',3'-dihydro-1'H-spiro[cyclohexane-1,4'-quinolin]-2-en-1'-yl)(pyridin-2-yl)methanone (2c):



Prepared according to general procedure **A**. from **1e** (51.0 mg, 0.15 mmol, 1.00 equiv) and $Pd(OAc)_2$ (3.4 mg, 0.10 equiv) at 110 °C for 2 hours to yield **2c** (42.0 mg, 82%) as a colorless oil. R_f = 0.40 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.8 Hz, 1H), 7.68 (t, *J* = 7.7 Hz, 1H), 7.54 – 7.23 (m, 2H), 7.14 (d, *J* = 8.6 Hz, 1H), 6.83 – 6.13 (m, 2H), 5.93 (d, *J* = 9.9 Hz, 1H), 5.50 (d, *J* = 10.0 Hz, 1H), 4.20 – 3.83 (m, 2H), 3.46 (s, 3H), 2.24 – 2.06 (m, 2H), 2.07 – 1.90 (m, 2H), 1.92 – 1.73 (m, 2H), 1.73 – 1.55 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.5, 157.5, 155.1, 149.3, 137.8, 136.7, 133.9, 130.1, 128.9, 128.3, 124.4, 123.3, 111.5, 109.9, 55.3, 42.6, 38.0, 36.2, 34.3, 25.2, 19.0. **^{1}H NMR** (600 MHz, Benzene-d_6, 70 °C) δ 8.13 (d, *J* = 4.7 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 9.8 Hz, 2H), 7.03 (t, *J* = 7.7 Hz, 1H), 6.68 (s, 1H), 6.60 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.54 (dd, *J* = 7.7, 4.3 Hz, 1H), 5.76 (dt, *J* = 9.9, 3.7 Hz, 1H), 5.47 (dt, *J* = 10.2, 2.3 Hz, 1H), 3.96 (dd, *J* = 8.0, 5.1 Hz, 2H), 3.18 (d, *J* = 2.5 Hz, 3H), 2.11 – 1.98 (m, 1H), 1.97 – 1.82 (m, 2H), 1.80 – 1.66 (m, 2H), 1.64 – 1.57 (m, 1H), 1.59 – 1.48 (m, 3H). **HRMS** (ESI): calcd for $C_{21}H_{22}N_2O_2Na^+$ [M+Na^+]: 357.1574, found 357.1571.

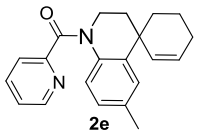
(6'-methoxy-2',3'-dihydro-1'H-spiro[cyclohexane-1,4'-quinolin]-2-en-1'-yl)(pyridin-2-yl)methanone (2d):



Prepared according to general procedure **A**. from **1c** (51.0 mg, 0.15 mmol, 1.00 equiv) and $Pd(OAc)_2$ (3.4 mg, 0.10 equiv) at 110 °C for 2 hours to yield **2d** (37.0 mg, 73%) as a colorless oil. R_f = 0.40 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.65 (s, 1H), 7.26 (d, *J* = 6.4 Hz, 3H), 6.81 (d, *J* = 2.7 Hz, 1H), 6.41 (s, 1H), 5.97 (dd, *J* = 9.4, 4.8 Hz, 1H), 5.52 (d, *J* = 10.0 Hz, 1H), 4.12 – 3.86 (m, 2H), 3.73 (s, 3H), 2.21 – 2.08 (m, 2H), 2.06 – 2.01 (m, 2H), 1.91 – 1.74 (m, 2H), 1.74 – 1.57 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.9, 156.4, 154.9, 149.1, 139.5, 136.4, 133.1, 130.2, 128.6, 125.9, 124.1, 123.3, 113.7, 110.8, 55.3, 41.7, 38.7, 35.9, 33.4, 25.1, 18.9. **^{1}H NMR** (600 MHz, Benzene-d_6, 70 °C) δ 8.16 (d, *J* = 4.8 Hz, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.08 (t, *J* = 7.7 Hz, 1H), 6.96 (d, *J* = 3.0 Hz, 2H), 6.58 (dd, *J* = 7.6, 4.8 Hz, 1H), 6.37 (dd, *J* = 8.9, 3.0 Hz, 1H), 5.75 (dt, *J* = 10.1, 3.8 Hz, 1H), 5.47 (dt, *J* = 10.1, 2.2 Hz, 1H), 4.02 (td, *J* = 11.2, 10.7, 6.2 Hz, 1H), 3.89 (ddd, *J* = 13.2, 6.6, 3.9 Hz, 1H), 3.34 (s, 3H), 2.20 – 2.06 (m, 1H), 1.96 – 1.78 (m, 2H),

1.76 – 1.65 (m, 2H), 1.65 – 1.58 (m, 1H), 1.57 – 1.44 (m, 2H). **^{13}C NMR** (101 MHz, Benzene-d_6) δ 168.0, 156.8, 156.2, 148.5, 139.5, 136.3, 133.9, 131.6, 126.3, 124.1, 123.9, 114.2, 111.1, 54.9, 42.5, 39.1, 36.5, 33.5, 25.4, 19.3. **HRMS** (ESI): calcd for $C_{21}H_{22}N_2O_2Na^+$ [M+Na$^+$]: 357.1574, found 357.1571.

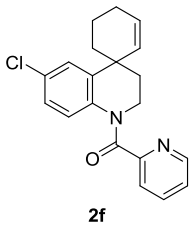
(6'-methyl-2',3'-dihydro-1'H-spiro[cyclohexane-1,4'-quinolin]-2-en-1'-yl)(pyridin-2-yl)methanone (2e):



2e

Prepared according to general procedure **A**. from **1b** (48.0 mg, 0.15 mmol, 1.00 equiv) and $Pd(OAc)_2$ (3.4 mg, 0.10 equiv) at 110 °C for 2 hours to yield **2e** (42.0 mg, 87%) as a colorless oil. R_f = 0.50 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.8 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.53 – 7.19 (m, 2.5H), 7.04 (d, *J* = 1.9 Hz, 1.5H), 6.69 (s, 1H), 5.95 (dt, *J* = 10.1, 3.7 Hz, 1H), 5.53 (dd, *J* = 10.1, 2.2 Hz, 1H), 4.03 – 3.89 (m, 2H), 2.25 (s, 3H), 2.22 – 2.06 (m, 2H), 2.05 – 1.91 (m, 2H), 1.92 – 1.75 (m, 2H), 1.75 – 1.59 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.2, 155.0, 149.1, 137.7, 136.5, 134.5, 134.0, 133.6, 128.5, 128.3, 126.6, 124.8, 124.2, 123.4, 42.3, 38.5, 36.1, 33.8, 25.2, 21.1, 21.1, 21.0, 19.0. **^{1}H NMR** (600 MHz, Benzene-d_6, 70 °C) δ 8.14 (d, *J* = 4.8 Hz, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.13 – 7.06 (m, 2H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.69 – 6.54 (m, 2H), 5.78 (dt, *J* = 10.0, 3.8 Hz, 1H), 5.50 (dt, *J* = 10.0, 2.4 Hz, 1H), 4.22 – 3.76 (m, 2H), 2.15 – 2.04 (m, 4H), 2.02 – 1.82 (m, 2H), 1.81 – 1.60 (m, 2H), 1.52 (pq, *J* = 6.7, 3.8 Hz, 2H). **^{13}C NMR** (101 MHz, Benzene-d_6) δ 168.3, 156.1, 148.5, 137.8, 136.3, 136.0, 134.3, 133.4, 128.7, 128.2, 127.8, 126.8, 125.2, 124.1, 123.9, 42.6, 38.8, 36.5, 33.7, 25.5, 21.0, 19.4.**HRMS** (ESI): calcd for $C_{21}H_{22}N_2ONa^+$ [M+Na$^+$]: 341.1624, found 341.1622.

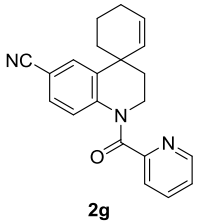
(6'-chloro-2',3'-dihydro-1'*H*-spiro[cyclohexane-1,4'-quinolin]-2-en-1'-yl)(pyridin-2-yl)methanone (**2f**).



2f

Prepared according to General Procedure **A**. from 3a (105 mg, 0.30 mmol, 1.00 equiv) and $Pd(OAc)_2$ (6.9 mg, 0.1 equiv) at 110 °C for 2 hours to yield **2f** (65 mg, 62.5%) as a brown liquid. R_f = 0.5 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.49 (d, *J* = 4.0 Hz, 1H), 7.69 (t, *J* = 7.6, 7.6 Hz, 1H), 7.46 (d, *J* = 7.2 Hz, 1H), 7.28 - 7.26 (m, 1H), 7.21 (s, 1H), 6.85 (s, 2H), 5.99 - 5.95 (m, 1H), 5.47 (d, *J* =10.4 Hz, 1H), 3.96 - 3.89 (m, 2H), 2.19 - 1.94 (m, 4H), 1.86 – 1.55 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 168.23, 154.26, 148.84, 139.47, 136.62, 135.62, 132.57, 129.60, 129.03, 127.87, 125.93, 125.83, 124.40, 123.44, 42.41, 38.48, 35.57, 33.38, 24.91, 18.65; **HRMS (ESI)**: calcd for $C_{20}H_{19}ClN_2NaO^+$ [M+Na$^+$]: 361.1074, found 361.1078.

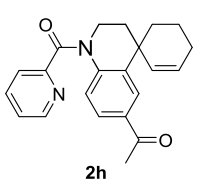
1'-picolinoyl-2',3'-dihydro-1'*H*-spiro[cyclohexane-1,4'-quinolin]-2-ene-6'-carbonitrile (**2g**).



2g

Prepared according to General Procedure **A**. from **1g** (100 mg, 0.30 mmol, 1.00 equiv) and $Pd(OAc)_2$ (6.7 mg, 0.1 equiv) at 110 °C for 2 hours to yield **2g** (59.1 mg, 59.5%) as a brown liquid. R_f = 0.5 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.46 (d, *J* = 4.8 Hz, 1H), 7.79 - 7.75 (m, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 1.6 Hz, 1H), 7.33 - 7.30 (m, 1H), 7.18 (dd, *J* = 7.2, 1.2 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.06 - 6.02 (m, 1H), 5.46 (d, *J* = 10.0 Hz, 1H), 4.06 - 4.01 (m, 1H), 3.93 - 3.86 (m, 1H), 2.16 - 1.95 (m, 4H), 1.89 - 1.53 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 168.81, 153.61, 148.73, 141.48, 138.32, 136.96, 132.29, 132.04, 129.81, 129.41, 125.05, 124.99, 123.92, 119.04, 107.09, 42.82, 38.30, 35.23, 33.36, 24.92, 18.55; **HRMS (ESI)**: calcd for $C_{21}H_{20}N_3O^+$ [M+H$^+$]: 330.1598, found 330.1600.

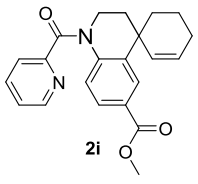
1-(1'-picolinoyl-2',3'-dihydro-1'H-spiro[cyclohexane-1,4'-quinolin]-2-en-6'-yl)ethan-1-one (2h):



2h

Prepared according to general procedure **A**. from **1h** (53.0 mg, 0.15 mmol, 1.00 equiv), $Pd(OAc)_2$ (6.8 mg, 0.20 equiv) and $PhI(OAc)_2$ (1.50 mmol, 5.0 equiv) at 110 °C for 3 hours to yield **2h** (33.0 mg, 61%) as a colorless oil. R_f = 0.35 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.63 – 8.41 (m, 1H), 7.88 (d, *J* = 2.1 Hz, 1H), 7.74 (td, *J* = 7.7, 1.8 Hz, 1H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.49 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.30 (ddd, *J* = 7.8, 4.8, 1.2 Hz, 1H), 6.94 (d, *J* = 8.5 Hz, 1H), 6.03 (dt, *J* = 10.1, 3.7 Hz, 1H), 5.54 (dt, *J* = 10.1, 2.1 Hz, 1H), 4.04 (ddd, *J* = 13.1, 6.4, 3.1 Hz, 1H), 3.93 (ddd, *J* = 13.3, 11.5, 5.5 Hz, 1H), 2.52 (s, 3H), 2.27 – 2.09 (m, 2H), 2.11 – 1.98 (m, 2H), 1.95 – 1.78 (m, 2H), 1.73 – 1.58 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.4, 168.9, 154.3, 149.1, 141.8, 137.7, 136.9, 133.0, 132.8, 129.4, 128.4, 126.3, 124.9, 124.7, 123.9, 42.9, 38.6, 35.6, 33.7, 26.6, 25.2, 18.9. **HRMS** (ESI): calcd for $C_{22}H_{22}N_2O_2Na^+$ [M+Na$^+$]: 369.1574, found 369.1570.

Methyl 1'-picolinoyl-2',3'-dihydro-1'H-spiro[cyclohexane-1,4'-quinolin]-2-ene-6'-carboxylate (2i):

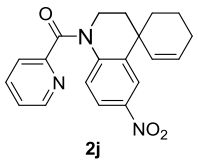


2i

Prepared according to general procedure **A**. from **1i** (55.0 mg, 0.15 mmol, 1.00 equiv), $Pd(OAc)_2$ (6.8 mg, 0.20 equiv) and $PhI(OAc)_2$ (1.50 mmol, 5.0 equiv) at 110 °C for 3 hours to yield **2i** (46.0 mg, 87%) as a colorless oil. R_f = 0.30 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.54 – 8.40 (m, 1H), 7.93 (d, *J* = 2.0 Hz, 1H), 7.72 (td, *J* = 7.7, 1.7 Hz, 1H), 7.62 – 7.46 (m, 2H), 7.32 – 7.27 (m, 1H), 6.87 (s, 1H), 6.02 (dt, *J* = 10.1, 3.7 Hz, 1H), 5.54 (dt, *J* = 10.1, 2.1 Hz, 1H), 4.04 (ddd, *J* = 13.1, 6.6, 3.2 Hz, 1H), 3.93 (ddd, *J* = 13.3, 11.5, 5.6 Hz, 1H), 3.87 (s, 3H), 2.27 – 2.08 (m, 2H), 2.09 – 1.99 (m, 2H), 1.93 – 1.76 (m, 2H), 1.77 – 1.52 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.9, 167.0,

154.3, 149.1, 141.7, 137.7, 136.9, 132.9, 129.7, 129.3, 127.4, 125.8, 124.8, 124.7, 123.8, 52.1, 42.8, 38.6, 35.7, 33.6, 25.2, 18.9. **HRMS** (ESI): calcd for $C_{22}H_{22}N_2O_3Na^+$ [M+Na$^+$]: 385.1523, found 385.1519.

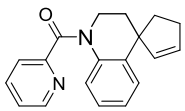
Methyl 1'-picolinoyl-2',3'-dihydro-1'H-spiro[cyclohexane-1,4'-quinolin]-2-ene-6'-carboxylate (2j):



2j

Prepared according to general procedure **A**. from **1j** (53.0 mg, 0.15 mmol, 1.00 equiv), $Pd(OAc)_2$ (6.8 mg, 0.20 equiv) and $PhI(OAc)_2$ (1.50 mmol, 5.0 equiv) at 110 ºC for 3 hours to yield **2j** (38.0 mg, 72%) as a colorless oil. R_f = 0.20 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, Benzene-d_6) δ 8.24 (d, J = 2.7 Hz, 1H), 7.99 – 7.89 (m, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.52 (dt, J = 9.0, 2.1 Hz, 1H), 7.00 (dq, J = 7.7, 1.8 Hz, 1H), 6.56 (dd, J = 9.2, 4.6 Hz, 1H), 6.47 (dt, J = 7.9, 3.9 Hz, 1H), 5.70 (dt, J = 9.9, 3.7 Hz, 1H), 5.19 (dd, J = 10.1, 2.1 Hz, 1H), 3.88 (ddd, J = 13.2, 6.6, 3.0 Hz, 1H), 3.74 (ddd, J = 13.0, 11.5, 5.9 Hz, 1H), 1.96 – 1.81 (m, 1H), 1.71 (t, J = 5.6 Hz, 2H), 1.55 – 1.43 (m, 1H), 1.45 – 1.29 (m, 4H). **^{13}C NMR** (101 MHz, Benzene-d_6) δ 168.8, 154.2, 148.4, 144.1, 144.0, 138.1, 136.8, 132.1, 130.0, 125.0, 125.0, 124.6, 123.6, 121.4, 42.9, 38.7, 35.4, 33.0, 25.1, 19.0. **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.1, 153.6, 148.9, 143.7, 143.5, 138.5, 137.2, 132.1, 130.2, 125.3, 124.9, 124.2, 123.8, 121.4, 43.1, 38.7, 35.3, 33.5, 25.1, 18.7. **HRMS** (ESI): calcd for $C_{20}H_{20}N_3O_3^+$ [M+H$^+$]: 350.1499, found 350.1497.

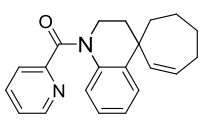
(2',3'-dihydro-1'H-spiro[cyclopentane-1,4'-quinolin]-2-en-1'-yl)(pyridin-2-yl)methanone (2k):



2k

Prepared according to general procedure **A**. from **1k** (90.0 mg, 0.30 mmol, 1.00 equiv), $Pd(OAc)_2$ (6.8 mg, 0.10 equiv) and $PhI(OAc)_2$ (1.50 mmol, 2.50 equiv) at 110 ºC for 2 hours to yield **2k** (64.0 mg, 71%) as a colorless oil. R_f = 0.40 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.8 Hz, 1H), 7.70 (t, *J* = 7.8 Hz, 1H), 7.55 – 7.41 (m, 1H), 7.33 – 7.27 (m, 1H), 7.23 – 7.17 (m, 1H), 7.15 – 6.84 (m, 3H), 5.96 (dt, *J* = 5.1, 2.3 Hz, 1H), 5.71 (dd, *J* = 5.3, 2.6 Hz, 1H), 4.07 (dt, *J* = 13.1, 4.9 Hz, 1H), 3.89 (dd, *J* = 14.0, 7.5 Hz, 1H), 2.58 – 2.44 (m, 2H), 2.12 (t, *J* = 7.1 Hz, 2H), 2.03 – 1.88 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.3, 154.8, 148.9, 137.8, 137.6, 137.1, 136.6, 131.5, 126.9, 125.8, 124.8, 124.5, 124.4, 123.6, 51.3, 43.4, 39.0, 35.5, 31.6. **HRMS** (ESI): calcd for $C_{19}H_{19}N_2O^+$ [M+H$^+$]: 291.1492, found 291.1491.

(2',3'-dihydro-1'H-spiro[cycloheptane-1,4'-quinolin]-2-en-1'-yl)(pyridin-2-yl)methanone (2l):

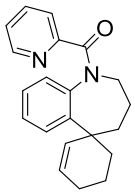


2l

Prepared according to general procedure **A**. from **1l** (50.0 mg, 0.15 mmol, 1.00 equiv), $Pd(OAc)_2$ (3.4 mg, 0.10 equiv) and $PhI(OAc)_2$ (0.375 mmol, 2.50 equiv) at 110 ºC for 2 hours to yield **2l** (46.0 mg, 92%) as a colorless oil. R_f = 0.40 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 4.8 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.47 – 7.37 (m, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.26 – 7.21 (m, 1H), 7.08 – 6.58 (m, 2H), 5.87 (dt, *J* = 11.7, 5.8 Hz, 1H),

5.56 (d, *J* = 11.8 Hz, 1H), 4.05 (q, *J* = 11.1, 9.0 Hz, 1H), 3.83 (dt, *J* = 13.1, 5.7 Hz, 1H), 2.37 – 2.22 (m, 2H), 2.24 – 2.07 (m, 2H), 2.07 – 1.94 (m, 1H), 1.92 – 1.81 (m, 1H), 1.82 – 1.64 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.4, 154.9, 149.1, 138.5, 136.9, 136.6, 131.3, 127.9, 125.9, 125.2, 124.8, 124.4, 123.6, 44.3, 42.5, 36.2, 35.3, 27.9, 27.7, 24.8. **HRMS** (ESI): calcd for $C_{21}H_{22}N_2ONa^+$ [M+Na^+]: 341.1624, found 341.1621.

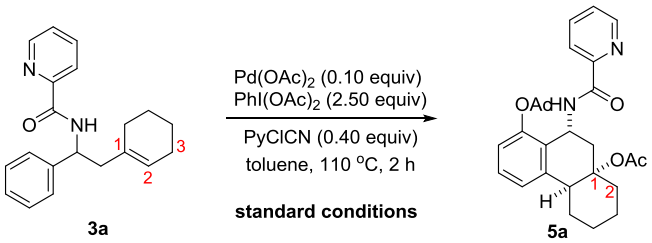
(3,4-dihydrospiro[benzo[b]azepine-5,1'-cyclohexan]-2'-en-1(2*H*)-yl)(pyridin-2-yl)methanone (**2n**).



2n

Prepared according to General Procedure **A**. from **1n** (96 mg, 0.30 mmol, 1.00 equiv) and $Pd(OAc)_2$ (6.7 mg, 0.1 equiv) at 110 °C for 2 hours to yield **2n** (41 mg, 43%) as a pale yellow liquid. R_f = 0.5 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 4.4 Hz, 1H), 7.59 - 7.51 (m, 2H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.06 - 7.00 (m, 2H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.54 (d, *J* = 7.6 Hz, 1H), 5.92 - 5.88 (m, 1H), 5.70 - 5.67 (m, 1H), 5.11 (d, *J* = 12.8 Hz, 1H), 2.97 - 2.94 (m, 1H), 2.78 (d, *J* = 12.8 Hz, 1H), 2.38 - 2.27 (m, 1H), 2.04 (s, 2H), 1.83 (d, *J* = 12.8 Hz, 2H), 1.72 -1.57 (m, 3H), 1.47 - 1.28 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 167.26, 154.37, 147.82, 142.57, 136.22, 135.88, 131.28, 128.99, 126.53, 126.14, 125.97, 123.59, 123.50, 47.45, 43.63, 40.19, 31.80, 25.70, 25.09, 19.03.; **HRMS (ESI)**: calcd for $C_{21}H_{22}N_2NaO^+$ [M+Na^+]: 341.1621, found 341.1624.

4. Optimization and Substrate Scope of α-Aryl Alkenyl Aamides



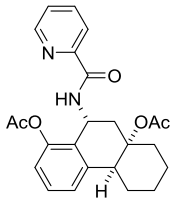
Scheme 2. Synthesis of α-Aryl Alkenyl Aamide.

General Procedure B: To a solution of **3** (0.3 mmol, 1.0 equiv) and $Pd(OAc)_2$ (0.015 mmol, 0.05 equiv) in anhydrous toluene (4 mL) at r.t. was added $PhI(OAc)_2$ (0.75 mmol, 2.5 equiv), 2-chloroisonicotinonitrile (16.6mg, 0.12 mmol, 0.4 equiv) in a 15 mL flame-dried sealed tube (purged with N_2, sealed with PTFE cap). The mixture was heated at 110 °C for 2 hours. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by silica gel flash chromatography (petroleum ether / EtOAc) to give the product **5**.

General Procedure C: To a solution of **3** (0.3 mmol, 1.0 equiv) and $Pd(OAc)_2$ (0.015 mmol, 0.05 equiv) in anhydrous toluene (4 mL) at r.t. was added $PhI(OAc)_2$ (0.75 mmol, 2.5 equiv), 2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl (S-phos, 12.5mg, 0.03 mmol, 0.1 equiv) in a 15 mL flame-dried sealed tube (purged with N_2,

sealed with PTFE cap). The mixture was heated at 110 ºC for 5 hours. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by silica gel flash chromatography (petroleum ether / EtOAc) to give the product **5**.

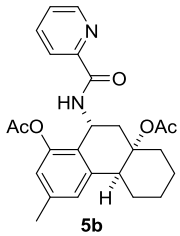
3'-(picolinamido)-2',3'-dihydrospiro[cyclohexane-1,1'-indene]-2,4'-diyl diacetate (5a)[4a]:



5a

Prepared according to general procedure **B**, from **3a** (92.0 mg, 0.3 mmol, 1.0 equiv) to give the desired product **5a** (78.0 mg, 60%) as a colorless oil; prepared according to general procedure **C**, from **3a** (92.0 mg, 0.3 mmol, 1.0 equiv) to give the desired product **5a** (47.0 mg, 55% brsm, 30.0 mg of **3a** was recovered) as a colorless oil R_f = 0.4 (silica gel, petroleum ether : EtOAc = 2 : 1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 4.7 Hz, 1H), 8.36 (d, *J* = 9.6 Hz, 1H), 8.22 (d, *J* = 7.8 Hz, 1H), 7.83 (td, *J* = 7.7, 1.7 Hz, 1H), 7.37 (dd, *J* = 7.6, 4.7 Hz, 1H), 7.30 (t, *J* = 7.8 Hz, 1H), 7.07 (d, *J* = 7.7 Hz, 1H), 6.92 (d, *J* = 7.9 Hz, 1H), 5.62 (dd, *J* = 9.4, 6.2 Hz, 1H), 3.52 (dd, *J* = 12.5, 4.8 Hz, 1H), 2.60 – 2.46 (m, 2H), 2.43 – 2.32 (m, 1H), 2.20 (dd, *J* = 13.4, 4.4 Hz, 1H), 2.14 (s, 3H), 2.01 (s, 3H), 1.98 – 1.89 (m, 1H), 1.74 (t, *J* = 13.9 Hz, 2H), 1.53 – 1.26 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.7, 169.9, 162.4, 150.0, 149.5, 148.0, 142.1, 137.4, 129.0, 127.2, 126.2, 125.9, 122.3, 120.9, 83.3, 44.3, 41.1, 36.1, 34.8, 32.0, 25.6, 23.6, 23.1, 21.1. **HRMS** (ESI): calcd for $C_{24}H_{26}N_2NaO_5^+$ [M+Na^+]: 445.1734, found 445.1719.

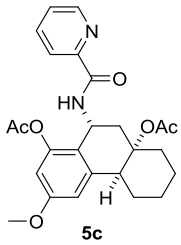
6'-methyl-3'-(picolinamido)-2',3'-dihydrospiro[cyclohexane-1,1'-indene]-2,4'-diyl diacetate (**5b**).



5b

Prepared according to General Procedure **B**. from **3b** (96 mg, 0.30 mmol, 1.00 equiv) and $Pd(OAc)_2$ (6.7 mg, 0.1 equiv) at 110 ºC for 2 hours to yield **5b** (55 mg, 42%) as a colorless liquid. R_f = 0.5 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.39 -8.32 (m, 2H), 8.21 (d, *J* = 7.2 Hz, 1H), 7.84 - 7.81 (m, 1H), 7.36 (s, 1H), 6.87 (s, 1H), 6.74 (s, 1H), 5.57 (s, 1H), 3.46 (d, *J* = 10.0 Hz, 1H), 2.55 - 2.44 (m, 2H), 2.38 - 2.32 (m, 4H), 2.19 - 2.12 (m, 4H), 2.00 (s, 3H), 1.94 - 1.91 (m, 1H), 1.73 - 1.70 (m, 2H), 1.48 - 1.27 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 170.59, 169.89, 162.22, 149.88, 149.22, 147.81, 141.62, 138.95, 137.27, 127.70, 126.03, 122.73, 122.08, 121.51, 83.31, 44.16, 40.83, 35.91, 34.62, 31.87, 25.47, 23.47, 22.99, 21.10, 20.91; **HRMS (ESI)**: calcd for $C_{25}H_{28}N_2NaO_5^+$ [M+Na^+]: 459.1886, found 459.1890.

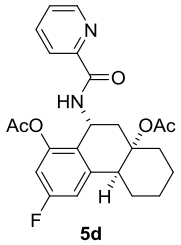
6'-methoxy-3'-(picolinamido)-2',3'-dihydrospiro[cyclohexane-1,1'-indene]-2,4'-diyl diacetate (**5c**).



5c

Prepared according to General Procedure **B**. from **3c** (101 mg, 0.30 mmol, 1.00 equiv) and $Pd(OAc)_2$ (6.7 mg, 0.1 equiv) at 110 ºC for 2 hours to yield **5c** (44 mg, 33%) as a colorless liquid. R_f = 0.5 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.40 (d, *J* = 4.8 Hz, 1H), 8.31 (d, *J* = 9.6 Hz, 1H), 8.20 (d, *J* = 7.6 Hz, 1H), 7.84 - 7.80 (m, 1H), 7.37 - 7.34 (m, 1H), 6.59 (d, *J* = 2.0 Hz, 1H), 6.50 (d, *J* = 2.4 Hz, 1H), 5.54 (q, *J* = 6.4, 2.4 Hz, 1H), 3.77 (s, 3H), 3.47 (q, *J* = 8.0, 4.4 Hz, 1H), 2.54 - 2.46 (m, 2H), 2.37 - 2.34 (m, 1H), 2.21 - 2.16 (m, 1H), 2.12 (s, 3H), 2.00 (s, 3H), 1.96 - 1.92 (m, 1H), 1.76 - 1.70 (m, 2H), 1.49 - 1.31 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 170.54, 169.62, 162.21, 159.69, 150.29, 149.99, 147.82, 142.74, 137.26, 126.00, 122.09, 118.07, 112.04, 107.41, 83.32, 55.38, 44.59, 40.77, 35.86, 34.64, 31.97, 25.49, 23.46, 22.97, 20.90; **HRMS (ESI)**: calcd for $C_{25}H_{28}N_2NaO_6^+$ [M+Na$^+$]: 475.1835, found 475.1839.

6'-fluoro-3'-(picolinamido)-2',3'-dihydrospiro[cyclohexane-1,1'-indene]-2,4'-diyl diacetate (**5d**).

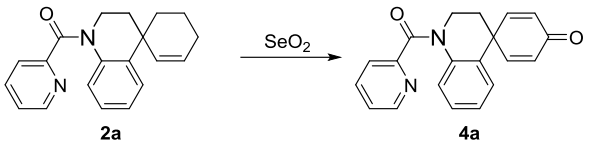


5d

Prepared according to General Procedure **B**. from **3d** (100 mg, 0.30 mmol, 1.00 equiv) and $Pd(OAc)_2$ (6.7 mg, 0.1 equiv) at 110 ºC for 2 hours to yield **5d** (42 mg, 31%) as a colorless liquid. R_f = 0.6 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.40 (d, *J* = 4.0 Hz, 1H), 8.31 (d, *J* = 9.6 Hz, 1H), 8.19 (d, *J* = 7.6 Hz, 1H), 7.82 (t, *J* = 8.0 Hz, 1H), 7.38 - 7.35 (m, 1H), 6.77 (d, *J* = 8.8 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 5.56 (t, *J* = 8.8 Hz, 1H), 3.50 - 3.46 (m, 1H), 2.50 - 2.43 (m, 2H), 2.37 - 2.34 (m, 1H), 2.18 - 2.15 (m, 1H), 2.12 (s, 3H), 2.00 (s, 3H), 1.92 - 1.89 (m, 1H), 1.73 - 1.70 (m, 2H), 1.45 - 1.30 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 170.45, 169.26, 162.27, 149.83, 147.87, 137.34, 126.13, 122.14, 113.48, 113.28, 109.30, 109.06, 82.97, 44.50, 40.65, 35.72, 34.52, 31.85, 28.06, 25.39, 23.39, 22.93, 20.83; **HRMS (ESI)**: calcd for $C_{24}H_{25}FN_2NaO_5^+$ [M+Na$^+$]: 463.1637, found 463.1639.

5. Versatile Transformations of the Product.

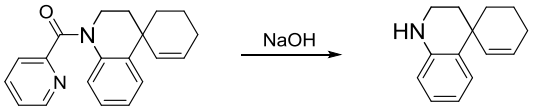
5.1 Synthesis of 2ab:



2a **4a**

A sealed tube was charged with alkene **2a** (92 mg, 0.30 mmol), monobasic sodium hydrogen phosphate (13mg, 0.11mmol), finely grounded selenium dioxide (66.0 mg, 0.60 mmol), quartz sand (150.0 mg) and 1, 4-dioxane (3.0 ml). The flask was evacuated and filled with N_2 (3 times). The solution was immersed in a 140°C oil bath. After stirring for 6 hours, the mixture was filtered through a short silica gel path and washed with ethyl acetate. The organic solvent was evacuated under vacuum and the resulting yellow oil was dissolved in methylene chloride and washed with 1N aqueous NaOH. The aqueous layer was extracted with methylene chloride. The combined organic layers were dried over sodium sulfate and concentrated in vacuo. The resulting slightly yellow oil was purified by flash chromatography (40% to 60% ethyl acetate in petroleum ether) to give **4a** (47.0 mg, 50%). R_f = 0.2 (silica gel, petroleum ether : EtOAc = 1 : 1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 4.9 Hz, 1H), 7.78 (t, *J* = 7.8 Hz, 1H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.31 (t, *J* = 6.2 Hz, 1H), 7.18 – 6.87 (m, 6H), 6.33 (d, *J* = 9.7 Hz, 2H), 4.08 (t, *J* = 6.0 Hz, 2H), 2.20 (t, *J* = 6.0 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 185.7, 168.3, 153.9, 152.7, 148.7, 138.2, 137.1, 128.4, 127.9, 127.7, 127.3, 125.5, 125.3, 125.0, 124.3, 43.4, 42.3, 34.4. **HRMS** (ESI): calcd for $C_{20}H_{16}N_2O_2Na^+$ [M+Na^+]: 339.1104, found 339.1102.

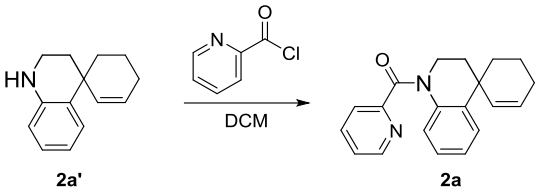
5.2 Synthesis of 2a':



2a **2a'**

To a mixture of THF/MeOH/H2O (16.0/4.0/4.0 mL) was added compound **2a** (200 mg, 0.66 mmol, 1.0 eq) and NaOH (200 mg, 0.33 mmol, 1.5 eq) at room temperature. The mixture was heated to 60 °C and stirred for 12 hours. Water was added and the mixture was extracted with DCM. The combined organic layers was washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel flash chromatography to give the desired product **2a'** (127.0 mg) in 97% yield. R_f = 0.8 (silica gel, petroleum ether : EtOAc = 2 : 1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.12 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.98 (td, *J* = 7.6, 1.5 Hz, 1H), 6.62 (td, *J* = 7.4, 1.2 Hz, 1H), 6.48 (dd, *J* = 7.9, 1.2 Hz, 1H), 5.91 (dt, *J* = 10.1, 3.8 Hz, 1H), 5.50 (dt, *J* = 10.1, 2.2 Hz,

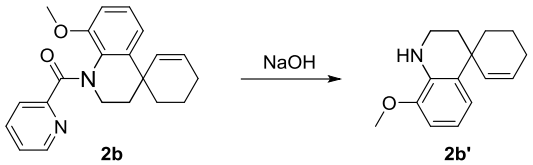
1H), 3.91 (bs, 1H), 3.45 (td, *J* = 11.5, 4.2 Hz, 1H), 3.29 (ddd, *J* = 11.4, 4.5, 3.2 Hz, 1H), 2.22 – 2.00 (m, 2H), 1.88 – 1.75 (m, 3H), 1.77 – 1.61 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.7, 135.5, 129.2, 128.3, 127.5, 127.1, 116.5, 114.0, 37.9, 36.9, 36.9, 34.3, 25.3, 18.4. **HRMS** (ESI): calcd for $C_{14}H_{18}N^+$ [M+H$^+$]: 200.1434, found 200.1432.



2a' **2a**

Prepared according to general procedure **SI-B**, from **2a'** (12.0 mg, 0.06 mmol, 1.0 equiv) to give the desired product **2a** (11.0 mg, 60%) as a colorless oil, R_f = 0.4 (silica gel, petroleum ether : EtOAc = 2 : 1);

5.2 Synthesis of 2b':



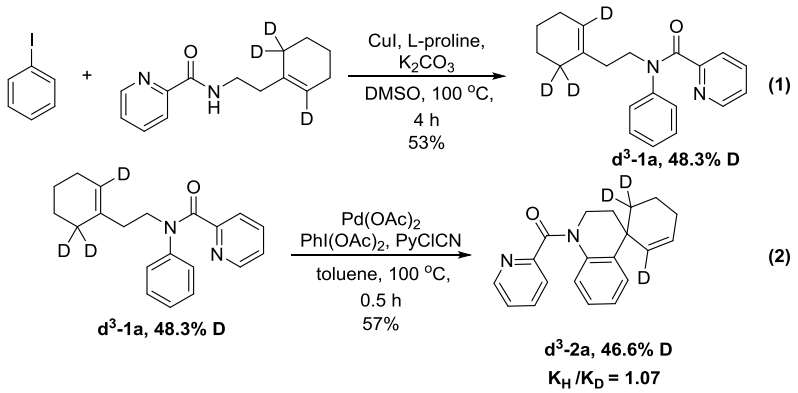
2b **2b'**

To a mixture of THF/MeOH/H2O (4.0/1.0/1.0 mL) was added compound **2b** (35.0 mg, 0.10 mmol, 1.0 eq) and NaOH (6.0 mg, 0.15 mmol, 1.5 eq) at room temperature. The mixture was heated to 60 °C and stirred for 12 hours. Water was added and the mixture was extracted with DCM. The combined organic layers was washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel flash chromatography to give the desired product **2b'** (10.0 mg) in 97% yield brsm and **2b** (20.0 mg was recovered). R_f = 0.6 (silica gel, petroleum ether : EtOAc = 5 : 1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.78 (dd, *J* = 7.7, 1.5 Hz, 1H), 6.68 – 6.61 (m, 1H), 6.57 (t, *J* = 7.8 Hz, 1H), 5.88 (dt, *J* = 10.1, 3.8 Hz, 1H), 5.49 (dd, *J* = 9.9, 2.3 Hz, 1H), 4.39 (s, 1H), 3.83 (s, 3H), 3.48 – 3.30 (m, 2H), 2.22 – 1.99 (m, 2H), 1.89 – 1.74 (m, 3H), 1.75 – 1.60 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.9, 135.7, 133.6, 128.3, 127.3, 121.4, 114.9, 107.5, 55.6, 37.4, 37.1, 36.9, 34.2, 25.3, 18.6. **MS** (ESI): calcd for $C_{15}H_{19}NO^+$ [M+H$^+$]: 230.2, found 230.2. **HRMS** (ESI): calcd for $C_{15}H_{20}NO^+$ [M+H$^+$]: 230.1539, found 230.1538

6. Deuterium Labeling Experiments and Mechanistic Studies

To explore the reaction mechanism for this C-H oxidative arylation reactions, some deuterium labeling experiments were conducted under the standard reaction condition.

6.1 Deuterium Labeling Experiments for sp^2 C-H oxidative arylation:



The substrate (**d^3-1a**, 52% deuterium) was prepared to distinguish double bond between at the 2, 3- and 5, 6-positions (**eq 1, Scheme 2**). Under the best reaction condition, **d^3-2a** was obtained in 30% yield at the 2, 3-position of the cyclohexene, and no 5,6-position double bond product generated. The kinetic isotope effect (KIE) was determined to briefly explore the reaction mechanism when PA was as DG. The KIE (kH/D = 1.07) was observed in the intermolecular competition experiment. The C-H bond of 2 positions is not involved with C−H cleavage.

6.1.1. A mixture of iodobenzene (0.36 g, 1.76 mmol, 1.10 eq), Amind **d^3-1a** (0.35 g, 1.60 mmol, 1.00 eq), K_2CO_3 (3.2 mmol), CuI (0.16 mmol), and L-proline (0.32 mmol) in 4 mL of DMSO was heated at 100 ℃ until the start material was consumed as indicated by TLC. The cooled mixture was partitioned between water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residual oil was loaded on a silica gel column and eluted with 1:20 to 1:5 ethyl acetate/petroleum ether to afford the corresponding product **d^3-1a** (260.0 mg, 53%).

6.1.2 To a flame-dried sealed tube was added $PhI(OAc)_2$ (120.0 mg, 0.375 mmol, 2.5 equiv), $Pd(OAc)_2$ (3.4 mg, 10 mol %), 2-chloroisonicotinonitrile (8.0 mg, 0.06 mmol, 0.4 equiv) and starting material (0.15 mmol, 1.0 equiv), then 2.0 mL dry toluene was added to dissolve the mixture under nitrogen. This was stirred at 90 ℃ with oil bath. Specificly, reaction would complete within 0.75 h, then cooled to room temperature. The reaction mixture next was purified by silica gel directly without remove solvent.

The calculation of deuterated percentage of **d^3-1a** based on the integration of NMR spectrum in

position **2**.

N_{SM}-H (hydrogen percentage in position 1 of starting material) = 51.7 %

N_{SM}-D (deuterated percentage in position 1 of starting material) = 48.3 %

N_{TM}-H (hydrogen percentage in position 1 of terminal material) = 53.4 %

N_{TM}-D (deuterated percentage in position 1 of terminal material) = 46.6 %

KH/KD = (N_{SM}-D*N_{TM}-H)/(N_{SM}-H*N_{TM}-D) = 1.07

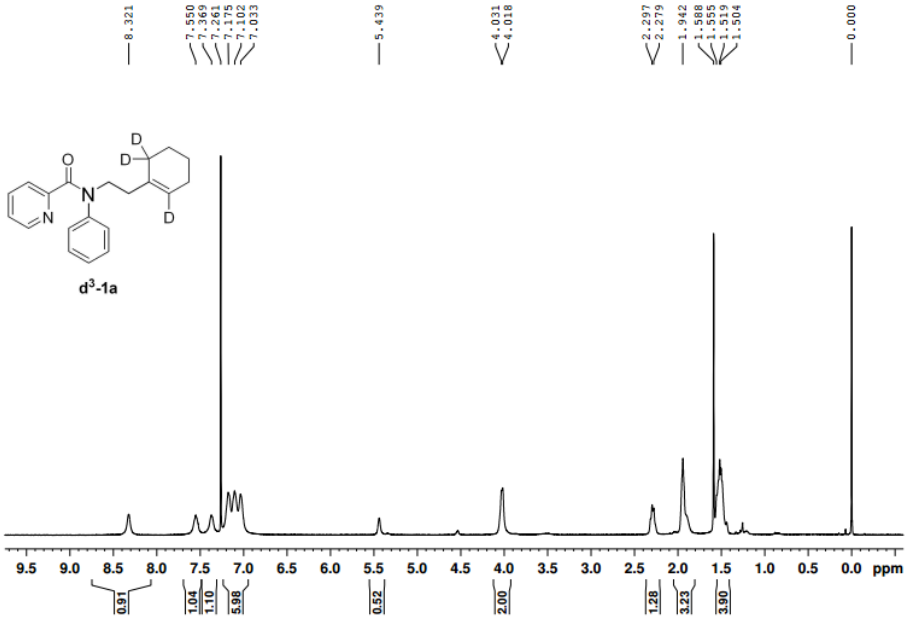


Figure S6.1 ^{1}H NMR spectrum of the substrates **d^3-1a**

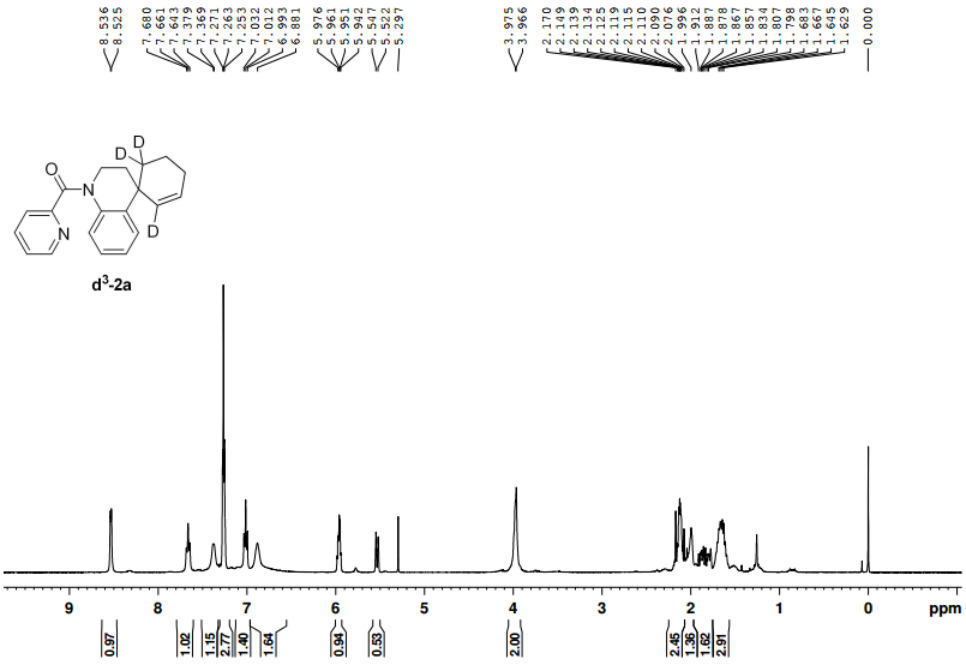
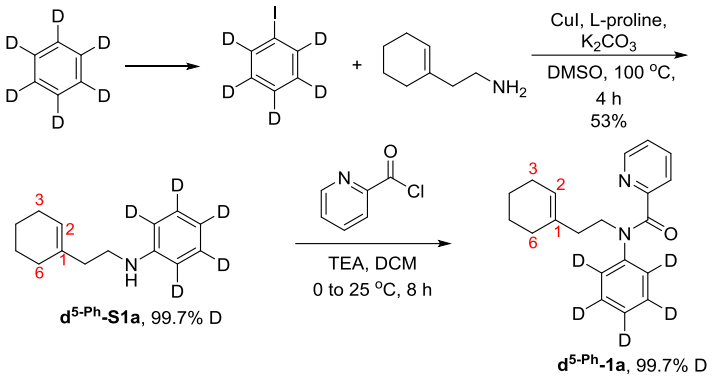


Figure S6.2 ^{1}H NMR spectrum of the substrates **d^3-2a**

6.2 Deuterium Labeling Experiments for sp^3 C-H acetoxylation 1:



6.2.1 The title compound was synthesized by following a similar procedure reported in the literature for the synthesis of iodobenzene[7] , by stirring a mixture of D^6-benzene (0.5 mL, 5.0 mmol), AgOTf (1280.0 mg, 2.5 mmol) and iodine (1270.0 mg, 2.5 mmol) in dry CH_2Cl_2 (10 mL) for 15 min at room temperature in dark condition. Reaction mixture was passed through a short celite plug and washed with CH_2Cl_2. Then combined filtrate was washed with dilute NH_4OH solution, dilute Na_2SO_3 and water, followed by organic solution was dried over Na_2SO_4, filtered and evapourated under reduced pressure. The resulting residue was utilized directly for next step.

6.2.2. A mixture of **$d^{5\text{-Ph}}$-iodobenzene** (0.60 g, 2.87 mmol, 1.00 eq), **Amine** (0.54 g, 4.30 mmol, 1.50 eq), K_2CO_3 (5.8 mmol), CuI (0.29 mmol), and L-proline (0.57 mmol) in 3 mL of DMSO was heated at 100 ℃ until the start material was consumed as indicated by TLC. The cooled mixture was partitioned between water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residual oil was loaded on a silica gel column and eluted with 1:20 to 1:5 ethyl acetate/petroleum ether to afford the corresponding product **$d^{5\text{-Ph}}$-S1a** (435.0 mg, 74%, 99.7% D). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.53 (s, 1H), 3.62 (s, 1H), 3.17 (t, *J* = 6.8 Hz, 2H), 2.27 (t, *J* = 6.9 Hz, 2H), 2.11 – 1.98 (m, 2H), 1.99 – 1.88 (m, 2H), 1.71 – 1.51 (m, 4H).

6.2.3 Procedure SI-B:

To a solution of the picolinic acid (10.50 mmol) in DCM (20 mL) at room temperature was added $SOCl_2$ (2 mL) and one drop of dry DMF. The reaction was allowed to stir at 40 ℃ for 4 hours. The solvent was then removed under reduced pressure to afford the corresponding crude acid chloride. Then DCM (20 mL) was added and the solution was cooled to 0 ℃ followed by dropwise addition of NEt_3 (3.5 mL), DMAP (0.25 mmol) and amine (10.0 mmol, 1.0 eq). The reaction mixture was stirred at room temperature overnight, extracted by DCM, the organic layer was dried over Na_2SO_4 and the solvent was evaporated, then purified by flash chromatography(petroleum ether/ EtOAc = 2 : 1) to give **$d^{5\text{-Ph}}$-1a** (2.0 g, 62%) as a white solid. R_f = 0.50 (silica, hexanes: EtOAc, 2:1); **^{1}H NMR** (400

MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.20 – 6.98 (m, 1H), 5.42 (s, 1H), 4.00 (d, *J* = 7.8 Hz, 2H), 2.28 (t, *J* = 7.7 Hz, 2H), 1.97 – 1.80 (m, 4H), 1.53 – 1.46 (m, 4H).

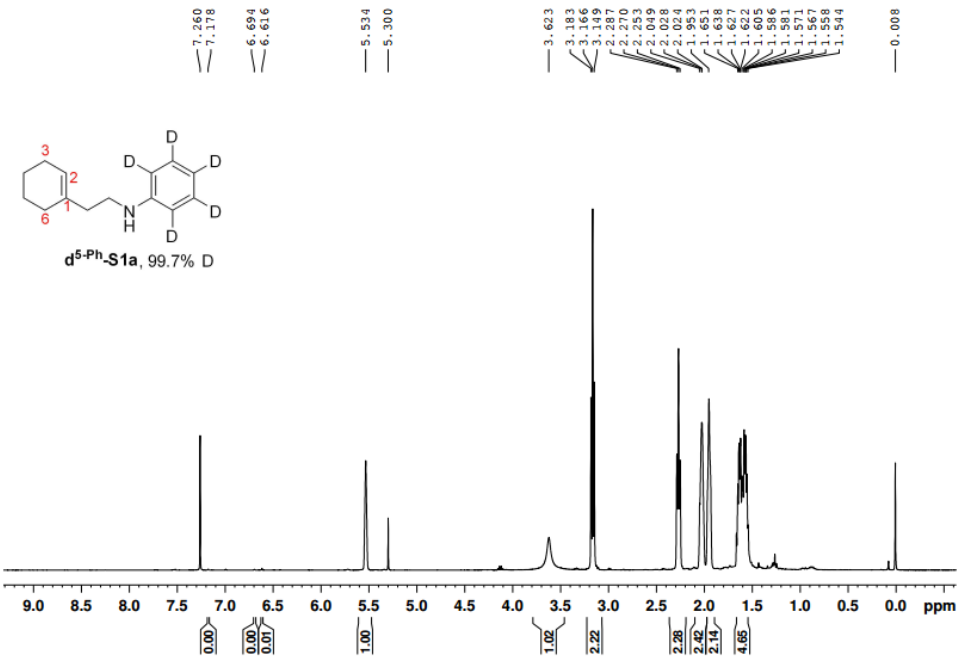


Figure S6.3 ^{1}H NMR spectrum of the substrates **$d^{5\text{-Ph}}$-S1a**

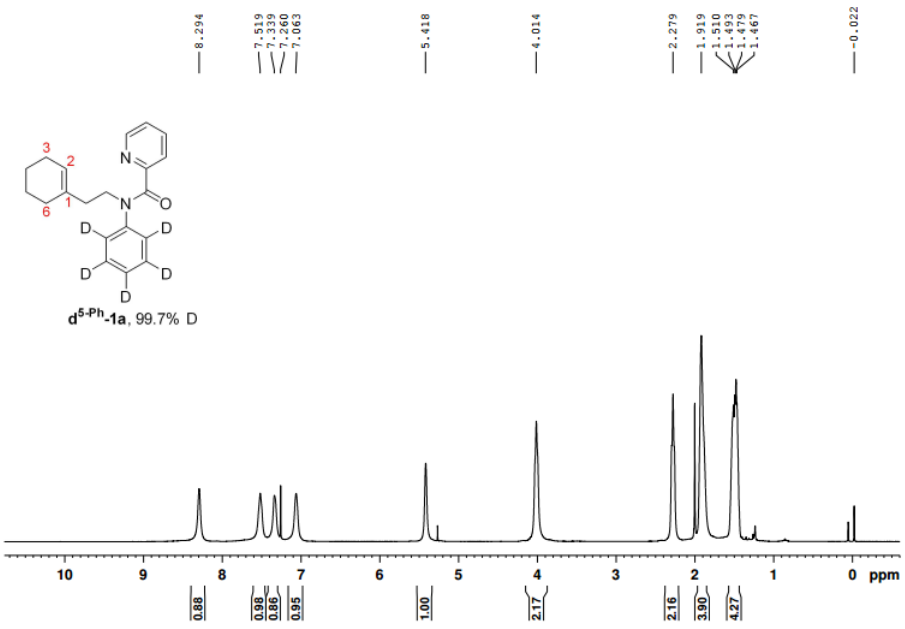


Figure S6.4 ^{1}H NMR spectrum of the substrates **$d^{5\text{-Ph}}$-S1a**

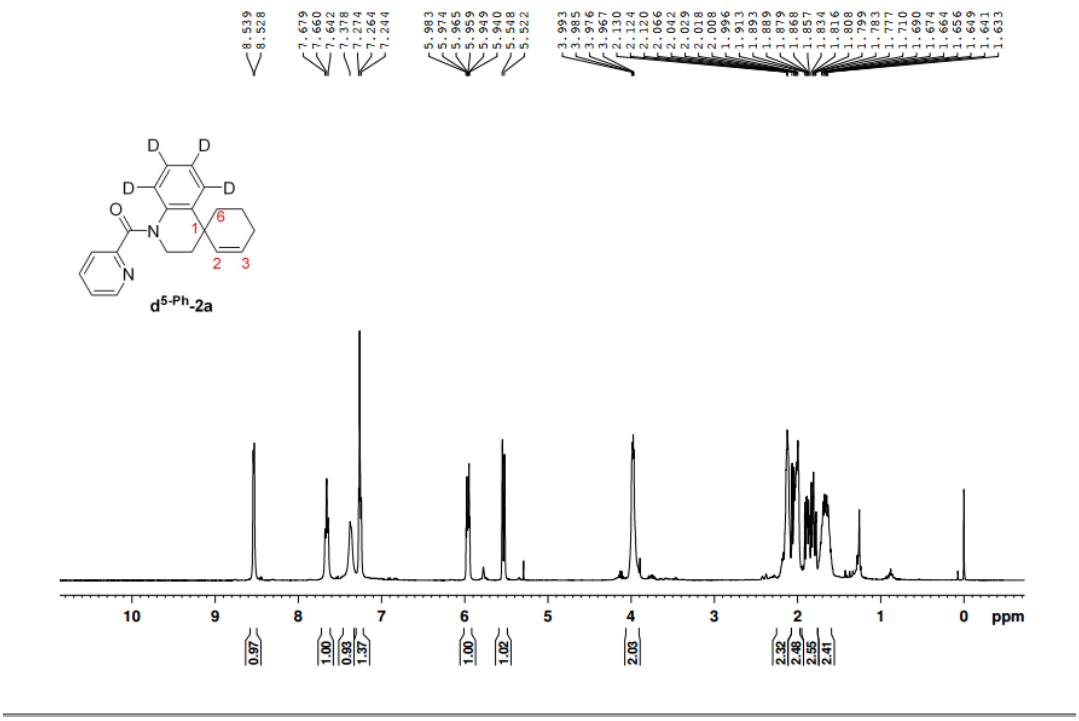
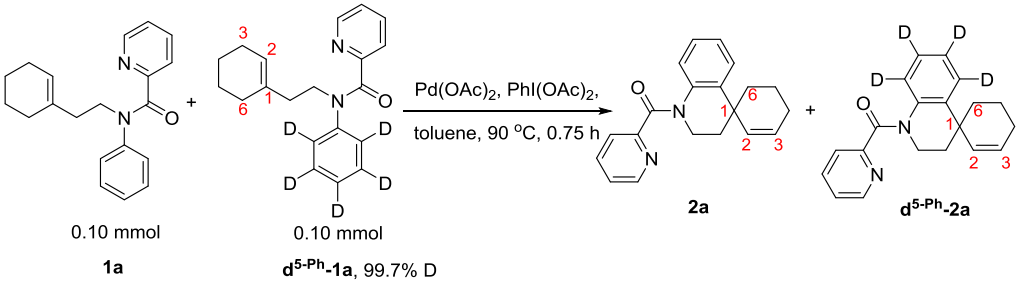


Figure S6.5 ^{1}H NMR spectrum of the substrates **d$^{5\text{-Ph}}$-2a**

6.2.4 To a solution of **d$^{5\text{-Ph}}$-1a** (43.0 mg, 0.15 mmol, 1.0 equiv) and $Pd(OAc)_2$ (0.015 mmol, 0.10 equiv) in anhydrous toluene (2 mL) at r.t. was added $PhI(OAc)_2$ (0.37 mmol, 2.5 equiv), 2-chloroisonicotinonitrile (8.0 mg, 0.06 mmol, 0.4 equiv) in a 15 mL flame-dried sealed tube (purged with N_2, sealed with PTFE cap). The mixture was heated at 110 °C for 2 hours. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by silica gel flash chromatography (petroleum ether / EtOAc) to give the product **d$^{5\text{-Ph}}$-2a** (23.0 mg, 53%).

6.2.5 Kinetic isotope effect studies



To a solution of **d$^{5\text{-Ph}}$-1a** (31.1 mg, 0.1 mmol, 1.0 equiv), **1a** (30.6 mg, 0.1 mmol, 1.0 equiv) and $Pd(OAc)_2$ (0.02 mmol, 0.10 equiv) in anhydrous toluene (3 mL) at r.t. was added $PhI(OAc)_2$ (0.50 mmol, 2.5 equiv), 2-chloroisonicotinonitrile (11.0 mg, 0.08 mmol, 0.4 equiv) in a 15 mL flame-dried sealed tube (purged with N_2, sealed with PTFE cap). The mixture was heated at 90 °C for 0.75 hour. The reaction mixture was cooled to room temperature,

and concentrated in vacuo. The resulting residue was purified by silica gel flash chromatography (petroleum ether / EtOAc) to give the product **$d^{5\text{-Ph}}$-2a and 2a** (13.0 mg, 34%). The KIE value was calculated as k_H/k_D = 3.39.

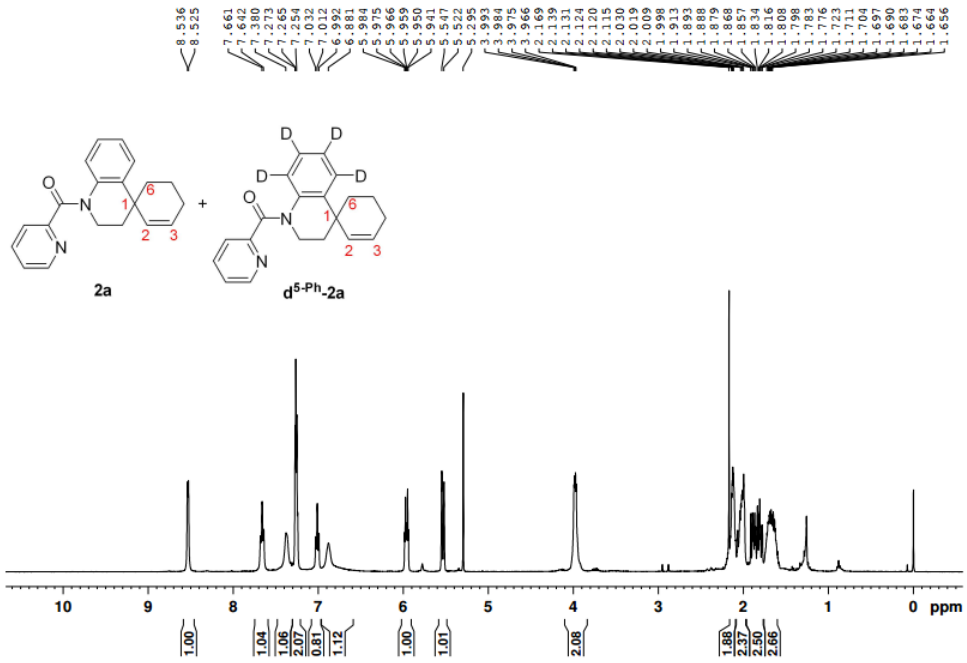
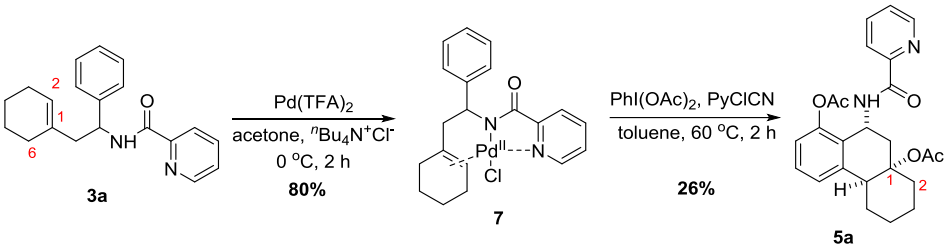


Figure S6.6 ^{1}H NMR spectrum of the substrates **2a** and **$d^{5\text{-Ph}}$-2a**

6.3 Deuterium Labeling Experiments for sp^3 C-H acetoxylation 2:



6.3.1 Procedure for Preparation of palladium Complexe **7**[6].

To a solution of N-(2-(cyclohex-1-en-1-yl)ethyl)-N,4-dimethylbenzenesulfonamide **3a** (45.0 mg, 0.15 mmol) in 4 mL of dried acetone was added palladium trifluoroacetate (46.0 mg, 0.15 mmol) and stirred at 0°C for 2 hours. A solution of tetra-*n*-butylammonium chloride (46.0 mg, 0.16 mmol) in 1 mL of dried acetone was added. The mixture was then stirred for 2 hours. It was then filtered through Celite to remove any metallic palladium, concentrated under reduced pressure to get the crude product. The residue was purified by flash chromatography on silica gel using hexanes/EtOAc 2:1 as eluent to afford the desired product **7** as yellow solid (**49.0 mg, 80%**). R_f = 0.15 (silica, hexanes: EtOAc, 1:1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.21 (dd, *J* = 5.5, 1.5 Hz, 1H), 8.07 (td, *J* = 7.6,

1.6 Hz, 1H), 7.98 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.56 (ddd, *J* = 7.4, 5.5, 1.7 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.22 (t, *J* = 7.1 Hz, 1H), 6.12 (d, *J* = 5.4 Hz, 1H), 5.28 (d, *J* = 8.0 Hz, 1H), 3.15 (dd, *J* = 16.8, 8.0 Hz, 1H), 2.87 (dd, *J* = 17.5, 10.0 Hz, 3H), 2.70 (dd, *J* = 16.7, 8.6 Hz, 1H), 2.31 – 2.04 (m, 3H), 2.00 – 1.76 (m, 2H), 1.58 – 1.44 (m, 1H), 1.39 – 1.22 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.0, 155.8, 148.4, 141.6, 140.8, 139.7, 129.0, 126.9, 125.9, 125.2, 99.7, 58.1, 45.9, 35.1, 26.6, 21.1, 21.0. **HRMS** (ESI): calcd for $C_{20}H_{22}ClN_2OPd^+$ [M^+]: 447.0455, found 447.0455, 413.0695, 471.0280.

Procedure for 4a: To a solution of **complex 7** (20.0 mg, 0.045 mmol) in anhydrous toluene (0.5 mL) at r.t. was added $PhI(OAc)_2$ (36.0 mg, 2.5 equiv), 2-chloroisonicotinonitrile (2.5 mg, 0.02 mmol, 0.4 equiv) in a 15 mL sealed tube (purged with N_2, sealed with PTFE cap). The mixture was heated at 100 °C for 1 hours. The reaction mixture was cooled to room temperature, and concentrated in vacuo. The resulting residue was purified by silica gel flash chromatography to give the product **5a** (5.0 mg, 26%).

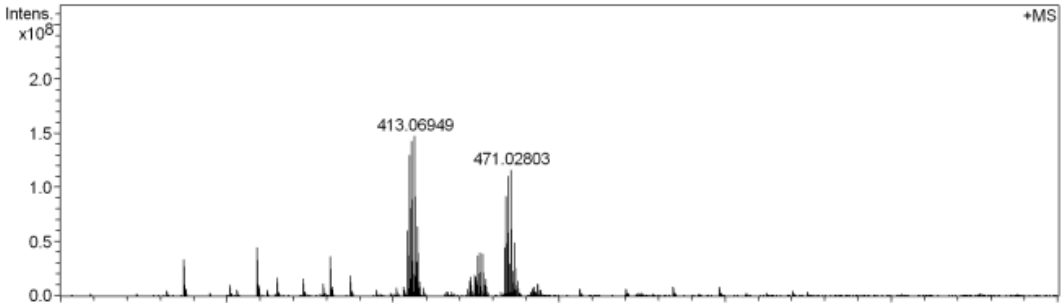
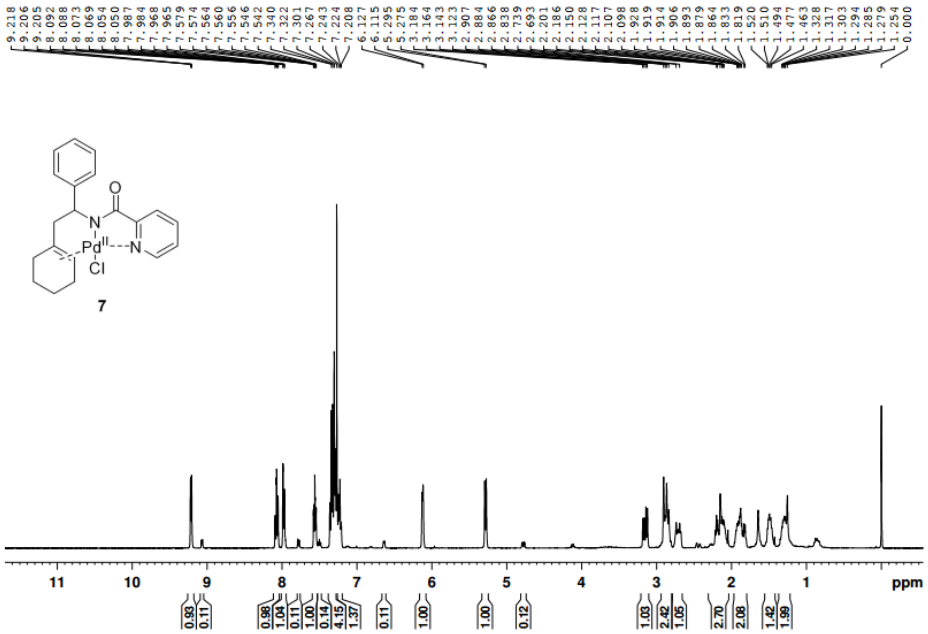


Figure S6.7 FTMS spectrum of the substrates **Pd complex 7**.



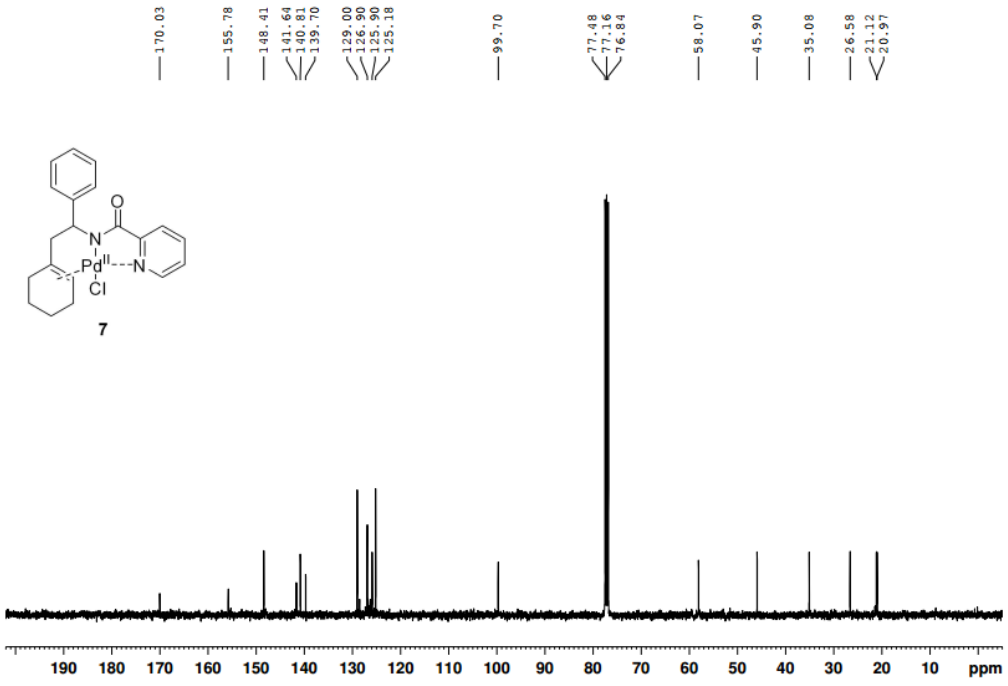
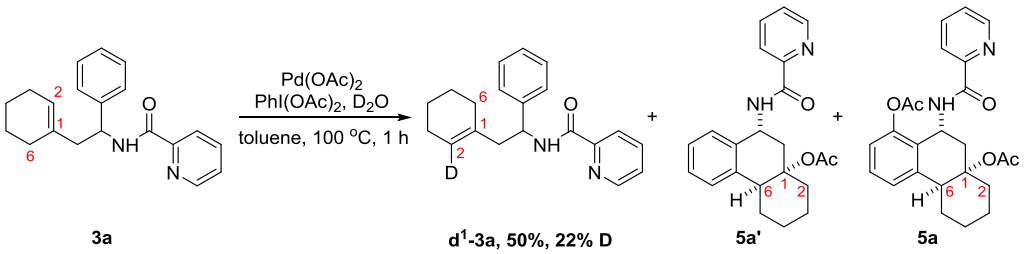


Figure S6.8 ^{1}H and ^{13}C NMR spectrum of the substrates **Pd complex 7**.

6.3.2 Procedure for Preparation

Significant deuteration occurred at the C2 position and acetoxylation product **5a** was formed when the reaction was carried out with D_2O under the standard conditions. This result suggests that acetoxylation firstly occurs through a sp^2 C–H activation process through the Pd intermediate at the 2-position of the cyclohexene.



To a flame-dried sealed tube was added $PhI(OAc)_2$ (120.0 mg, 0.375 mmol, 2.5 equiv), $Pd(OAc)_2$ (3.4 mg, 10 mol %), 2-chloroisonicotinonitrile (8.0 mg, 0.06 mmol, 0.4 equiv) and starting material **3a** (0.15 mmol, 1.0 equiv), then 2.0 mL dry toluene was added to dissolve the mixture under nitrogen. This was stirred at 110 ℃ for 2h, then cooled to room temperature. The reaction mixture next was purified by silica gel directly without remove solvent using hexanes/EtOAc 5:1 to 2:1 as eluent to afford the desired product **5a** as a pale yellow oil (3.0 mg, 9.5% brsm), R_f = 0.30 (silica, hexanes: EtOAc, 2:1); the single acetoxylation product **5a'** (5.0 mg, 9%); and start material **d^1-3a** (23.0 mg, 50%, 22% D).

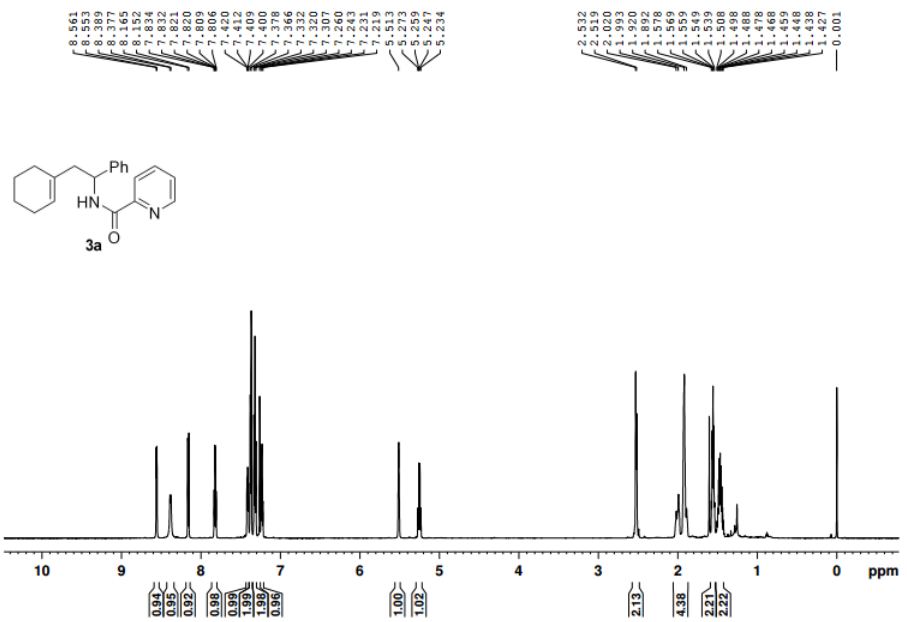


Figure S6.9 ^{1}H NMR spectrum of the substrates**3a**

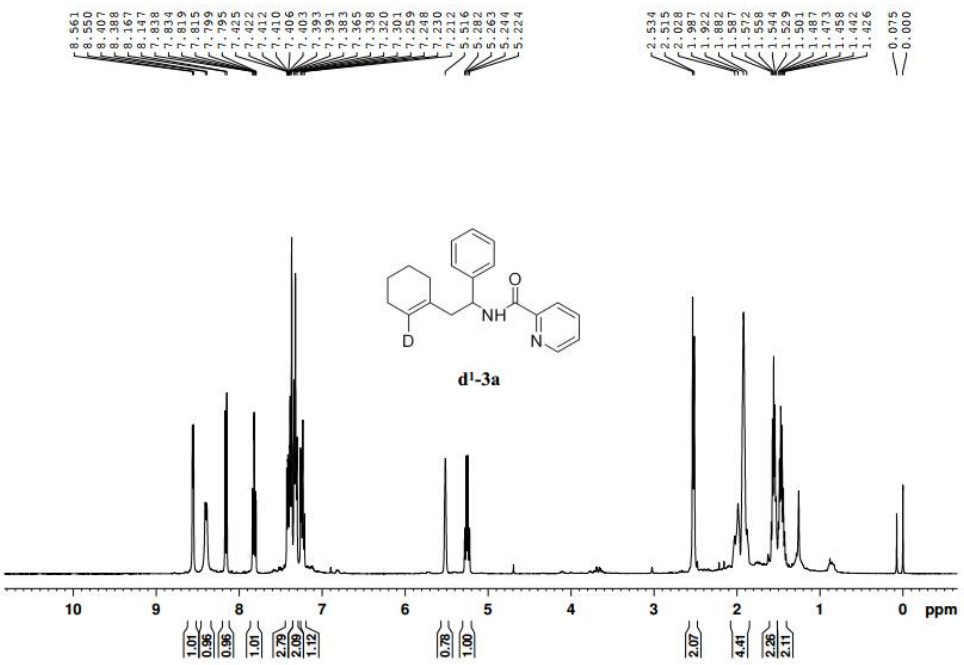


Figure S6.10 ^{1}H NMR spectrum of the substrates **d^{1}-3a**

7. X-ray Crystallographic Data of Compound 2n, 5c and 7:

The crystal **2n, 5c, 7** were prepared from the solution of **2n** in DCM/ hexane at ambient temperature.

7.1 X-ray crystallographic Data of Compound **2n**:

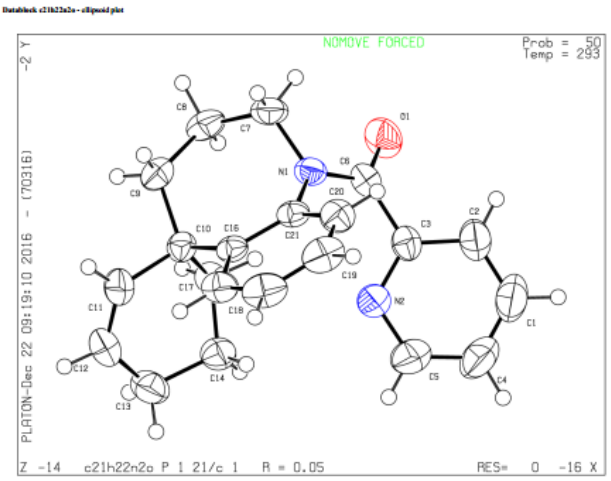


Figure 1. X-ray derived ORTEP representation of **2n**.

Crystal data and structure refinement for 2n (CCDC: 1528891)

Identification code	C21H22N2O
Empirical formula	C21H22N2O
Formula weight	318.40
Temperature/K	293(2)
Crystal system	monoclinic
Space group	P21/c
a/Å	16.8116(9)
b/Å	12.2054(7)
c/Å	8.3966(4)
α/°	90
β/°	95.080(5)
γ/°	90
Volume/Å3	1716.15(16)

Z	4
ρcalcg/cm3	1.232
μ/mm-1	0.076
F(000)	680.0
Crystal size/mm3	? ×? ×?
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	7.106 to 52.744
Index ranges	-21 ≤ h ≤ 12, -7 ≤ k ≤ 15, -9 ≤ l ≤ 10
Reflections collected	7488
Independent reflections	3505 [Rint = 0.0224, Rsigma = 0.0414]
Data/restraints/parameters	3505/0/217
Goodness-of-fit on F2	1.090
Final R indexes [I>=2σ (I)]	R1 = 0.0541, wR2 = 0.1231
Final R indexes [all data]	R1 = 0.0823, wR2 = 0.1401
Largest diff. peak/hole / e Å-3	0.17/-0.21

7.2 X-ray crystallographic Data of Compound **5c**:

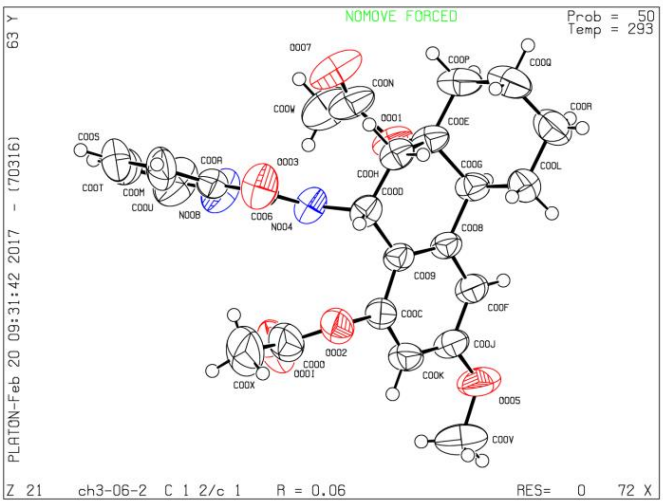


Figure 2. X-ray derived ORTEP representation of **5c**.

Crystal data and structure refinement for 5c (CCDC: 1534514)

Empirical formula	$C_{25}H_{28}N_2O_6$
Formula weight	452.49
Temperature/K	293(2)
Crystal system	monoclinic
Space group	C2/c
a/Å	25.1784(14)
b/Å	10.2826(5)
c/Å	19.7614(11)
α/°	90
β/°	110.072(6)
γ/°	90
Volume/Å^3	4805.5(5)
Z	8
ρ_{calc}g/cm^3	1.251
μ/mm^{-1}	0.090
F(000)	1920.0
Crystal size/mm^3	0.48 × 0.35 × 0.27
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.782 to 52.738
Index ranges	-31 ≤ h ≤ 17, -11 ≤ k ≤ 12, -24 ≤ l ≤ 24
Reflections collected	9927
Independent reflections	4893 [R_{int} = 0.0188, R_{sigma} = 0.0336]
Data/restraints/parameters	4893/0/302
Goodness-of-fit on F^2	1.089
Final R indexes [I>=2σ (I)]	R_1 = 0.0623, wR_2 = 0.1752
Final R indexes [all data]	R_1 = 0.0964, wR_2 = 0.1988
Largest diff. peak/hole / e Å^{-3}	0.16/-0.16

7.3 X-ray crystallographic Data of Compound **7**:

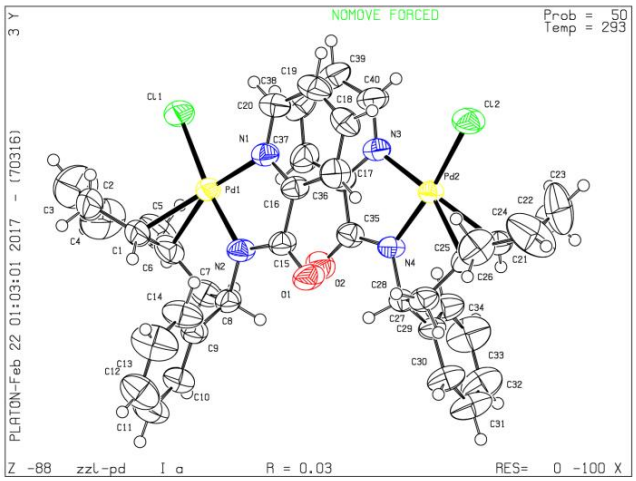


Figure 2. X-ray derived ORTEP representation of **7**.

Crystal data and structure refinement for 7 (CCDC: 1534515)

Empirical formula	$C_{20}H_{19}ClN_2OPd$
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Crystal system	monoclinic
Space group	Ia
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b/Å	9.0821(2)
c/Å	26.7621(6)
α/°	90
β/°	107.248(2)
γ/°	90
Volume/Å^3	3802.94(14)
Z	8
ρ_{calc}g/cm^3	1.555
μ/mm^{-1}	1.126
F(000)	1792.0
Crystal size/mm^3	? × ? × ?
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/ °	6.698 to 52.718
Index ranges	-20 ≤ h ≤ 20, -11 ≤ k ≤ 11, -33 ≤ l ≤ 33
Reflections collected	28393
Independent reflections	7762 [R_{int} = 0.0291, R_{sigma} = 0.0284]
Data/restraints/parameters	7762/9/451
Goodness-of-fit on F^2	1.060
Final R indexes [I>=2σ (I)]	R_1 = 0.0323, wR_2 = 0.0864
Final R indexes [all data]	R_1 = 0.0391, wR_2 = 0.0919
Largest diff. peak/hole / e Å^{-3}	0.97/-0.38
Flack parameter	-0.048(10)

8. References:

[1] a) Zhang, H.; Cai, Q.; Ma, D.-W. *J. Org. Chem*. **2005**, *70*, 5164; b) Pan, X.-H.; Cai, Q.; Ma, D.-W.Cai, Q.; Ma, D.-W. *Org. Lett.* **2004**, *6*, 1809.

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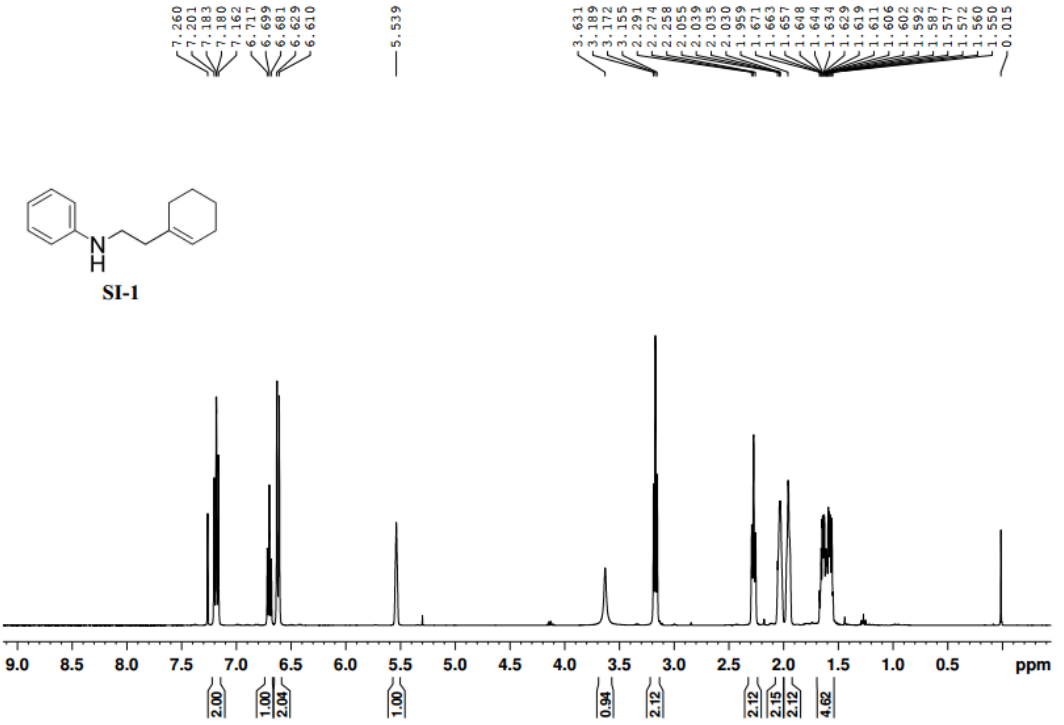
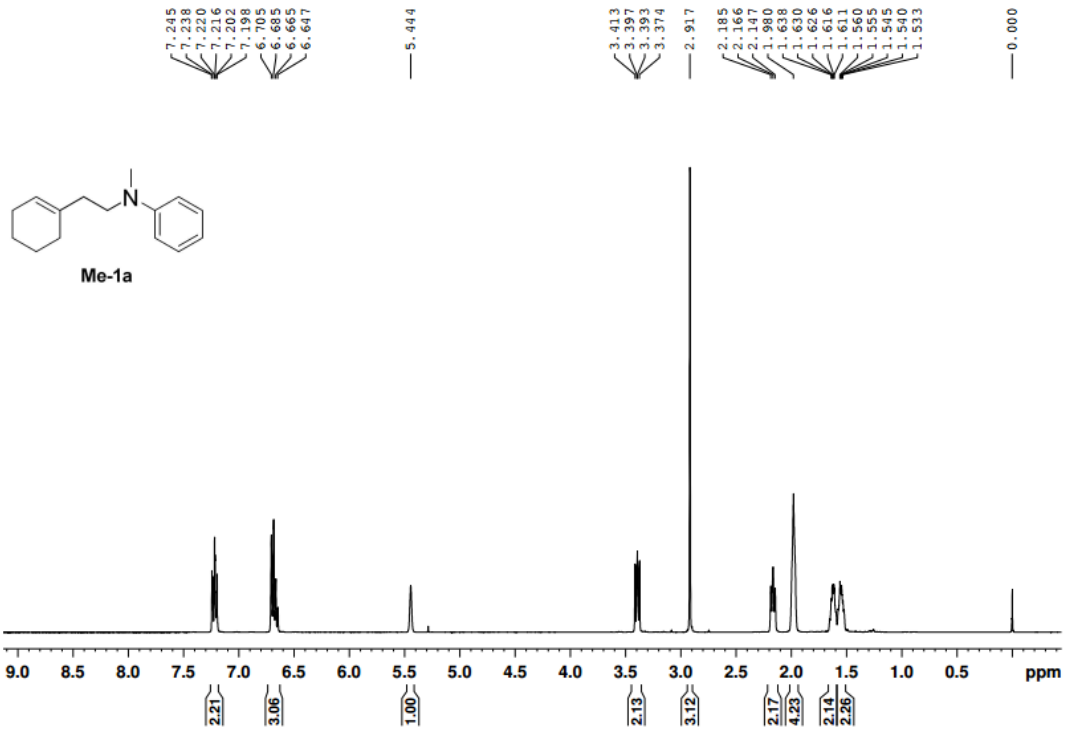
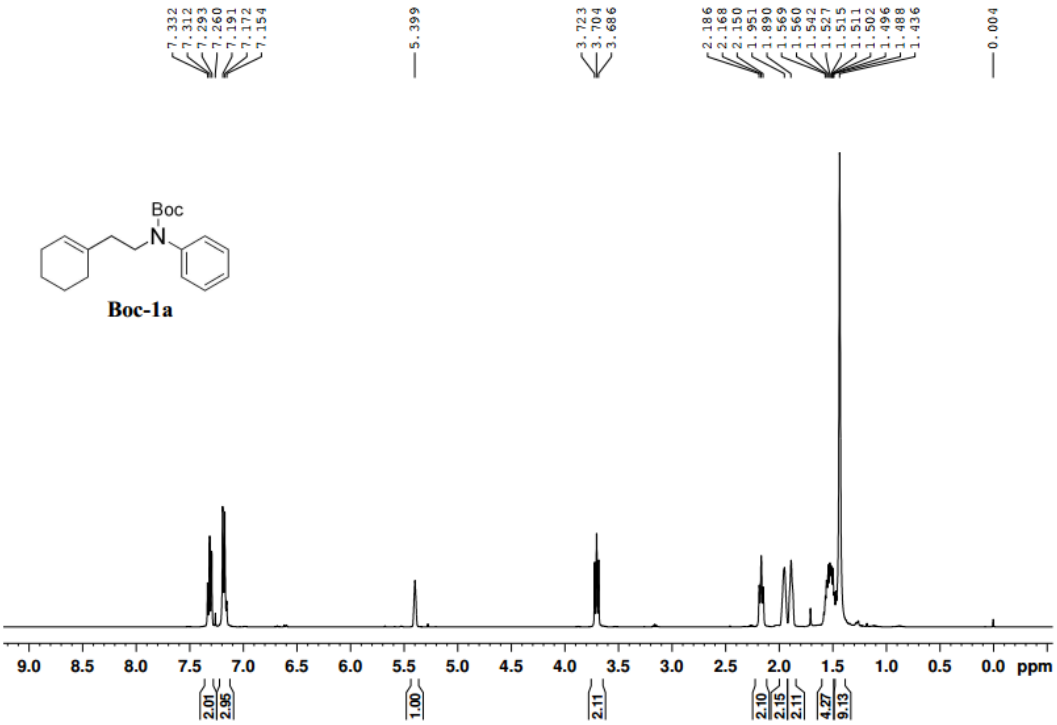
9. Experimental Spectra:

9.1 Experimental Spectra of sp^2 C–H Acetoxylation



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2.150
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1.527
1.515
1.511
1.502
1.496
1.488
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Boc
N
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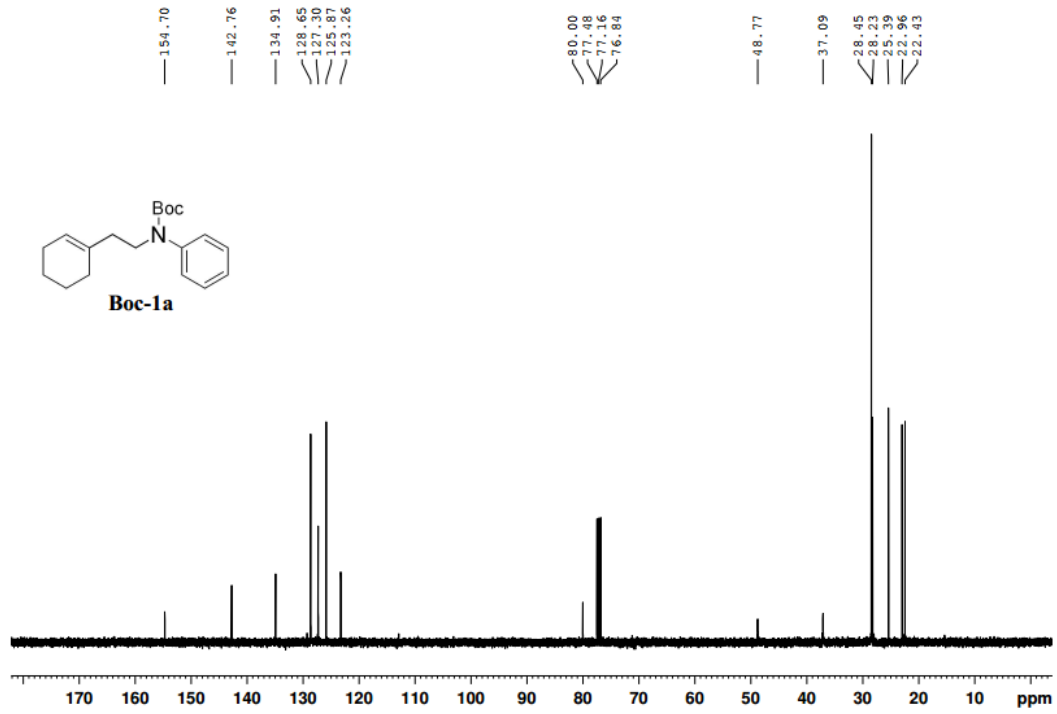
2.15
2.11
4.27
9.13

Boc-1a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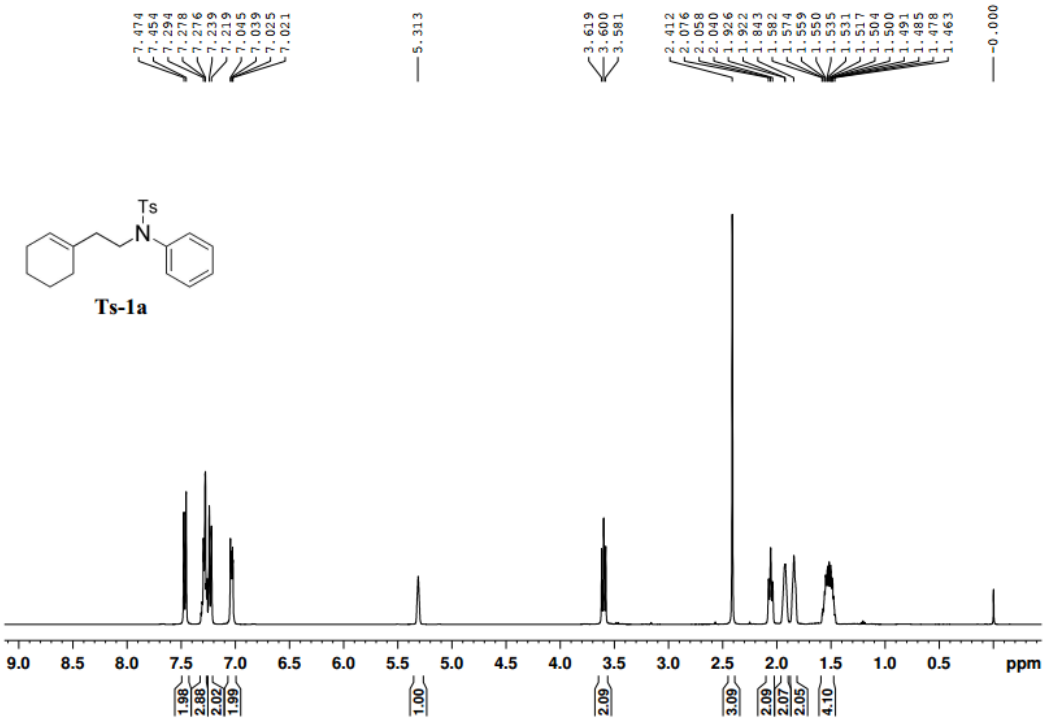
Boc-1a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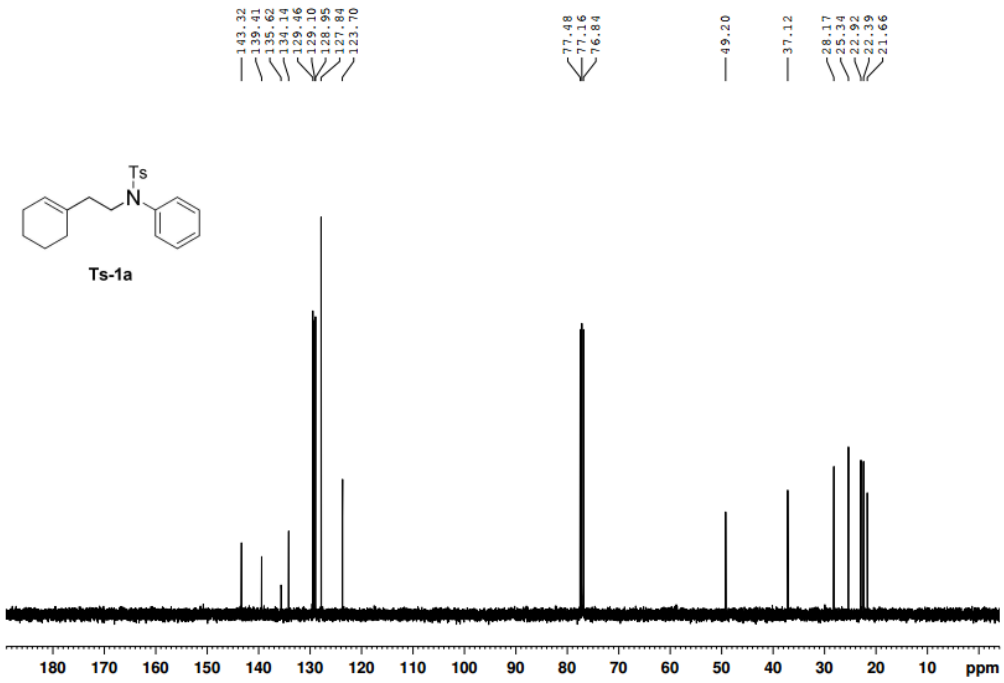
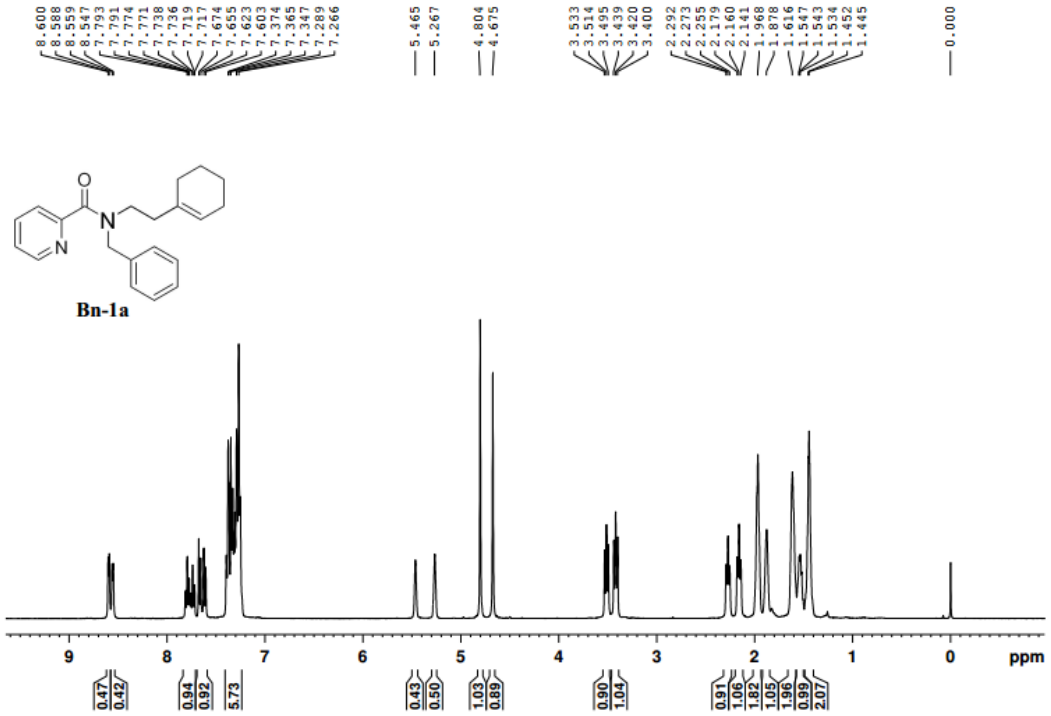
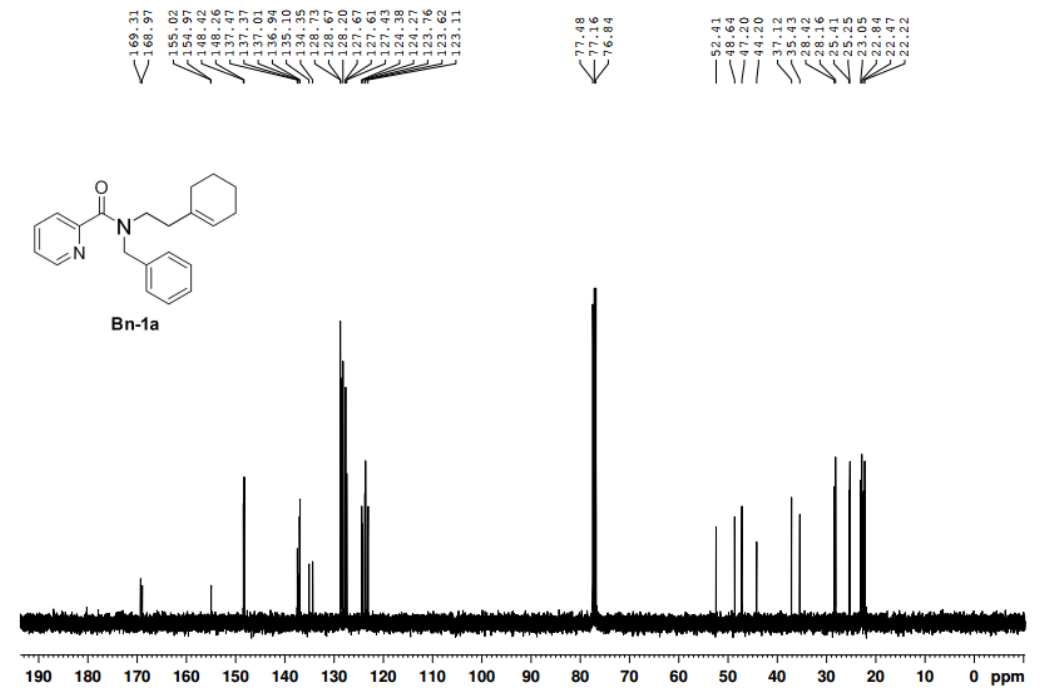
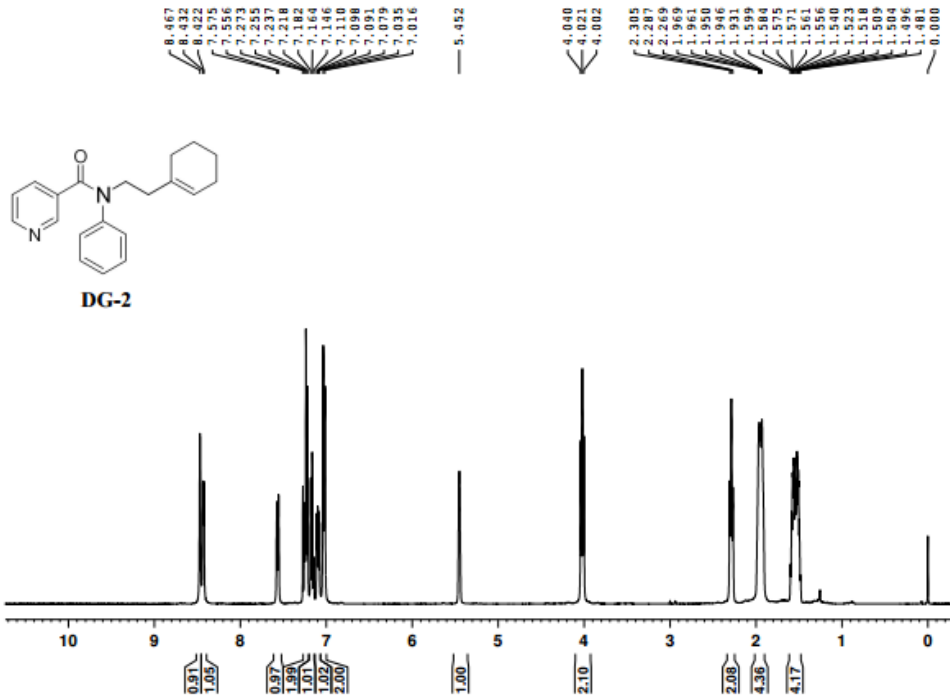
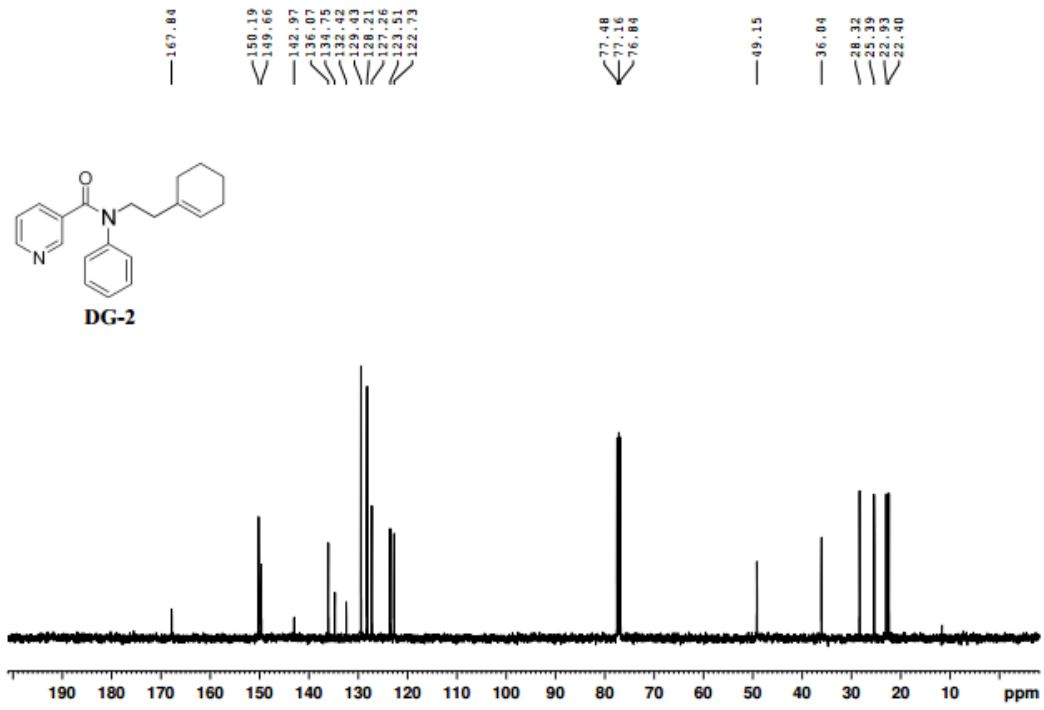
1.531
1.517
1.504
1.500
1.491
1.485
1.478
1.463
0.000
Ts
N
Ts-1a
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.98
2.88
2.02
1.99
1.00
2.09
3.09
2.09
2.07
2.05
4.10


143.32
139.41
135.62
134.14
129.46
129.10
128.95
127.84
123.70
77.48
77.16
76.84
49.20
37.12
28.17
25.34
22.92
22.39
21.66
Ts
N
Ts-1a
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

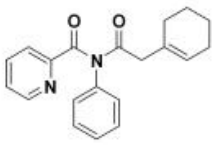

8.600
8.588
8.559
8.547
7.793
7.791
7.774
7.771
7.738
7.736
7.719
7.717
7.674
7.655
7.623
7.603
7.374
7.365
7.347
7.289
7.266
5.465
5.267
4.804
4.675
3.533
3.514
3.495
3.439
3.420
3.400
2.292
2.273
2.255
2.179
2.160
2.141
1.968
1.878
1.616
1.547
1.543
1.534
1.452
1.445
0.000
O
N
N
Bn-1a
9
8
7
6
5
4
3
2
1
0
ppm
0.47
0.42
0.94
0.92
5.73
0.43
0.50
1.03
0.89
0.90
1.04
0.91
1.06
1.82
1.05
1.96
0.99
2.07


169.31
168.97
155.02
154.97
148.42
148.26
137.47
137.37
137.01
136.94
135.10
134.35
128.73
128.67
128.20
127.67
127.61
127.43
124.38
124.27
123.76
123.62
123.11
77.48
77.16
76.84
52.41
48.64
47.20
44.20
37.12
35.43
28.42
28.16
25.41
25.25
23.05
22.84
22.47
22.22
O
N
N
Bn-1a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

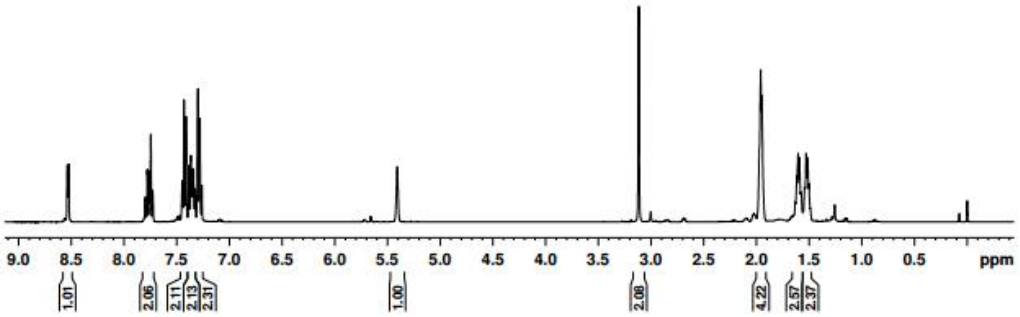

8.467
8.432
8.422
7.575
7.556
7.273
7.255
7.237
7.218
7.182
7.164
7.146
7.110
7.098
7.091
7.079
7.035
7.016
5.452
4.040
4.021
4.002
2.305
2.287
2.269
1.969
1.961
1.950
1.946
1.931
1.599
1.584
1.575
1.571
1.561
1.556
1.540
1.523
1.518
1.509
1.504
1.496
1.481
0.000
DG-2
10
9
8
7
6
5
4
3
2
1
0
ppm
0.91
1.05
0.97
1.99
1.01
1.02
2.00
1.00
2.10
2.08
4.36
4.17

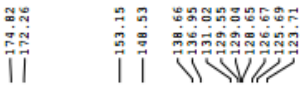

167.84
150.19
149.66
142.97
136.07
134.75
132.42
129.43
128.21
127.26
123.51
122.73
77.48
77.16
76.84
49.15
36.04
28.32
25.39
22.93
22.40
DG-2
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

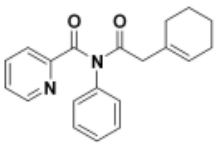

7.797
7.794
7.777
7.774
7.759
7.755
7.744
7.725
7.446
7.429
7.409
7.381
7.363
7.355
7.352
7.343
7.339
7.334
7.325
7.322
7.299
7.296
7.278
7.259
5.408
3.116
1.959
1.948
1.617
1.604
1.594
1.590
1.578
1.541
1.529
1.525
1.515
1.502
0.000



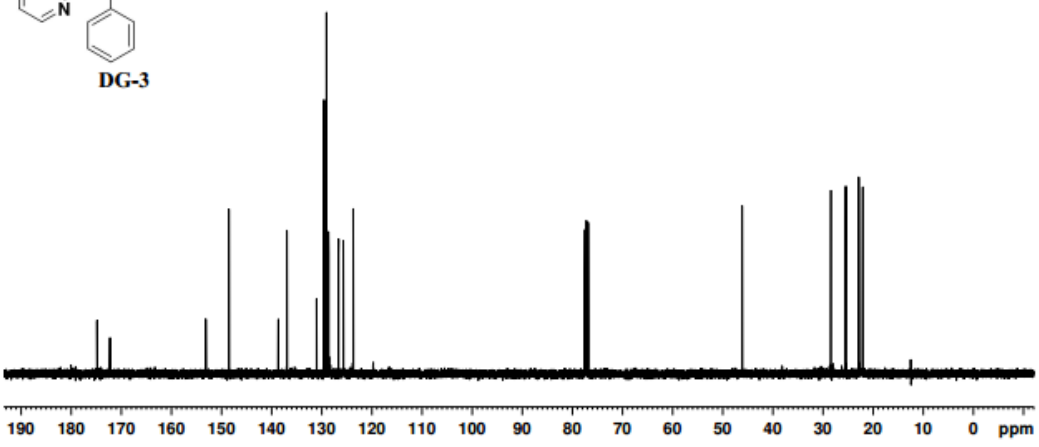
DG-3

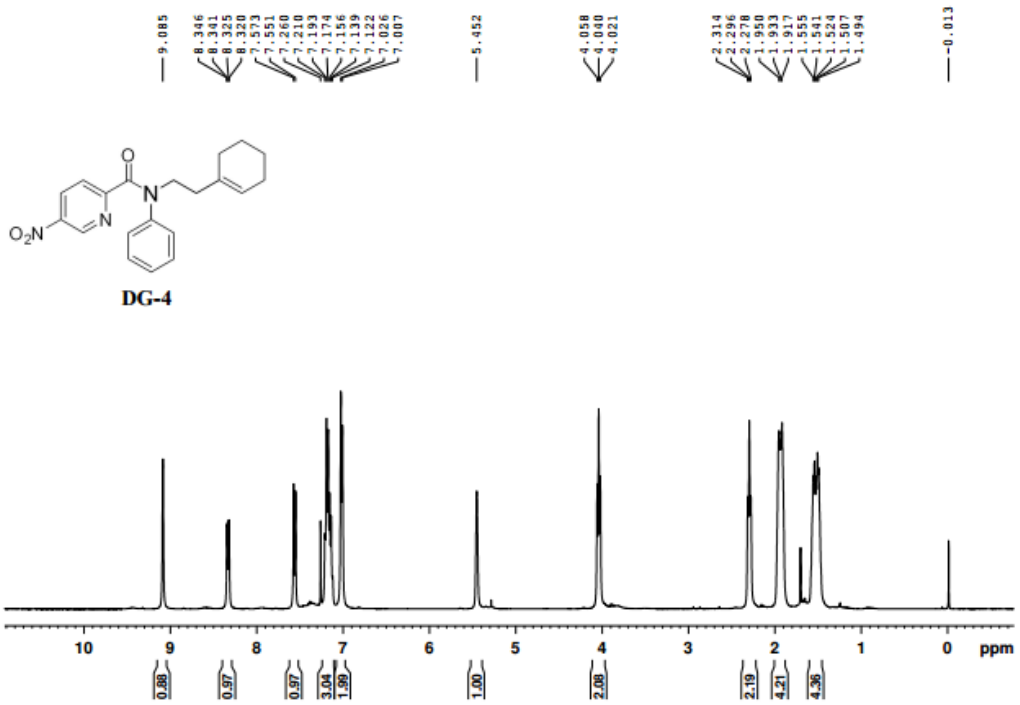

9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.01
2.06
2.11
2.13
2.37
1.00
2.08
4.22
2.57
2.37

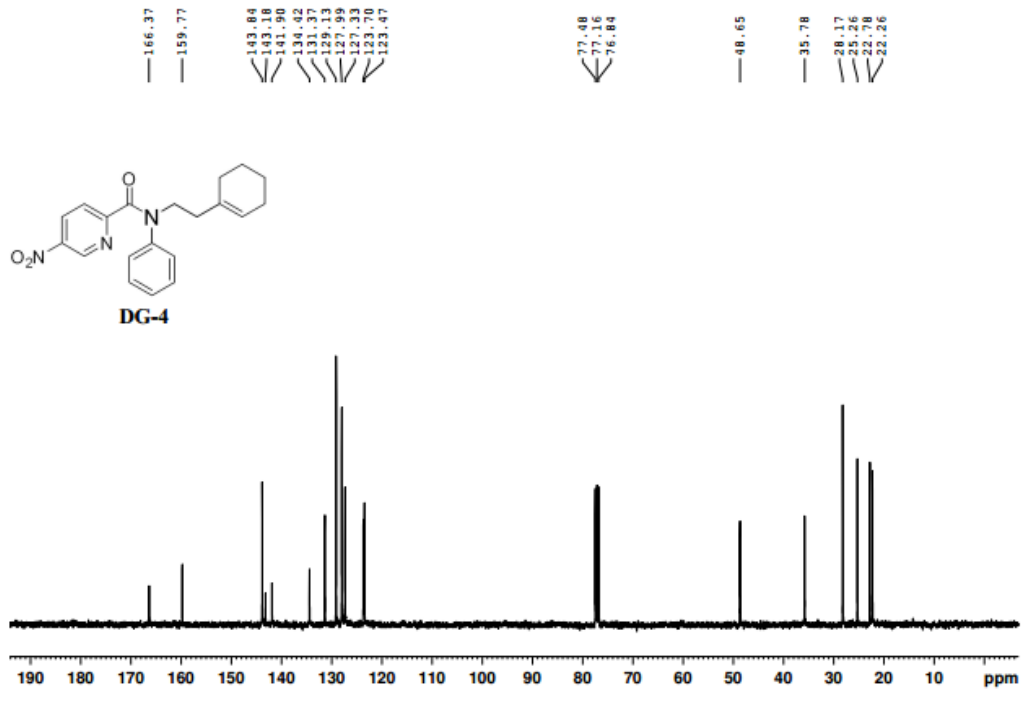

174.82
172.26
153.15
148.53
138.66
136.95
131.02
129.55
129.04
128.65
126.67
125.69
123.71
77.48
77.16
76.84
46.12
28.40
25.44
22.83
22.04

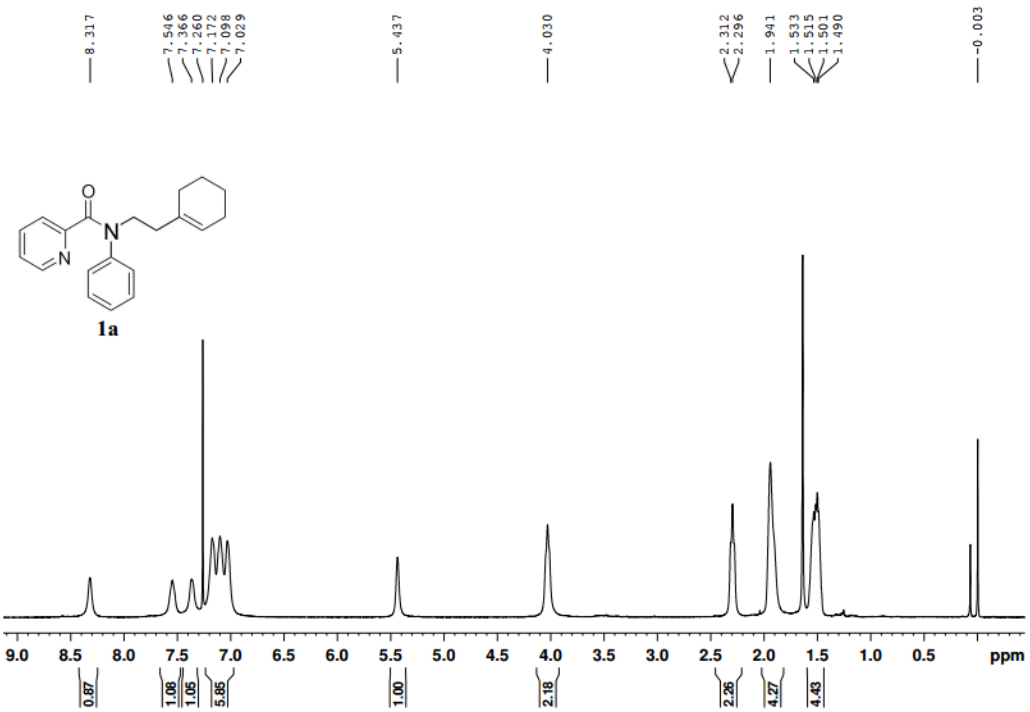


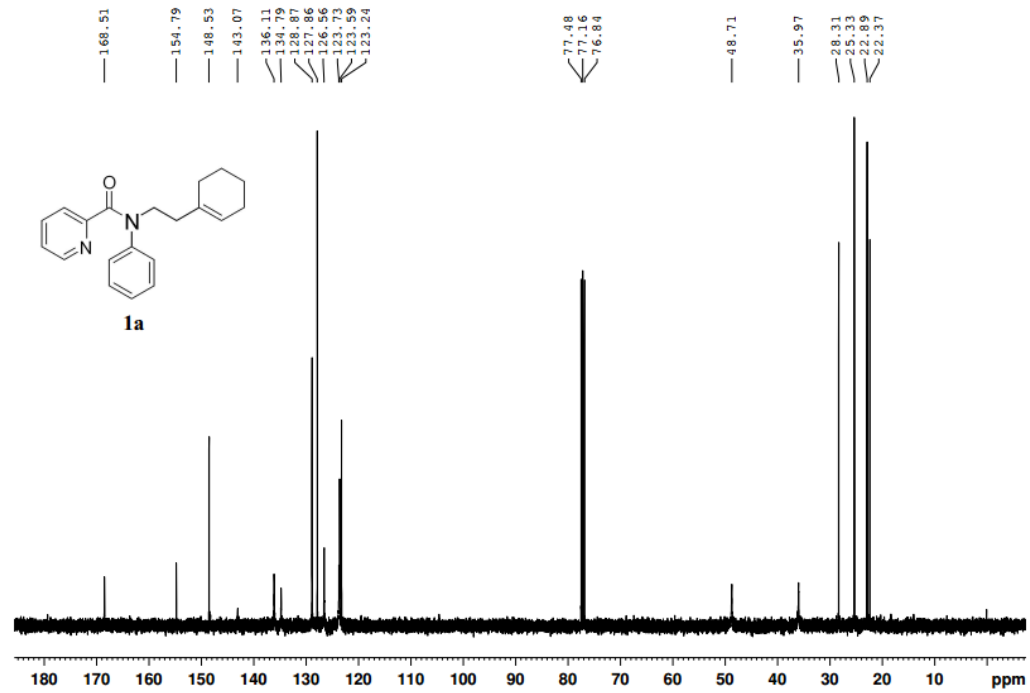
DG-3

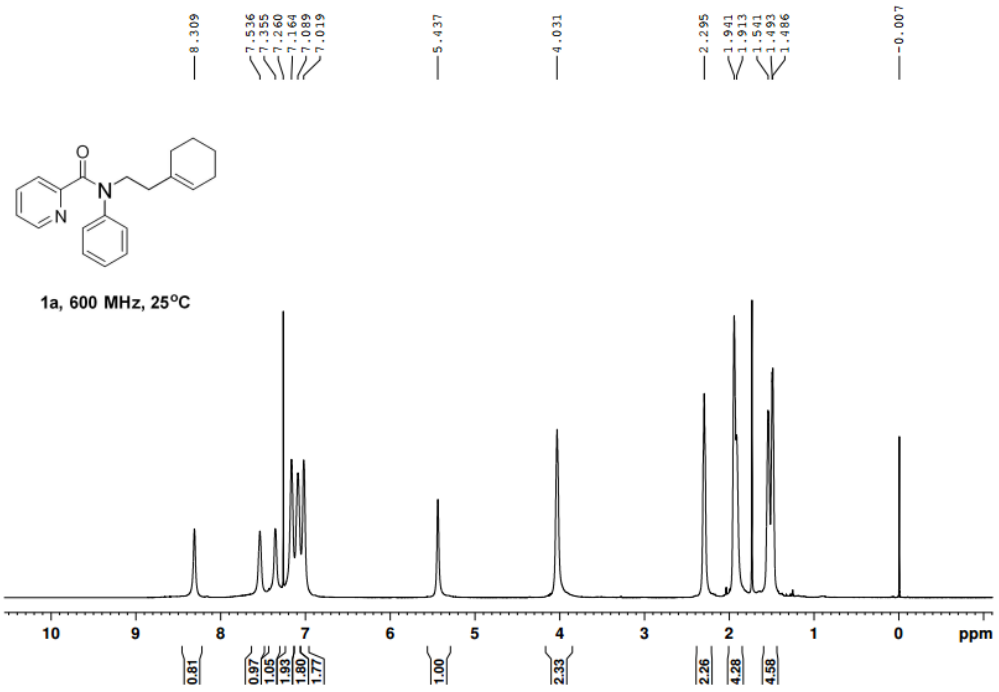

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

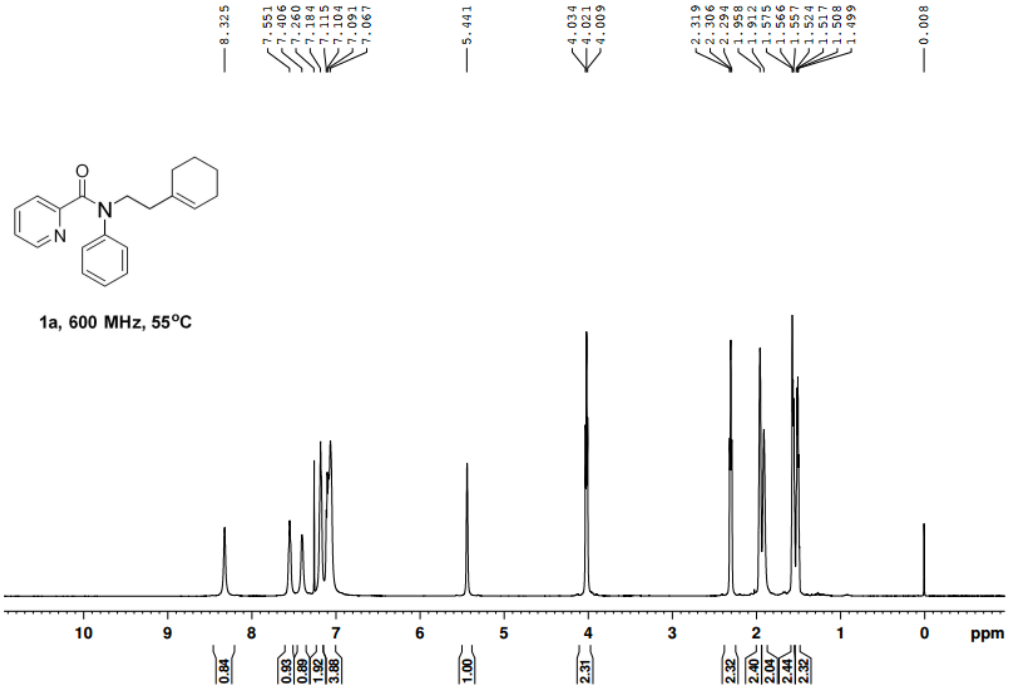

9.085
8.346
8.341
8.325
8.320
7.573
7.551
7.260
7.210
7.193
7.174
7.156
7.139
7.122
7.026
7.007
5.452
4.058
4.040
4.021
2.314
2.296
2.278
1.950
1.933
1.917
1.555
1.541
1.524
1.507
1.494
0.013
O2N
N
O
N
DG-4
10
9
8
7
6
5
4
3
2
1
0
ppm
0.88
0.97
0.97
3.04
1.99
1.00
2.08
2.19
4.21
4.36

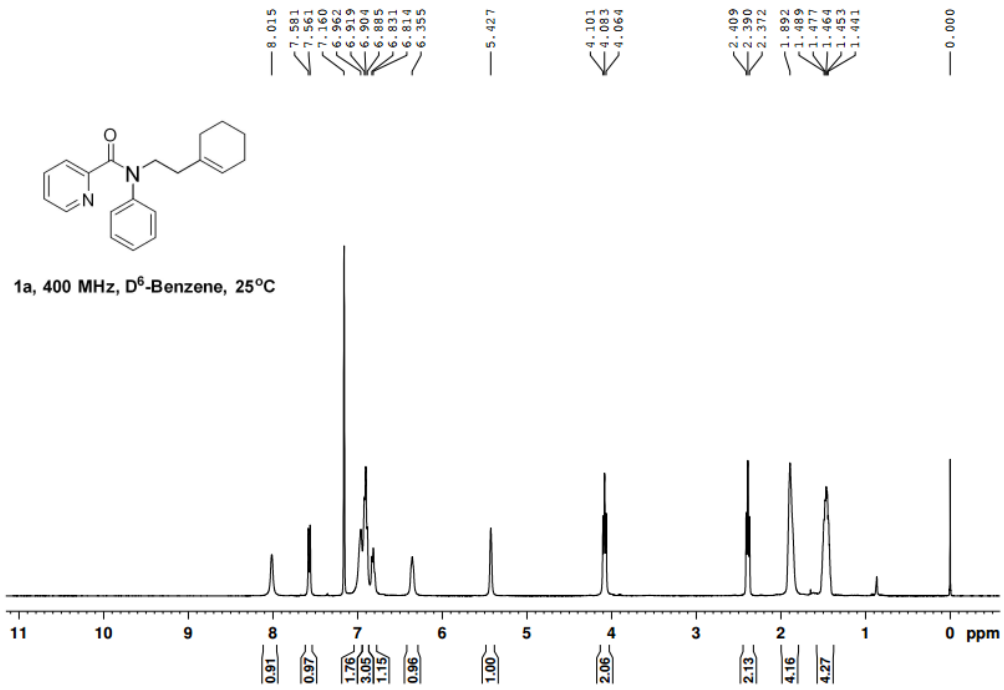

166.37
159.77
143.84
143.18
141.90
134.42
131.37
129.13
127.99
127.33
123.70
123.47
77.48
77.16
76.84
48.65
35.78
28.17
25.26
22.78
22.26
O2N
N
O
N
DG-4
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

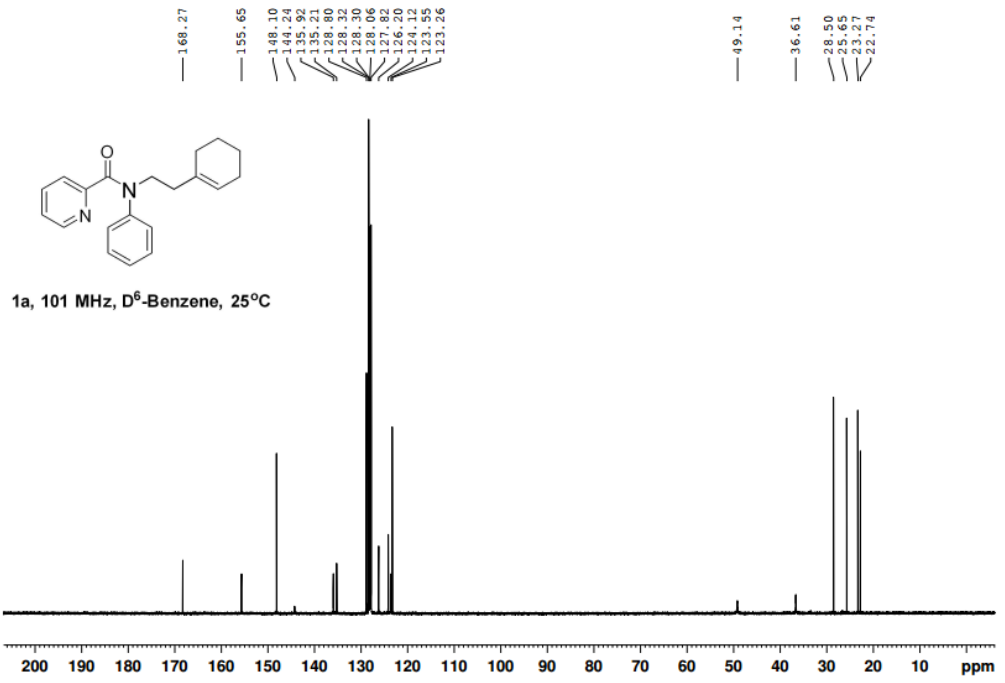

8.317
7.546
7.366
7.260
7.172
7.098
7.029
5.437
4.030
2.312
2.296
1.941
1.533
1.515
1.501
1.490
-0.003
1a
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.87
1.08
1.05
5.85
1.00
2.18
2.26
4.27
4.43

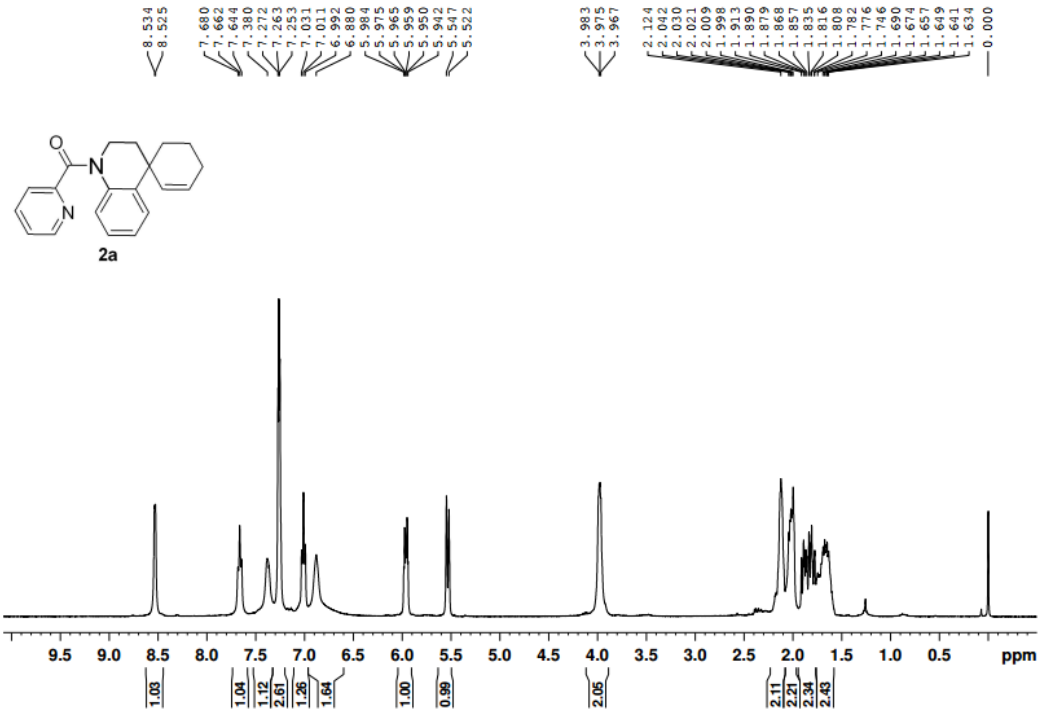

168.51
154.79
148.53
143.07
136.11
134.79
128.87
127.86
126.56
123.73
123.59
123.24
77.48
77.16
76.84
48.71
35.97
28.31
25.33
22.89
22.37
1a
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

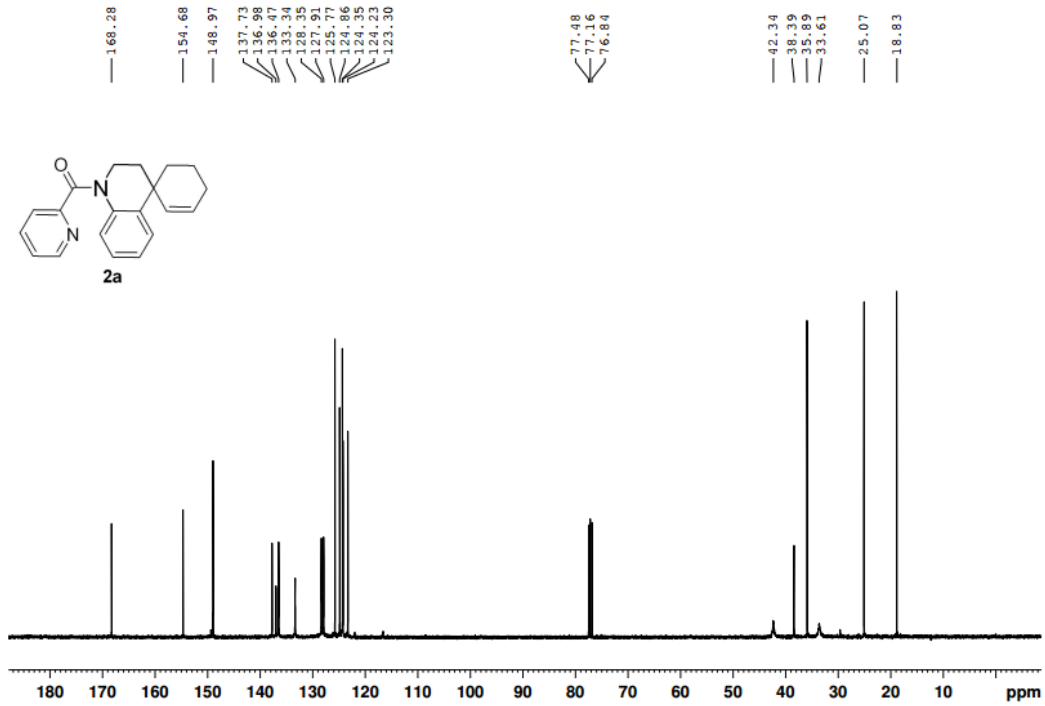

8.309
7.536
7.355
7.260
7.164
7.089
7.019
5.437
4.031
2.295
1.941
1.913
1.541
1.493
1.486
0.007
1a, 600 MHz, 25°C
10
9
8
7
6
5
4
3
2
1
0
ppm
0.81
0.97
1.05
1.93
1.80
1.77
1.00
2.33
2.26
4.28
4.58

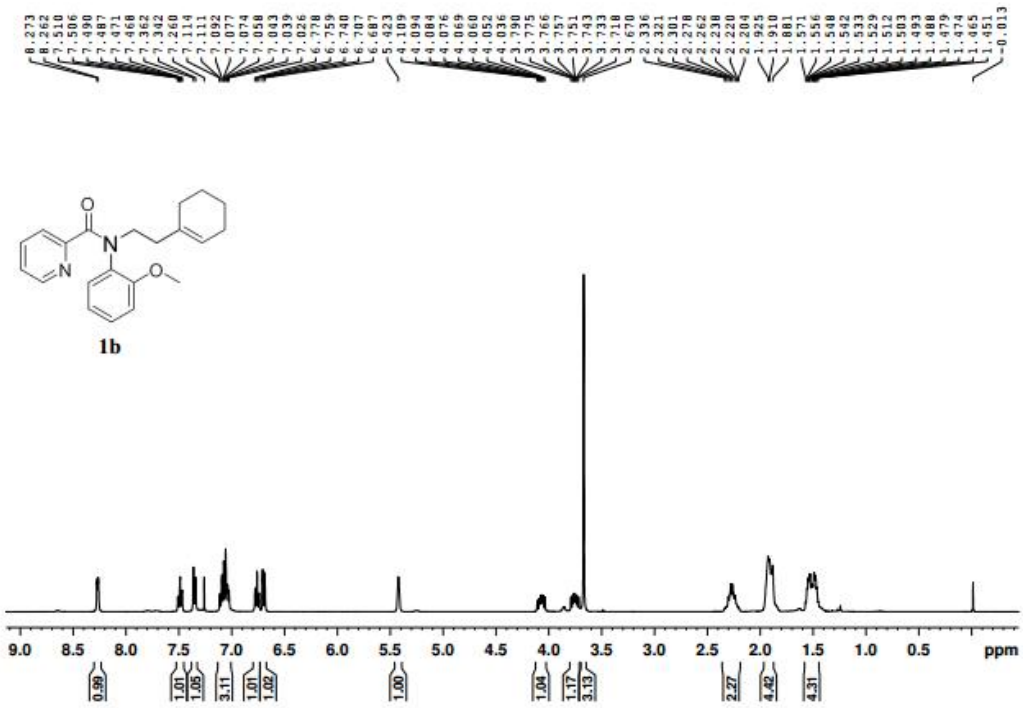

8.325
7.551
7.406
7.260
7.184
7.115
7.104
7.091
7.067
5.441
4.034
4.021
4.009
2.319
2.306
2.294
1.958
1.912
1.575
1.566
1.557
1.524
1.517
1.508
1.499
0.008
1a, 600 MHz, 55°C
10
9
8
7
6
5
4
3
2
1
0
ppm
0.84
0.93
0.89
1.92
3.88
1.00
2.31
2.32
2.40
2.04
2.44
2.32

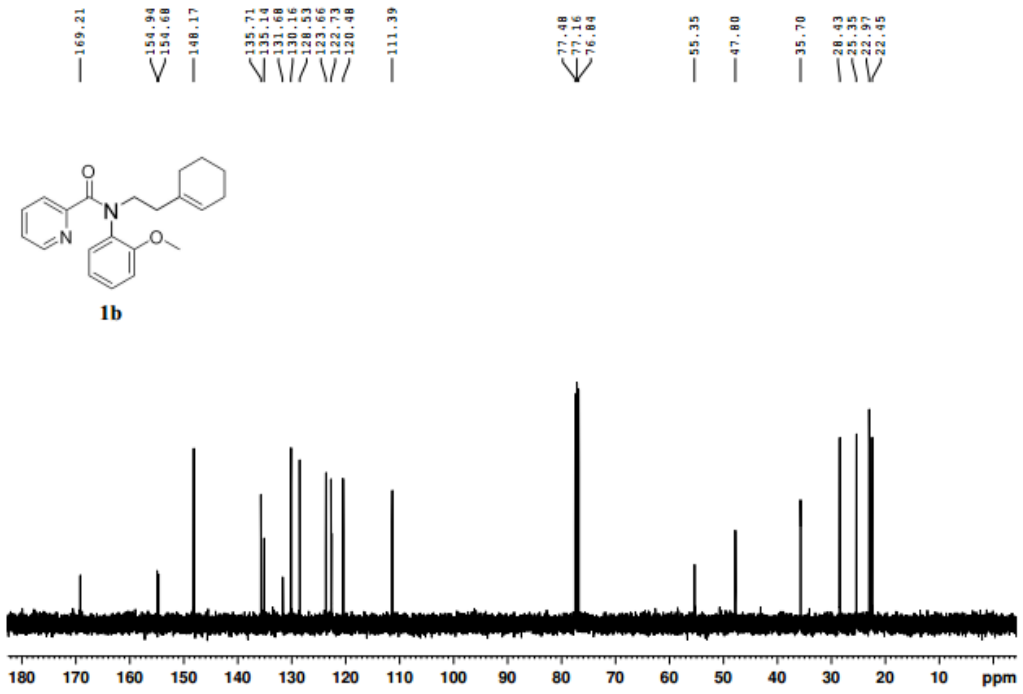

8.015
7.581
7.561
7.160
6.962
6.919
6.904
6.885
6.831
6.814
6.355
5.427
4.101
4.083
4.064
2.409
2.390
2.372
1.892
1.489
1.477
1.464
1.453
1.441
0.000
1a, 400 MHz, D6-Benzene, 25°C
11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.91 0.97 1.76 3.05 1.15 0.96 1.00 2.06 2.13 4.16 4.27

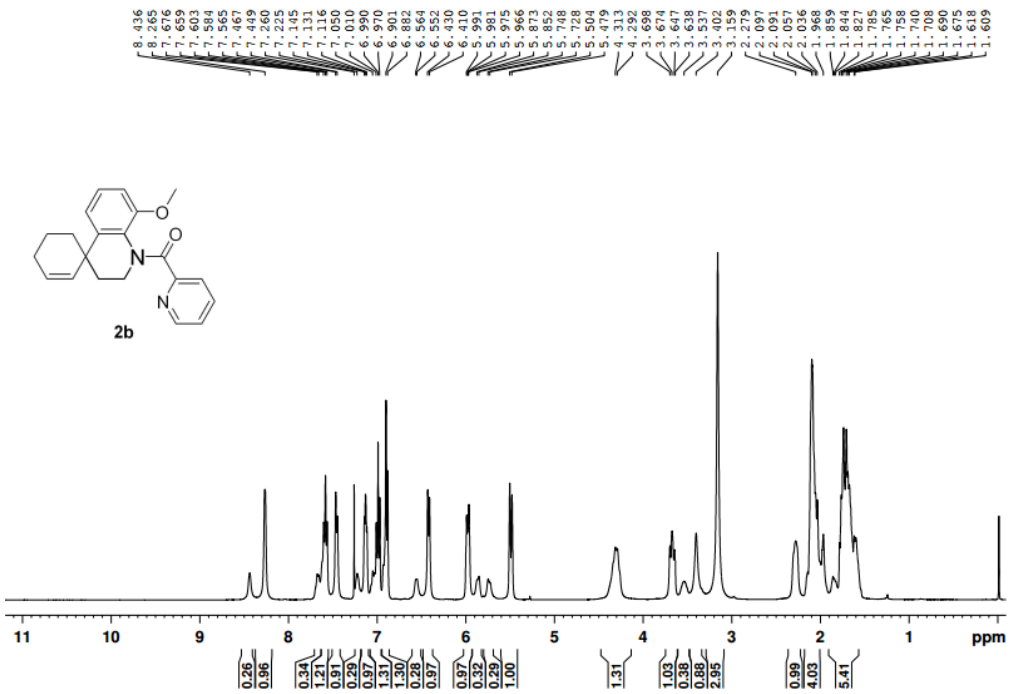

168.27
155.65
148.10
144.24
135.92
135.21
128.80
128.32
128.30
128.06
127.82
126.20
124.12
123.55
123.26
49.14
36.61
28.50
25.65
23.27
22.74
1a, 101 MHz, D6-Benzene, 25°C
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

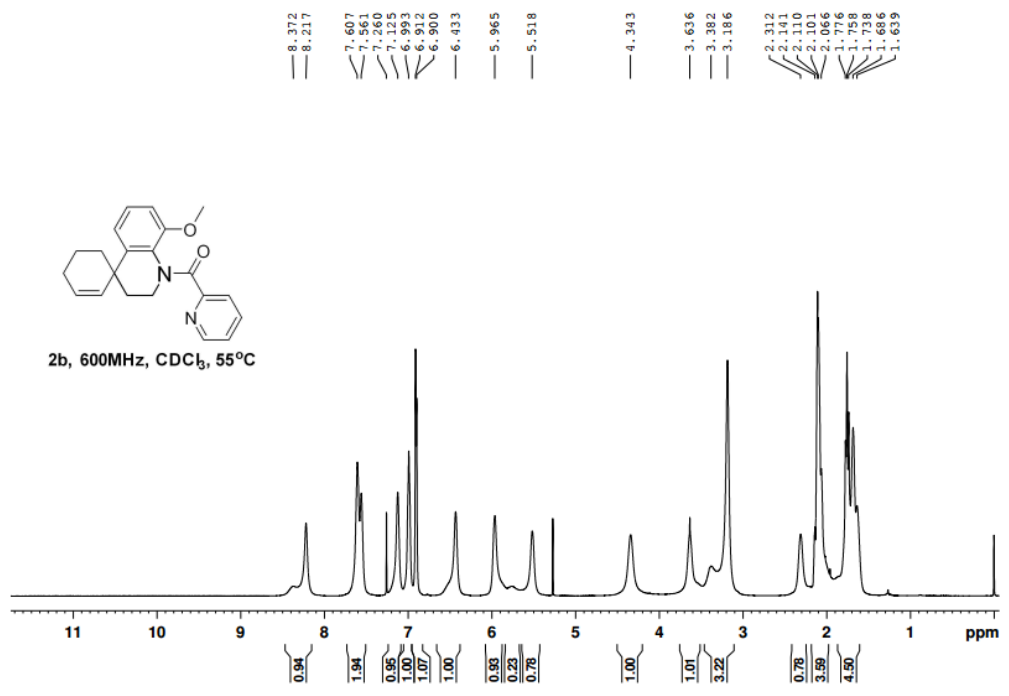

8.534
8.525
7.680
7.662
7.644
7.380
7.272
7.263
7.253
7.031
7.011
6.992
6.880
5.984
5.975
5.965
5.959
5.950
5.942
5.547
5.522
3.983
3.975
3.967
2.124
2.042
2.030
2.021
2.009
1.998
1.913
1.890
1.879
1.868
1.857
1.835
1.816
1.808
1.782
1.776
1.746
1.690
1.674
1.657
1.649
1.641
1.634
0.000
2a
9.5 9.0 8.5 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 ppm
1.03
1.04
1.12
2.61
1.26
1.64
1.00
0.99
2.05
2.11
2.21
2.34
2.43

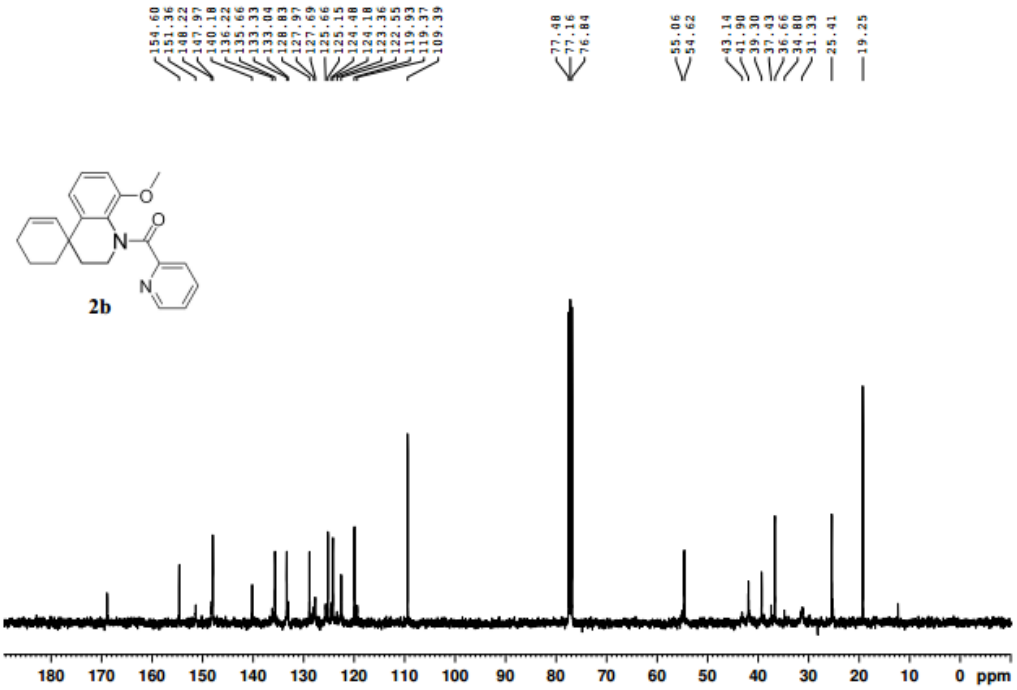

168.28
154.68
148.97
137.73
136.98
136.47
133.34
128.35
127.91
125.77
124.86
124.35
124.23
123.30
77.48
77.16
76.84
42.34
38.39
35.89
33.61
25.07
18.83
2a
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

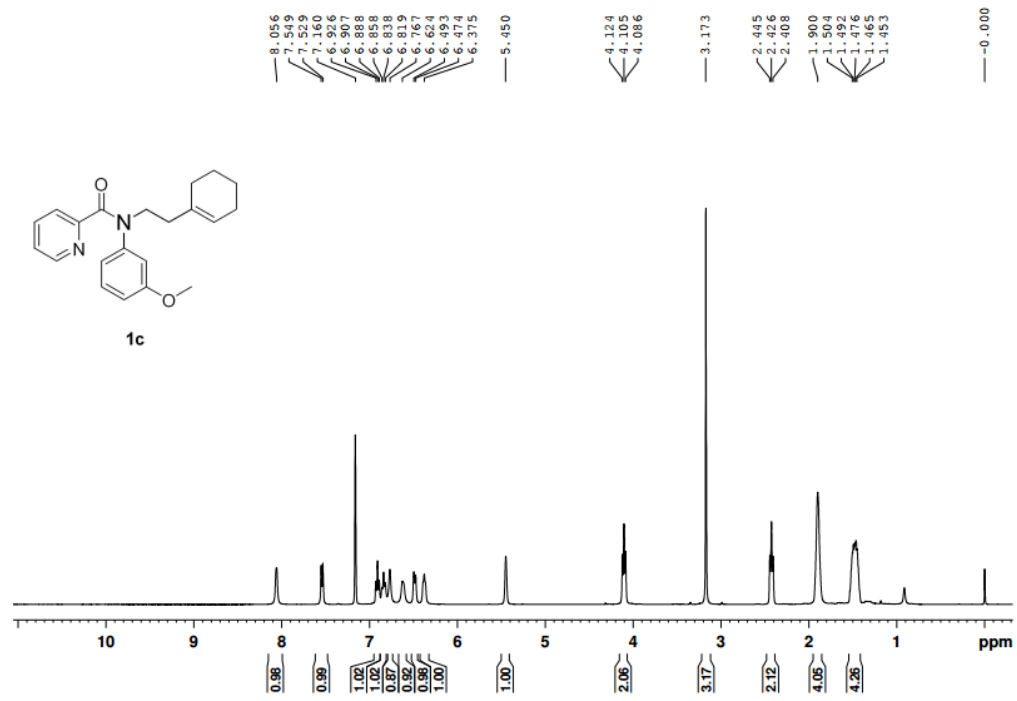

8.273
8.262
7.510
7.506
7.490
7.487
7.471
7.468
7.362
7.342
7.260
7.114
7.111
7.092
7.077
7.074
7.058
7.043
7.039
7.026
6.778
6.759
6.740
6.707
6.687
5.423
4.109
4.094
4.084
4.076
4.069
4.060
4.052
4.036
3.790
3.775
3.766
3.757
3.751
3.743
3.733
3.718
3.670
2.336
2.321
2.301
2.278
2.262
2.238
2.220
2.204
1.925
1.910
1.881
1.571
1.556
1.548
1.542
1.533
1.529
1.512
1.503
1.493
1.488
1.479
1.474
1.465
1.451
-0.013
O
N
N
O
1b
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 ppm
0.99
1.01
1.05
3.11
1.01
1.02
1.00
1.04
1.17
3.13
2.27
4.42
4.31

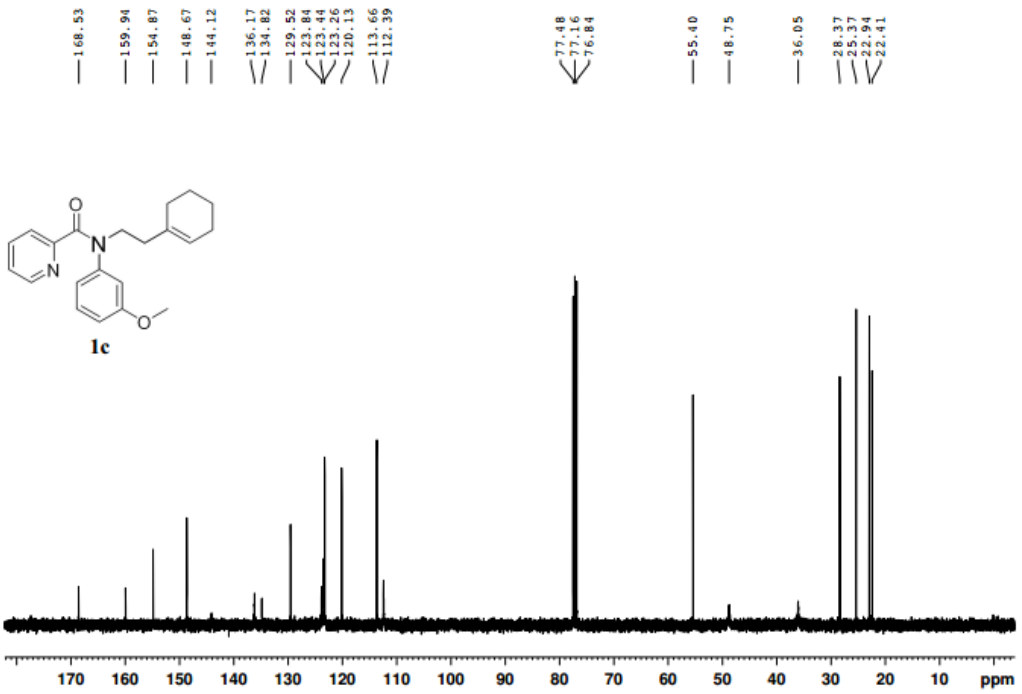

169.21
154.94
154.68
148.17
135.71
135.14
131.68
130.16
128.53
123.66
122.73
120.48
111.39
77.48
77.16
76.84
55.35
47.80
35.70
28.43
25.35
22.97
22.45
O
N
N
O
1b
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

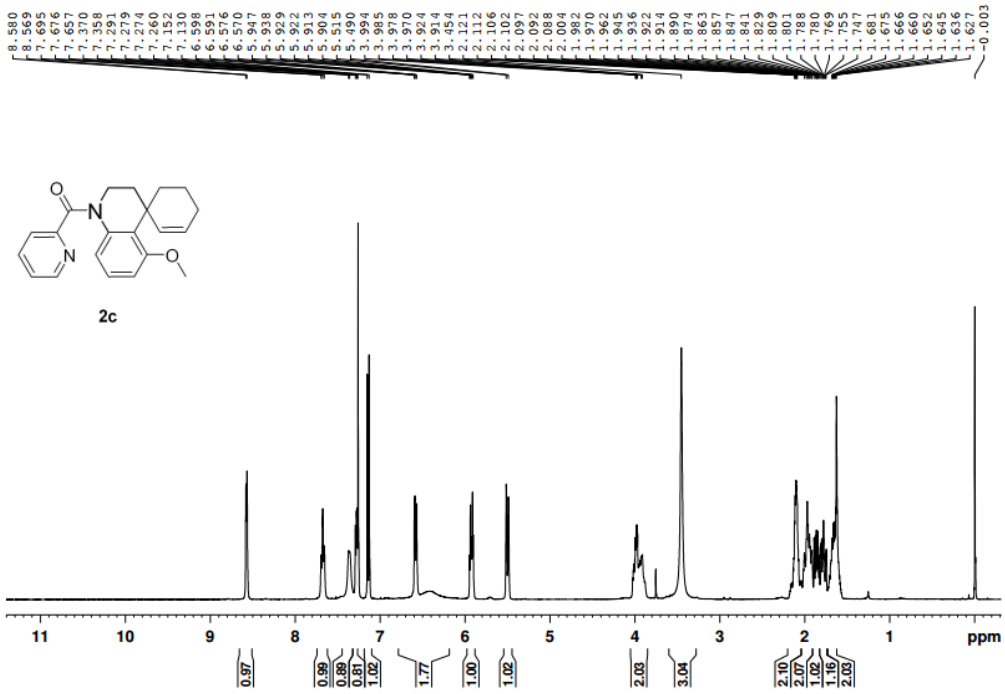

8.436
8.265
7.676
7.659
7.603
7.584
7.565
7.467
7.449
7.260
7.225
7.145
7.131
7.116
7.050
7.010
6.990
6.970
6.901
6.882
6.564
6.552
6.430
6.410
5.991
5.981
5.975
5.966
5.873
5.852
5.748
5.728
5.504
5.479
4.313
4.292
3.698
3.674
3.647
3.638
3.537
3.402
3.159
2.279
2.097
2.091
2.057
2.036
1.968
1.859
1.844
1.827
1.785
1.765
1.758
1.740
1.708
1.690
1.675
1.618
1.609
2b
11
10
9
8
7
6
5
4
3
2
1
ppm
0.26
0.96
0.34
1.21
0.91
0.29
0.97
1.31
1.30
0.28
0.97
0.97
0.32
0.29
1.00
1.31
1.03
0.38
0.88
2.95
0.99
4.03
5.41

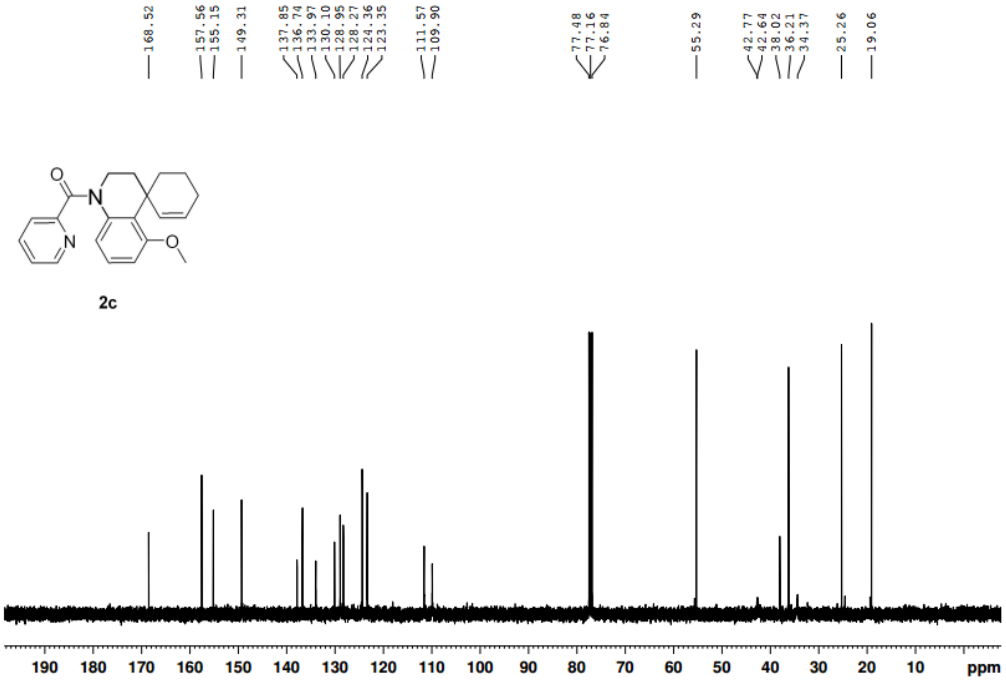

8.372
8.217
7.607
7.561
7.260
7.125
6.993
6.912
6.900
6.433
5.965
5.518
4.343
3.636
3.382
3.186
2.312
2.141
2.110
2.101
2.066
1.776
1.758
1.738
1.686
1.639
2b, 600MHz, CDCl3, 55°C
11
10
9
8
7
6
5
4
3
2
1
ppm
0.94
1.94
0.95
1.00
1.07
1.00
0.93
0.23
0.78
1.00
1.01
3.22
0.78
3.59
4.50

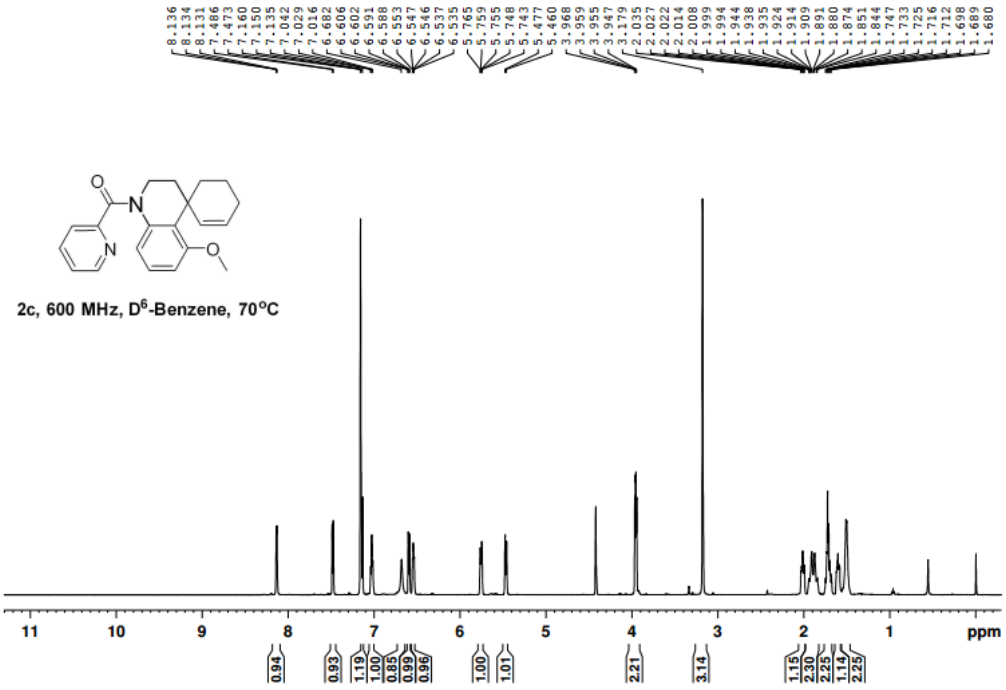

154.60
151.36
148.22
147.97
140.18
136.22
135.66
133.33
133.04
128.83
127.97
127.69
125.66
125.15
124.48
124.18
123.36
122.55
119.93
119.37
109.39
77.48
77.16
76.84
55.06
54.62
43.14
41.90
39.30
37.43
36.66
34.80
31.33
25.41
19.25
2b
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

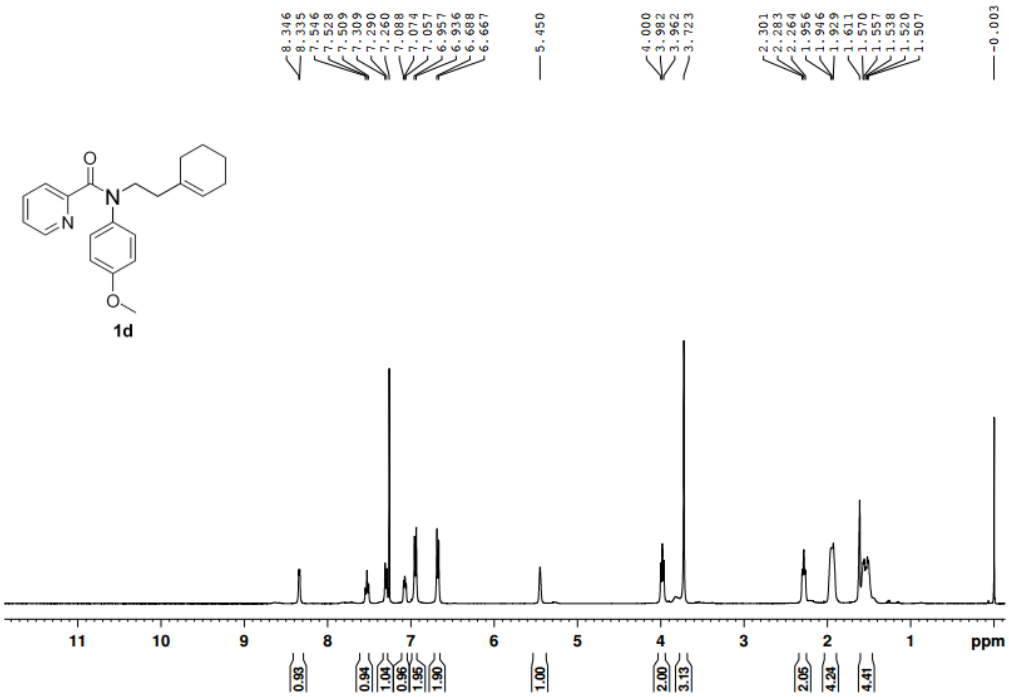

8.056
7.549
7.529
7.160
6.926
6.907
6.888
6.858
6.838
6.819
6.767
6.624
6.493
6.474
6.375
5.450
4.124
4.105
4.086
3.173
2.445
2.426
2.408
1.900
1.504
1.492
1.476
1.465
1.453
-0.000
1c
10 9 8 7 6 5 4 3 2 1 ppm
0.98
0.99
1.00
1.02
0.87
0.92
0.98
1.00
1.00
2.06
3.17
2.12
4.05
4.26

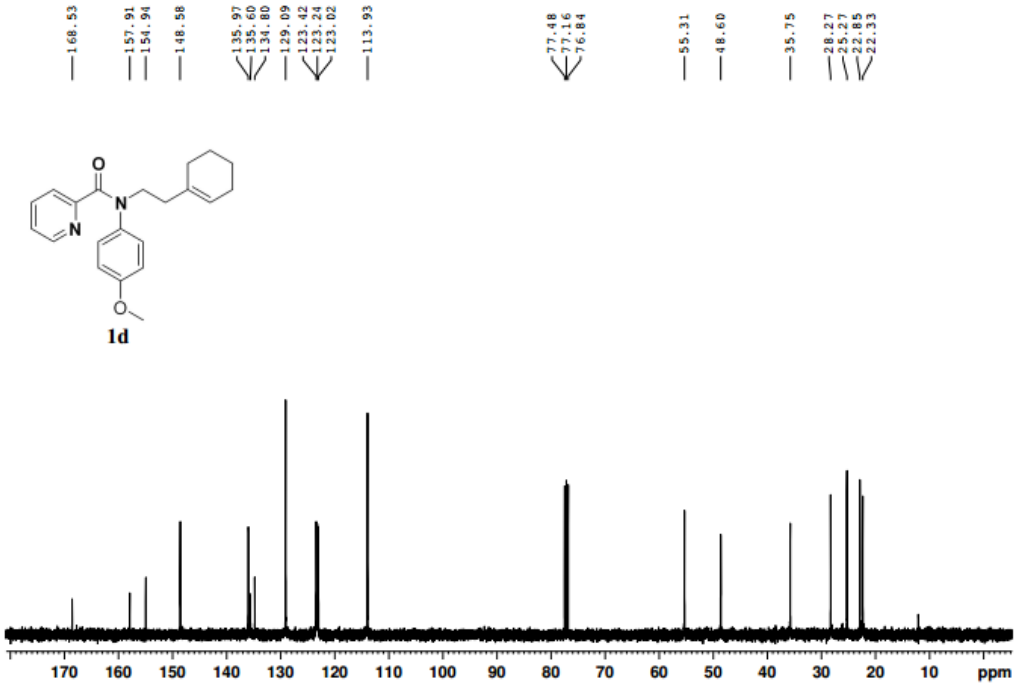

168.53
159.94
154.87
148.67
144.12
136.17
134.82
129.52
123.84
123.44
123.26
120.13
113.66
112.39
77.48
77.16
76.84
55.40
48.75
36.05
28.37
25.37
22.94
22.41
1c
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

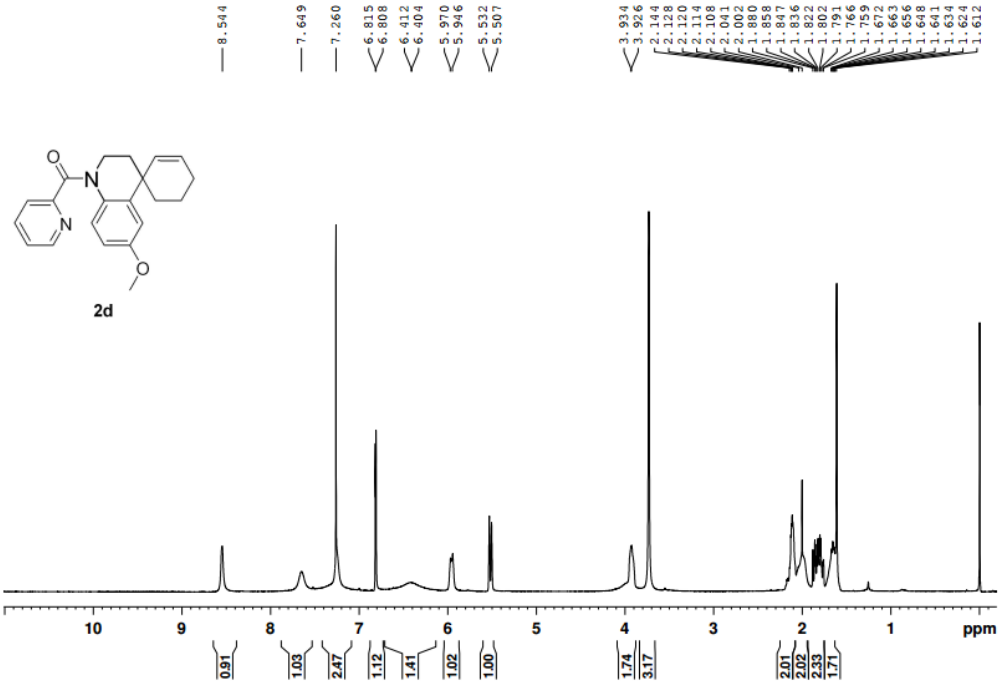

2c
11 10 9 8 7 6 5 4 3 2 1 ppm
0.97
0.99
0.88
0.81
1.02
1.77
1.00
1.02
2.03
3.04
2.10
2.07
1.02
1.16
2.03

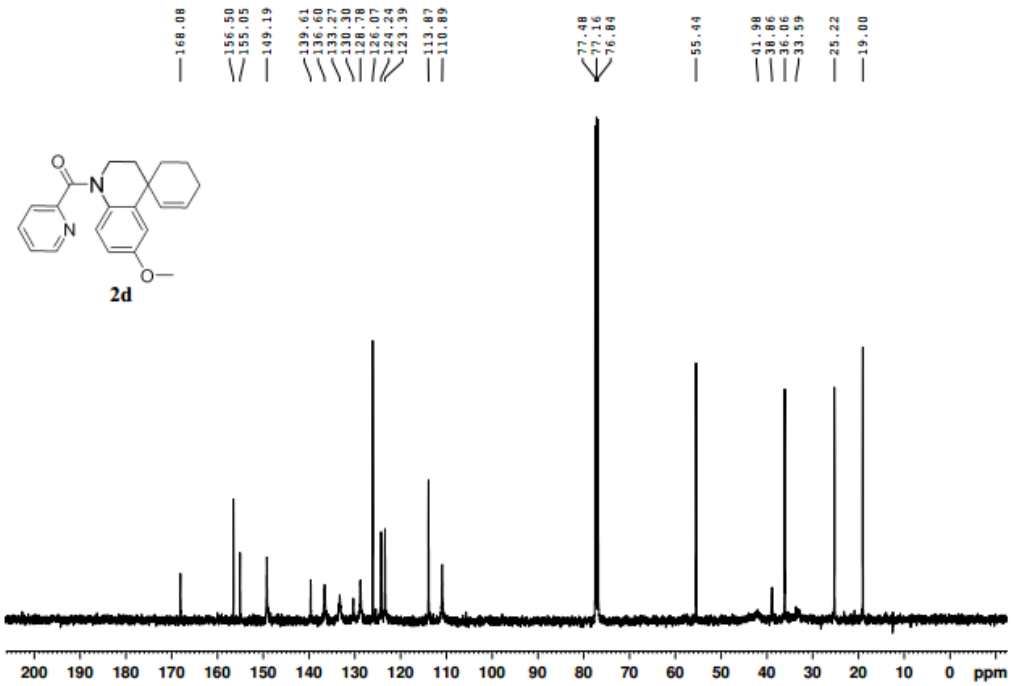

168.52
157.56
155.15
149.31
137.85
136.74
133.97
130.10
128.95
128.27
124.36
123.35
111.57
109.90
77.48
77.16
76.84
55.29
42.77
42.64
38.02
36.21
34.37
25.26
19.06
2c
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

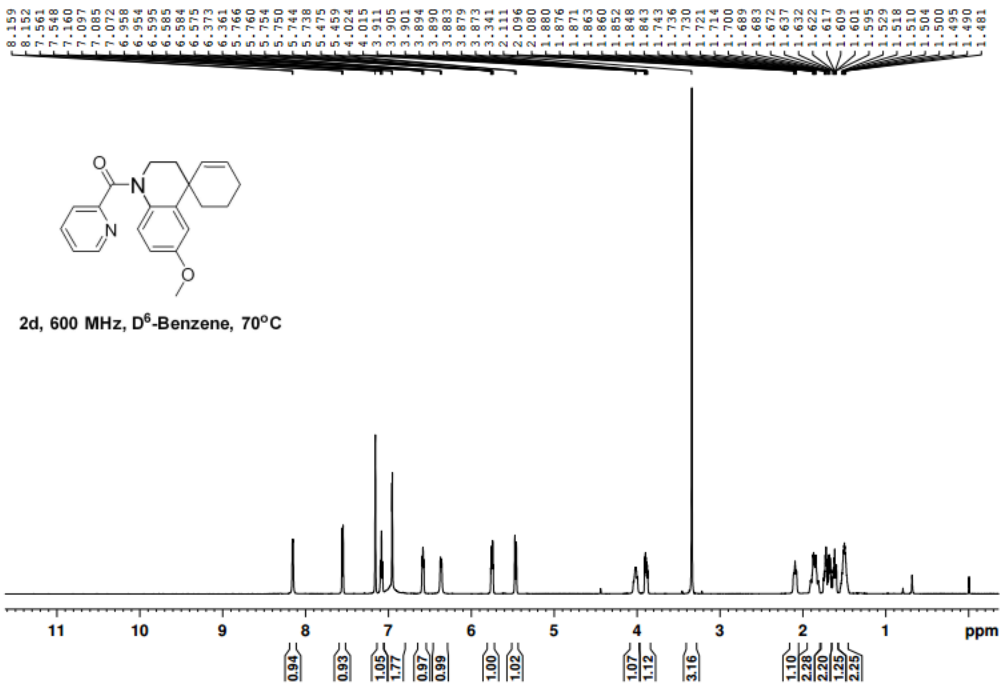

8.136
8.134
8.131
7.486
7.473
7.160
7.150
7.135
7.042
7.029
7.016
6.682
6.606
6.602
6.591
6.588
6.553
6.547
6.546
6.537
6.535
5.765
5.759
5.755
5.748
5.743
5.477
5.460
3.968
3.959
3.955
3.947
3.179
3.135
2.027
2.022
2.014
2.008
1.999
1.994
1.944
1.938
1.935
1.924
1.914
1.909
1.891
1.880
1.874
1.851
1.844
1.747
1.733
1.725
1.716
1.712
1.698
1.689
1.680
2c, 600 MHz, D6-Benzene, 70°C
11 10 9 8 7 6 5 4 3 2 1 ppm
0.94
0.93
1.19
1.00
0.85
0.99
0.96
1.00
1.01
2.21
3.14
1.15
2.30
2.25
1.14
2.25

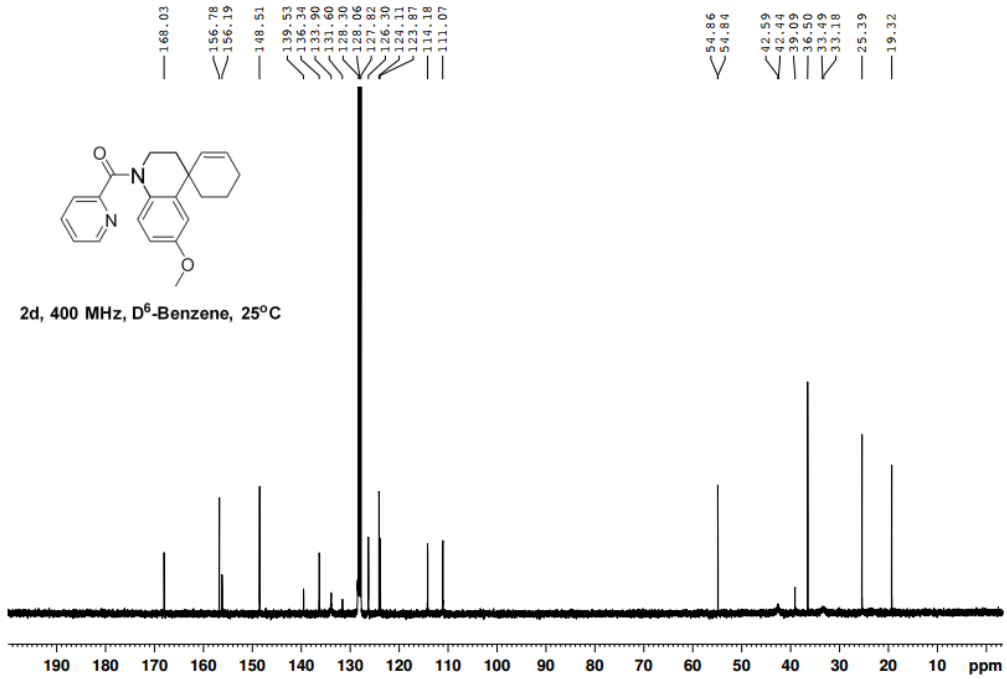

8.346
8.335
7.546
7.528
7.509
7.309
7.290
7.260
7.088
7.074
7.057
6.957
6.936
6.688
6.667
5.450
4.000
3.982
3.962
3.723
2.301
2.283
2.264
1.956
1.946
1.929
1.611
1.570
1.557
1.538
1.520
1.507
-0.003
1d
11
10
9
8
7
6
5
4
3
2
1
ppm
0.93
0.94
1.04
0.96
1.95
1.90
1.00
2.00
3.13
2.05
4.24
4.41

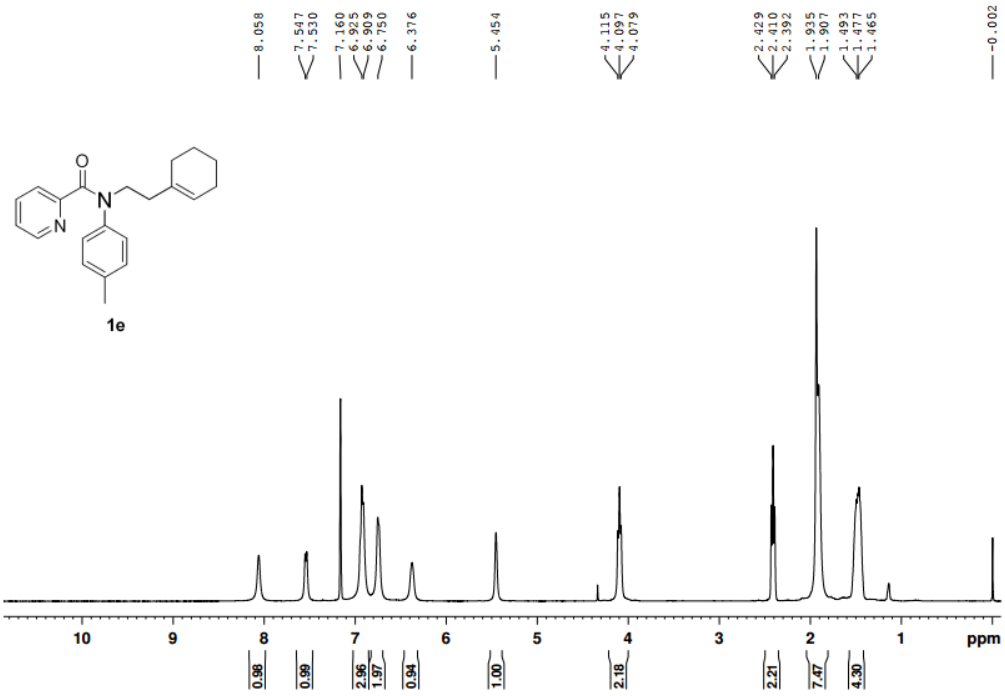

168.53
157.91
154.94
148.58
135.97
135.60
134.80
129.09
123.42
123.24
123.02
113.93
77.48
77.16
76.84
55.31
48.60
35.75
28.27
25.27
22.85
22.33
1d
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

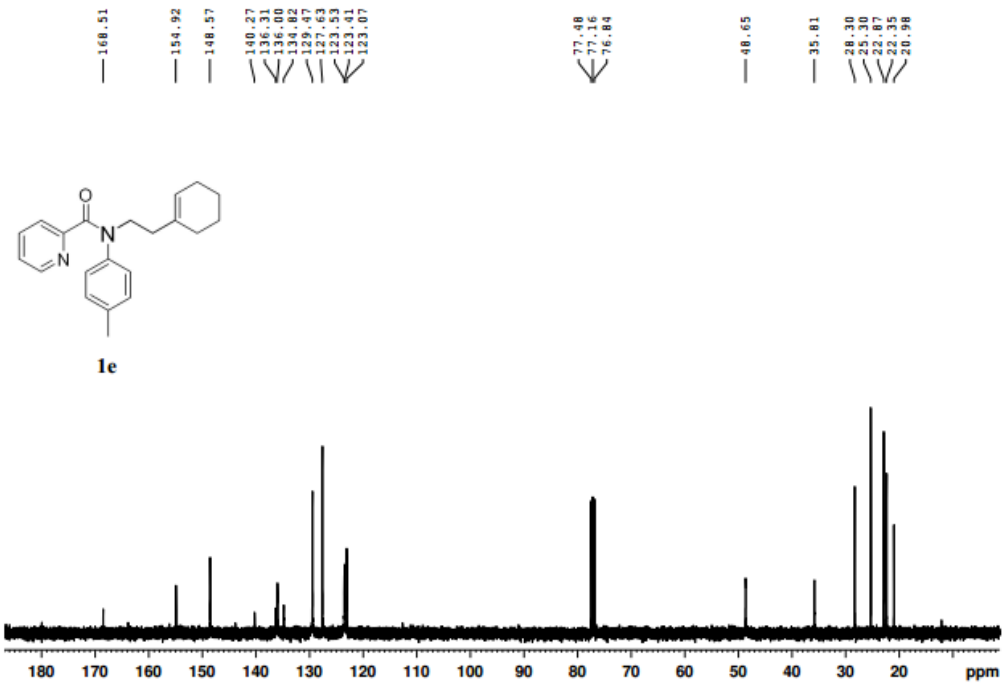

8.544
7.649
7.260
6.815
6.808
6.412
6.404
5.970
5.946
5.532
5.507
3.934
3.926
2.144
2.128
2.120
2.114
2.108
2.041
2.002
1.880
1.858
1.847
1.836
1.822
1.802
1.791
1.766
1.759
1.672
1.663
1.656
1.648
1.641
1.634
1.624
1.612
2d
10
9
8
7
6
5
4
3
2
1
ppm
0.91
1.03
2.47
1.12
1.41
1.02
1.00
1.74
3.17
2.01
2.02
2.33
1.71

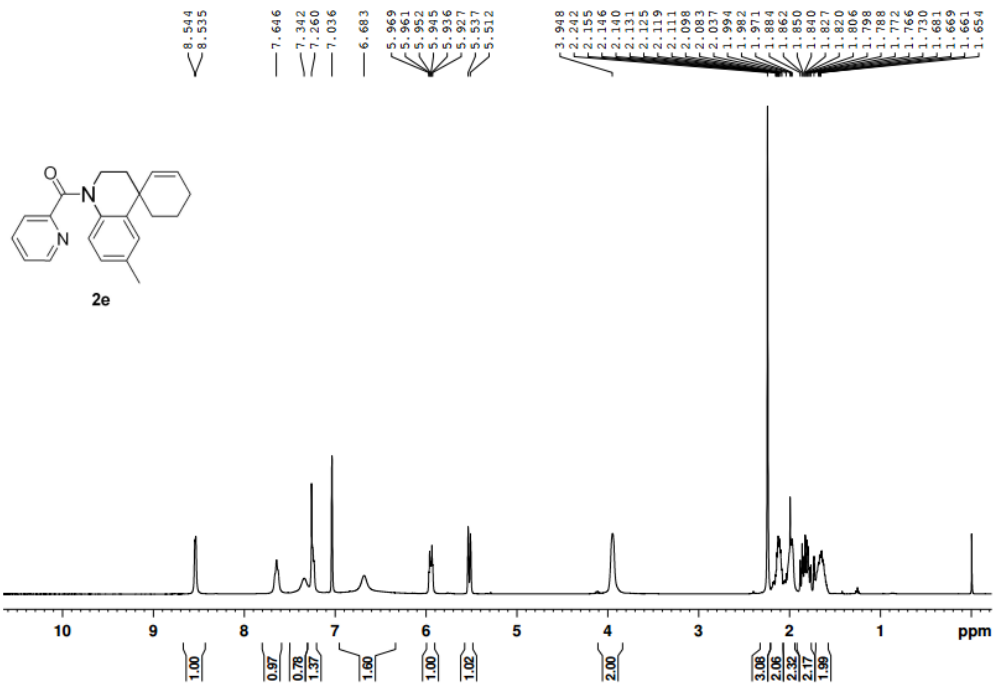

168.08
156.50
155.05
149.19
139.61
136.60
133.27
130.30
128.78
126.07
124.24
123.39
113.87
110.89
77.48
77.16
76.84
55.44
41.98
38.86
36.06
33.59
25.22
19.00
2d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

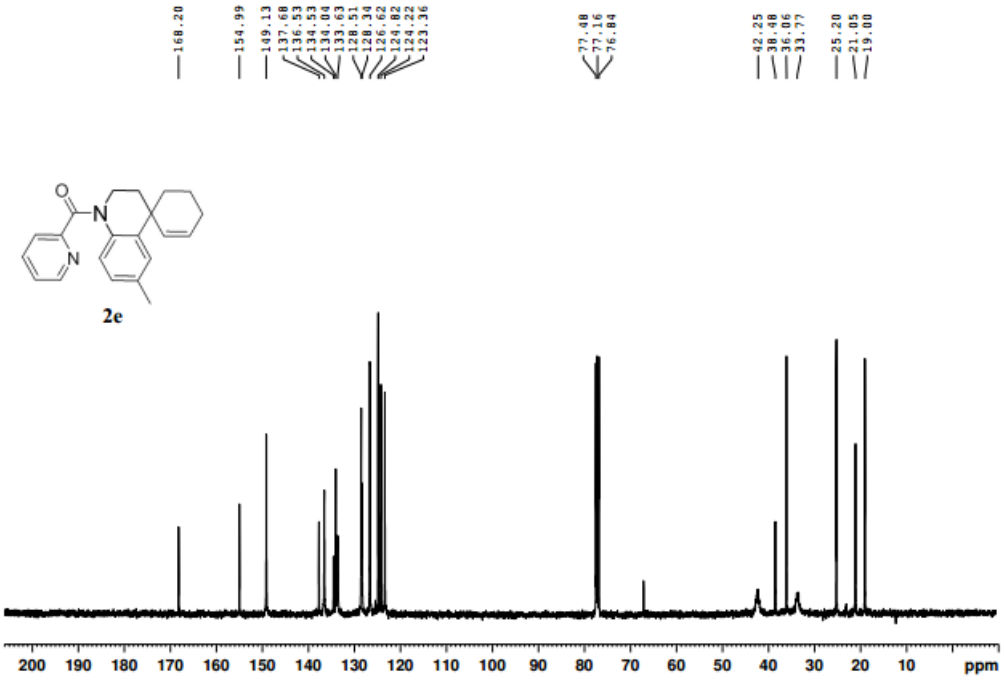

8.159
8.152
7.561
7.548
7.160
7.097
7.085
7.072
6.958
6.954
6.595
6.585
6.584
6.575
6.373
6.361
5.766
5.760
5.754
5.750
5.744
5.738
5.475
5.459
4.024
4.015
3.911
3.905
3.901
3.894
3.890
3.883
3.879
3.873
3.341
2.111
2.096
2.080
1.880
1.876
1.871
1.863
1.860
1.852
1.848
1.843
1.743
1.736
1.730
1.721
1.714
1.700
1.689
1.683
1.672
1.637
1.632
1.622
1.617
1.609
1.601
1.595
1.529
1.518
1.510
1.504
1.500
1.495
1.490
1.481
O
N
N
O
2d, 600 MHz, D6-Benzene, 70°C
11
10
9
8
7
6
5
4
3
2
1
ppm
0.94
0.93
1.05
1.77
0.97
0.99
1.00
1.02
1.07
1.12
3.16
1.10
2.26
2.20
1.25
2.25

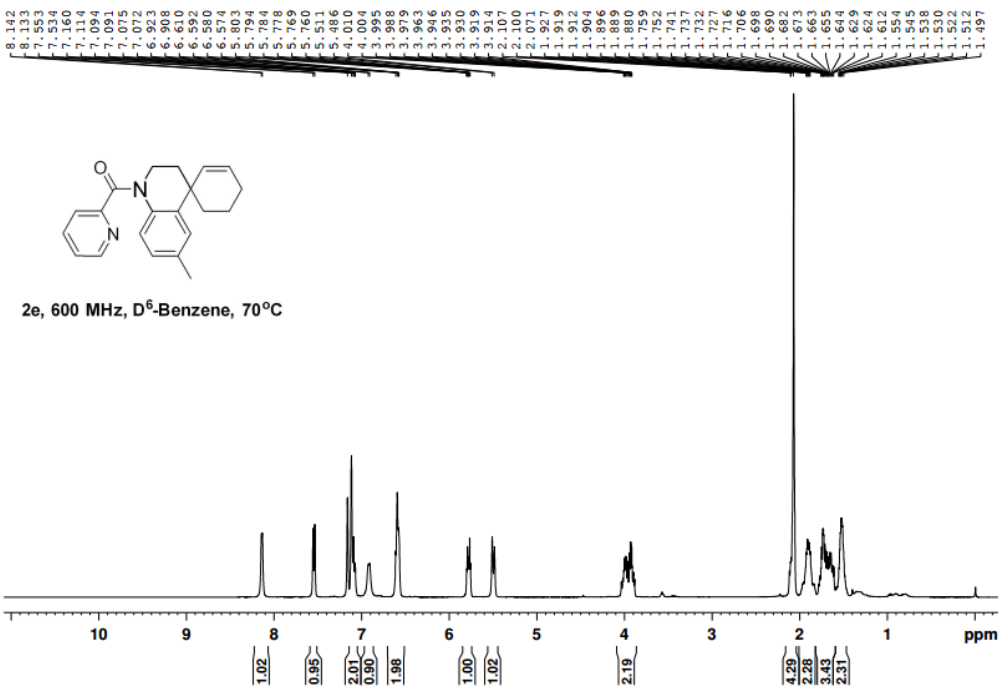

168.03
156.78
156.19
148.51
139.53
136.34
133.90
131.60
128.30
128.06
127.82
126.30
124.11
123.87
114.18
111.07
54.86
54.84
42.59
42.44
39.09
36.50
33.49
33.18
25.39
19.32
O
N
N
O
2d, 400 MHz, D6-Benzene, 25°C
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

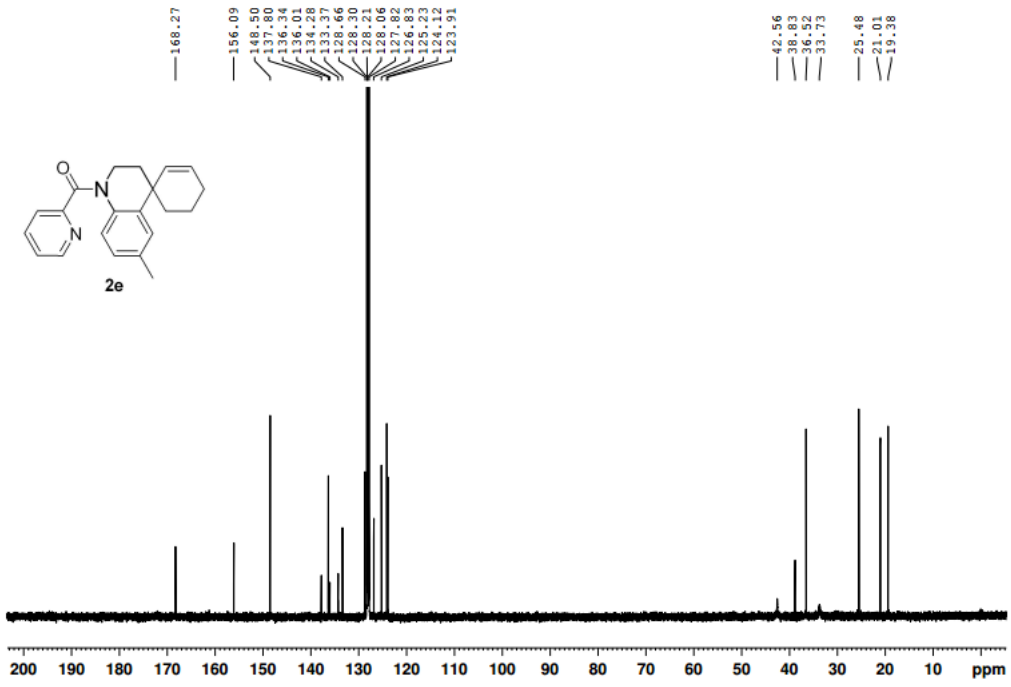

8.058
7.547
7.530
7.160
6.925
6.909
6.750
6.376
5.454
4.115
4.097
4.079
2.429
2.410
2.392
1.935
1.907
1.493
1.477
1.465
-0.002
1e
10
9
8
7
6
5
4
3
2
1
ppm
0.98
0.99
2.96
1.97
0.94
1.00
2.18
2.21
7.47
4.30

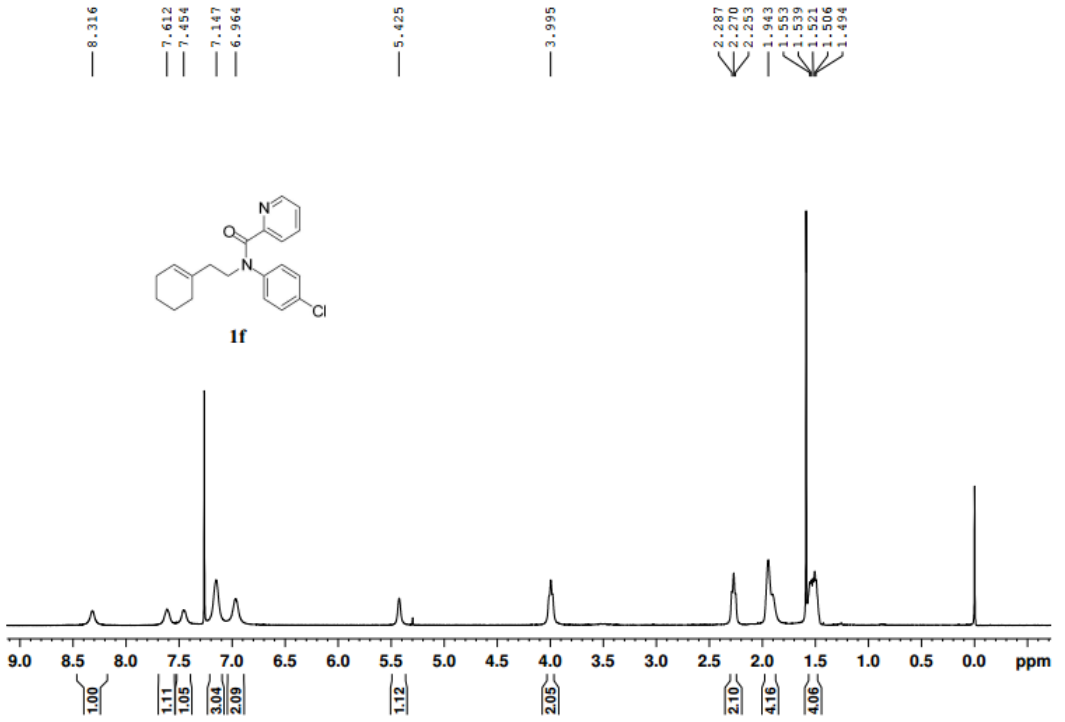

168.51
154.92
148.57
140.27
136.31
136.00
134.82
129.47
127.63
123.53
123.41
123.07
77.48
77.16
76.84
48.65
35.81
28.30
25.30
22.87
22.35
20.98
1e
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

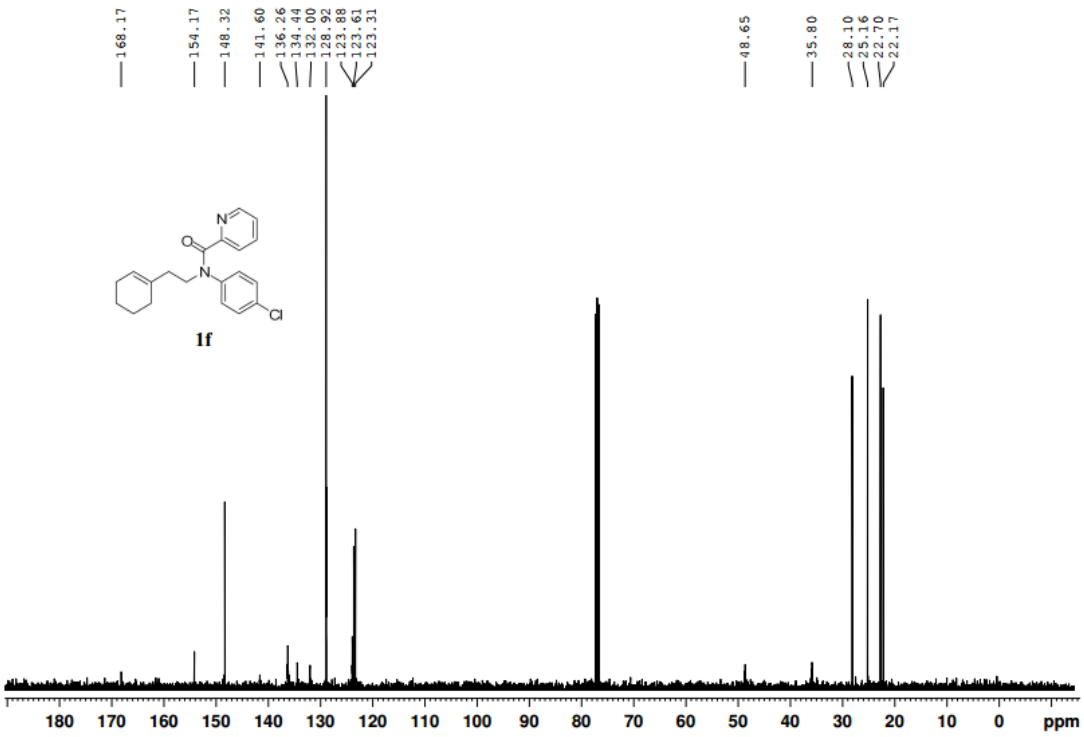

8.544
8.535
7.646
7.342
7.260
7.036
6.683
5.969
5.961
5.952
5.945
5.936
5.927
5.537
5.512
3.948
2.242
2.155
2.146
2.140
2.131
2.125
2.119
2.111
2.098
2.083
2.037
1.994
1.982
1.971
1.884
1.862
1.850
1.840
1.827
1.820
1.806
1.798
1.788
1.772
1.766
1.730
1.681
1.669
1.661
1.654
O
N
N
2e
10
9
8
7
6
5
4
3
2
1
ppm
1.00
0.97
0.78
1.37
1.60
1.00
1.02
2.00
3.08
2.06
2.32
2.17
1.99

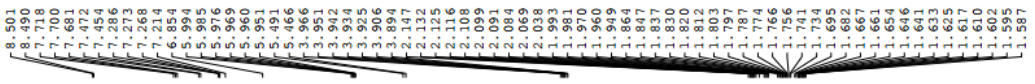

168.20
154.99
149.13
137.68
136.53
134.53
134.04
133.63
128.51
128.34
126.62
124.82
124.22
123.36
77.48
77.16
76.84
42.25
38.48
36.06
33.77
25.20
21.05
19.00
O
N
N
2e
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


8.142
8.133
7.553
7.534
7.160
7.114
7.094
7.091
7.075
7.072
6.923
6.908
6.610
6.592
6.580
6.574
5.803
5.794
5.784
5.778
5.769
5.760
5.511
5.486
4.010
4.004
3.995
3.988
3.979
3.963
3.946
3.935
3.930
3.919
3.914
2.107
2.100
2.071
1.927
1.919
1.912
1.904
1.896
1.889
1.880
1.759
1.752
1.741
1.737
1.732
1.727
1.716
1.706
1.698
1.690
1.682
1.673
1.663
1.655
1.644
1.629
1.624
1.612
1.554
1.545
1.538
1.530
1.522
1.512
1.497
O
N
N
2e, 600 MHz, D6-Benzene, 70°C
10
9
8
7
6
5
4
3
2
1
ppm
1.02
0.95
2.01
0.90
1.98
1.00
1.02
2.19
4.29
2.28
3.43
2.31


168.27
156.09
148.50
137.80
136.34
136.01
134.28
133.37
128.66
128.30
128.21
128.06
127.82
126.83
125.23
124.12
123.91
42.56
38.83
36.52
33.73
25.48
21.01
19.38
O
N
N
2e
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


8.316
7.612
7.454
7.147
6.964
5.425
3.995
2.287
2.270
2.253
1.943
1.553
1.539
1.521
1.506
1.494
1f
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 0.0 ppm
1.00 1.11 1.05 3.04 2.09 1.12 2.05 2.10 4.16 4.06


168.17
154.17
148.32
141.60
136.26
134.44
132.00
128.92
123.88
123.61
123.31
48.65
35.80
28.10
25.16
22.70
22.17
1f
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.501
8.490
7.718
7.700
7.681
7.472
7.454
7.286
7.273
7.268
7.214
6.854
5.994
5.985
5.976
5.969
5.960
5.951
5.491
5.466
3.966
3.951
3.942
3.934
3.925
3.906
3.894
2.147
2.132
2.125
2.116
2.108
2.099
2.091
2.084
2.069
2.038
1.993
1.981
1.970
1.960
1.949
1.864
1.847
1.837
1.830
1.820
1.812
1.803
1.797
1.787
1.774
1.766
1.756
1.741
1.734
1.695
1.682
1.667
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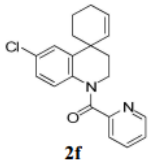
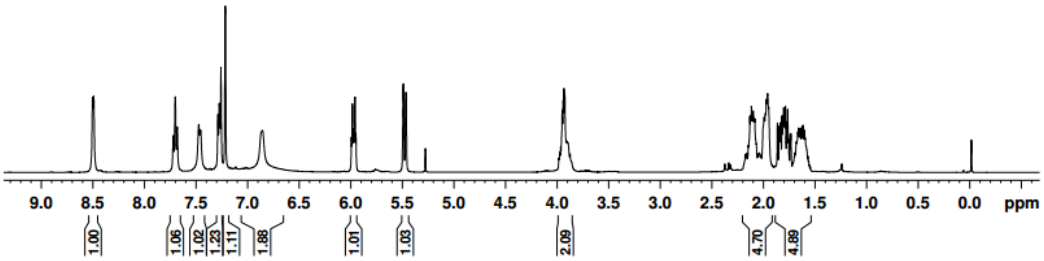
1.646
1.641
1.633
1.625
1.617
1.610
1.602
1.595
1.587


Cl
N
O
N

2f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7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
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1.02
1.23
1.11
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1.01
1.03
2.09
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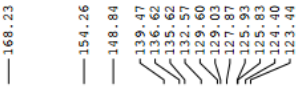
4.80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148.84
139.47
136.62
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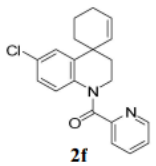
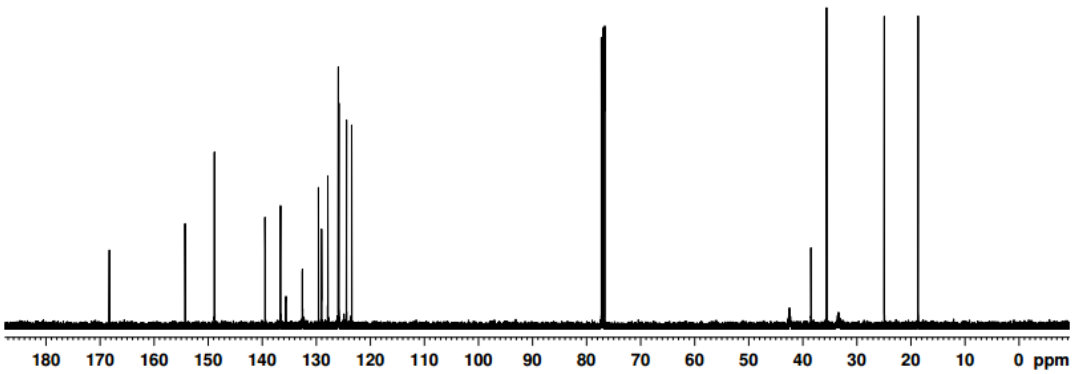
132.57
129.60
129.03
127.87
125.93
125.83
124.40
123.44
42.41
38.48
35.57
33.38
24.91
18.65


Cl
N
O
N

2f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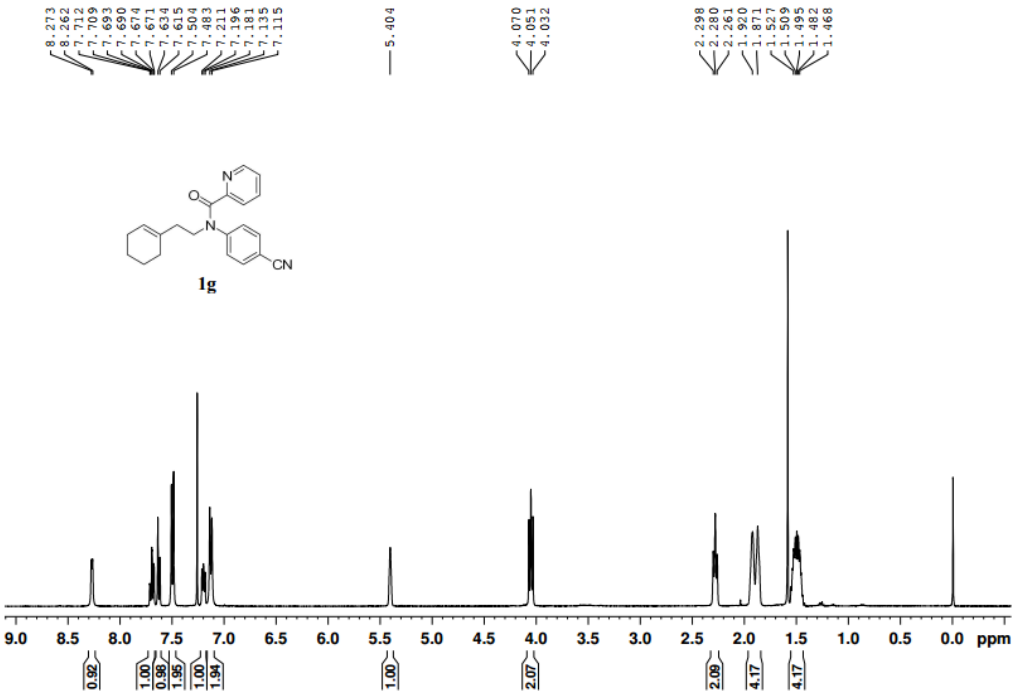
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm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8.262
7.712
7.709
7.693
7.690
7.674
7.671
7.634
7.615
7.504
7.483
7.211
7.196
7.181
7.135
7.115
5.404
4.070
4.051
4.032
2.298
2.280
2.261
1.920
1.871
1.527
1.509
1.495
1.482
1.468
N
O
N
CN
1g
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 0.0 ppm
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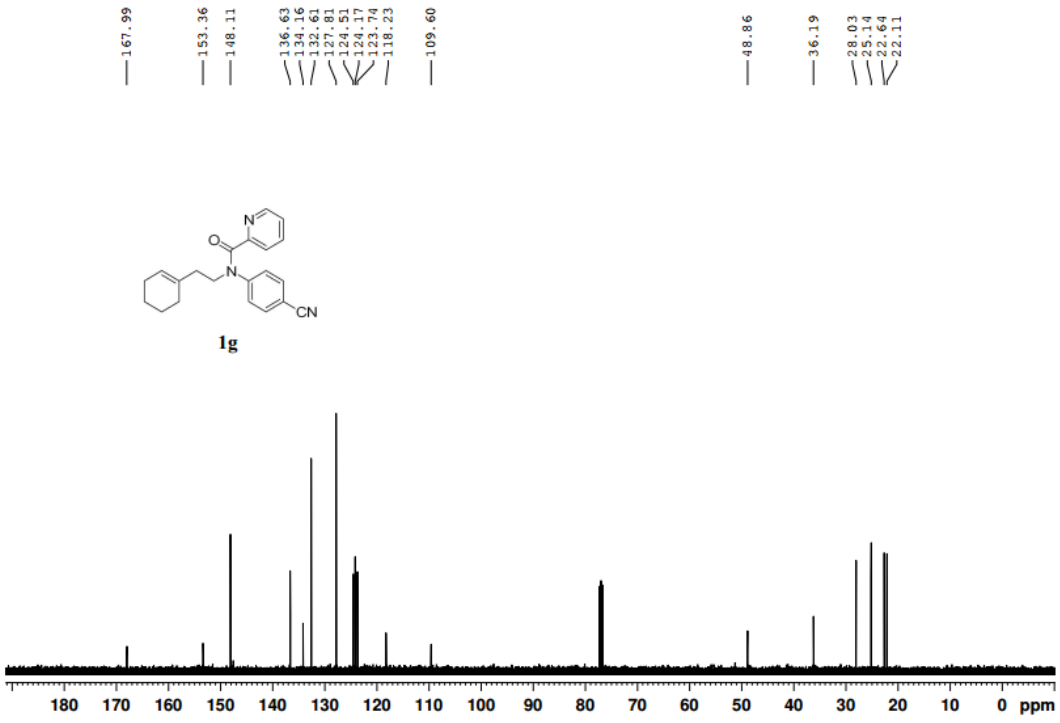
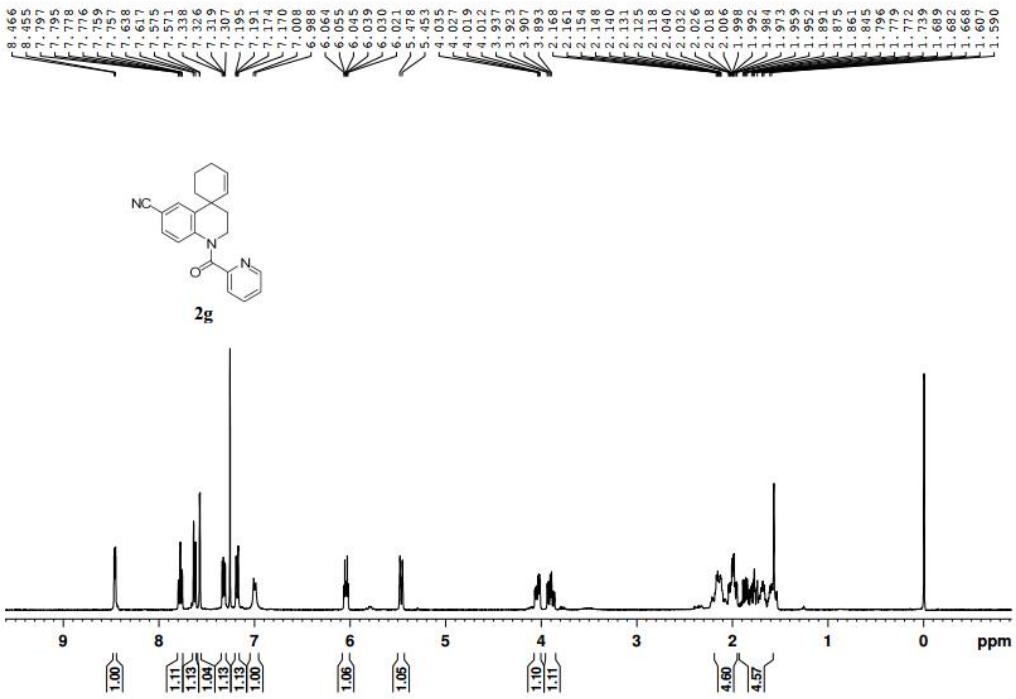
1.00
0.98
1.95
1.00
1.94
1.00
2.07
2.09
4.17
4.17


167.99
153.36
148.11
136.63
134.16
132.61
127.81
124.51
124.17
123.74
118.23
109.60
48.86
36.19
28.03
25.14
22.64
22.11
N
O
N
CN
1g
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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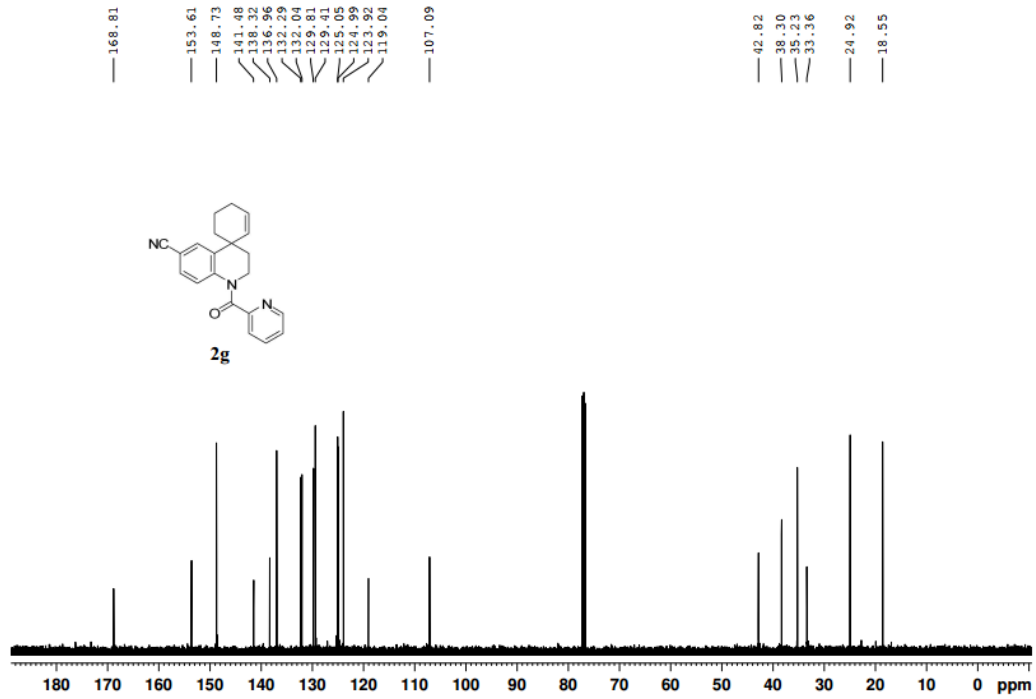
7.797
7.795
7.778
7.776
7.759
7.757
7.638
7.617
7.575
7.571
7.338
7.326
7.319
7.307
7.195
7.191
7.174
7.170
7.008
6.988
6.064
6.055
6.045
6.039
6.030
6.021
5.478
5.453
4.035
4.027
4.019
4.012
3.937
3.923
3.907
3.893
2.168
2.161
2.154
2.148
2.140
2.131
2.125
2.118
2.040
2.032
2.026
2.018
2.006
1.998
1.992
1.984
1.973
1.959
1.952
1.891
1.875
1.861
1.845
1.796
1.779
1.772
1.739
1.689
1.682
1.668
1.607
1.590
NC
N
O
N
2g
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.11
1.13
1.04
1.13
1.13
1.00
1.06
1.05
1.10
1.11
4.60
4.57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153.61
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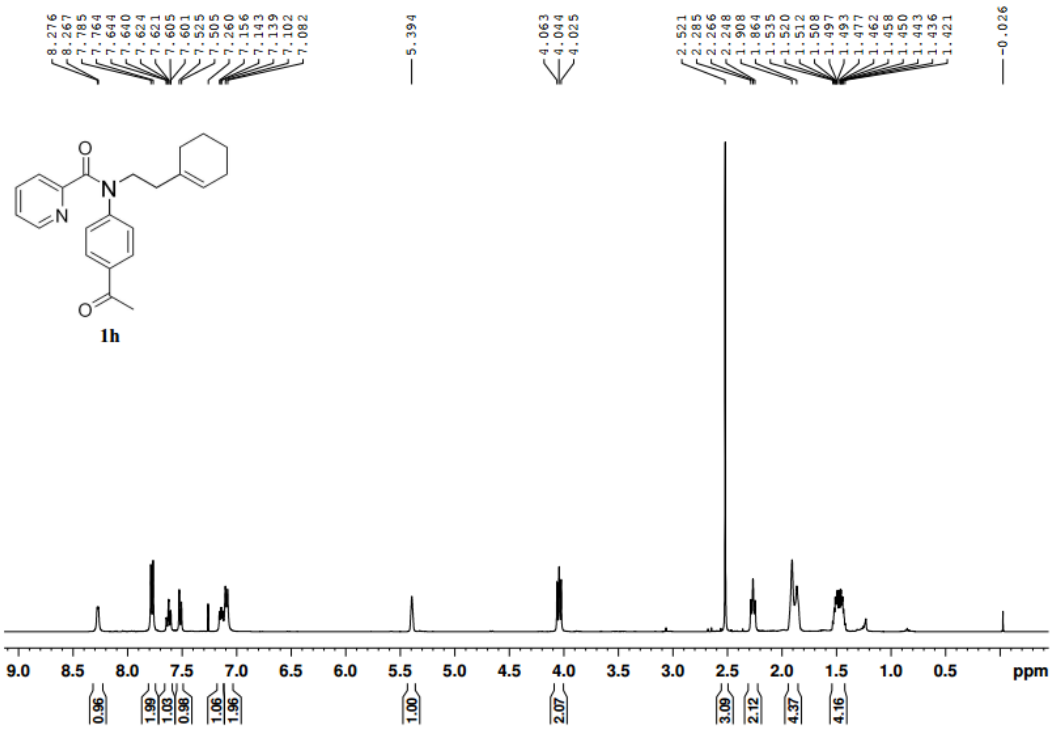
141.48
138.32
136.96
132.29
132.04
129.81
129.41
125.05
124.99
123.92
119.04
107.09
42.82
38.30
35.23
33.36
24.92
18.55
NC
N
O
N
2g
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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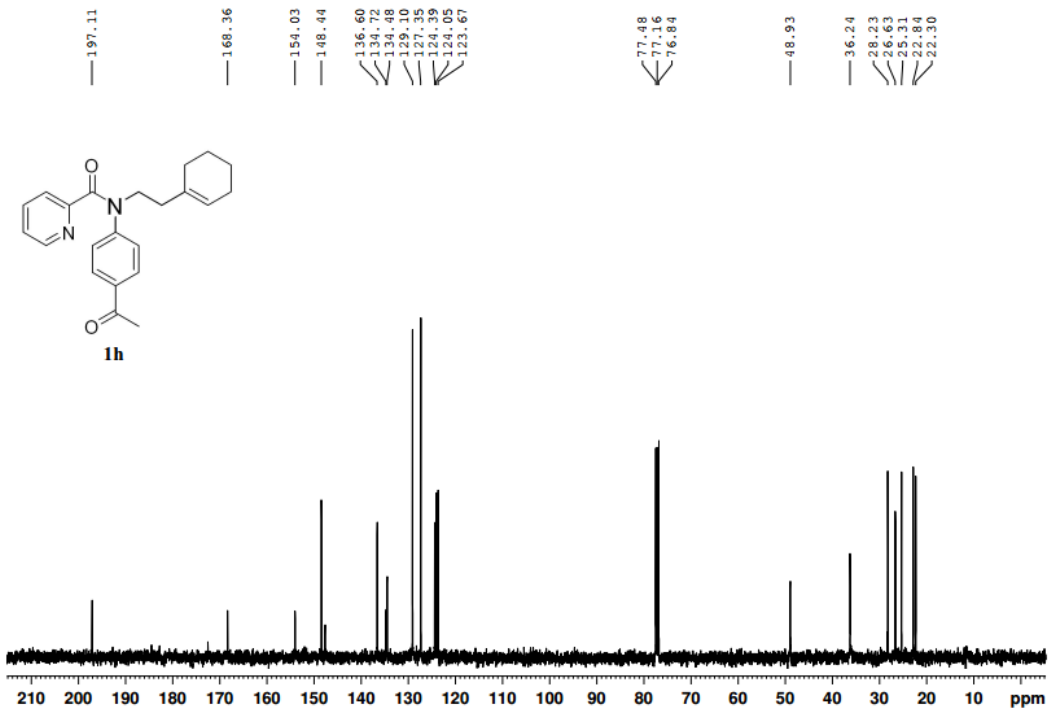
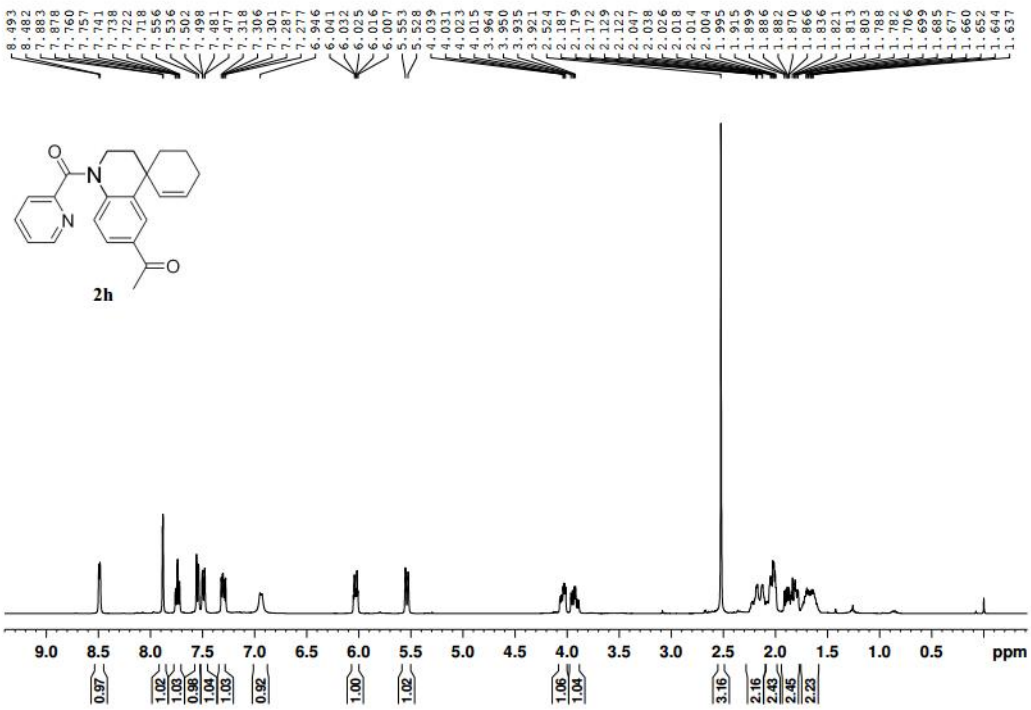
7.764
7.644
7.640
7.624
7.621
7.605
7.601
7.525
7.505
7.260
7.156
7.143
7.139
7.102
7.082
5.394
4.063
4.044
4.025
2.521
2.285
2.266
2.248
2.208
1.864
1.535
1.520
1.512
1.508
1.497
1.493
1.477
1.462
1.458
1.450
1.443
1.436
1.421
-0.026
O
N
N
O
1h
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.96
1.99
1.03
0.98
1.06
1.96
1.00
2.07
3.09
2.12
4.37
4.16


197.11
168.36
154.03
148.44
136.60
134.72
134.48
129.10
127.35
124.39
124.05
123.67
77.48
77.16
76.84
48.93
36.24
28.23
26.63
25.31
22.84
22.30
O
N
N
O
1h
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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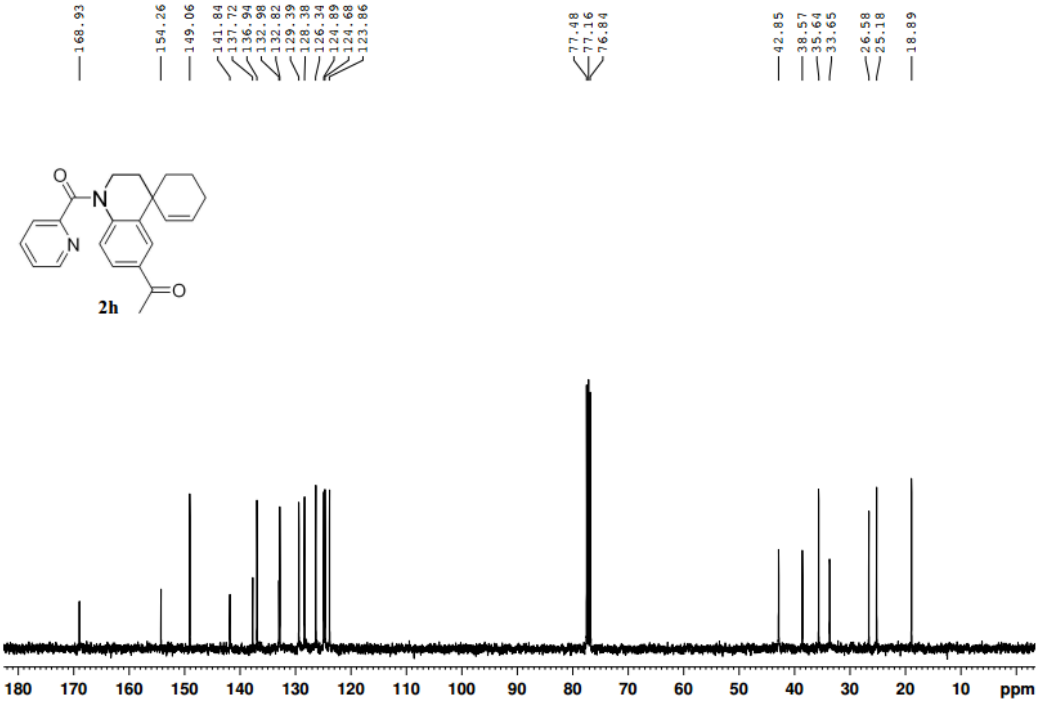
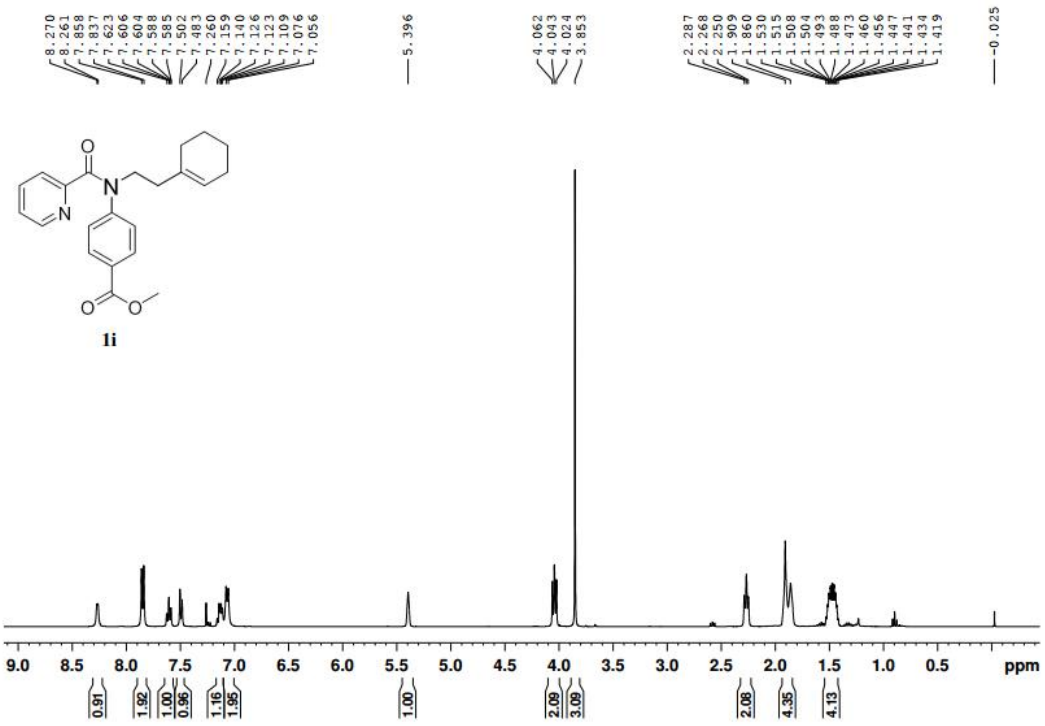
7.760
7.757
7.741
7.738
7.722
7.718
7.556
7.536
7.502
7.498
7.481
7.477
7.318
7.306
7.301
7.287
7.277
6.946
6.041
6.032
6.025
6.016
6.007
5.553
5.528
4.039
4.031
4.023
4.015
3.964
3.950
3.935
3.921
2.524
2.187
2.179
2.172
2.129
2.122
2.047
2.038
2.026
2.018
2.014
2.004
1.995
1.915
1.899
1.886
1.882
1.870
1.866
1.836
1.821
1.813
1.803
1.788
1.782
1.706
1.699
1.685
1.677
1.660
1.652
1.644
1.637
2h
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 ppm
0.97
1.02
1.03
0.98
1.04
1.03
0.92
1.00
1.02
1.06
1.04
3.16
2.16
2.43
2.45
2.23


168.93
154.26
149.06
141.84
137.72
136.94
132.98
132.82
129.39
128.38
126.34
124.89
124.68
123.86
77.48
77.16
76.84
42.85
38.57
35.64
33.65
26.58
25.18
18.89
2h
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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7.837
7.623
7.606
7.604
7.588
7.585
7.502
7.483
7.260
7.159
7.140
7.126
7.123
7.109
7.076
7.056
5.396
4.062
4.043
4.024
3.853
2.287
2.268
2.250
1.909
1.860
1.530
1.515
1.508
1.504
1.493
1.488
1.473
1.460
1.456
1.447
1.441
1.434
1.419
-0.025
1i
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 ppm
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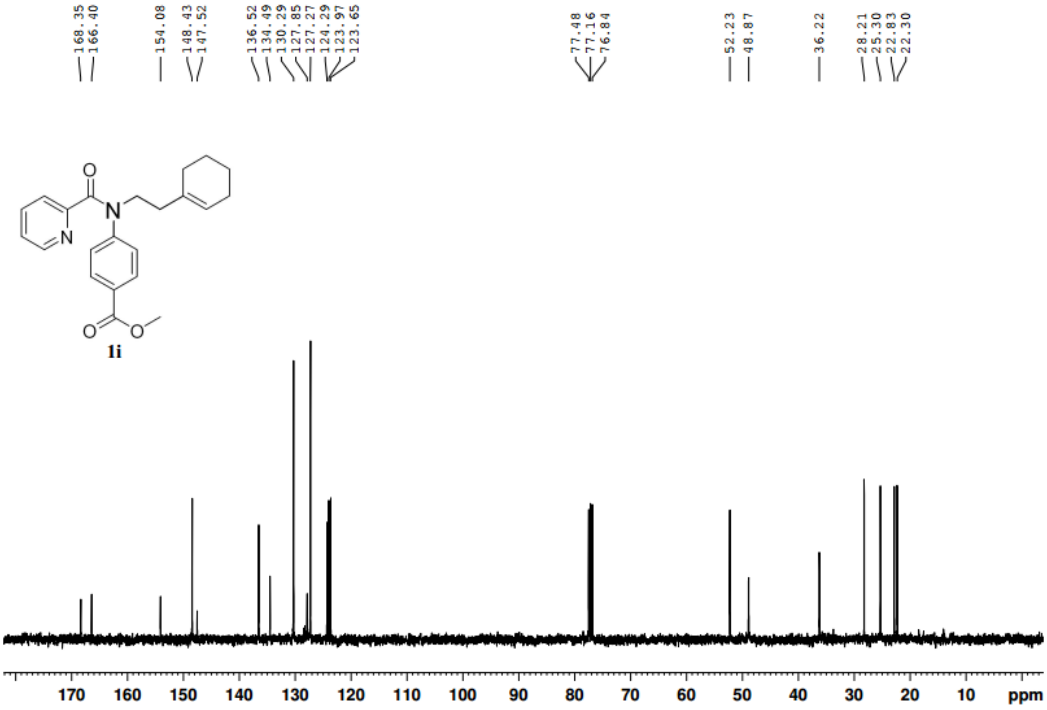
1.92
1.00
0.96
1.16
1.95
1.00
2.09
3.09
2.08
4.35
4.13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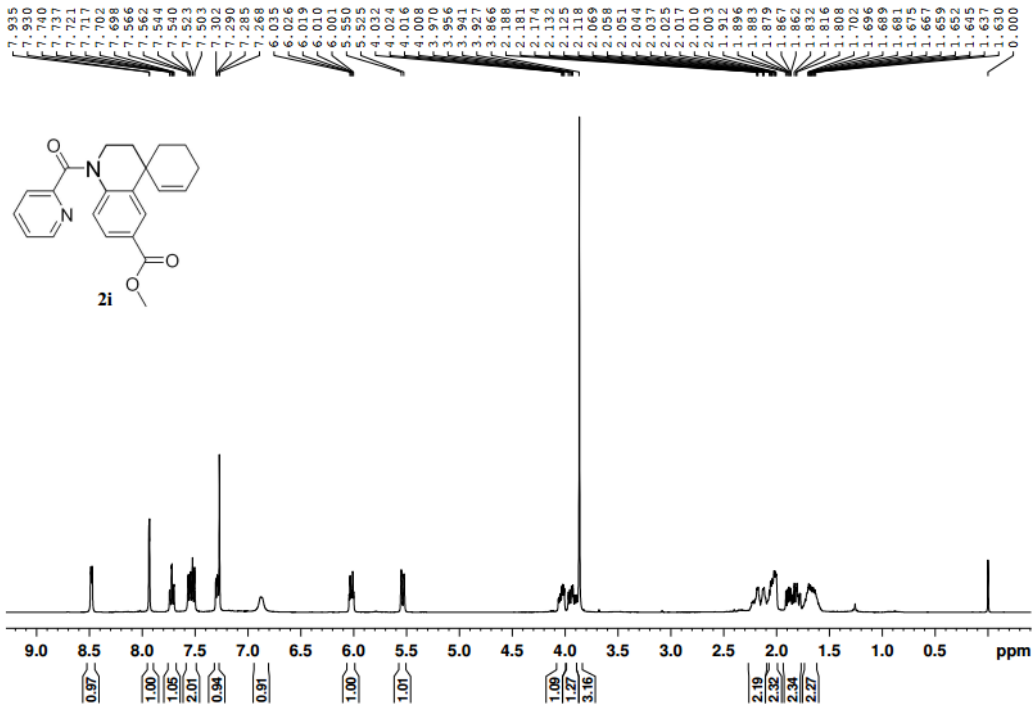
154.08
148.43
147.52
136.52
134.49
130.29
127.85
127.27
124.29
123.97
123.65
77.48
77.16
76.84
52.23
48.87
36.22
28.21
25.30
22.83
22.30
1i
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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7.930
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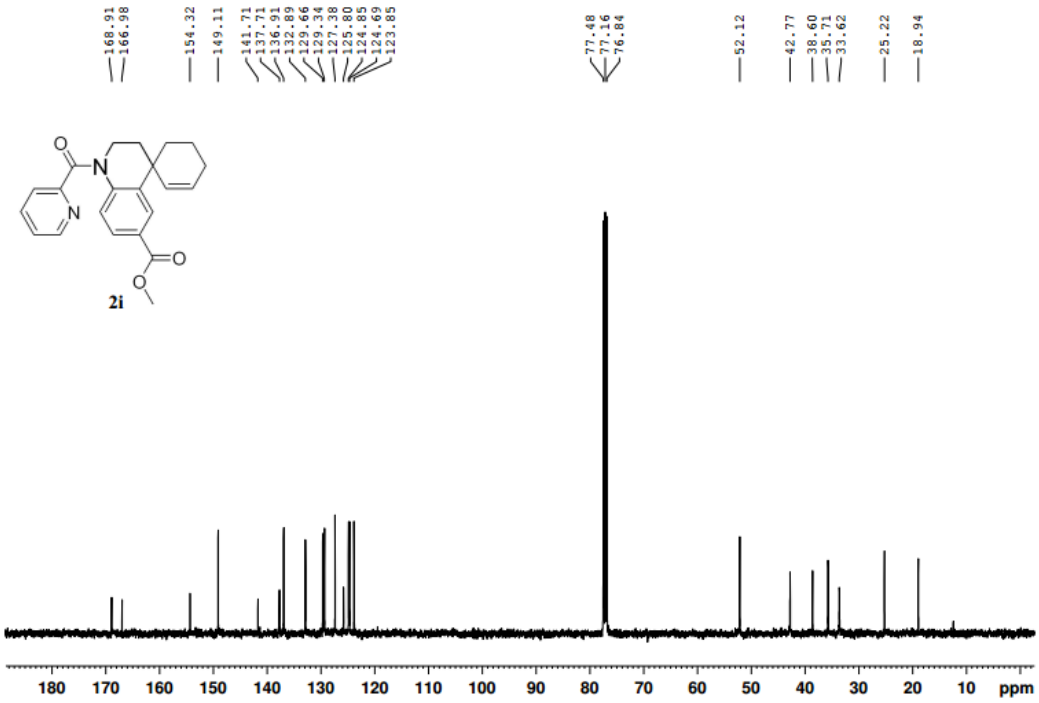
7.737
7.721
7.717
7.702
7.698
7.566
7.562
7.544
7.540
7.523
7.503
7.302
7.290
7.285
7.268
6.035
6.026
6.019
6.010
6.001
5.550
5.525
4.032
4.024
4.016
4.008
3.970
3.956
3.941
3.927
3.866
2.188
2.181
2.174
2.132
2.125
2.118
2.069
2.058
2.051
2.044
2.037
2.025
2.017
2.010
2.003
1.912
1.896
1.883
1.879
1.867
1.862
1.832
1.816
1.808
1.702
1.696
1.689
1.681
1.675
1.667
1.659
1.652
1.645
1.637
1.630
0.000
2i
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
ppm
0.97
1.00
1.05
2.01
0.94
0.91
1.00
1.01
1.09
1.27
3.16
2.19
2.32
2.34
2.27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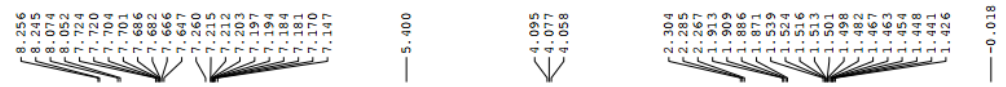
137.71
136.91
132.89
129.66
129.34
127.38
125.80
124.85
124.69
123.85
77.48
77.16
76.84
52.12
42.77
38.60
35.71
33.62
25.22
18.94
2i
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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8.052
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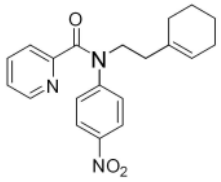
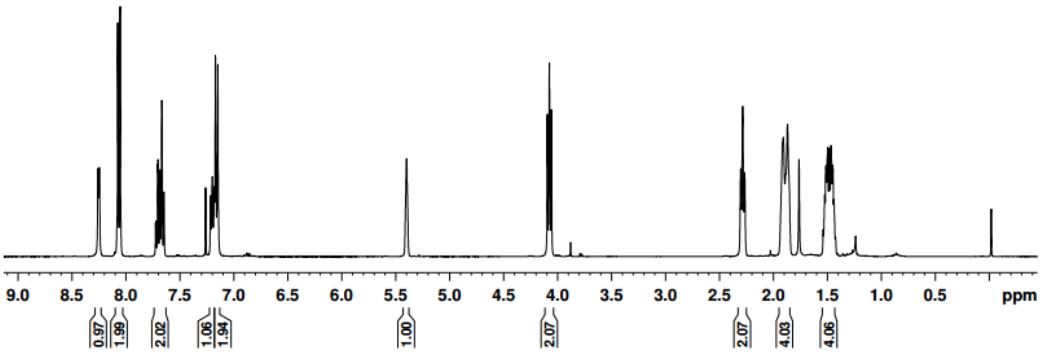
7.720
7.704
7.701
7.686
7.682
7.666
7.647
7.260
7.215
7.212
7.203
7.197
7.194
7.184
7.181
7.170
7.147
5.400
4.095
4.077
4.058
2.304
2.285
2.267
1.913
1.909
1.886
1.871
1.539
1.524
1.516
1.513
1.501
1.498
1.482
1.467
1.463
1.454
1.448
1.441
1.426
-0.018


O
N
N
NO2

1j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8.0
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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
ppm
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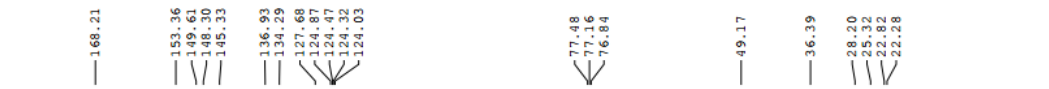
1.99
2.02
1.06
1.94
1.00
2.07
2.07
4.03
4.06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145.33
136.93
134.29
127.68
124.87
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124.03
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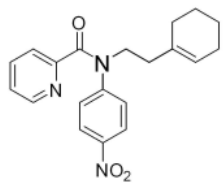
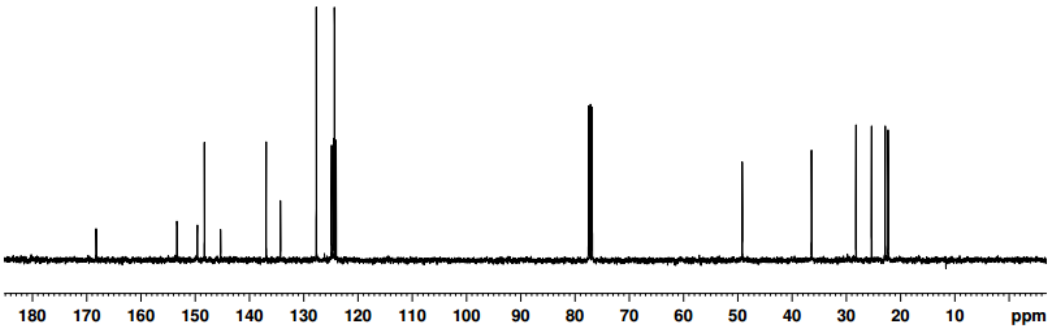
49.17
36.39
28.20
25.32
22.82
22.28


O
N
N
NO2

1j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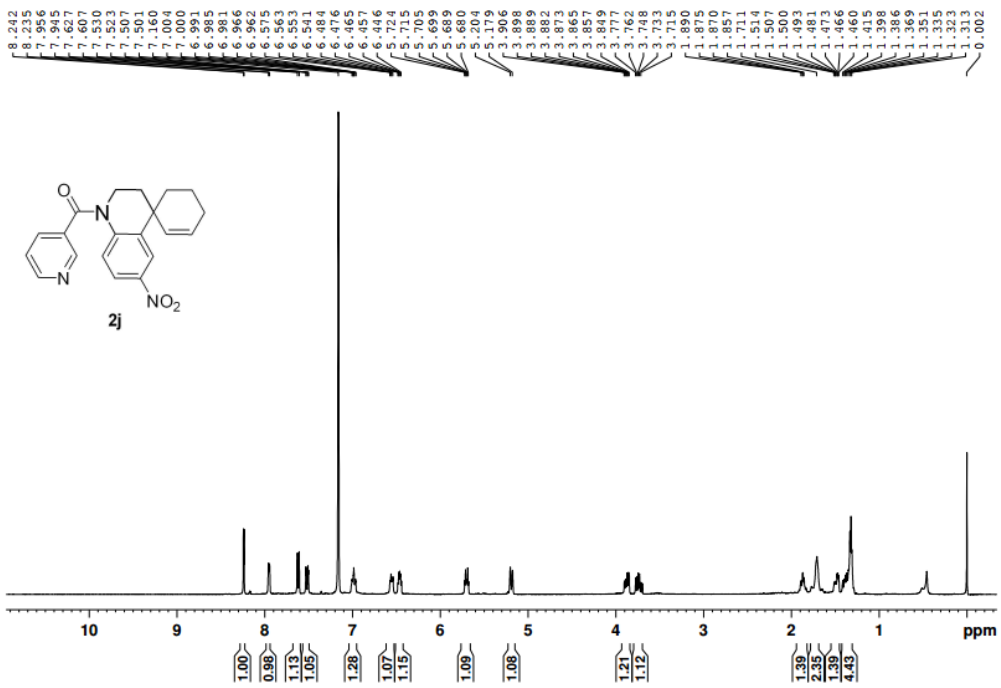
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.523
7.507
7.501
7.160
7.004
7.000
6.991
6.985
6.981
6.966
6.962
6.575
6.563
6.553
6.541
6.484
6.476
6.465
6.457
6.446
5.724
5.715
5.705
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3.849
3.777
3.762
3.748
3.733
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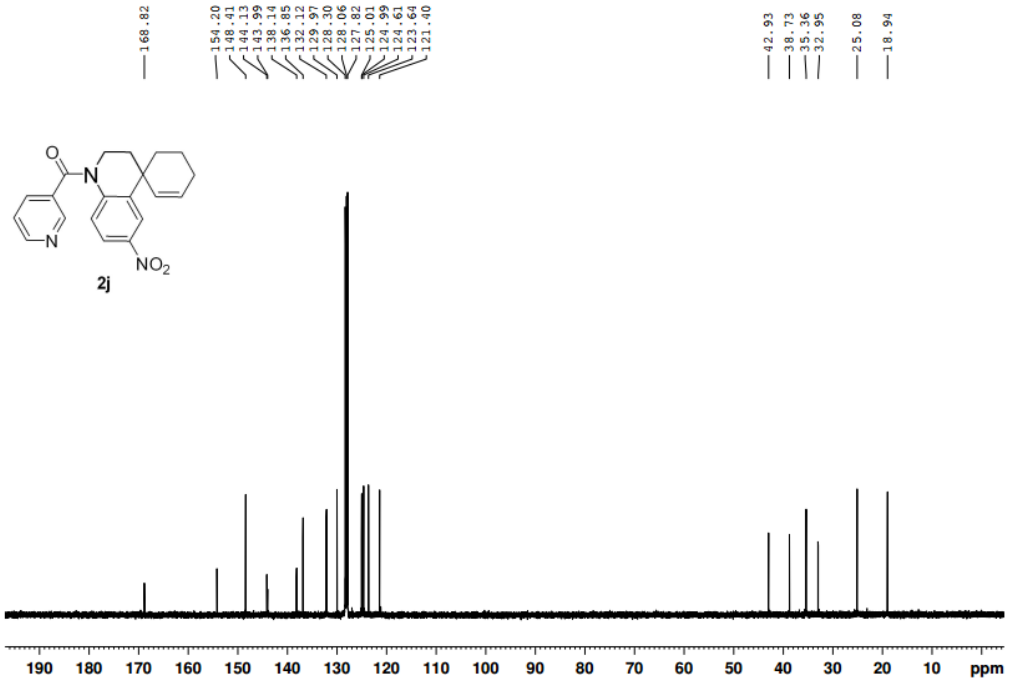
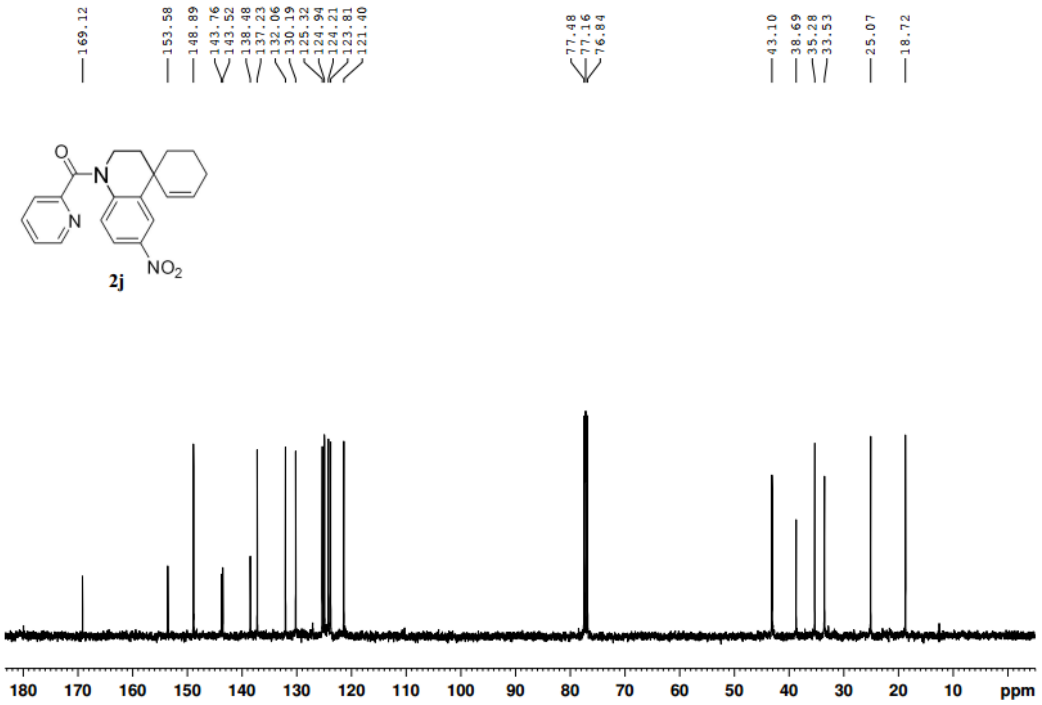
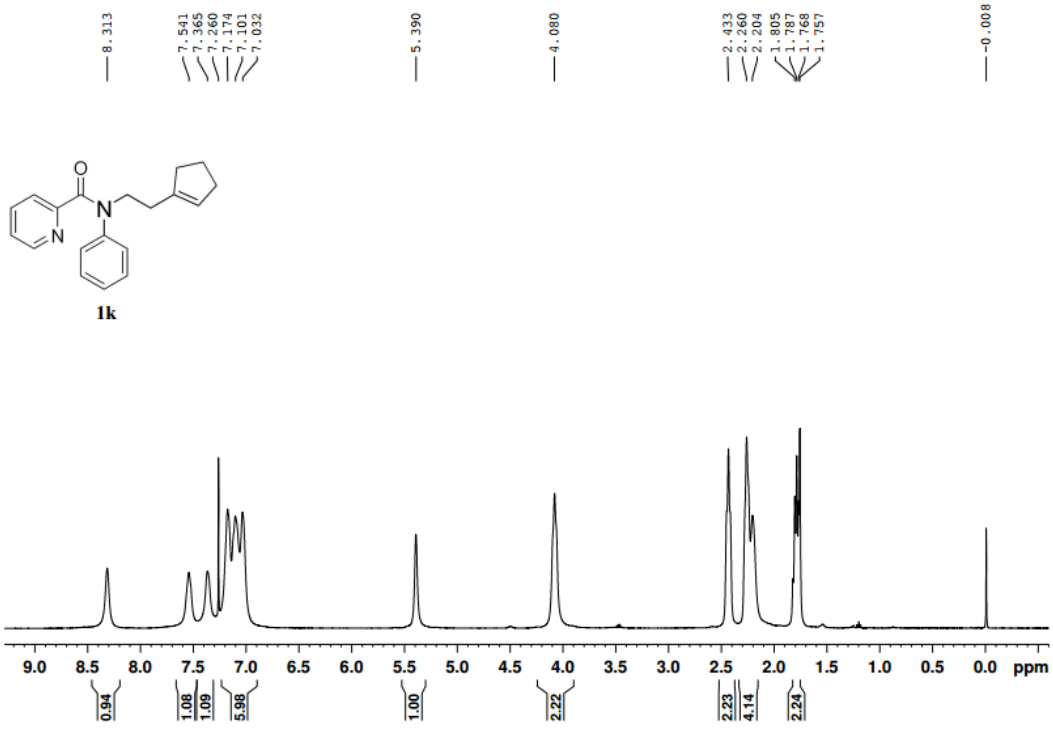
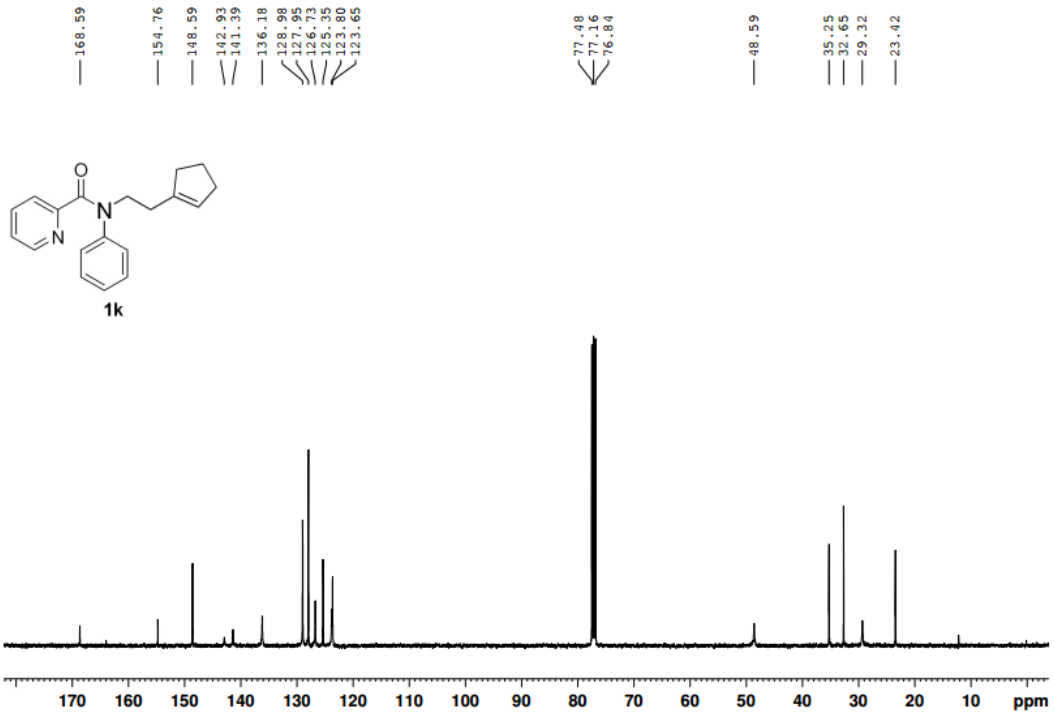
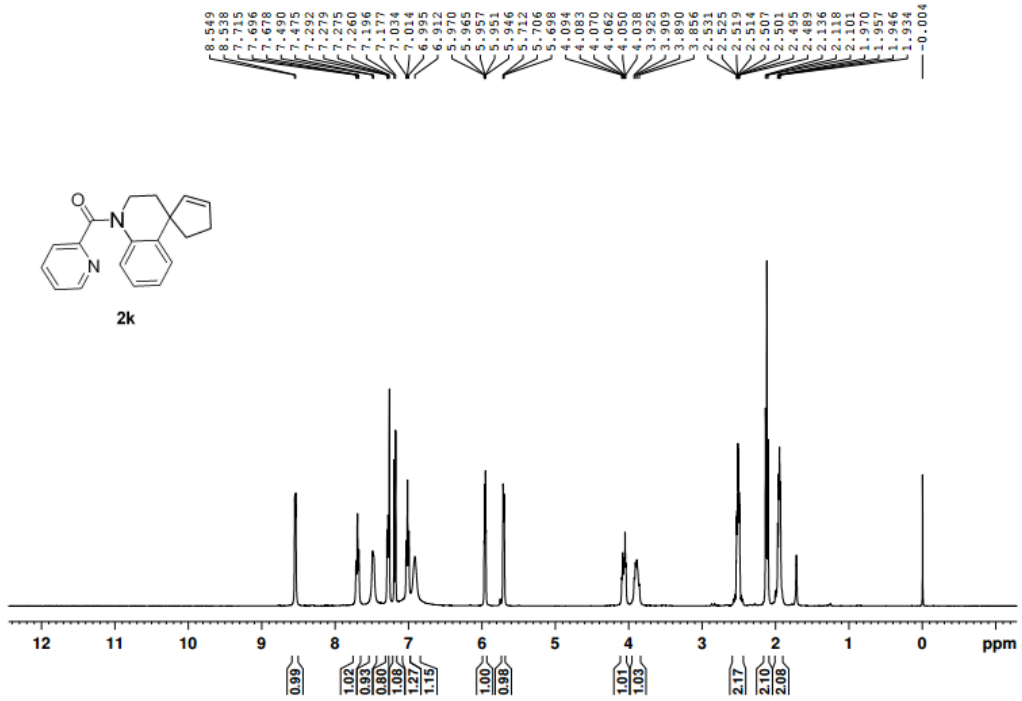
1.870
1.857
1.711
1.514
1.507
1.500
1.493
1.481
1.473
1.466
1.460
1.415
1.398
1.386
1.369
1.351
1.335
1.323
1.313
0.002
O
N
N
NO2
2j
10
9
8
7
6
5
4
3
2
1
ppm
1.00
0.98
1.13
1.05
1.28
1.07
1.15
1.09
1.08
1.21
1.12
1.39
2.35
1.39
4.43

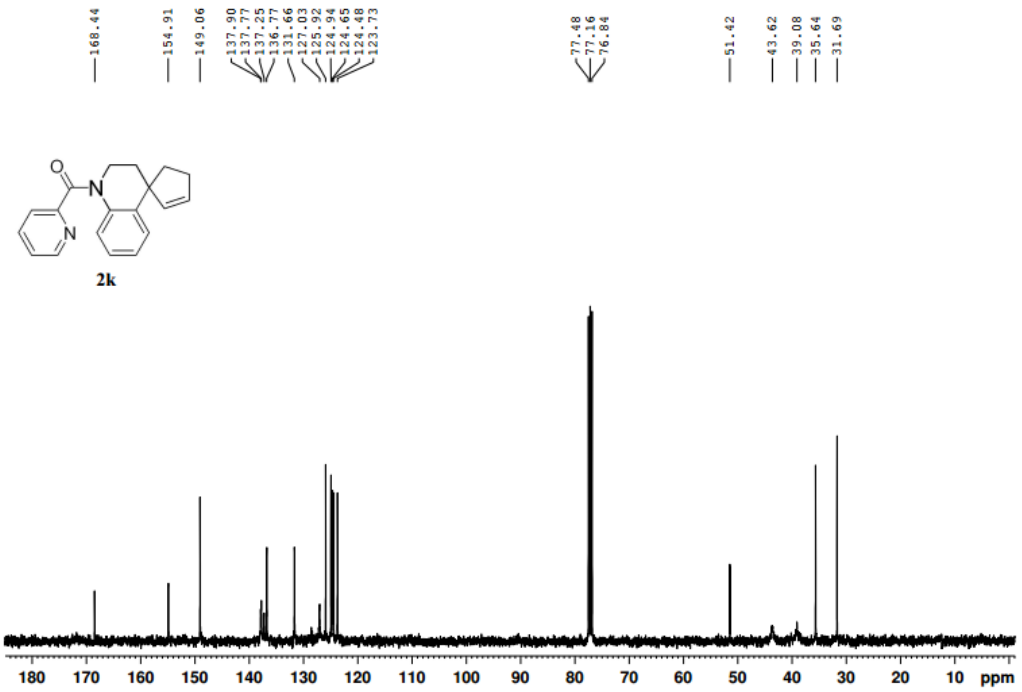

168.82
154.20
148.41
144.13
143.99
138.14
136.85
132.12
129.97
128.30
128.06
127.82
125.01
124.99
124.61
123.64
121.40
42.93
38.73
35.36
32.95
25.08
18.94
O
N
N
NO2
2j
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


169.12
153.58
148.89
143.76
143.52
138.48
137.23
132.06
130.19
125.32
124.94
124.21
123.81
121.40
77.48
77.16
76.84
43.10
38.69
35.28
33.53
25.07
18.72
O
N
N
NO2
2j
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


8.313
7.541
7.365
7.260
7.174
7.101
7.032
5.390
4.080
2.433
2.260
2.204
1.805
1.787
1.768
1.757
-0.008
O
N
N
1k
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 0.0 ppm
0.94
1.08
1.09
5.98
1.00
2.22
2.23
4.14
2.24


168.59
154.76
148.59
142.93
141.39
136.18
128.98
127.95
126.73
125.35
123.80
123.65
77.48
77.16
76.84
48.59
35.25
32.65
29.32
23.42
1k
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


8.549
8.538
7.715
7.696
7.678
7.490
7.475
7.292
7.279
7.275
7.260
7.196
7.177
7.034
7.014
6.995
6.912
5.970
5.965
5.957
5.951
5.946
5.712
5.706
5.698
4.094
4.083
4.070
4.062
4.050
4.038
3.925
3.909
3.890
3.856
2.531
2.525
2.519
2.514
2.507
2.501
2.495
2.489
2.136
2.118
2.101
1.970
1.957
1.946
1.934
-0.004
2k
12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.99
1.02
0.93
0.80
1.08
1.27
1.15
1.00
0.98
1.01
1.03
2.17
2.10
2.08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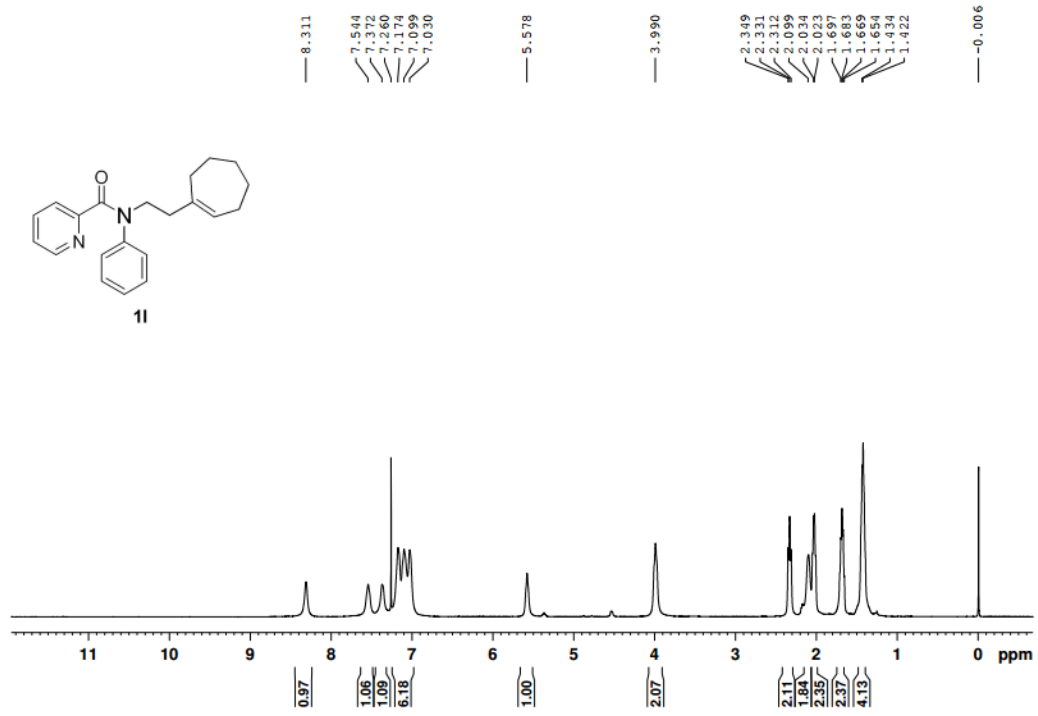
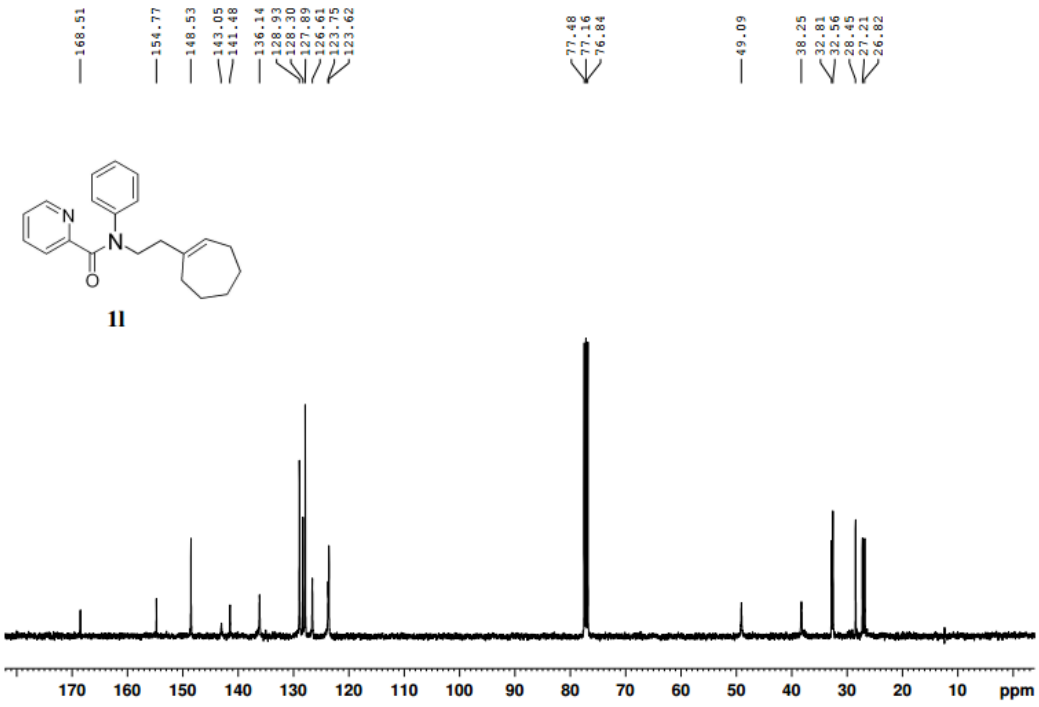
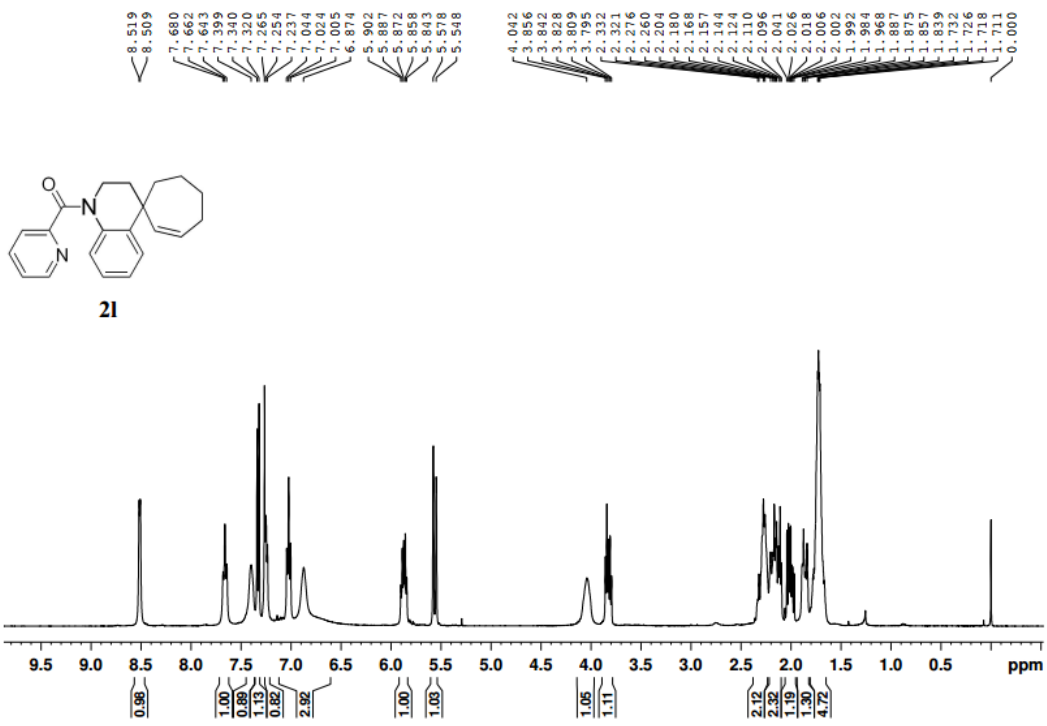
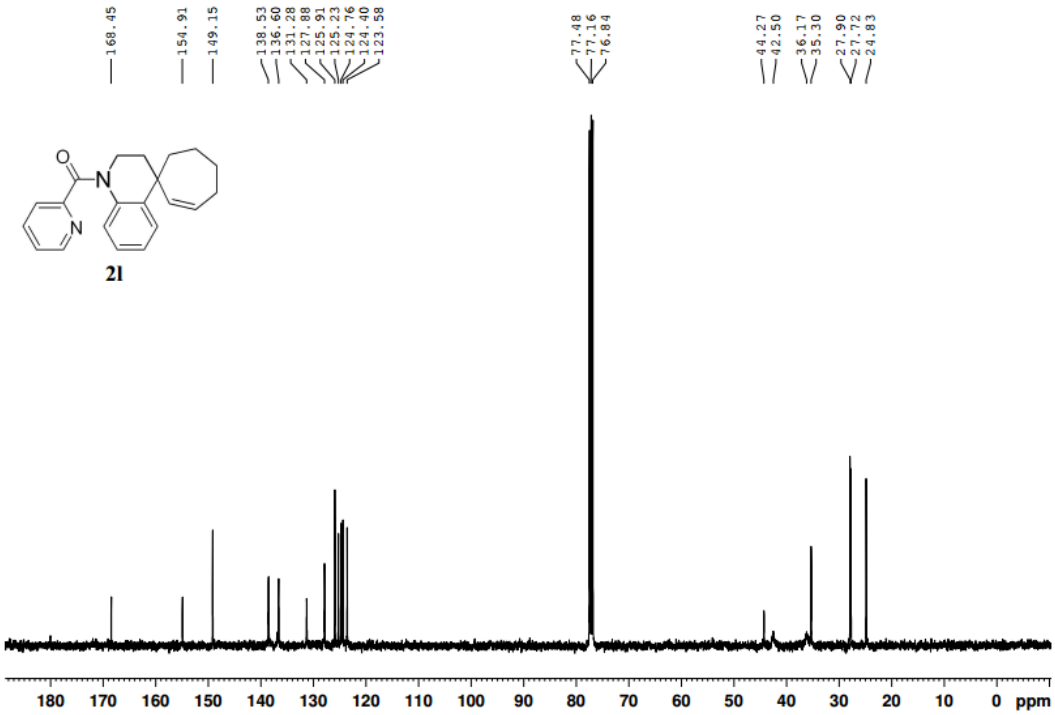
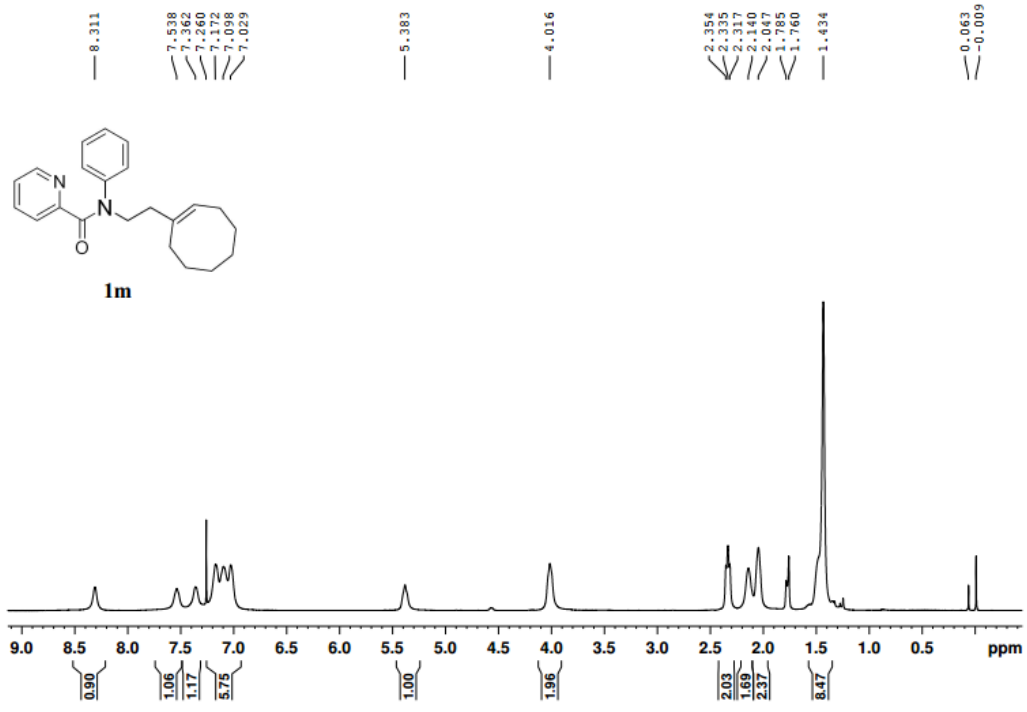
154.91
149.06
137.90
137.77
137.25
136.77
131.66
127.03
125.92
124.94
124.65
124.48
123.73
77.48
77.16
76.84
51.42
43.62
39.08
35.64
31.69
O
N
N
2k
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

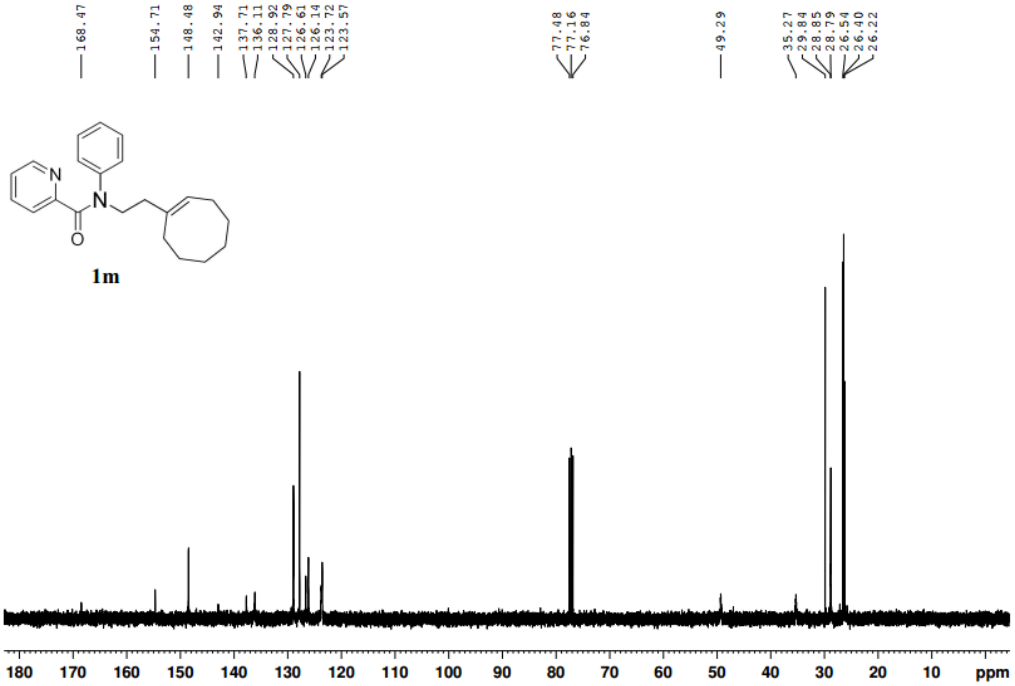

8.311
7.544
7.372
7.260
7.174
7.099
7.030
5.578
3.990
2.349
2.331
2.312
2.099
2.034
2.023
1.697
1.683
1.669
1.654
1.434
1.422
-0.006
O
N
N
1l
11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.97
1.06
1.09
6.18
1.00
2.07
2.11
1.84
2.35
2.37
4.13


168.51
154.77
148.53
143.05
141.48
136.14
128.93
128.30
127.89
126.61
123.75
123.62
77.48
77.16
76.84
49.09
38.25
32.81
32.56
28.45
27.21
26.82
1l
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

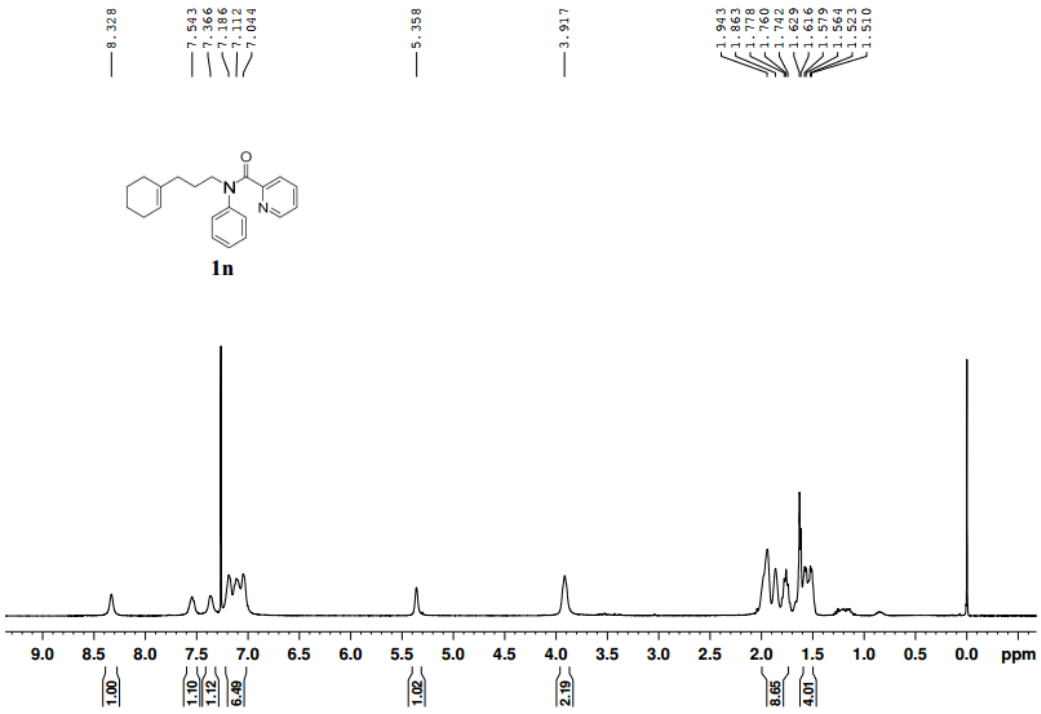

8.519
8.509
7.680
7.662
7.643
7.399
7.340
7.320
7.265
7.254
7.237
7.044
7.024
7.005
6.874
5.902
5.887
5.872
5.858
5.843
5.578
5.548
4.042
3.856
3.842
3.828
3.809
3.795
2.332
2.321
2.276
2.260
2.204
2.180
2.168
2.157
2.144
2.124
2.110
2.096
2.041
2.026
2.018
2.006
2.002
1.992
1.984
1.968
1.887
1.875
1.857
1.839
1.732
1.726
1.718
1.711
0.000
2l
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 ppm
0.98
1.00
0.88
1.13
0.82
2.92
1.00
1.03
1.05
1.11
2.12
2.32
1.19
1.30
4.72


168.45
154.91
149.15
138.53
136.60
131.28
127.88
125.91
125.23
124.76
124.40
123.58
77.48
77.16
76.84
44.27
42.50
36.17
35.30
27.90
27.72
24.83
O
N
N
2l
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

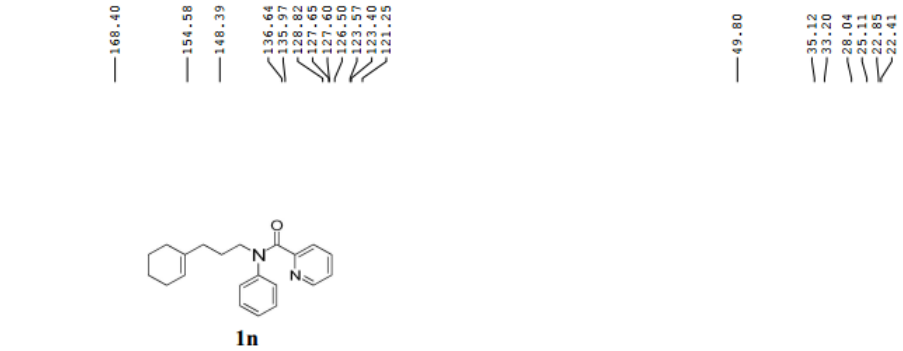

8.311
7.538
7.362
7.260
7.172
7.098
7.029
5.383
4.016
2.354
2.335
2.317
2.140
2.047
1.785
1.760
1.434
0.063
-0.009
N
N
O
1m
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.90
1.06
1.17
5.75
1.00
1.96
2.03
1.69
2.37
8.47


168.47
154.71
148.48
142.94
137.71
136.11
128.92
127.79
126.61
126.14
123.72
123.57
77.48
77.16
76.84
49.29
35.27
29.84
28.85
28.79
26.54
26.40
26.22
N
N
O
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

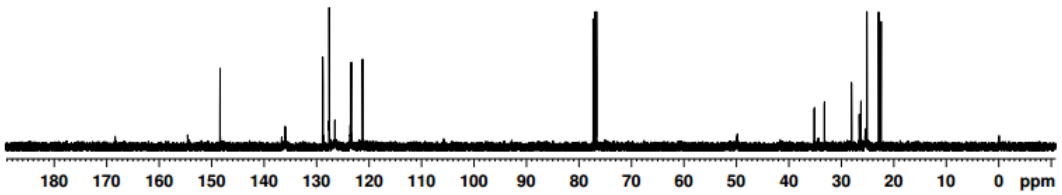
1m

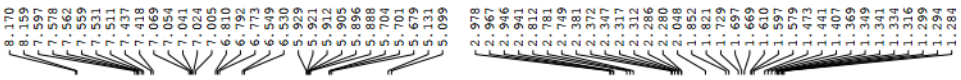

8.328
7.543
7.366
7.186
7.112
7.044
5.358
3.917
1.943
1.863
1.778
1.760
1.742
1.629
1.616
1.579
1.564
1.523
1.510
O
N
N
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
1.10
1.12
6.49
1.02
2.19
8.65
4.01

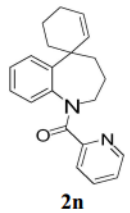
1n


168.40
154.58
148.39
136.64
135.97
128.82
127.65
127.60
126.50
123.57
123.40
121.25
49.80
35.12
33.20
28.04
25.11
22.85
22.41
O
N
N

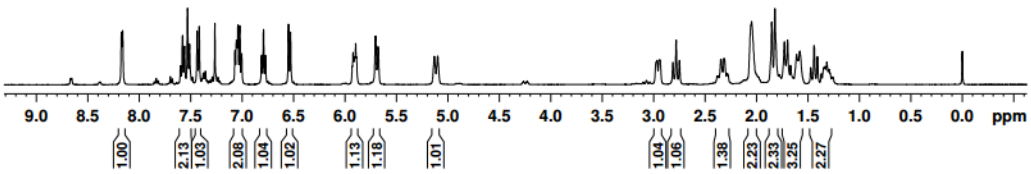
1n

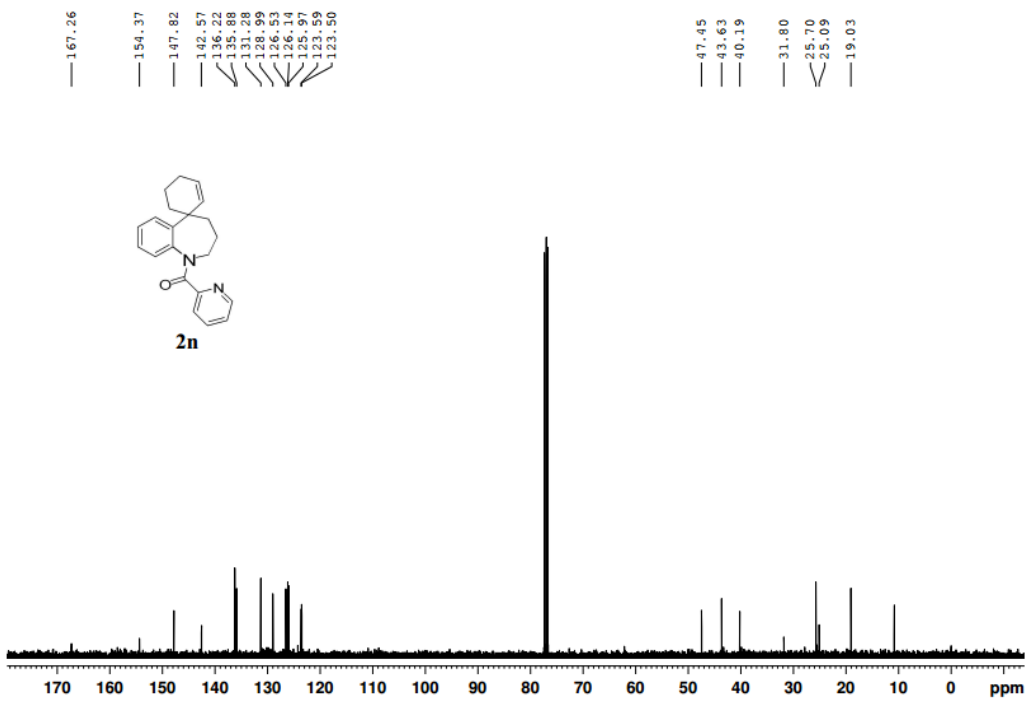

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

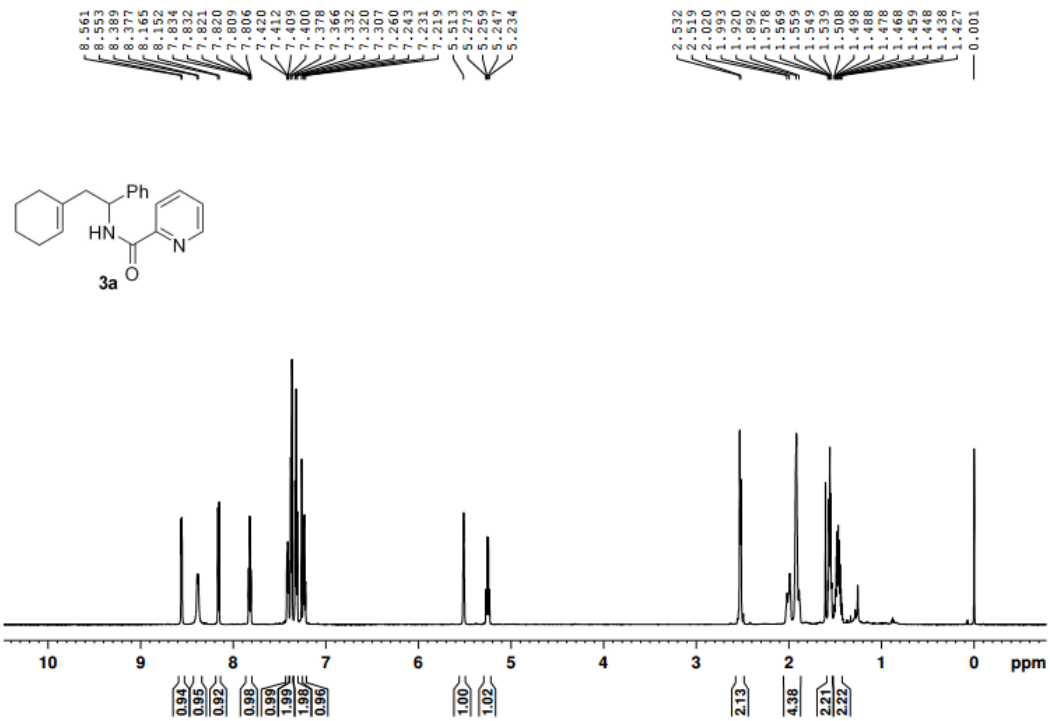

8.170
8.159
7.597
7.578
7.562
7.559
7.531
7.511
7.437
7.418
7.069
7.054
7.041
7.024
7.005
6.810
6.792
6.773
6.549
6.530
5.929
5.921
5.912
5.905
5.896
5.888
5.704
5.701
5.679
5.131
5.099
2.978
2.967
2.946
2.941
2.812
2.781
2.749
2.381
2.372
2.347
2.317
2.312
2.286
2.280
2.048
1.852
1.821
1.729
1.697
1.669
1.610
1.597
1.579
1.473
1.441
1.407
1.369
1.349
1.341
1.334
1.316
1.299
1.294
1.284

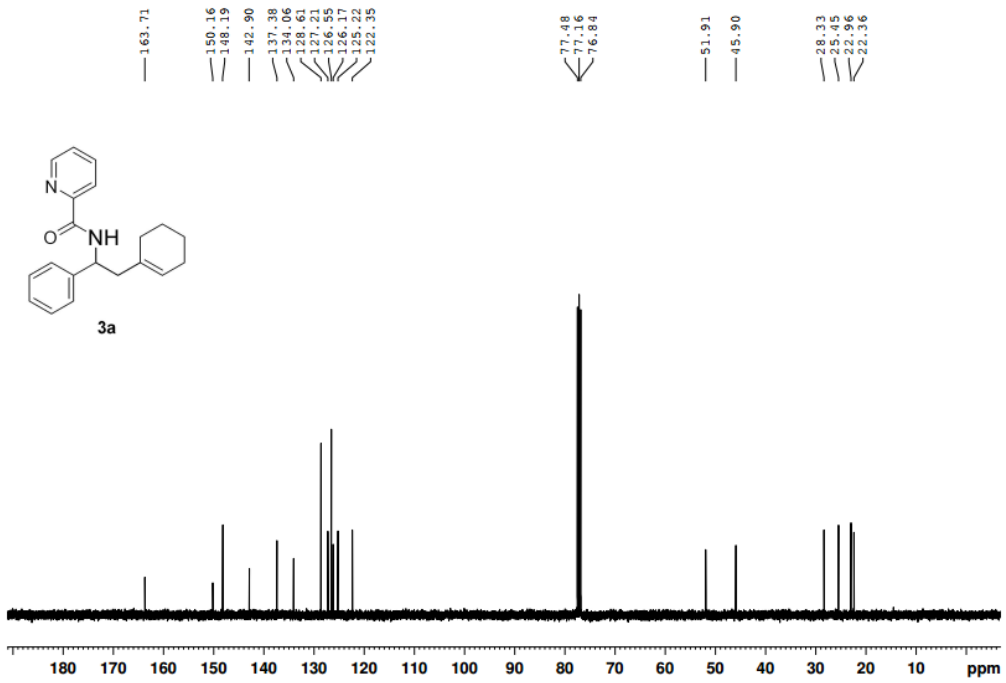

N
O
N

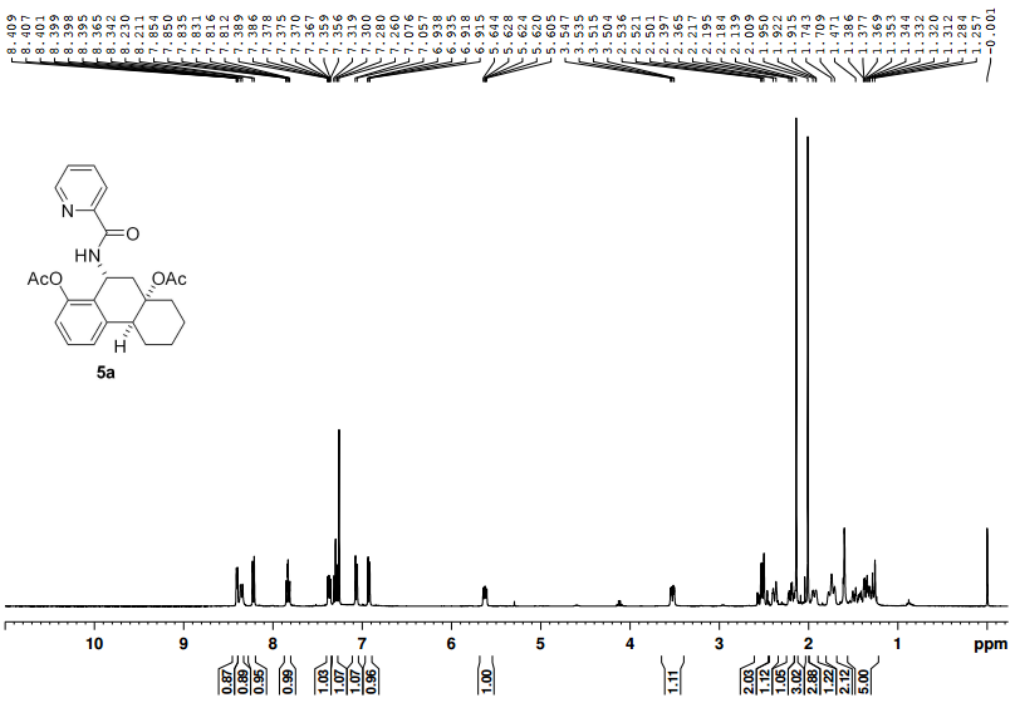
2n

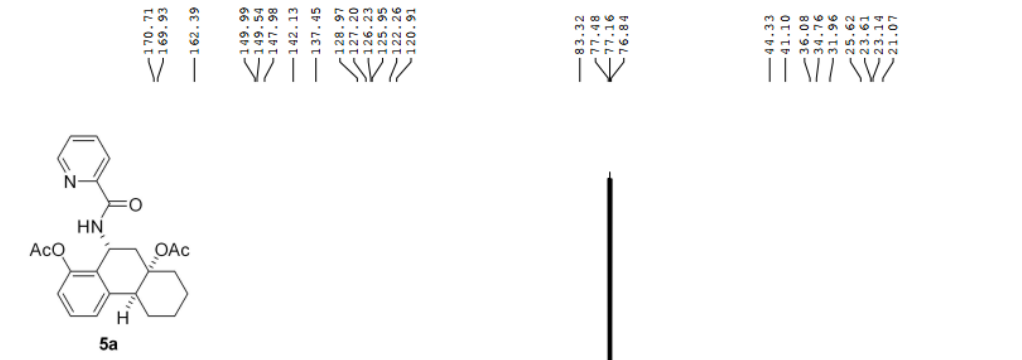

9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00
2.13
1.03
2.08
1.04
1.02
1.13
1.18
1.01
1.04
1.06
1.38
2.23
2.33
3.25
2.27

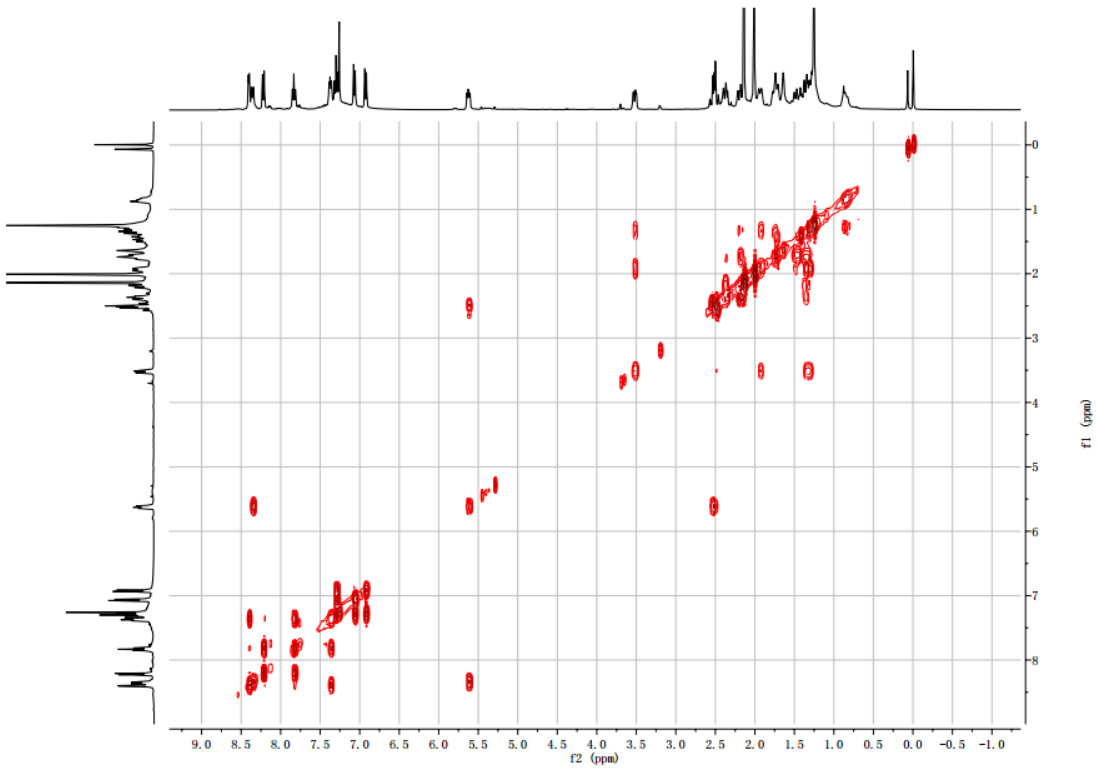

167.26
154.37
147.82
142.57
136.22
135.88
131.28
128.99
126.53
126.14
125.97
123.59
123.50
47.45
43.63
40.19
31.80
25.70
25.09
19.03
2n
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.561
8.553
8.389
8.377
8.165
8.152
7.834
7.832
7.821
7.820
7.809
7.806
7.420
7.412
7.409
7.400
7.378
7.366
7.332
7.320
7.307
7.260
7.243
7.231
7.219
5.513
5.273
5.259
5.247
5.234
2.532
2.519
2.020
1.993
1.920
1.892
1.578
1.569
1.559
1.549
1.539
1.508
1.498
1.488
1.478
1.468
1.459
1.448
1.438
1.427
0.001
Ph
HN
N
O
3a
10 9 8 7 6 5 4 3 2 1 0 ppm
0.94
0.95
0.92
0.98
0.99
1.99
1.98
0.96
1.00
1.02
2.13
4.38
2.21
2.22

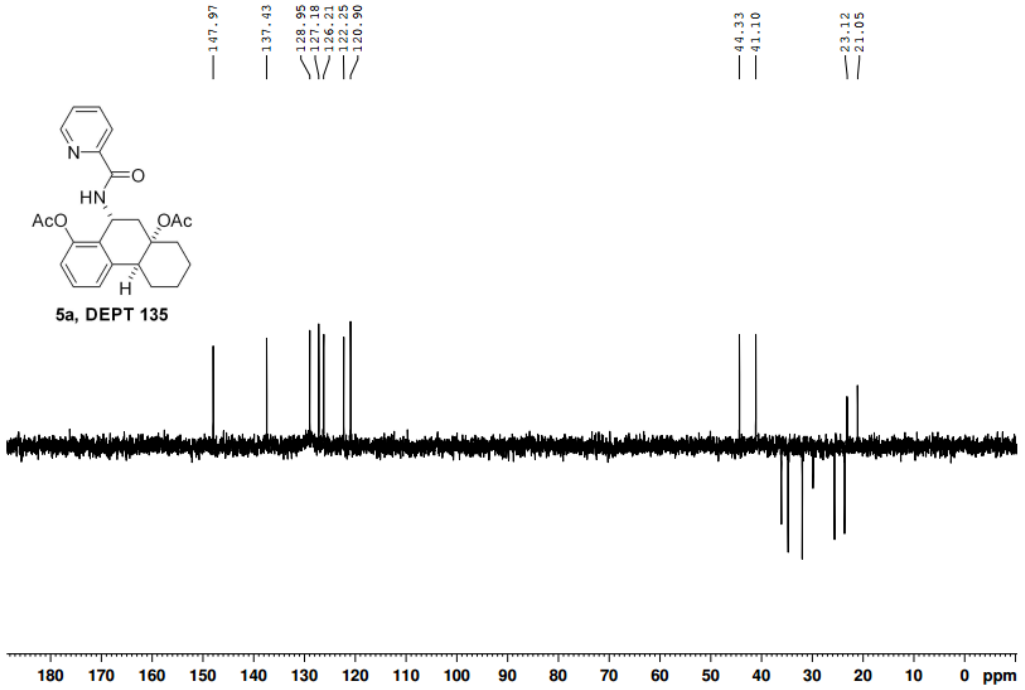

163.71
150.16
148.19
142.90
137.38
134.06
128.61
127.21
126.55
126.17
125.22
122.35
77.48
77.16
76.84
51.91
45.90
28.33
25.45
22.96
22.36
N
O
NH
3a
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


8.409
8.407
8.401
8.399
8.398
8.395
8.365
8.342
8.230
8.211
7.854
7.850
7.835
7.831
7.816
7.812
7.389
7.386
7.378
7.375
7.370
7.367
7.359
7.356
7.319
7.300
7.280
7.260
7.076
7.057
6.938
6.935
6.918
6.915
5.644
5.628
5.624
5.620
5.605
3.547
3.535
3.515
3.504
2.536
2.521
2.501
2.397
2.365
2.217
2.195
2.184
2.139
2.009
1.950
1.922
1.915
1.743
1.709
1.471
1.386
1.377
1.369
1.353
1.344
1.332
1.320
1.312
1.284
1.257
-0.001
N
O
HN
AcO
OAc
H
5a
10 9 8 7 6 5 4 3 2 1 ppm
0.87
0.89
0.95
0.99
1.03
1.07
1.07
0.96
1.00
1.11
2.03
1.12
1.05
3.02
2.88
1.22
2.12
5.00

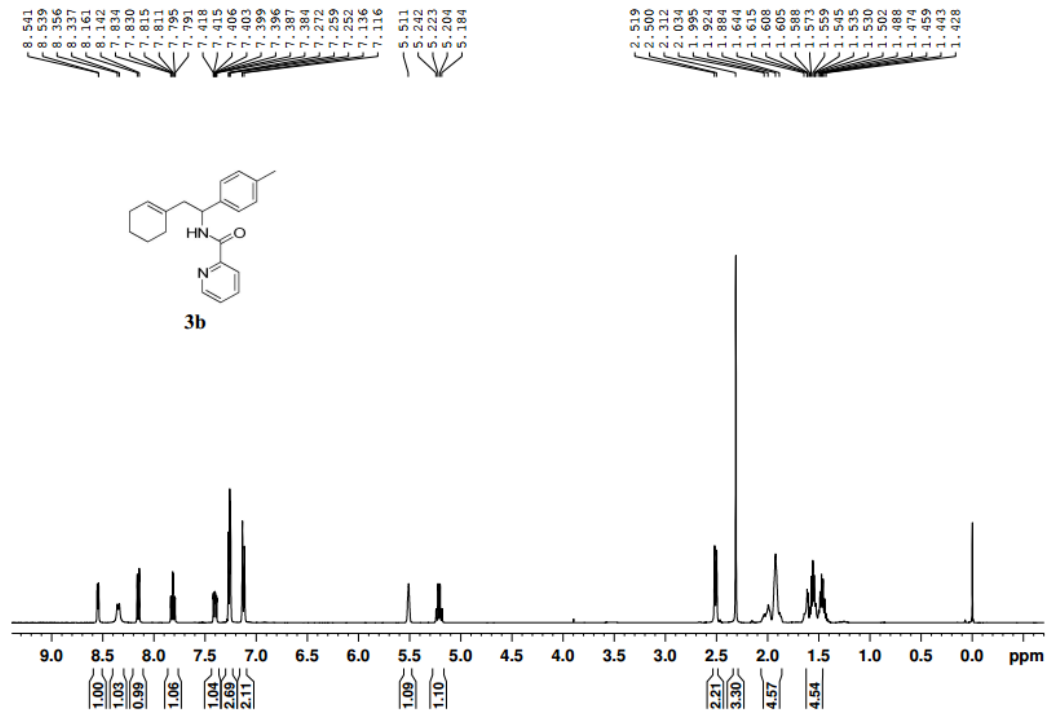




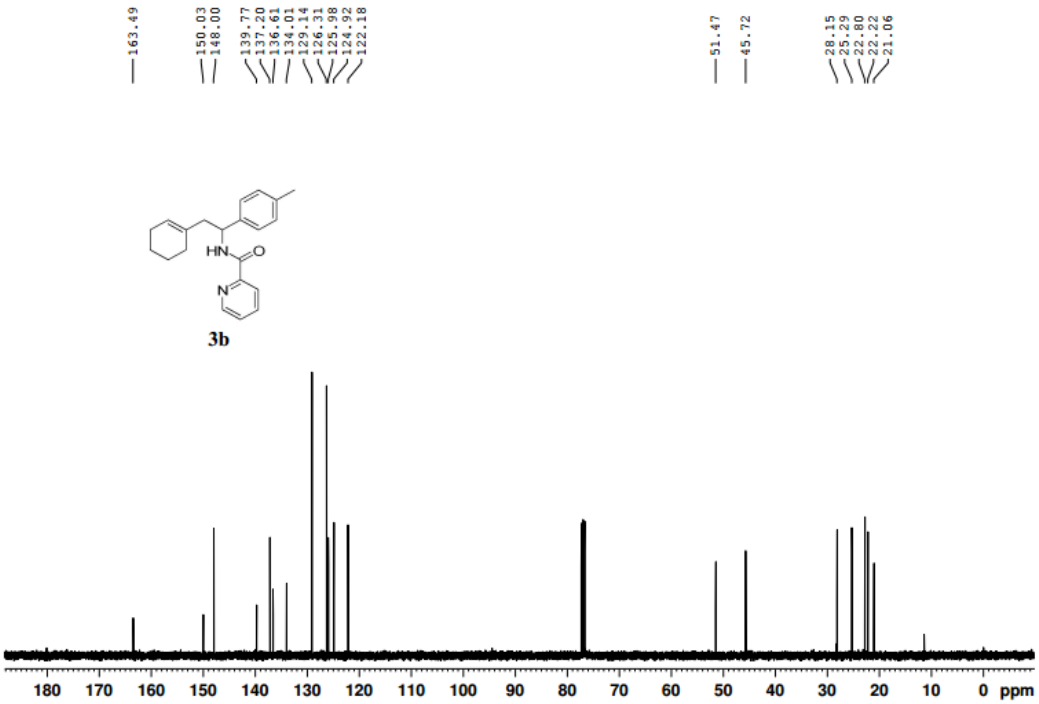
^{1}H-^{1}H COSY of compound 5a

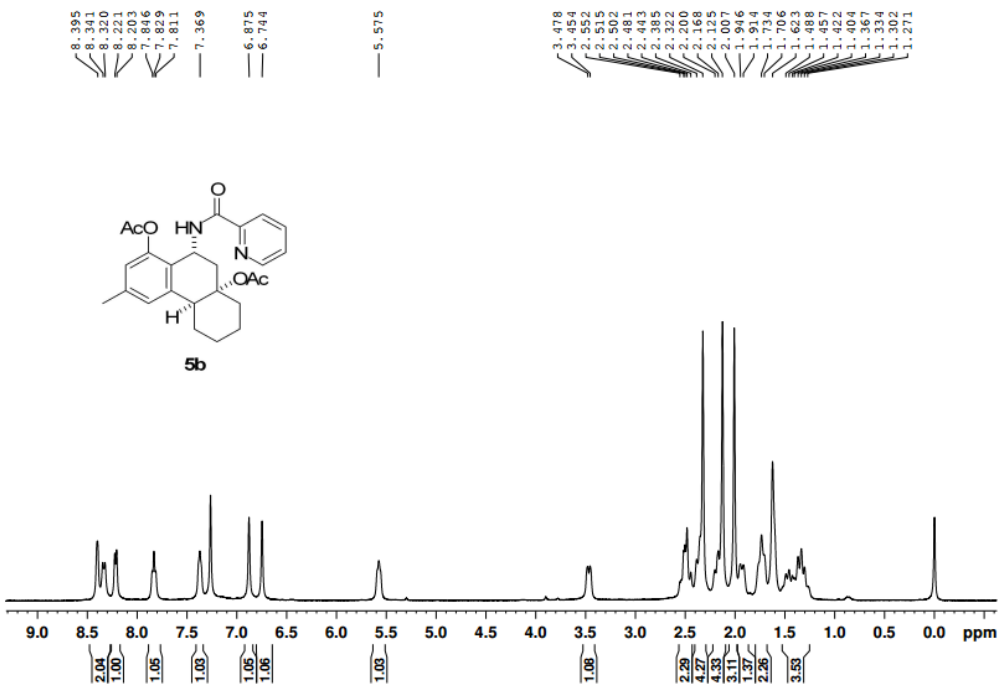


5a, DEPT 135



3b


163.49
150.03
148.00
139.77
137.20
136.61
134.01
129.14
126.31
125.98
124.92
122.18
51.47
45.72
28.15
25.29
22.80
22.22
21.06
HN
O
N
3b
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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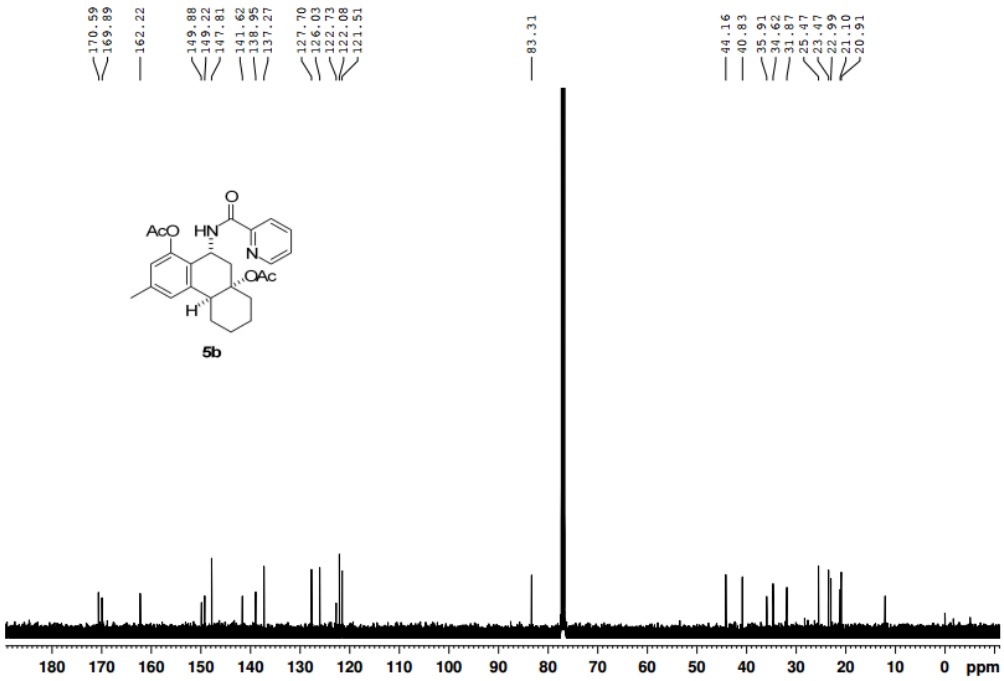
8.341
8.320
8.221
8.203
7.846
7.829
7.811
7.369
6.875
6.744
5.575
3.478
3.454
2.552
2.515
2.502
2.481
2.443
2.385
2.322
2.200
2.168
2.125
2.007
1.946
1.914
1.734
1.706
1.623
1.488
1.457
1.422
1.404
1.367
1.334
1.302
1.271
AcO
HN
O
N
OAc
H
5b
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.04
1.00
1.05
1.03
1.05
1.06
1.03
1.08
2.29
4.27
4.33
3.11
1.37
2.26
3.53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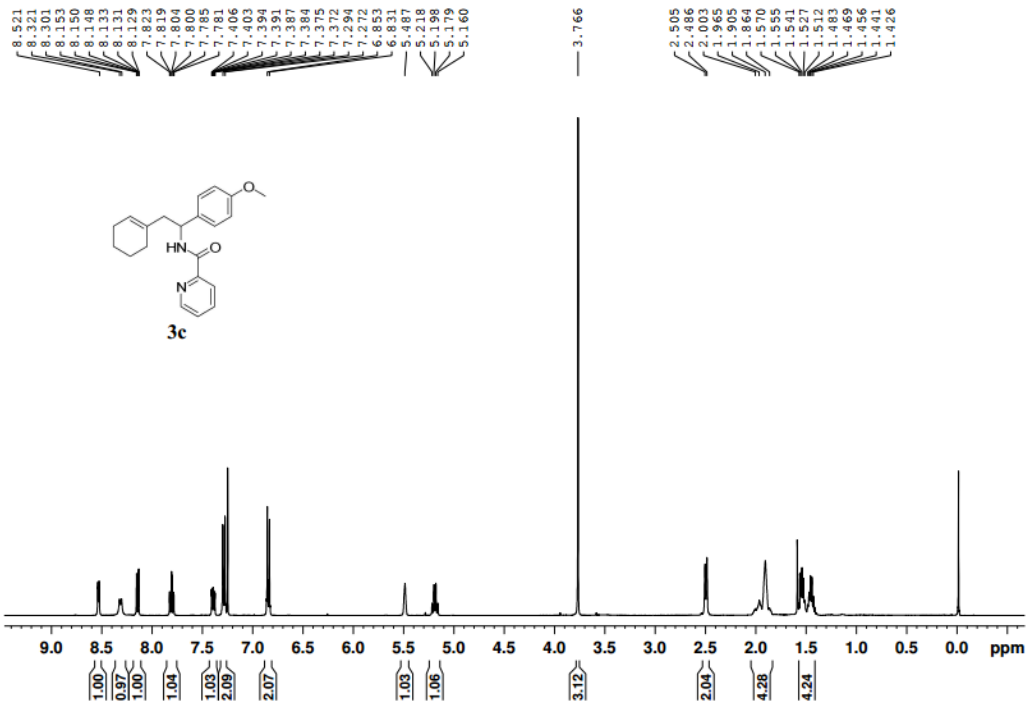
169.89
162.22
149.88
149.22
147.81
141.62
138.95
137.27
127.70
126.03
122.73
122.08
121.51
83.31
44.16
40.83
35.91
34.62
31.87
25.47
23.47
22.99
21.10
20.91
AcO
HN
O
N
OAc
H
5b
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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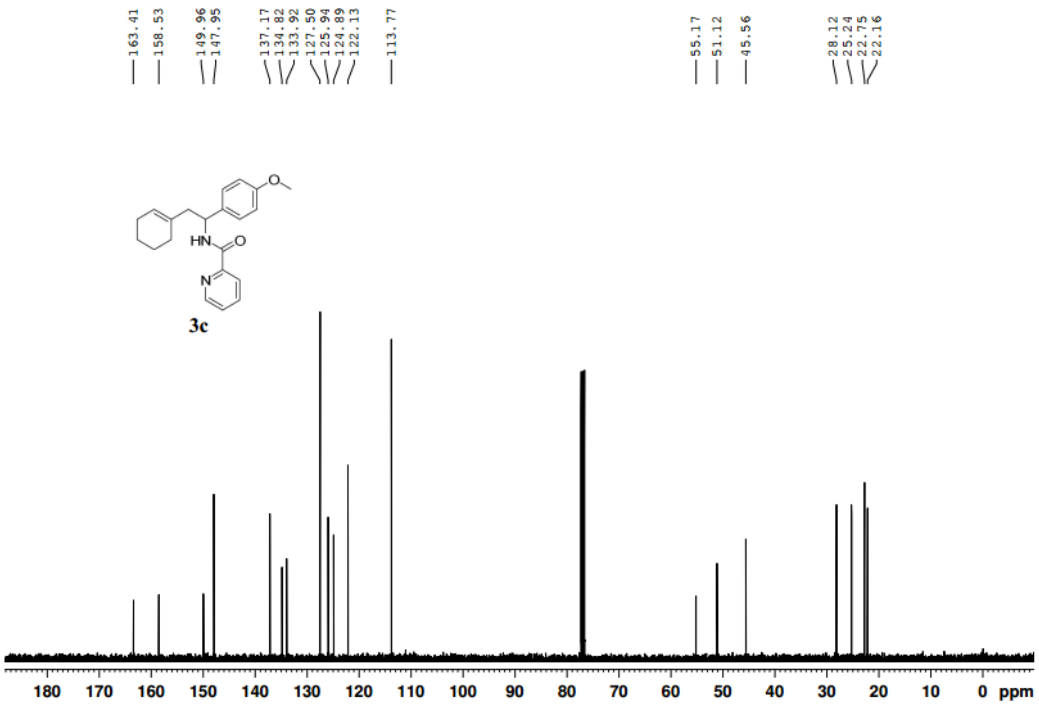
8.321
8.301
8.153
8.150
8.148
8.133
8.131
8.129
7.823
7.819
7.804
7.800
7.785
7.781
7.406
7.403
7.394
7.391
7.387
7.384
7.375
7.372
7.294
7.272
6.853
6.831
5.487
5.218
5.198
5.179
5.160
3.766
2.505
2.486
2.003
1.965
1.905
1.864
1.570
1.555
1.541
1.527
1.512
1.483
1.469
1.456
1.441
1.426
O
HN
O
N
3c
9.0 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 0.0 ppm
1.00
0.97
1.00
1.04
1.03
2.09
2.07
1.03
1.06
3.12
2.04
4.28
4.24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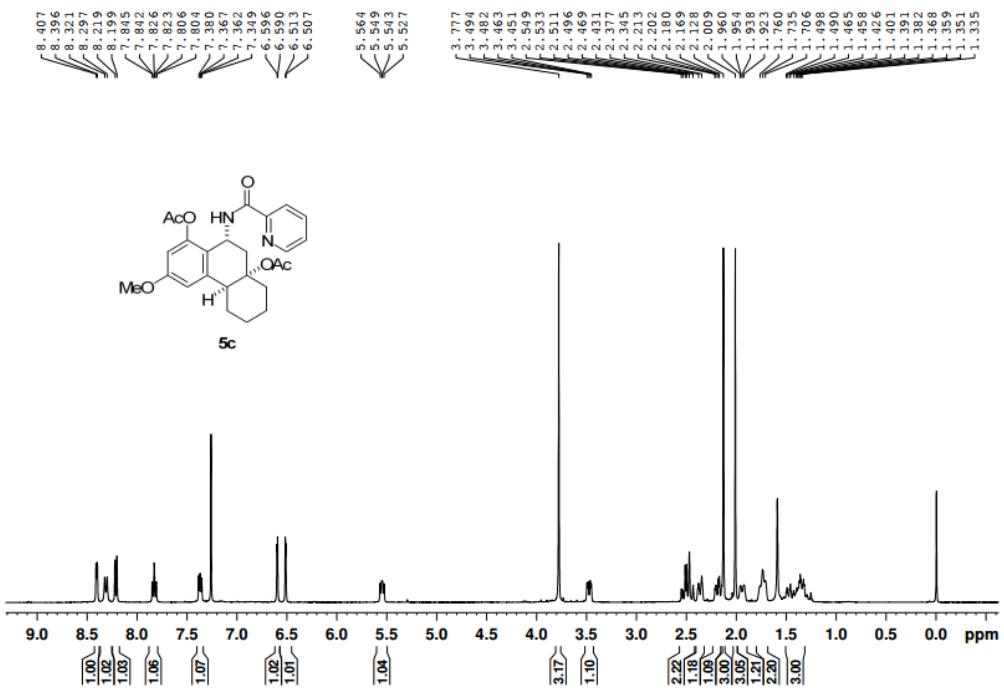
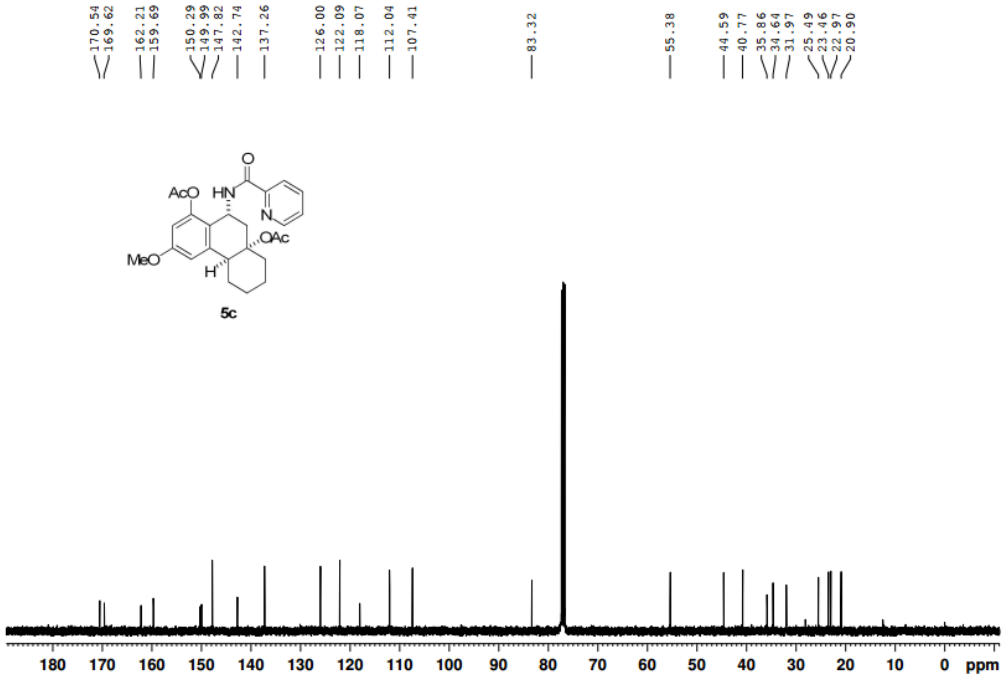
158.53
149.96
147.95
137.17
134.82
133.92
127.50
125.94
124.89
122.13
113.77
55.17
51.12
45.56
28.12
25.24
22.75
22.16
HN
O
N
O
3c
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.407
8.396
8.321
8.297
8.219
8.199
7.845
7.842
7.826
7.823
7.806
7.804
7.380
7.367
7.362
7.349
6.596
6.590
6.513
6.507
5.564
5.549
5.543
5.527
3.777
3.494
3.482
3.463
3.451
2.549
2.533
2.511
2.496
2.469
2.431
2.377
2.345
2.213
2.202
2.180
2.169
2.128
2.009
1.960
1.954
1.938
1.923
1.760
1.735
1.706
1.498
1.490
1.465
1.458
1.426
1.401
1.391
1.382
1.368
1.359
1.351
1.335
AcO
HN
O
N
OAc
MeO
H
5c
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 0.0 ppm
1.00
1.02
1.03
1.06
1.07
1.02
1.01
1.04
3.17
1.10
2.22
1.16
1.09
3.00
3.05
1.21
2.20
3.00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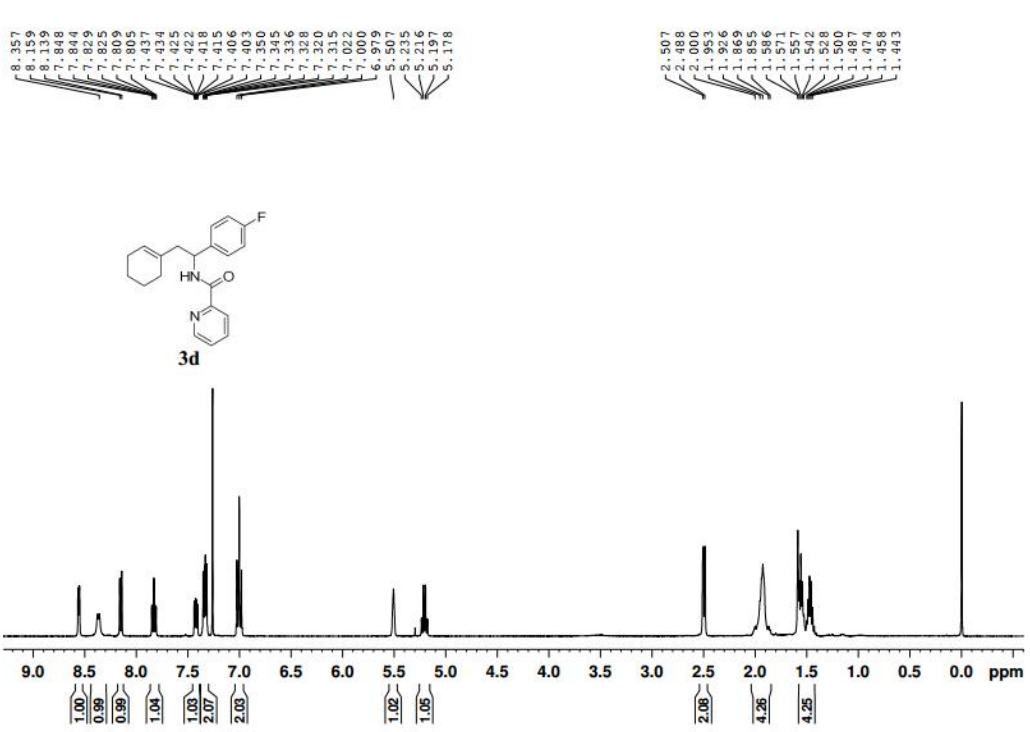
169.62
162.21
159.69
150.29
149.99
147.82
142.74
137.26
126.00
122.09
118.07
112.04
107.41
83.32
55.38
44.59
40.77
35.86
34.64
31.97
25.49
23.46
22.97
20.90
AcO
HN
O
N
OAc
MeO
H
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

5c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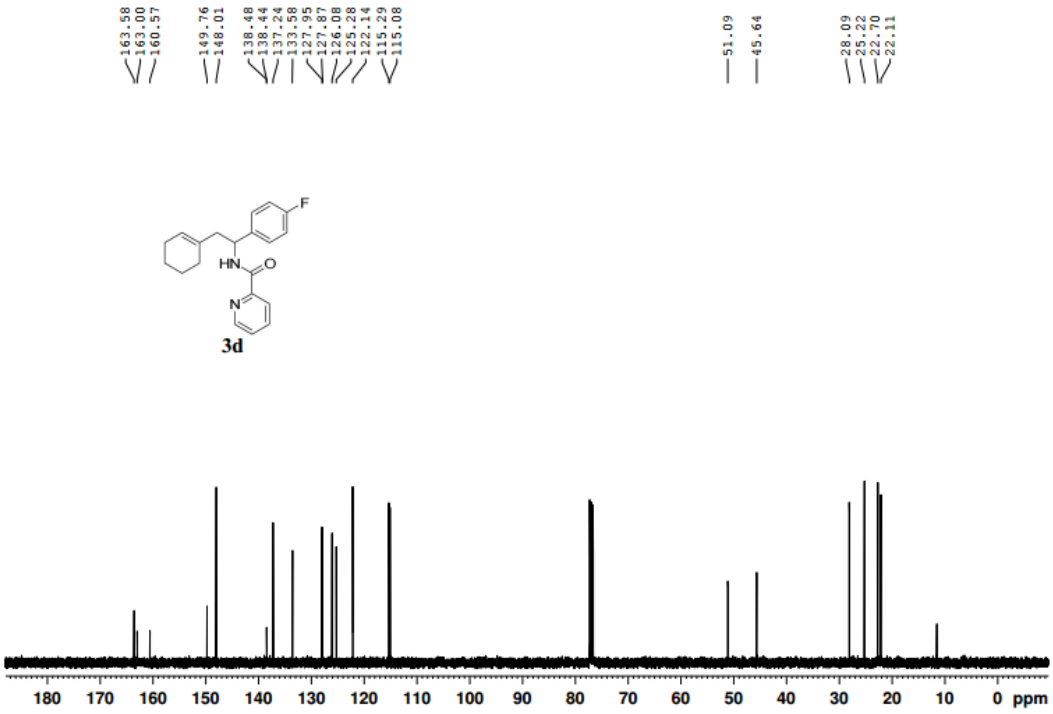
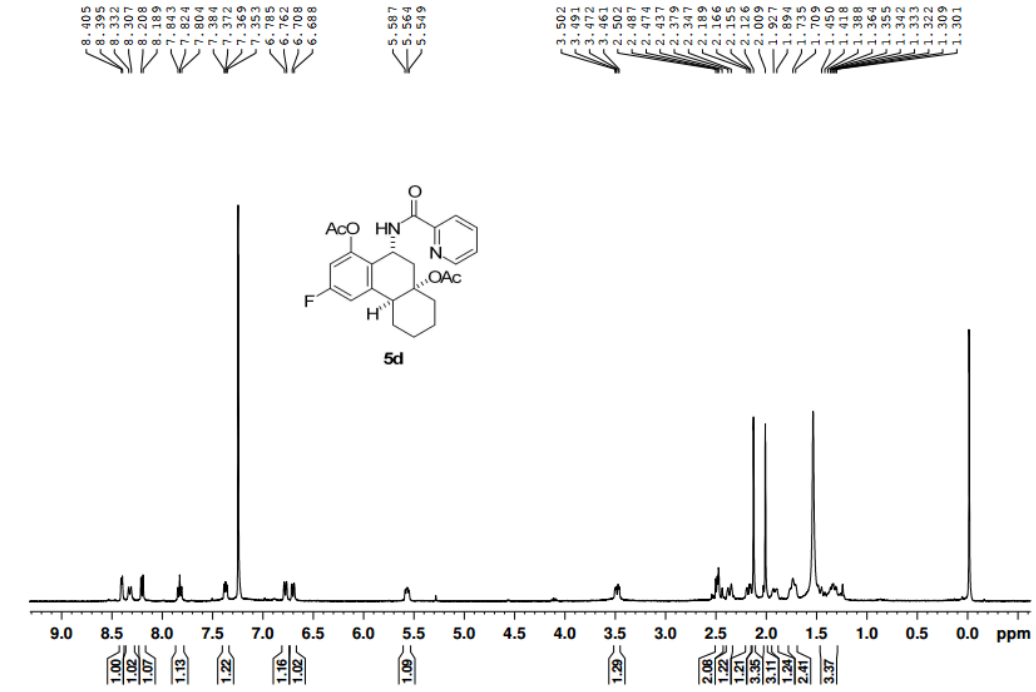
8.159
8.139
7.848
7.844
7.829
7.825
7.809
7.805
7.437
7.434
7.425
7.422
7.418
7.415
7.406
7.403
7.350
7.345
7.336
7.328
7.320
7.315
7.022
7.000
6.979
5.507
5.235
5.216
5.197
5.178
2.507
2.488
2.000
1.953
1.926
1.869
1.855
1.586
1.571
1.557
1.542
1.528
1.500
1.487
1.474
1.458
1.443
F
HN
O
N
9.0 8.5 8.0 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 0.0 ppm
1.00
0.99
0.99
1.04
1.03
2.07
2.03
1.02
1.05
2.08
4.26
4.25

3d


163.58
163.00
160.57
149.76
148.01
138.48
138.44
137.24
133.58
127.95
127.87
126.08
125.28
122.14
115.29
115.08
51.09
45.64
28.09
25.22
22.70
22.11
F
HN
O
N
3d
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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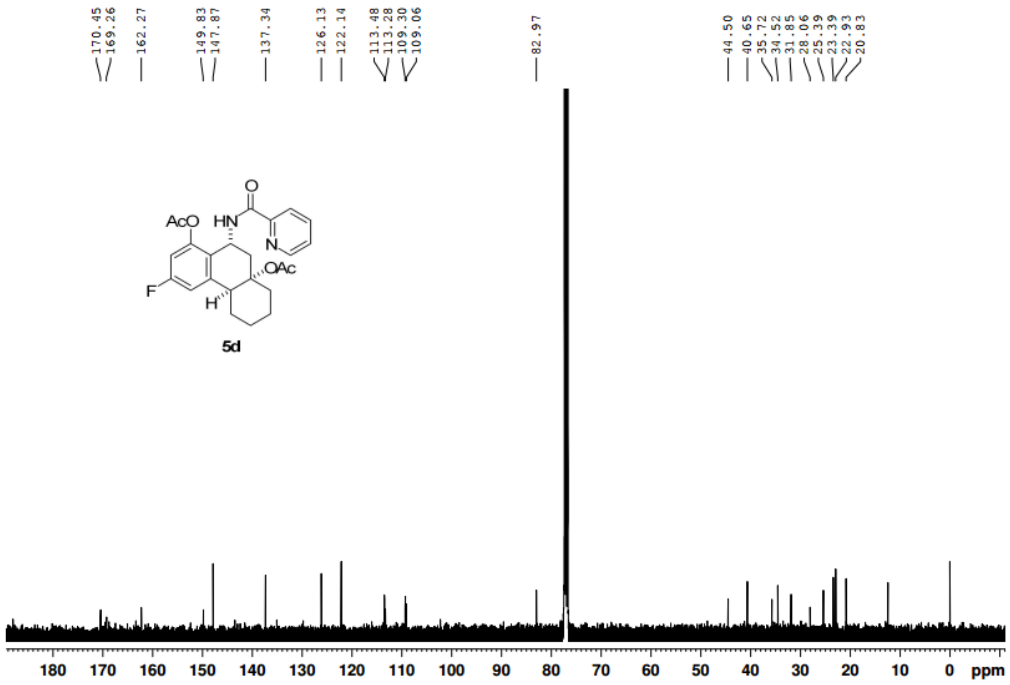
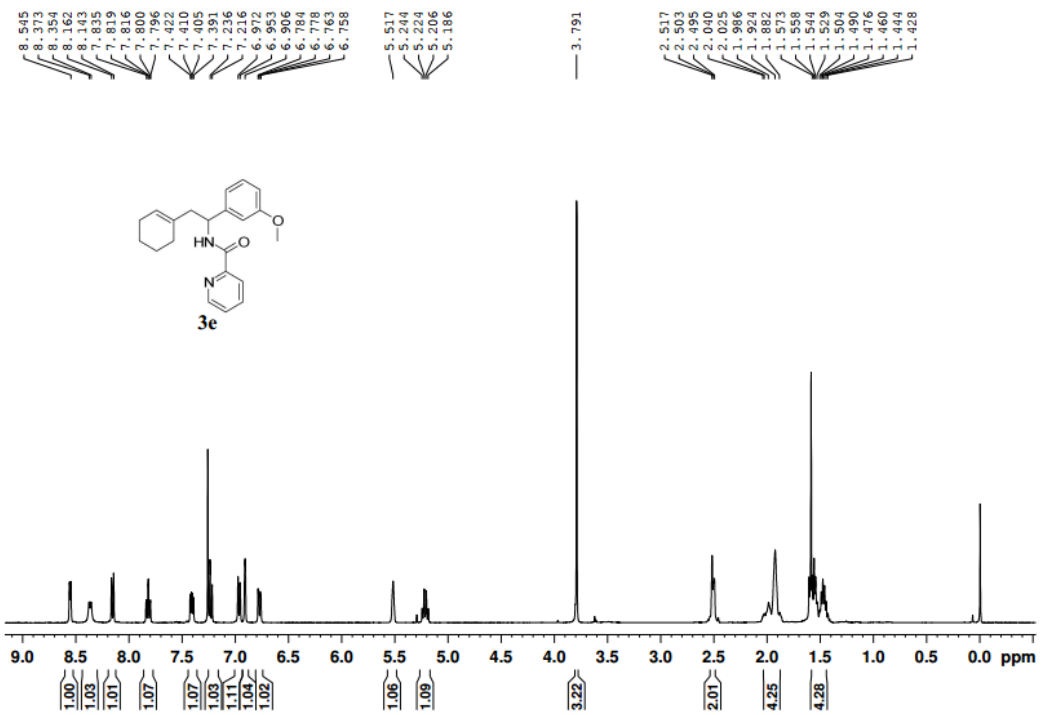
8.395
8.332
8.307
8.208
8.189
7.843
7.824
7.804
7.384
7.372
7.369
7.353
6.785
6.762
6.708
6.688
5.587
5.564
5.549
3.502
3.491
3.472
3.461
2.502
2.487
2.474
2.437
2.379
2.347
2.189
2.166
2.155
2.126
2.009
1.927
1.894
1.735
1.709
1.450
1.418
1.388
1.364
1.355
1.342
1.333
1.322
1.309
1.301
AcO
HN
O
N
OAc
F
H
5d
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 0.0 ppm
1.00
1.02
1.07
1.13
1.22
1.16
1.02
1.09
1.29
2.06
1.22
1.21
3.35
3.11
1.24
2.41
3.37


170.45
169.26
162.27
149.83
147.87
137.34
126.13
122.14
113.48
113.28
109.30
109.06
82.97
44.50
40.65
35.72
34.52
31.85
28.06
25.39
23.39
22.93
20.83
AcO
HN
O
N
OAc
F
H
5d
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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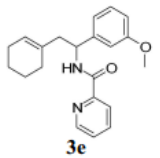
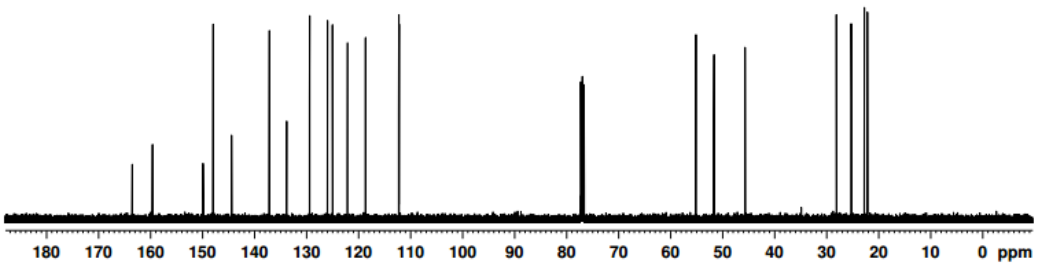
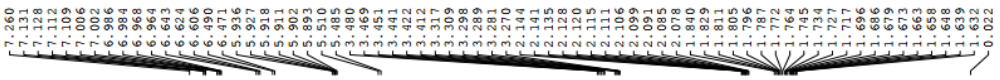
8.373
8.354
8.162
8.143
7.835
7.819
7.816
7.800
7.796
7.422
7.410
7.405
7.391
7.236
7.216
6.972
6.953
6.906
6.784
6.778
6.763
6.758
5.517
5.244
5.224
5.206
5.186
3.791
2.517
2.503
2.495
2.040
2.025
1.986
1.924
1.882
1.573
1.558
1.544
1.529
1.504
1.490
1.476
1.460
1.444
1.428
HN
O
N
O
3e
9.0 8.5 8.0 7.5 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 0.0 ppm
1.00
1.03
1.01
1.07
1.07
1.03
1.11
1.04
1.02
1.06
1.09
3.22
2.01
4.25
4.28

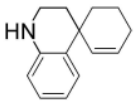

163.51
159.62
149.89
147.97
144.42
137.16
133.83
129.42
125.97
125.00
122.13
118.66
112.27
112.21
55.12
51.66
45.67
28.10
25.24
22.74
22.15


HN
O
N

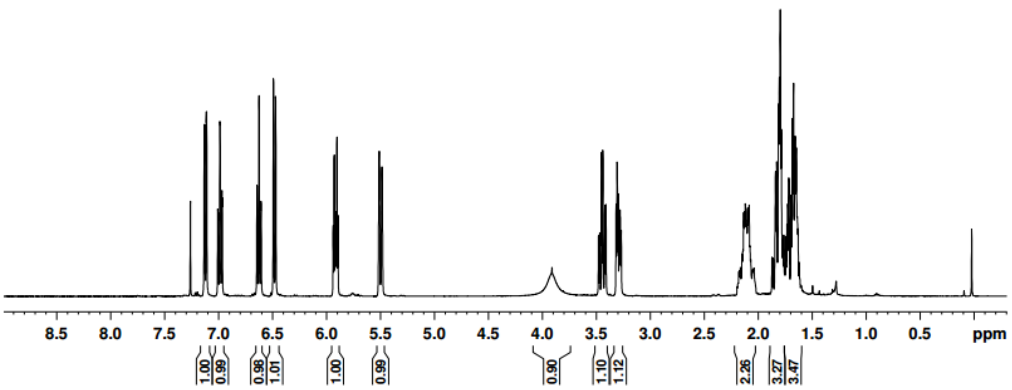
3e

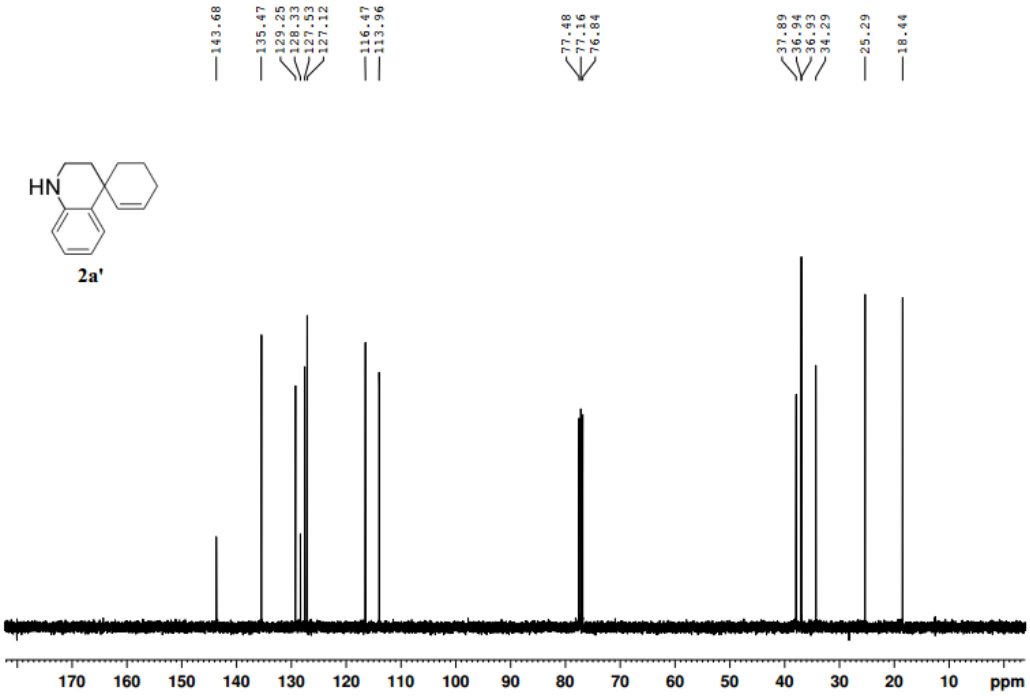

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

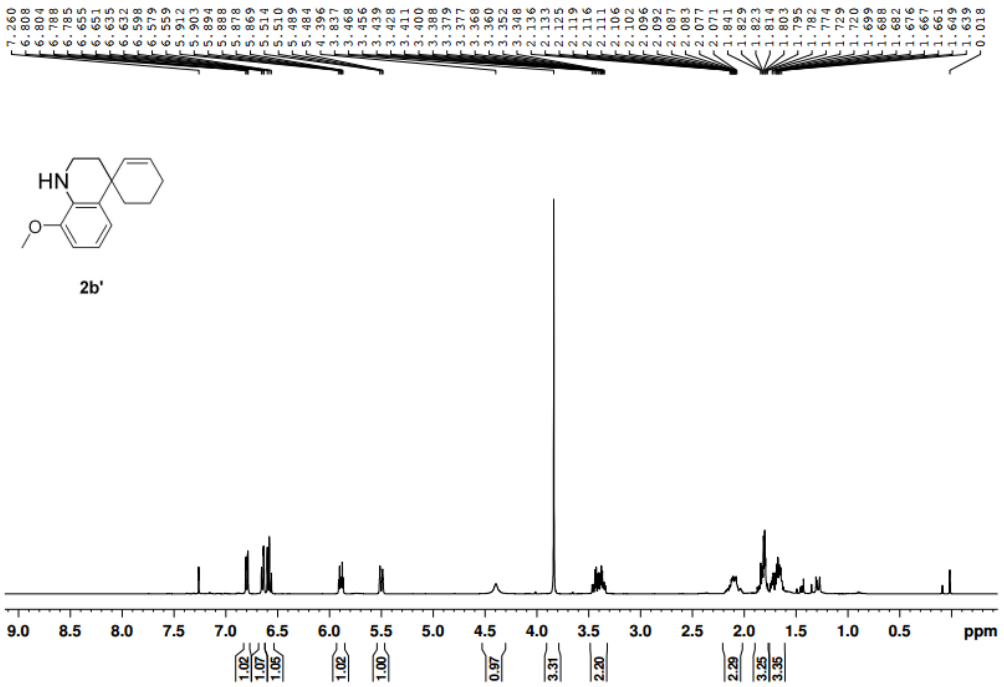

7.260
7.131
7.128
7.122
7.109
7.006
7.002
6.986
6.984
6.968
6.964
6.643
6.624
6.606
6.490
6.471
5.936
5.927
5.918
5.911
5.902
5.893
5.510
5.485
3.480
3.469
3.451
3.441
3.422
3.412
3.317
3.309
3.298
3.289
3.281
3.270
2.144
2.141
2.135
2.128
2.120
2.115
2.111
2.106
2.099
2.091
2.085
2.078
1.840
1.829
1.811
1.805
1.796
1.787
1.772
1.764
1.745
1.734
1.727
1.717
1.696
1.686
1.679
1.673
1.663
1.658
1.648
1.639
1.632
0.022

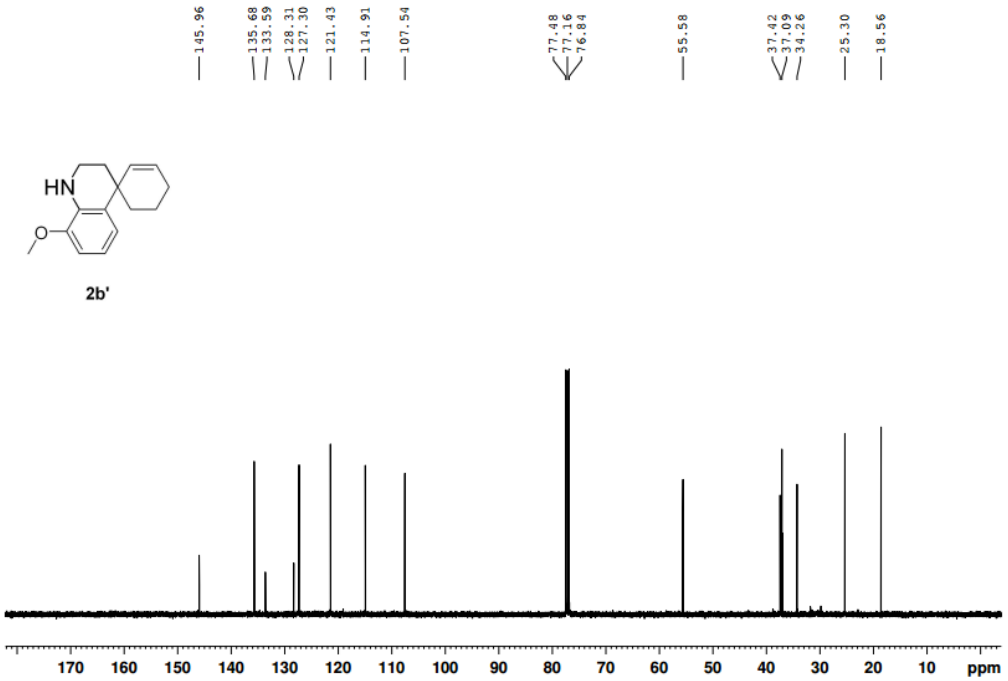

HN

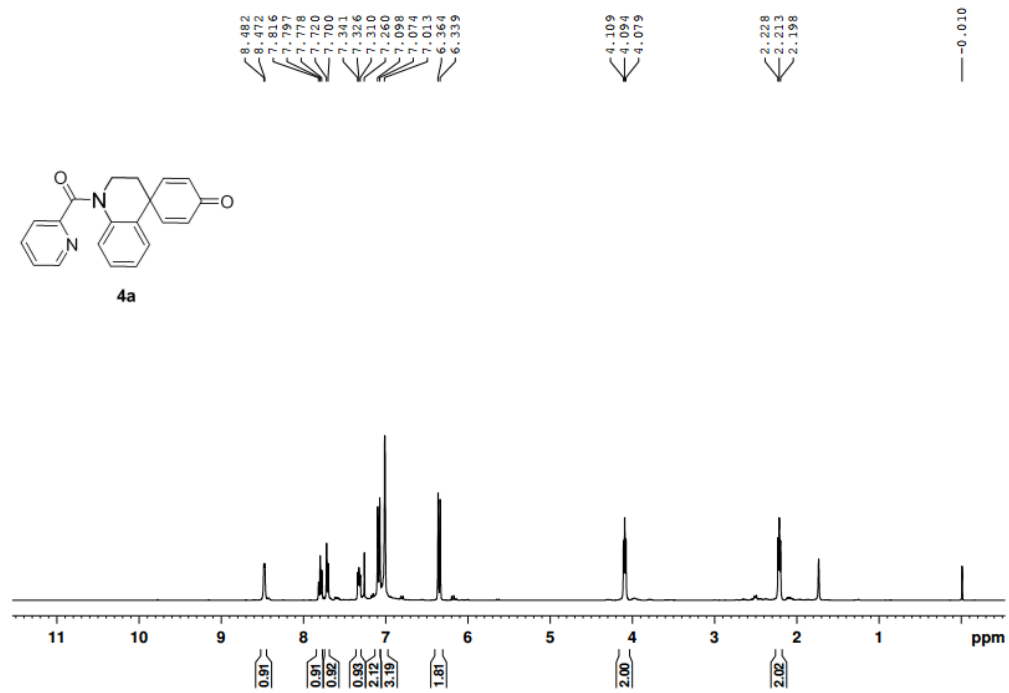
2a'

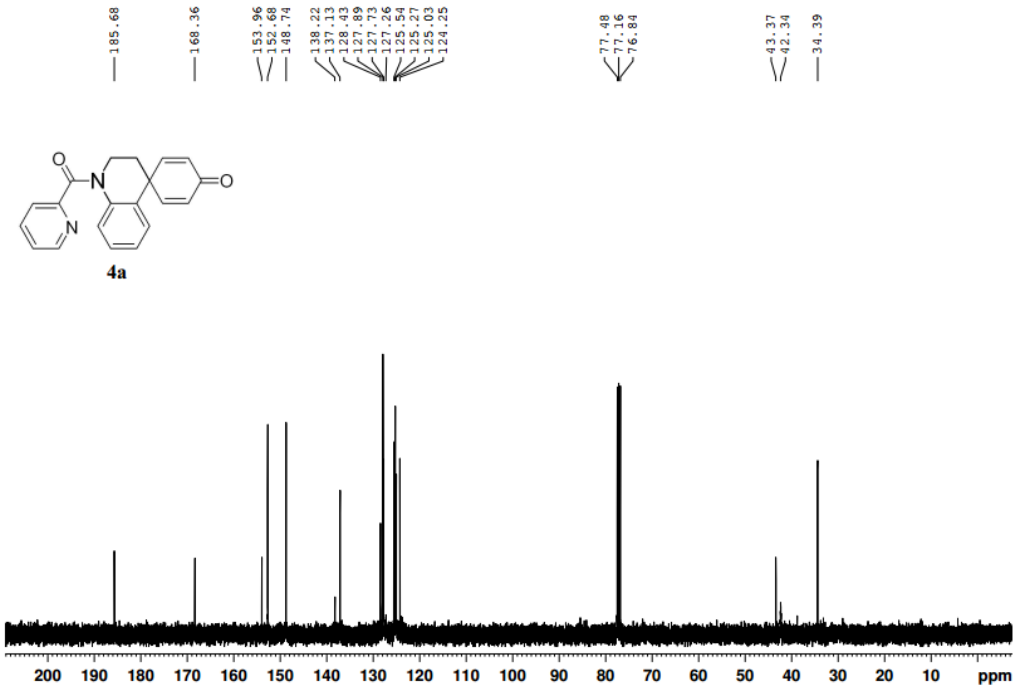

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
0.99
0.98
1.01
1.00
0.99
0.90
1.10
1.12
2.26
3.27
3.47


143.68
135.47
129.25
128.33
127.53
127.12
116.47
113.96
77.48
77.16
76.84
37.89
36.94
36.93
34.29
25.29
18.44
HN
2a'
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.260
6.808
6.804
6.788
6.785
6.655
6.651
6.635
6.632
6.598
6.579
6.559
5.912
5.903
5.894
5.888
5.878
5.869
5.514
5.510
5.489
5.484
4.396
3.837
3.468
3.456
3.439
3.428
3.411
3.400
3.388
3.379
3.377
3.368
3.360
3.352
3.348
2.136
2.133
2.125
2.119
2.116
2.111
2.106
2.102
2.096
2.092
2.087
2.083
2.077
2.071
1.841
1.829
1.823
1.814
1.803
1.795
1.782
1.774
1.729
1.720
1.699
1.688
1.682
1.676
1.667
1.661
1.649
1.639
0.018
HN
O
2b'
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 ppm
1.00
1.07
1.05
1.02
1.00
0.97
3.31
2.20
2.29
3.25
3.35


145.96
135.68
133.59
128.31
127.30
121.43
114.91
107.54
77.48
77.16
76.84
55.58
37.42
37.09
34.26
25.30
18.56
HN
O
2b'
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


8.482
8.472
7.816
7.797
7.778
7.720
7.700
7.341
7.326
7.310
7.260
7.098
7.074
7.013
6.364
6.339
4.109
4.094
4.079
2.228
2.213
2.198
-0.010
O
N
O
N
4a
11 10 9 8 7 6 5 4 3 2 1 ppm
0.91
0.91
0.92
0.93
2.12
3.19
1.81
2.00
2.02


185.68
168.36
153.96
152.68
148.74
138.22
137.13
128.43
127.89
127.73
127.26
125.54
125.27
125.03
124.25
77.48
77.16
76.84
43.37
42.34
34.39
O
N
N
O
4a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm