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Facile Synthesis of 6-Acylated Pyrido[2,1-a]isoindoles from 2-Arylpyridines and γ -Substituted *tert*-Propargyl Alcohols via Rhodium-Catalyzed C-H Bond Activation and β -Carbon Elimination

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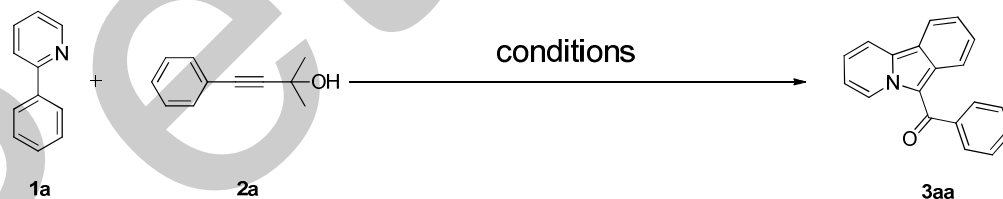
Supporting Information

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I. General methods Unless otherwise noted, all reagents and solvents were obtained from commercial suppliers and used without further purification. All glassware was dried overnight at 110 °C prior to use. Chromatography was performed on 300-400 mesh silica gel. NMR chemical shifts are reported in ppm relative to CHCl_3 (7.283 ppm for ^1H , and 77.005 ppm for ^{13}C NMR). The following abbreviations were used to describe peak splitting patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = overlapped. Coupling constants, J, were reported in Hertz unit (Hz). IR spectra were recorded on a Nicolet Avatar 330 FTIR spectrometer equipped with an attenuated total reflectance accessory or a Nicolet 6700 FT-IR equipped with an attenuated total reflectance accessory, and only partial data are listed. Melting points were determined on a Mel-Temp apparatus and are reported uncorrected. Mass spectra (HRMS) were obtained on Bruker En Apex ultra 7.0T FT-MS by the Public Instrument Platform of College of Chemistry and Chemical Engineering at Xiamen University. Single-crystal X-ray diffraction data were recorded on Oxford single-crystal diffractometer.

II. Experimental for screening of reaction conditions and preparation of substrates

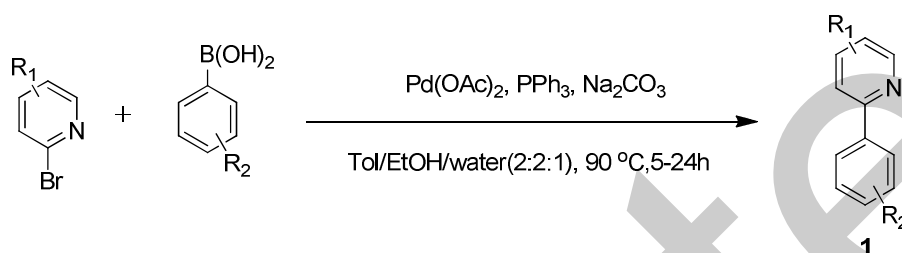
IIa Experimental for screening of reaction conditions



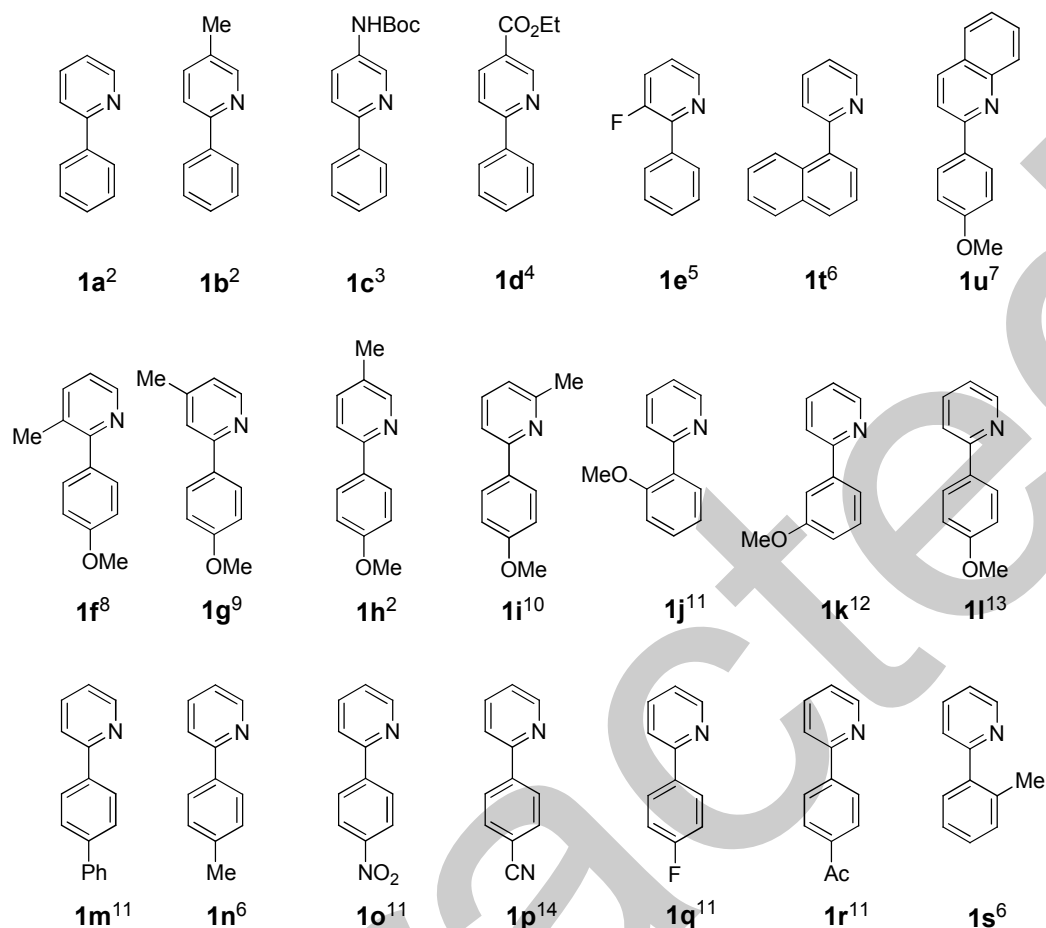
A mixture of **1a** (1.0 mmol), **2a** (1.5 mmol), [M] (2.5 mol %), $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (2.5 mmol) and solvents was added to a Schlenk tube under an air atmosphere. Then the mixture was stirred at 130 °C (bath temperature) under air for 24h. Then the reaction mixture was filtered through a short plug of silica gel, washed with ethyl acetate and concentrated, the residue was purified by chromatography (hexane/ethyl acetate = 5/1) to afford the desired products.

Structure of the byproduct 1,4-diphenylbuta-1,3-diyne was confirmed by ^1H NMR and ^{13}C NMR according to the standard sample of literature report.¹

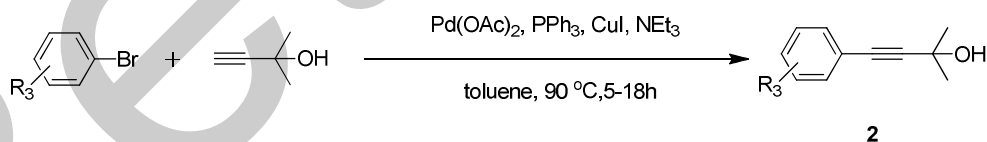
IIb General procedure of Suzuki cross-coupling reactions for the synthesis of functionalized 2-arylpyridines.²



To a Schlenk tube was added 2-bromopyridine derivatives (8.0 mmol), aryl-boronic acid (8.5 mmol), $\text{Pd}(\text{OAc})_2$ (5.0 mol%), triphenylphosphine (20 mol%) and sodium carbonate (20 mmol), toluene (10 mL), EtOH (10 mL), and water (5 mL) was added to the mixture under N_2 , then the mixture was stirred at 90°C for desired time until complete consumption of starting materials judged by TLC (5-24h). Water (30 mL) was added to the mixture and the resulting residue was extracted with ethyl acetate (10 mL $\times$ 3). The combined organic portions were dried with anhydrous sodium sulfate, filtered and taken to dryness. The residue was filtered, concentrated, and purified by chromatography (hexane/ethyl acetate) to afford the desired products. And all the 2-arylpyridines were known compounds and references were cited at the end of supporting information.

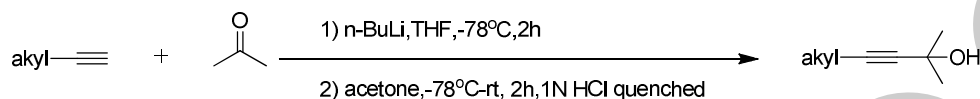


IIc General procedure for the synthesis of γ -arylated *tert*-propargyl alcohols (Sonogashira cross-coupling) and γ -alkylated *tert*-propargyl alcohols.

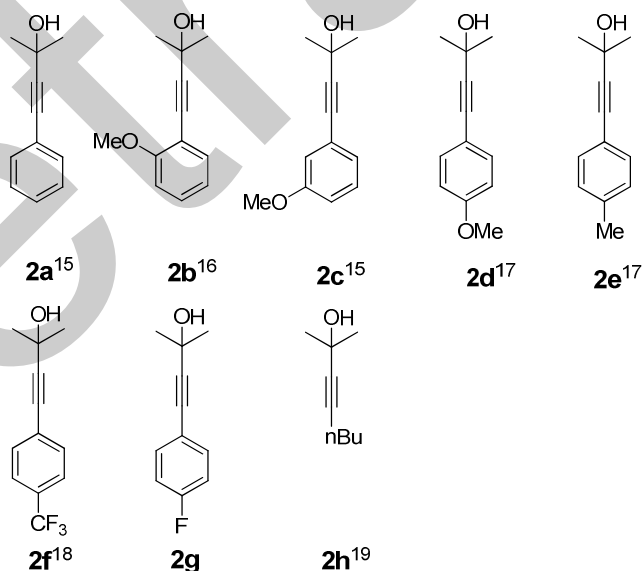


A mixture of aryl-bromide (12.0 mmol), 2- methyl -3-butyn-2-ol (1.2 g, 14.0 mmol), Pd(OAc)₂(21 mg, 0.1 mmol) , CuI (19 mg, 0.1mmol) and triphenylphosphine (393 mg, 1.5 mmol), NEt₃ (2 mL, 20 mmol) and toluene (15 mL) was added to a dry Schlenk tube, then the reaction mixture was degassed with N₂ and stirred at 80 °C for desired time until complete consumption of starting materials judged by TLC (5-18h) . After cooling, water (50 mL) was added to the mixture and the resulting residue was

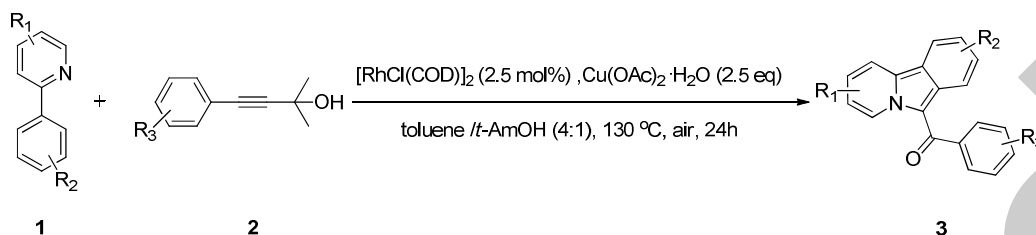
extracted with ethyl acetate (15 mL×3), and the organics were further washed with brine and dried with anhydrous sodium sulfate. The residue was filtered, concentrated, and purified by chromatography (hexane/ethyl acetate = 10/1) to afford the desired products. And all the products were known compounds and references were cited at the end of supporting information.



Under N₂ at -78°C, to a solution of alkynes (12.0 mmol) and THF (15 mL) in a dry Schlenk tube was added 5 mL n-BuLi (2.5M in hexane, 12.5 mmol) in a drop wise manner for 20 min, then the reaction mixture was at -78°C for 1 h, then acetone (3 mL) was added to mixture in a dropwise manner, and the mixture was stirred for 2h until the temperature raised up to rt slowly, then the resulting residue was quenched by 20 mL 1N HCl and extracted with ethyl acetate (15 mL×3), the organic layer were further washed with brine and dried with anhydrous sodium sulfate. The residue was filtered, concentrated, and purified by chromatography (hexane/ethyl acetate = 30/1) to afford the desired products.



III. General procedure for Rh-catalyzed pyrido[2,1-a]isoindoles syntheses



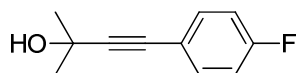
A mixture of 2-arylpyridine derivatives (1.0 mmol), *tert*-propargyl alcohols (1.5 mmol), $[\text{RhCl}(\text{COD})]_2$ (24 mg, 2.5 mol%), $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (500 mg, 2.5 mmol), toluene (8 mL) and *t*-AmOH (2 mL) was added to a Schlenk tube under an air atmosphere. Then the mixture was stirred at 130 °C (bath temperature) under air for desired time (usually 24h) until complete consumption of starting materials judged by TLC. Then the reaction mixture was filtered through a short plug of silica gel, washed with ethyl acetate and concentrated, the residue was purified by chromatography (hexane/ethyl acetate = 5/1) to afford the desired products.

IV. References

1. Wang, L. *J. Chem. Res.* **2005**, 2, 112-115.
2. Liu, C.; Yang, W. *Chem. Commun.* **2009**, 6267-6269.
3. WO2005030213.
4. Bonnet, V.; Mongin, F.; Trécourt, F.; Quéguiner, G.; Knochel, P. *Tetrahedron Lett.* **2001**, 42, 5717-5719.
5. Guo, P.; Joo, J. M.; Rakshit, S.; Sames, D. *J. Am. Chem. Soc.* **2011**, 133, 16338-16341.
6. So, C. M.; Yeung, C. C.; Lau, C. P.; Kwong, F. Y. *J. Org. Chem.* **2008**, 73, 7803-7806.
7. Knochel, P.; Korn, T.; Schade, M.; Cheemala, M.; Wirth, S.; Guevara, S.; Cahiez, G. *Synthesis* **2006**, 2006, 3547-3574.
8. Gao, K.; Lee, P.-S.; Fujita, T.; Yoshikai, N. *J. Am. Chem. Soc.* **2010**, 132, 12249-12251.
9. Filosa, R.; Peduto, A.; de Caprariis, P.; Saturnino, C.; Festa, M.; Petrella, A.; Pau, A.; Pinna, G. A.; La Colla, P.; Busonera, B.; Loddo, R. *Eur. J. Med. Chem.* **2007**, 42, 293-306.
10. Zhao, Y.-L.; Li, Y.; Li, S.-M.; Zhou, Y.-G.; Sun, F.-Y.; Gao, L.-X.; Han, F.-S. *Adv. Synth. Catal.* **2011**, 353, 1543-1550.

11. Luzung, M. R.; Patel, J. S.; Yin, J. *J. Org. Chem.* **2010**, *75*, 8330-8332.
12. Chau, N. T. T.; Meyer, M.; Komagawa, S.; Chevallier, F.; Fort, Y.; Uchiyama, M.; Mongin, F.; Gros, P. C. *Chem. Eur. J.* **2010**, *16*, 12425-12433.
13. Liu, N.; Wang, Z.-X. *J. Org. Chem.* **2011**, *76*, 10031-10038.
14. Wang, W.; Luo, F.; Zhang, S.; Cheng, J. *J. Org. Chem.* **2010**, *75*, 2415-2418.
15. Zou, H.; Zhou, L.; Li, Y.; Cui, Y.; Zhong, H.; Pan, Z.; Yang, Z.; Quan, J. *J. Med. Chem.* **2010**, *53*, 994-1003.
16. Ma, Y.; Song, C.; Jiang, W.; Wu, Q.; Wang, Y.; Liu, X.; Andrus, M. B. *Org. Lett.* **2003**, *5*, 3317-3319.
17. Cheng, J.; Sun, Y.; Wang, F.; Guo, M.; Xu, J.-H.; Pan, Y.; Zhang, Z. *J. Org. Chem.* **2004**, *69*, 5428-5432.
18. Shirakawa, E.; Kitabata, T.; Otsuka, H.; Tsuchimoto, T. *Tetrahedron* **2005**, *61*, 9878-9885.
19. Ma, S.; Wu, B.; Jiang, X.; Zhao, S. *J. Org. Chem.* **2005**, *70*, 2568-2575.

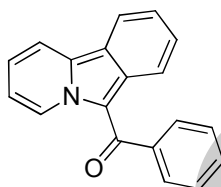
V. Spectra data for characterized compounds



2g

2g: 1.75 g, yield: 82%; light yellow oil.

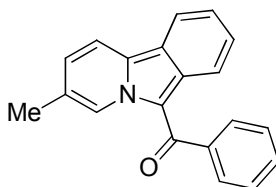
^1H NMR (500 MHz, CDCl_3): δ 7.43-7.40 (m, 2 H), 7.01 (t, $J = 8.6$ Hz, 2 H), 2.10 (br, 1 H), 1.63 (s, 6 H); ^{13}C NMR (125 MHz, CDCl_3): δ 162.52 (d, $J_{\text{C-F}} = 249.3$ Hz), 133.52 (d, $J_{\text{C-F}} = 8.5$ Hz), 118.82 (d, $J_{\text{C-F}} = 3.6$ Hz), 115.51 (d, $J_{\text{C-F}} = 22.1$ Hz), 93.45, 81.11, 65.60, 31.48.



3aa

3aa: 195 mg, yield: 72%; yellow solid; m.p: 123-125 °C.

^1H NMR (500 MHz, CDCl_3): δ 10.66 (d, $J = 6.8$ Hz, 1 H), 8.22 (d, $J = 8.4$ Hz, 1 H), 8.12 (d, $J = 8.0$ Hz, 1 H), 7.71 (d, $J = 8.0$ Hz, 2 H), 7.59-7.53 (comp, 4 H), 7.39 (t, $J = 7.2$ Hz, 1 H), 7.26 (m, 2 H), 6.87 (d, $J = 7.6$ Hz, 1 H); ^{13}C NMR (125 MHz, CDCl_3): δ 183.28, 142.58, 134.87, 132.55, 130.13, 129.42, 128.54, 128.19, 128.13, 125.13, 121.28, 119.96, 119.68, 119.24, 118.37, 117.21, 114.19; IR (KBr): 1565, 1432, 1320, 943, 756 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{19}\text{H}_{13}\text{NO}$ ($\text{M}+\text{Na}^+$): 294.0895, found: 294.0889.

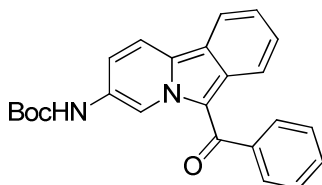


3ba

3ba: 211 mg, yield: 74%; yellow solid; m.p: 248-250 °C.

^1H NMR (500 MHz, CDCl_3): δ 10.53 (s, 1 H), 8.13 (d, $J = 8.6$ Hz, 1 H), 8.05 (m, 1 H), 7.70 (m, 2 H), 7.58-7.52 (comp, 3 H), 7.42 (dd, $J = 8.6$ Hz, $J = 1.0$ Hz, 1 H),

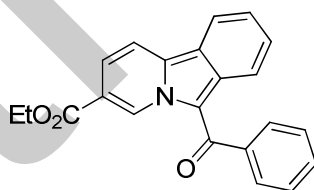
7.58-7.52 (m, 2 H), 6.82 (m, 1 H), 2.58 (s, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 183.01, 142.71, 133.57, 132.54, 130.02, 128.83, 128.54, 128.08, 128.03, 127.93, 127.83, 121.15, 120.05, 119.48, 119.21, 116.54, 113.92, 19.09; IR (KBr): 1548, 1457, 1341, 1300, 1121, 756, 706 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{20}\text{H}_{15}\text{NO}$ ($\text{M}+\text{Na}^+$): 308.1046, found: 308.1041.



3ca

3ca: 212 mg, yield: 55%; yellow solid; m.p: 119-121 $^{\circ}\text{C}$.

^1H NMR (500 MHz, CDCl_3): δ 10.86 (s, 1 H), 8.13 (d, $J = 9.1$ Hz, 1 H), 8.05 (m, 1 H), 7.71-7.68 (m, 2 H), 7.67 (br, 1 H), 7.57-7.50 (comp, 4 H), 6.80-6.78 (m, 1 H), 7.71-7.68 (m, 2 H), 1.56 (s, 9 H); ^{13}C NMR (125MHz, CDCl_3): δ 182.96, 153.08, 142.47, 132.60, 132.49, 131.82, 130.06, 128.50, 128.16, 127.60, 121.37, 120.32, 119.91, 119.58, 119.25, 119.07, 116.75, 114.39, 81.40, 28.33; IR (KBr): 1727, 1544, 1457, 1403, 1333, 1225, 1158, 711 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_3$ ($\text{M}+\text{Na}^+$): 409.1523, found: 409.1529.

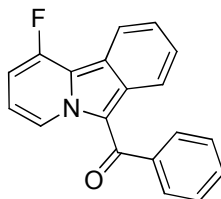


3da

3da: 223 mg, yield: 65%; yellow solid; m.p: 225-227 $^{\circ}\text{C}$.

^1H NMR (500 MHz, CDCl_3): δ 10.24 (s, 1 H), 8.28 (d, $J = 9.0$ Hz, 1 H), 8.15 (d, $J = 7.5$ Hz, 1 H), 8.11 (dd, $J = 9.0$ Hz, $J = 1.4$ Hz, 1 H), 7.74 (m, 2 H), 7.62-7.53 (comp, 3 H), 7.34-7.27 (m, 2 H), 6.95 (d, $J = 8.0$ Hz, 1 H), 4.52 (q, $J = 7.0$ Hz, 2 H), 4.52 (t, $J = 7.0$ Hz, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 184.03, 164.89, 141.97, 135.14, 133.43, 132.19, 130.64, 128.98, 128.60, 128.28, 124.39, 122.00, 121.95, 120.11, 119.52, 119.43, 116.75, 114.85, 61.82, 14.32; IR (KBr): 1718, 1565, 1453, , 1287,

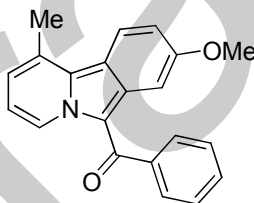
1105, 756 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{22}\text{H}_{17}\text{NO}_3$ ($\text{M}+\text{Na}^+$): 366.1106, found: 366.1106.



3ea

3ea: 197 mg, yield: 68%; yellow solid; m.p: 148-150 $^{\circ}\text{C}$.

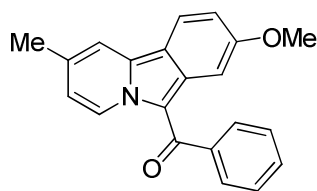
^1H NMR (500 MHz, CDCl_3): δ 10.40 (d, $J = 7.0$ Hz, 1 H), 8.33 (d, $J = 5.4$ Hz, 1 H), 7.73 (m, 2 H), 7.64-7.53 (m, 3 H), 7.33-7.22 (comp, 4 H), 6.92 (m, 1 H); ^{13}C NMR (125 MHz, CDCl_3): δ 184.22, 156.02 (d, $J_{\text{C-F}} = 249.8$ Hz), 142.04, 131.98, 130.59, 128.61, 128.24, 128.07, 125.25, 125.20, 122.14, 122.08, 119.08, 118.25 (d, $J_{\text{C-F}} = 4.0$ Hz), 117.33 (d, $J_{\text{C-F}} = 7.3$ Hz), 115.73, 109.01 (d, $J_{\text{C-F}} = 17.2$ Hz); IR (KBr): 1590, 1573, 1420, 1287, 1154, 935, 789, 702 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{19}\text{H}_{12}\text{FNO}$ ($\text{M}+\text{Na}^+$): 312.0801, found: 312.791.



3fa

3fa: 107 mg, yield: 34%; yellow solid; m.p: 163-165 $^{\circ}\text{C}$.

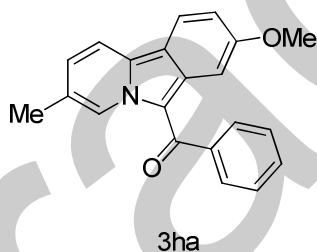
^1H NMR (500 MHz, CDCl_3): δ 10.58 (d, $J = 6.8$ Hz, 1 H), 8.11 (d, $J = 8.9$ Hz, 1 H), 7.69-7.66 (m, 2 H), 7.57-7.54 (comp, 3 H), 7.30 (t, $J = 6.7$ Hz, 1 H), 7.22 (t, $J = 7.0$ Hz, 1 H), 6.85 (dd, $J = 8.9$ Hz, $J = 2.3$ Hz, 1 H), 6.07 (d, $J = 2.3$ Hz, 1 H), 3.47 (s, 3 H), 2.90 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3): δ 182.97, 159.19, 142.95, 134.95, 134.16, 129.79, 129.27, 128.69, 127.82, 127.57, 127.25, 123.62, 116.72, 115.72, 114.00, 113.72, 98.76, 54.63, 20.67; IR (KBr): 1557, 1544, 1428, 1221, 1225, 1117, 835, 781, 715 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{21}\text{H}_{17}\text{NO}_2$ ($\text{M}+\text{Na}^+$): 338.1152, found: 338.1152.



3ga

3ga: 180 mg, yield: 57%; yellow solid; m.p: 192-194 °C.

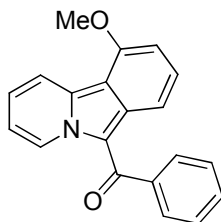
^1H NMR (500 MHz, CDCl_3): δ 10.51 (d, $J = 7.0$ Hz, 1 H), 7.90 (d, $J = 8.9$ Hz, 1 H), 7.86 (m, 1 H), 7.68-7.62 (m, 2 H), 7.55 (comp, 3 H), 7.15 (dd, $J = 7.0$ Hz, $J = 1.7$ Hz, 1 H), 6.82 (dd, $J = 8.9$ Hz, $J = 2.2$ Hz, 1 H), 6.00 (d, $J = 2.2$ Hz, 1 H), 3.48 (s, 3 H), 2.60 (s, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 182.10, 160.14, 142.92, 137.75, 135.82, 134.93, 129.59, 129.47, 128.60, 127.77, 121.00, 119.30, 115.74, 114.39, 113.66, 113.54, 98.88, 54.71, 21.49; IR (KBr): 1540, 1453, 1416, 1266, 1117, 814, 706 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{21}\text{H}_{17}\text{NO}_2$ ($\text{M}+\text{Na}^+$): 338.1152, found: 338.1147.



3ha

3ha: 135 mg, yield: 43%; yellow solid; m.p: 231-233 °C.

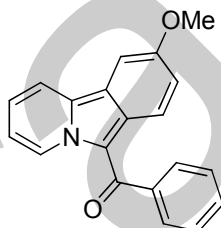
^1H NMR (500 MHz, CDCl_3): δ 10.47 (s, 1 H), 7.99 (d, $J = 8.9$ Hz, 1 H), 7.91 (d, $J = 8.9$ Hz, 1 H), 7.68 (m, 2 H), 7.56-7.54 (comp, 3 H), 7.39 (dd, $J = 8.6$ Hz, $J = 1.0$ Hz, 1 H), 6.84 (dd, $J = 8.9$ Hz, $J = 2.2$ Hz, 1 H), 6.01 (d, $J = 2.2$ Hz, 1 H), 3.48 (s, 3 H), 2.55 (s, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 182.69, 159.81, 142.88, 134.38, 133.94, 129.70, 128.61, 128.48, 128.33, 127.79, 127.48, 120.71, 115.76, 114.91, 113.90, 113.60, 99.06, 54.72, 18.94; IR (KBr): 1540, 1478, 1266, 1217, 846, 806, 702 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{21}\text{H}_{17}\text{NO}_2$ ($\text{M}+\text{Na}^+$): 338.1152, found: 338.1153.



3ja

3ja: 96 mg, yield: 32%; yellow solid; m.p: 211-213 °C.

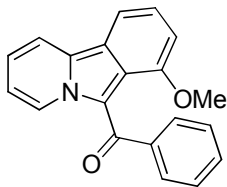
^1H NMR (500 MHz, CDCl_3): δ 10.63 (d, $J = 6.9$ Hz, 1 H), 8.63 (d, $J = 8.6$ Hz, 1 H), 7.71-7.69 (m, 2 H), 7.58-7.51 (comp, 4 H), 7.36 (td, $J = 6.9$ Hz, $J = 1.4$ Hz, 1 H), 7.18 (t, $J = 8.0$ Hz, 1 H), 6.60 (d, $J = 7.7$ Hz, 1 H), 6.42 (d, $J = 8.6$ Hz, 1 H), 4.10 (s, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 183.53, 155.95, 142.62, 134.46, 134.41, 130.06, 129.01, 128.80, 128.51, 128.14, 125.58, 120.75, 117.67, 114.36, 111.52, 110.77, 100.19, 55.40; IR (KBr): 1548, 1428, 1312, 1241, 976, 715 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{20}\text{H}_{15}\text{NO}_2$ ($\text{M}+\text{Na}^+$): 324.0995, found: 324.0993.



3ka-1

3ka-1: 154 mg, yield: 51%; yellow solid; m.p: 175-177 °C.

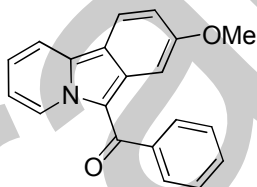
^1H NMR (500 MHz, CDCl_3): δ 10.59 (d, $J = 6.9$ Hz, 1 H), 8.15 (d, $J = 8.6$ Hz, 1 H), 7.70-7.69 (m, 2 H), 7.58-7.46 (comp, 4 H), 7.42 (d, $J = 2.1$ Hz, 1 H), 7.18 (td, $J = 7.0$ Hz, $J = 1.0$ Hz, 1 H), 6.97 (dd, $J = 9.1$ Hz, $J = 2.3$ Hz, 1 H), 6.77 (d, $J = 9.1$ Hz, 1 H), 3.92 (s, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 182.79, 155.14, 142.54, 134.03, 130.13, 129.33, 128.55, 128.18, 127.82, 124.34, 120.78, 120.56, 120.38, 118.05, 117.23, 114.00, 98.93, 55.56; IR (KBr): 1541, 1416, 1304, 1221, 1142, 702 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{20}\text{H}_{15}\text{NO}_2$ ($\text{M}+\text{Na}^+$): 324.0995, found: 324.1001.



3ka-2

3ka-2: 30 mg, yield: 10%; yellow solid; m.p: 149-151 °C.

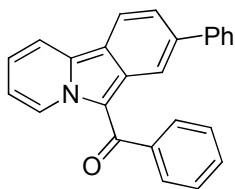
^1H NMR (500 MHz, CDCl_3): δ 10.26 (d, J = 6.9 Hz, 1 H), 8.20 (d, J = 8.6 Hz, 1 H), 7.77 (d, J = 8.0 Hz, 1 H), 7.66 (m, 2 H), 7.49-7.36 (comp, 4 H), 7.28-7.21 (m, 2 H), 6.73 (d, J = 7.5 Hz, 1 H), 3.23 (s, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 185.85, 151.55, 144.36, 133.22, 130.09, 128.65, 127.78, 127.25, 123.39, 123.02, 122.02, 120.98, 117.86, 117.67, 114.34, 111.76, 106.70, 54.39; IR (KBr): 1565, 1424, 1308, 1262, 1026, 752 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{20}\text{H}_{15}\text{NO}_2$ ($\text{M}+\text{Na}^+$): 324.0995, found: 324.1000.



3la

3la: 157 mg, yield: 52%; yellow solid; m.p: 184-186 °C.

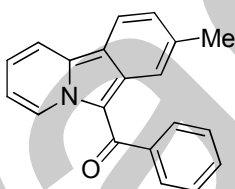
^1H NMR (500 MHz, CDCl_3): δ 10.59 (d, J = 6.8 Hz, 1 H), 8.06 (d, J = 8.5 Hz, 1 H), 7.93 (d, J = 8.9 Hz, 1 H), 7.68 (m, 2 H), 7.56 (comp, 3 H), 7.50 (t, J = 7.5 Hz, 1 H), 7.29 (t, J = 6.8 Hz, 1 H), 6.85 (d, J = 8.9 Hz, 1 H), 6.04 (s, 1 H), 3.23 (s, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 182.95, 160.07, 142.74, 135.22, 134.43, 129.83, 129.67, 128.63, 127.82, 125.77, 120.96, 117.16, 116.41, 114.85, 114.09, 113.95, 98.84, 54.73; IR (KBr): 1635, 1544, 1487, 1266, 769, 702 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{20}\text{H}_{15}\text{NO}_2$ ($\text{M}+\text{Na}^+$): 324.0995, found: 324.1001.



3ma

3ma: 295 mg, yield: 85%; yellow solid; m.p: 181-183 °C.

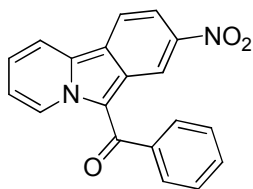
^1H NMR (500 MHz, CDCl_3): δ 10.67 (d, J = 6.8 Hz, 1 H), 8.25 (d, J = 8.5 Hz, 1 H), 8.18 (d, J = 8.5 Hz, 1 H), 7.75 (m, 2 H), 7.61-7.59 (comp, 4 H), 7.53 (d, J = 8.5 Hz, 1 H), 7.41-7.38 (m, 5 H), 7.33 m, 1 H), 7.03 (s, 1 H); ^{13}C NMR (125MHz, CDCl_3): δ 183.25, 142.66, 141.29, 140.79, 134.80, 133.08, 130.14, 129.53, 128.71, 128.63, 128.16, 127.38, 127.27, 125.41, 121.14, 120.12, 119.15, 118.36, 117.48, 117.26, 114.42; IR (KBr): 1545, 1460, 1436, 1320, 764, 698 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{25}\text{H}_{17}\text{NO}$ ($\text{M}+\text{Na}^+$): 370.1202, found: 370.1208.



3na

3na: 214 mg, yield: 75%; yellow solid; m.p: 183-185 °C.

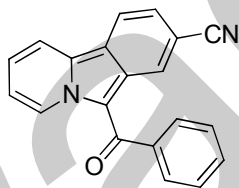
^1H NMR (500 MHz, CDCl_3): δ 10.62 (d, J = 6.9 Hz, 1 H), 8.13 (d, J = 8.5 Hz, 1 H), 7.97 (d, J = 8.9 Hz, 1 H), 7.71 (m, 2 H), 7.59-7.47 (comp, 4 H), 7.30 (td, J = 6.9 Hz, J = 1.3 Hz, 1 H), 7.07 (d, J = 8.5 Hz, 1 H), 6.60 (s, 1 H), 2.29 (s, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 183.08, 142.63, 138.32, 135.03, 133.11, 130.08, 129.49, 128.51, 128.14, 125.30, 123.55, 119.44, 118.57, 118.28, 117.95, 116.91, 113.86, 22.54; IR (KBr): 1545, 1436, 1312, 1121, 765, 702 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{20}\text{H}_{15}\text{NO}$ ($\text{M}+\text{Na}^+$): 308.1046, found: 308.1041.



30a

30a: 88 mg, yield: 28%; yellow solid; m.p: decomp. >250 °C.

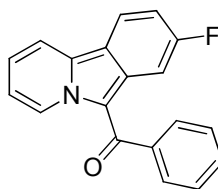
¹H NMR (500 MHz, CDCl₃): δ 10.64 (d, *J* = 6.9 Hz, 1 H), 8.36 (d, *J* = 8.5 Hz, 1 H), 8.25 (d, *J* = 8.9 Hz, 1 H), 8.03 (dd, *J* = 8.9 Hz, *J* = 1.9 Hz, 1 H), 7.82 (d, *J* = 1.9 Hz, 1 H), 7.74-7.66 (comp, 4 H), 7.63-7.59 (m, 2 H), 7.54 (td, *J* = 6.9 Hz, *J* = 1.0 Hz, 1 H), 6.60 (s, 1 H), 2.29 (s, 3 H); ¹³C NMR (125MHz, CDCl₃): δ 184.05, 147.58, 141.35, 133.55, 131.26, 130.74, 129.43, 128.90, 128.13, 125.90, 121.51, 120.89, 119.92, 118.32, 116.25, 115.22, 115.04; IR (KBr): 1573, 1436, 1295, 1250, 773, 706 cm⁻¹; HRMS (ESI): Calcd for C₁₉H₁₂N₂O₃ (M+Na⁺): 339.0740, found: 339.0740.



3pa

3pa: 107 mg, yield: 36%; yellow solid; m.p: decomp. >250 °C.

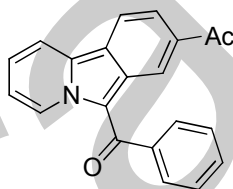
¹H NMR (500 MHz, CDCl₃): 10.61 (d, *J* = 6.9 Hz, 1 H), 8.32 (d, *J* = 8.5 Hz, 1 H), 8.22 (d, *J* = 8.9 Hz, 1 H), 7.70-7.64 (comp, 4 H), 7.60-7.57 (m, 2 H), 7.52 (t, *J* = 6.9 Hz, 1 H), 7.40 (d, *J* = 8.5 Hz, 1 H), 7.32 (s, 1 H); ¹³C NMR (125MHz, CDCl₃): δ 183.91, 141.52, 133.78, 131.19, 130.71, 129.34, 128.90, 128.06, 125.76, 125.14, 122.21, 120.92, 120.57, 119.77, 119.54, 118.05, 114.11, 111.19; IR (KBr): 2224, 1565, 1461, 1312, 1129, 773, 702 cm⁻¹; HRMS (ESI): Calcd for C₂₀H₁₂N₂O (M+Na⁺): 319.0842, found: 319.0847.



3qa

3qa: 156 mg, yield: 54%; yellow solid; m.p: 161-163 °C.

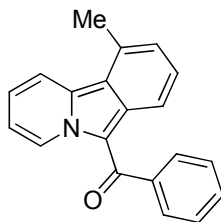
^1H NMR (500 MHz, CDCl_3): δ 10.61 (d, $J = 7.0$ Hz, 1 H), 8.18 (d, $J = 8.5$ Hz, 1 H), 8.07 (m, 1 H), 7.69-7.67 (m, 2 H), 7.61-7.55 (comp, 4 H), 7.39 (t, $J = 6.9$ Hz, 1 H), 6.99 (dt, $J = 8.8$ Hz, $J = 2.0$ Hz, 1 H), 6.42 (dd, $J = 11.2$ Hz, $J = 1.8$ Hz, 1 H); ^{13}C NMR (125MHz, CDCl_3): δ 183.44, 162.93 (d, $J_{\text{C-F}} = 244.9$ Hz), 142.04, 134.73, 133.61 (d, $J_{\text{C-F}} = 11.7$ Hz), 130.45, 129.59, 128.73, 127.93, 125.87, 121.79 (d, $J_{\text{C-F}} = 10.8$ Hz), 118.15, 116.90, 116.65, 114.24 (d, $J_{\text{C-F}} = 5.3$ Hz), 111.31 (d, $J_{\text{C-F}} = 26.5$ Hz), 103.77 (d, $J_{\text{C-F}} = 26.5$ Hz); IR (KBr): 1548, 1436, 1308, 1175, 764, 706 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{19}\text{H}_{12}\text{FNO}$ ($\text{M}+\text{Na}^+$): 312.0795, found: 312.0799.



3ra

3ra: 213 mg, yield: 68%; yellow solid; m.p: 239-241 °C.

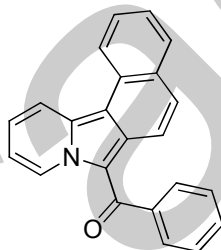
^1H NMR (500 MHz, CDCl_3): δ 10.63 (d, $J = 6.9$ Hz, 1 H), 8.27 (d, $J = 8.5$ Hz, 1 H), 8.13 (d, $J = 8.5$ Hz, 1 H), 7.82 (dd, $J = 8.5$ Hz, $J = 1.3$ Hz, 1 H), 7.72 (m, 2 H), 7.64-7.58 (comp, 4 H), 7.45 (td, $J = 7.0$ Hz, $J = 1.1$ Hz, 1 H), 7.37 (s, 1 H), 2.29 (s, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 198.23, 183.47, 142.30, 136.40, 134.11, 131.60, 130.45, 129.37, 128.67, 128.12, 125.52, 122.00, 121.56, 119.98, 119.52, 119.27, 118.01, 114.71, 26.16; IR (KBr): 1561, 1420, 1308, 1262, 1026, 748 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{21}\text{H}_{15}\text{NO}_2$ ($\text{M}+\text{Na}^+$): 336.0995, found: 336.1001.



3sa

3sa: 160 mg, yield: 56%; yellow solid; m.p: 184-186 °C.

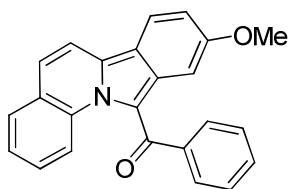
^1H NMR (500 MHz, CDCl_3): δ 10.63 (d, $J = 6.9$ Hz, 1 H), 8.62 (d, $J = 8.4$ Hz, 1 H), 7.70 (m, 2 H), 7.58-7.51 (comp, 4 H), 7.36 (d, $J = 6.9$ Hz, $J = 1.4$ Hz, 1 H), 7.17 (t, $J = 8.0$ Hz, 1 H), 6.60 (d, $J = 7.6$ Hz, 1 H), 6.42 (d, $J = 8.5$ Hz, 1 H), 4.09 (s, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 183.52, 155.95, 142.64, 134.44, 134.40, 130.05, 129.00, 128.79, 128.50, 128.14, 125.54, 120.74, 117.65, 114.37, 111.52, 110.77, 100.19, 55.39; IR (KBr): 1548, 1424, 1308, 1241, 976, 785, 752, 711 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{20}\text{H}_{15}\text{NO}$ ($\text{M}+\text{Na}^+$): 308.1046, found: 308.1042.



3ta

3ta: 238 mg, yield: 74%; yellow solid; m.p: 209-211 °C.

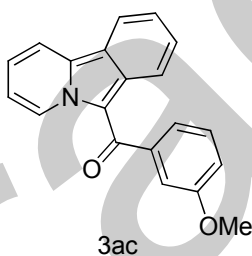
^1H NMR (500 MHz, CDCl_3): δ 10.55 (d, $J = 6.9$ Hz, 1 H), 8.67 (d, $J = 8.9$ Hz, 1 H), 8.64 (d, $J = 8.5$ Hz, 1 H), 7.87 (d, $J = 7.9$ Hz, 1 H), 7.76 (m, 2 H), 7.71 (t, $J = 7.9$ Hz, 1 H), 7.63-7.50 (comp, 6 H), 7.31 (t, $J = 6.9$ Hz, 1 H), 6.92 (d, $J = 9.1$ Hz, 1 H); ^{13}C NMR (125MHz, CDCl_3): δ 184.74, 142.30, 134.43, 131.75, 130.77, 130.16, 129.35, 129.30, 129.16, 128.67, 128.61, 128.48, 127.57, 125.46, 124.29, 122.48, 119.42, 119.03, 116.12, 115.49, 112.71; IR (KBr): 1585, 1392, 1217, 1138, 818, 744 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{23}\text{H}_{15}\text{NO}$ ($\text{M}+\text{Na}^+$): 344.1046, found: 344.1047.



3ua

3ua: 249 mg, yield: 71%; yellow solid; m.p: 192-194 °C.

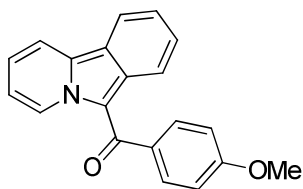
^1H NMR (500 MHz, CDCl_3): δ 8.17 (d, J = 8.6 Hz, 1 H), 8.01 (m, 2 H), 7.94-7.91 (m, 2 H), 7.85 (d, J = 7.8 Hz, 1 H), 7.70 (d, J = 8.9 Hz, 1 H), 7.62-7.54 (comp, 4 H), 7.49 (t, J = 7.2 Hz, 1 H), 6.87 (d, J = 8.9 Hz, 1 H), 6.42 (s, 1 H), 3.56 (s, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 184.17, 159.92, 141.24, 135.46, 133.65, 133.07, 131.84, 129.61, 128.70, 128.65, 128.36, 126.16, 126.06, 125.37, 122.04, 121.01, 118.35, 115.58, 115.43, 115.01, 97.65, 54.78; IR (KBr): 1590, 1349, 1221, 802 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{24}\text{H}_{17}\text{NO}_2$ ($\text{M}+\text{Na}^+$): 374.11151, found: 374.1155.



3ac

3ac: 190 mg, yield: 63%; yellow solid; m.p: 105-106 °C.

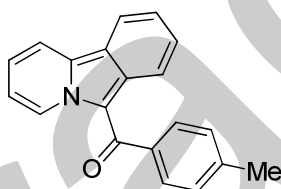
^1H NMR (500 MHz, CDCl_3): δ 10.66 (d, J = 7.0 Hz, 1 H), 8.25 (d, J = 8.4 Hz, 1 H), 8.13 (d, J = 8.0 Hz, 1 H), 7.57 (t, J = 7.4 Hz, 1 H), 7.45 (t, J = 7.8 Hz, 1 H), 7.41 (td, J = 7.0 Hz, J = 1.4 Hz, 1 H), 7.30-7.25 (comp, 4 H), 7.13 (dd, J = 8.0 Hz, J = 2.5 Hz, 1 H), 6.93 (d, J = 8.5 Hz, 1 H), 3.87 (s, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 182.87, 159.82, 143.86, 134.98, 132.56, 129.67, 129.47, 128.29, 125.31, 121.36, 120.55, 119.99, 119.69, 119.36, 118.45, 117.24, 116.55, 114.05, 112.70, 55.43; IR (KBr): 1565, 1548, 1436, 1324, 1246, 1204, 760, 715 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{20}\text{H}_{15}\text{NO}_2$ ($\text{M}+\text{Na}^+$): 324.0995, found: 324.0997.



3ad

3ad: 154 mg, yield: 51%; yellow solid; m.p: 120-122 °C.

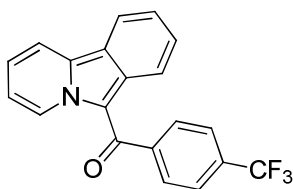
^1H NMR (500 MHz, CDCl_3): δ 10.54 (d, $J = 7.0$ Hz, 1 H), 8.24 (d, $J = 8.4$ Hz, 1 H), 8.13 (d, $J = 7.9$ Hz, 1 H), 7.73 (d, $J = 8.5$ Hz, 1 H), 7.52 (t, $J = 7.6$ Hz, 1 H), 7.38-7.25 (comp, 4 H), 7.11 (d, $J = 8.5$ Hz, 1 H), 7.05 (m, 2 H), 3.95 (s, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 182.97, 161.58, 134.87, 134.41, 132.28, 130.50, 130.05, 129.08, 127.96, 124.55, 121.08, 119.67, 119.36, 118.14, 117.25, 114.32, 113.75, 55.41; IR (KBr): 1606, 1436, 1329, 1266, 1100, 1022, 806 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{20}\text{H}_{15}\text{NO}_2$ ($\text{M}+\text{Na}^+$): 324.0995, found: 324.1001.



3ae

3ae: 194 mg, yield: 68%; yellow solid; m.p: 127-129 °C.

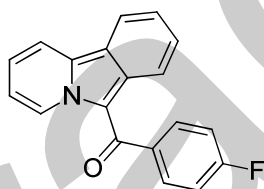
^1H NMR (500 MHz, CDCl_3): δ 10.61 (d, $J = 7.0$ Hz, 1 H), 8.25 (d, $J = 8.5$ Hz, 1 H), 8.13 (d, $J = 7.7$ Hz, 1 H), 7.63 (m, 2 H), 7.55 (t, $J = 7.6$ Hz, 1 H), 7.39 (t, $J = 6.7$ Hz, 1 H), 7.35-7.25 (comp, 4 H), 7.00 (d, $J = 8.5$ Hz, 1 H), 2.51 (s, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 183.51, 140.47, 139.67, 134.61, 132.43, 129.28, 129.16, 128.38, 128.03, 124.85, 121.16, 119.80, 119.65, 119.39, 118.27, 117.22, 114.30, 21.60; IR (KBr): 1544, 1436, 1324, 1300, 943, 756 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{20}\text{H}_{15}\text{NO}$ ($\text{M}+\text{Na}^+$): 308.1046, found: 308.1043.



3af

3af: 159 mg, yield: 47%; yellow solid; m.p: 140-142 °C.

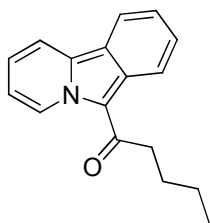
¹H NMR (500 MHz, CDCl₃): δ 10.69 (d, *J* = 6.8 Hz, 1 H), 8.28 (d, *J* = 8.4 Hz, 1 H), 8.15 (m, 1 H), 7.82 (br, 4 H), 7.63 (t, *J* = 8.0 Hz, 1 H), 7.45 (t, *J* = 7.1 Hz, 1 H), 7.34-7.27 (m, 2 H), 6.79 (d, *J* = 8.4 Hz, 1 H); ¹³C NMR (125MHz, CDCl₃): δ 181.08, 145.89, 135.51, 133.74, 132.47, 131.87 (q, *J*_{C-F} = 32.5 Hz), 129.70, 128.72, 128.46, 126.10, 125.68 (q, *J*_{C-F} = 3.8 Hz), 124.17 (q, *J*_{C-F} = 274.1 Hz), 121.68, 120.29, 119.95, 118.79, 117.30, 113.86; IR (KBr): 1548, 1432, 1320, 1241, 1163, 1121, 843, 769, 752 cm⁻¹; HRMS (ESI): Calcd for C₂₀H₁₂F₃NO (M+Na⁺): 362.0763, found: 362.0758.



3ag

3ag: 75 mg, yield: 26%; yellow solid; m.p: 154-156 °C.

¹H NMR (500 MHz, CDCl₃): δ 10.60 (d, *J* = 7.0 Hz, 1 H), 8.23 (d, *J* = 8.4 Hz, 1 H), 8.13 (d, *J* = 8.0 Hz, 1 H), 7.75-7.72 (m, 2 H), 7.57-7.54 (m, 1 H), 7.39 (td, *J* = 7.1 Hz, *J* = 1.2 Hz, 1 H), 7.33-7.21 (comp, 4 H), 6.94 (d, *J* = 8.4 Hz, 1 H); ¹³C NMR (125MHz, CDCl₃): δ 181.64, 164.13 (d, *J*_{C-F} = 250.2 Hz), 138.62 (d, *J*_{C-F} = 3.4 Hz), 134.97, 132.43, 130.54 (d, *J*_{C-F} = 8.2 Hz), 129.36, 128.33, 125.33, 121.38, 119.98, 119.82, 119.02, 118.46, 117.26, 115.57 (d, *J*_{C-F} = 21.4 Hz), 114.04; IR (KBr): 1598, 1565, 1432, 1324, 1291, 1212, 1121, 769, 719, 603 cm⁻¹; HRMS (ESI): Calcd for C₁₉H₁₂FNO (M+Na⁺): 312.0795, found: 312.0794.

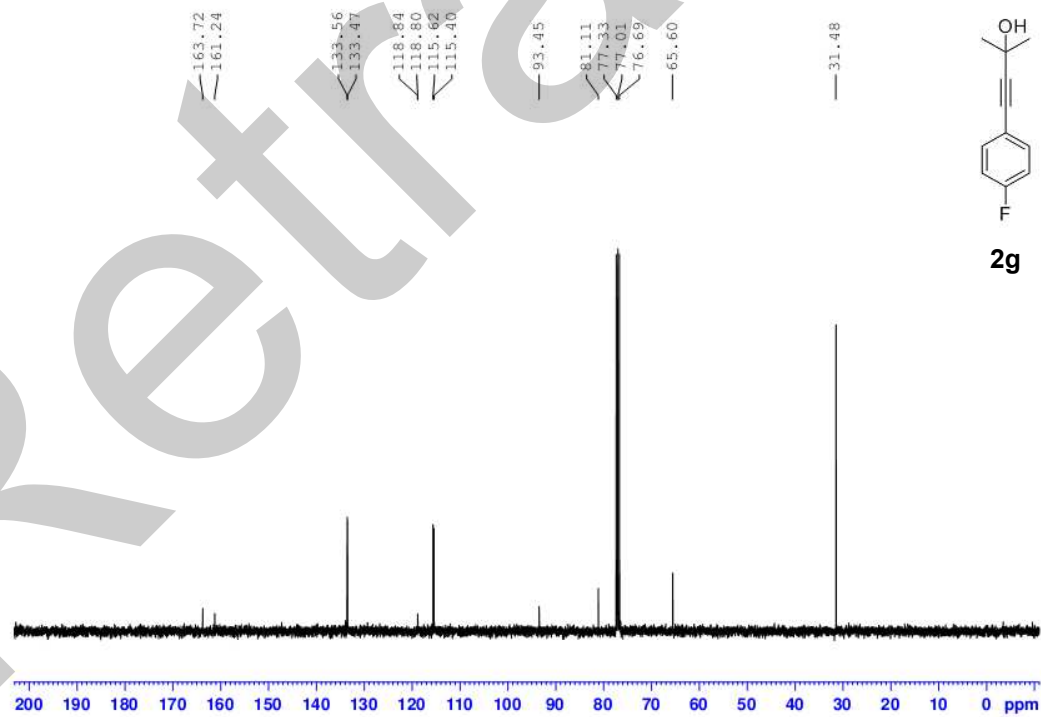
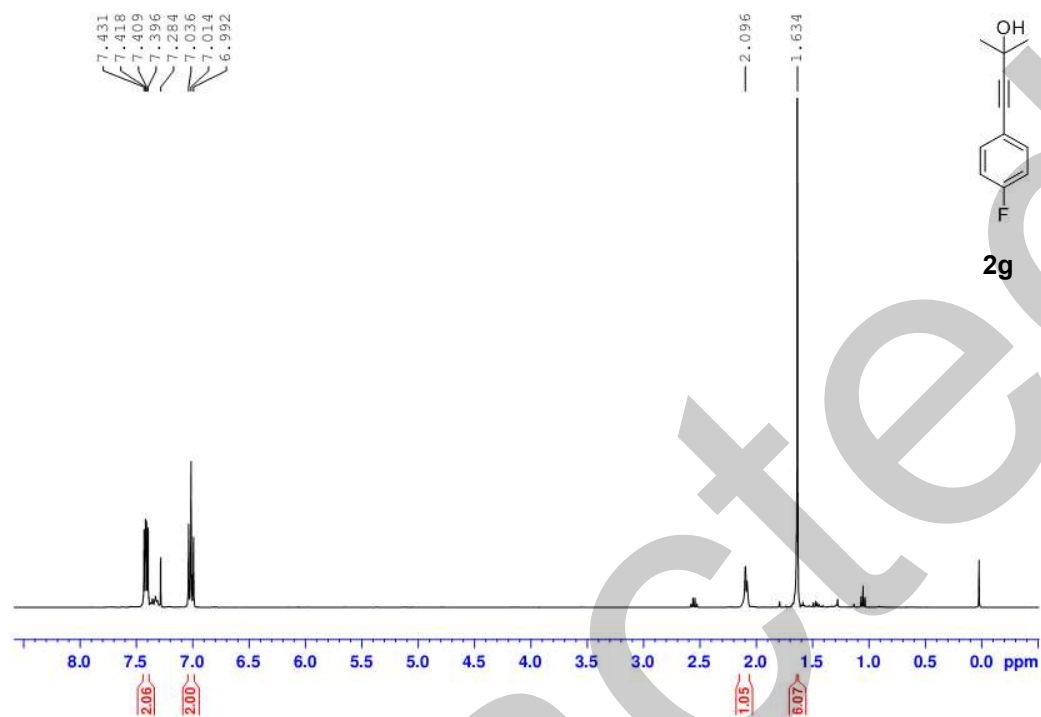


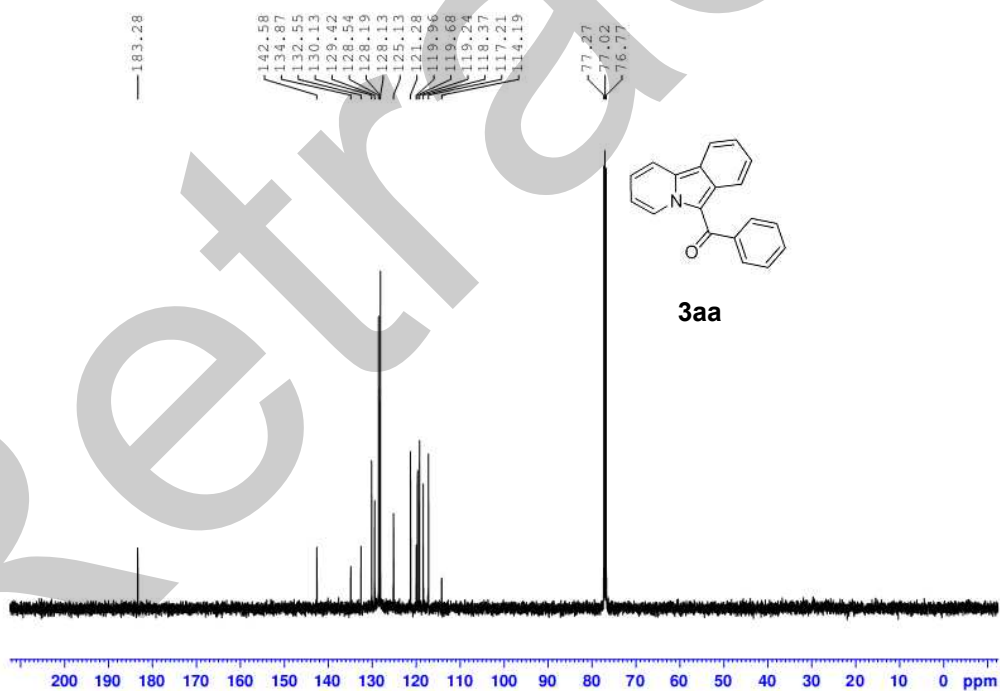
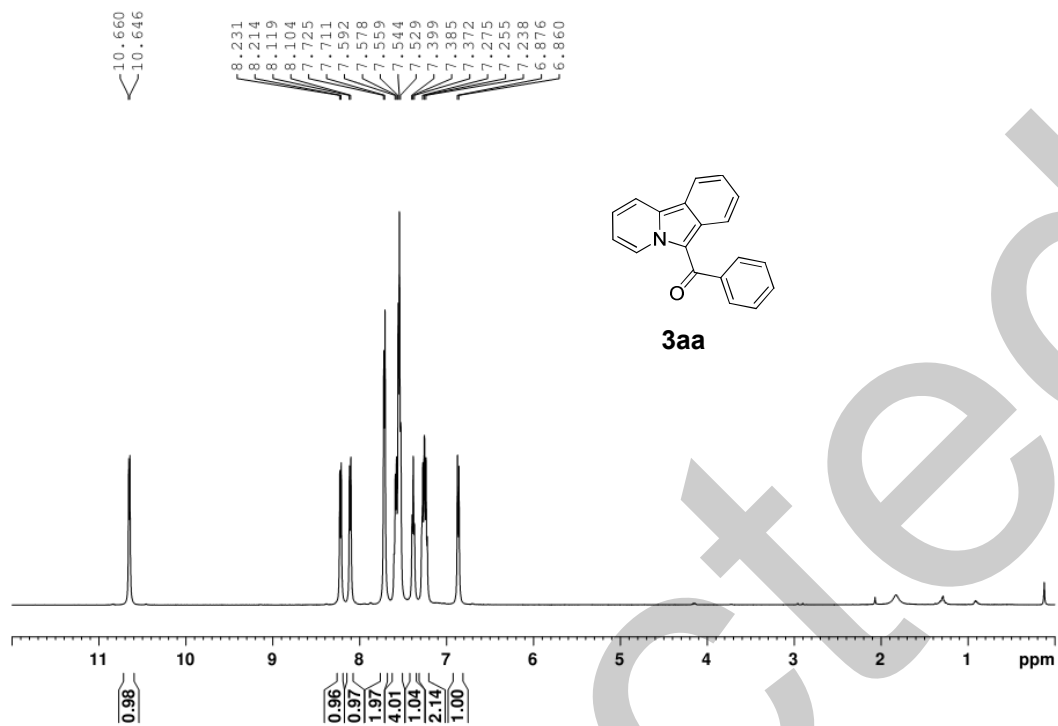
3ah

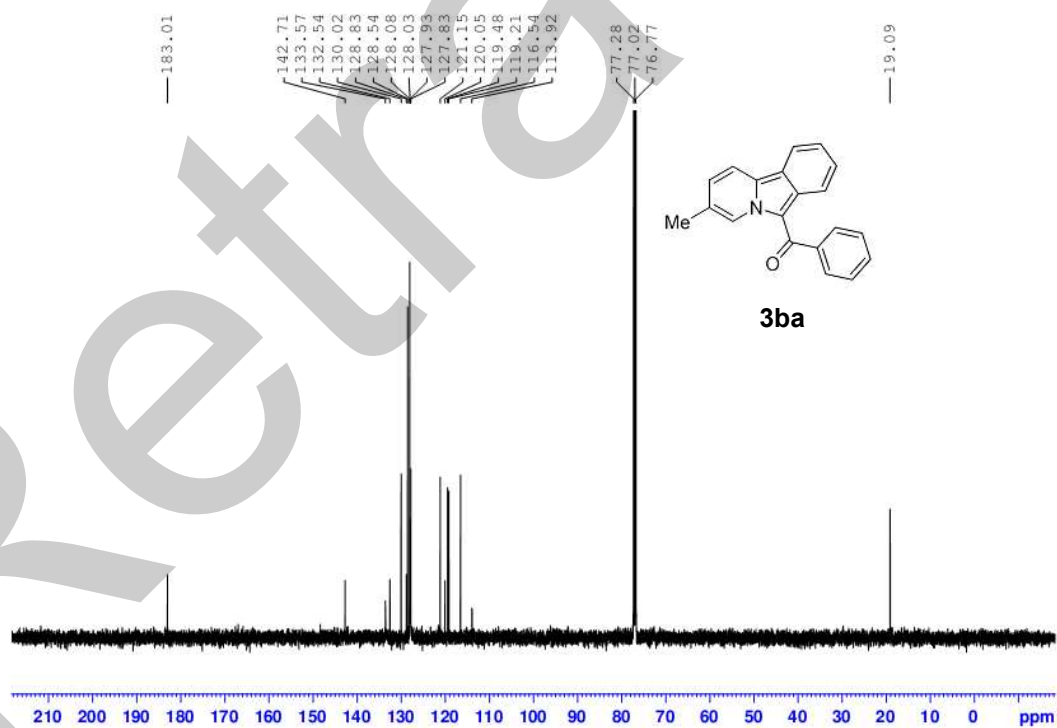
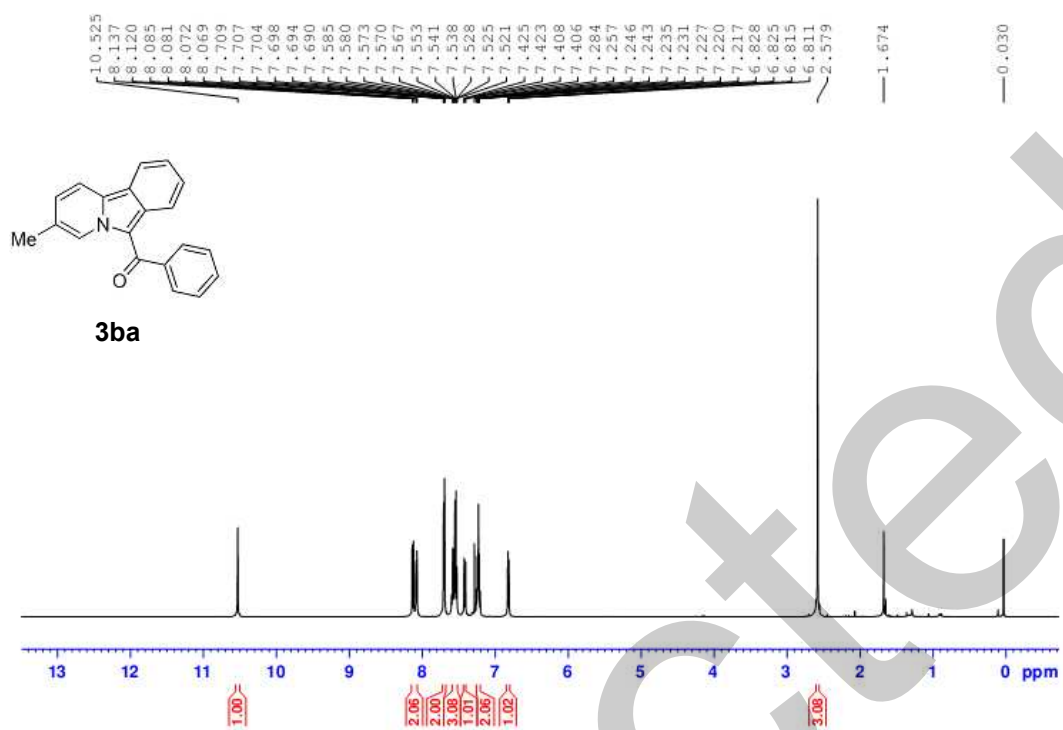
3ah: 98 mg, yield: 39%; yellow solid; m.p: 124-126 °C.

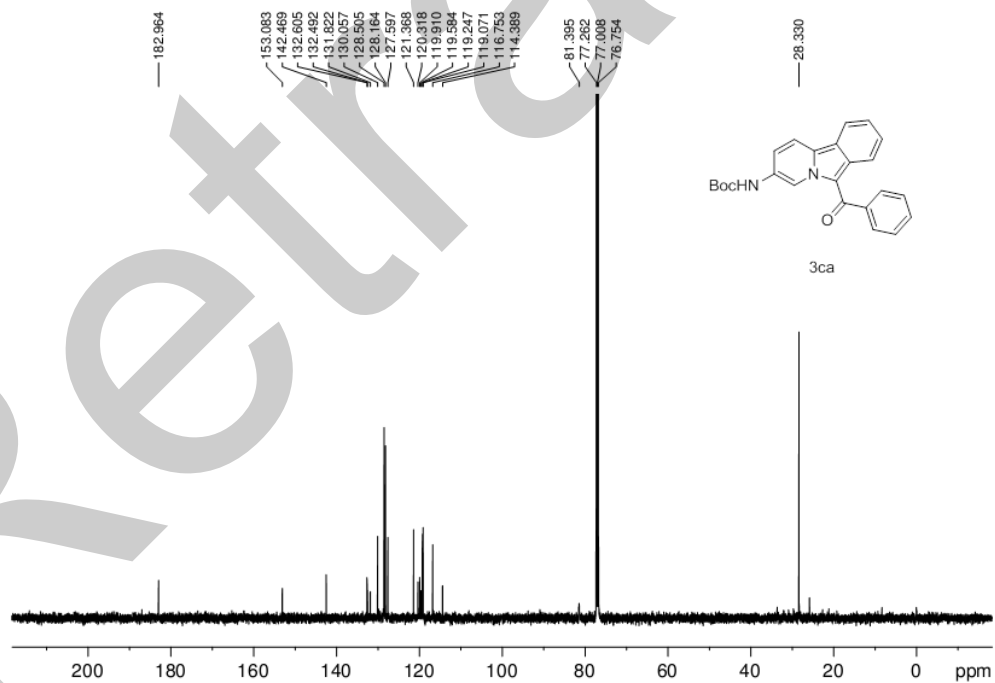
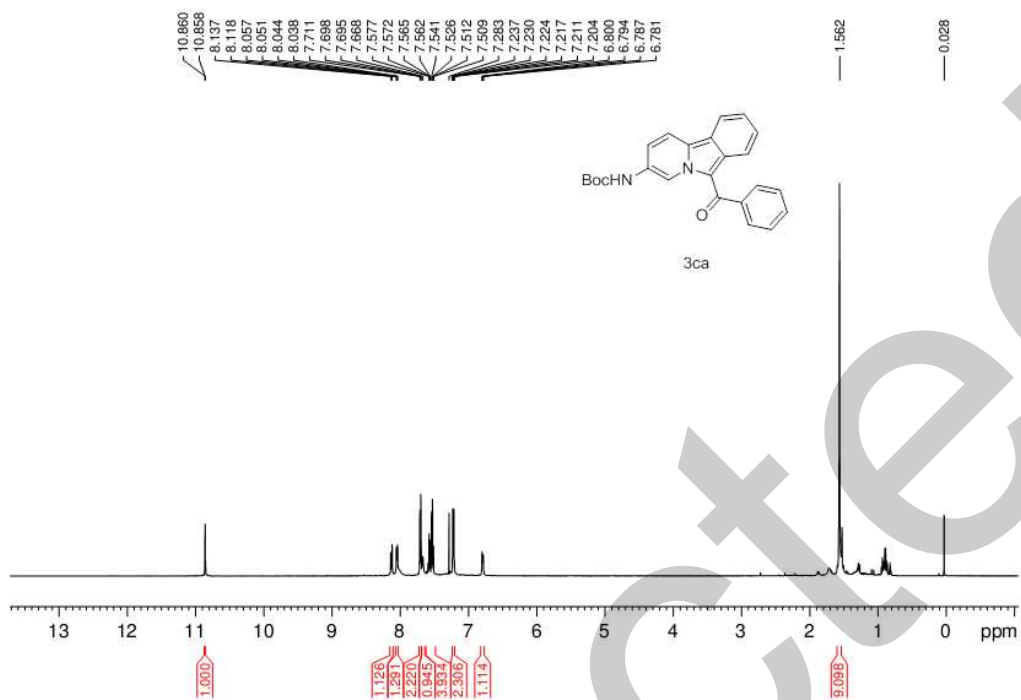
^1H NMR (500 MHz, CDCl_3): δ 10.74 (d, $J = 7.0$ Hz, 1 H), 8.22-8.18 (m, 2 H), 8.03 (d, $J = 8.5$ Hz, 1 H), 7.64 (t, $J = 8.0$ Hz, 1 H), 7.48 (t, $J = 8.0$ Hz, 1 H), 7.36-7.31 (m, 2 H), 3.17 (t, $J = 7.6$ Hz, 2 H), 1.92 (m, 2 H), 1.58 (m, 2 H), 1.05 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (125MHz, CDCl_3): δ 187.69, 133.82, 130.90, 129.29, 128.79, 124.22, 120.73, 120.21, 119.82, 118.99, 118.28, 116.96, 114.37, 41.63, 27.22, 22.89, 14.10; IR (KBr): 2958, 1582, 1432, 1250, 1167, 1084, 968, 756, 715 cm^{-1} ; HRMS (ESI): Calcd for $\text{C}_{17}\text{H}_{17}\text{NO}$ ($\text{M}+\text{Na}^+$): 274.1202, found: 274.1201.

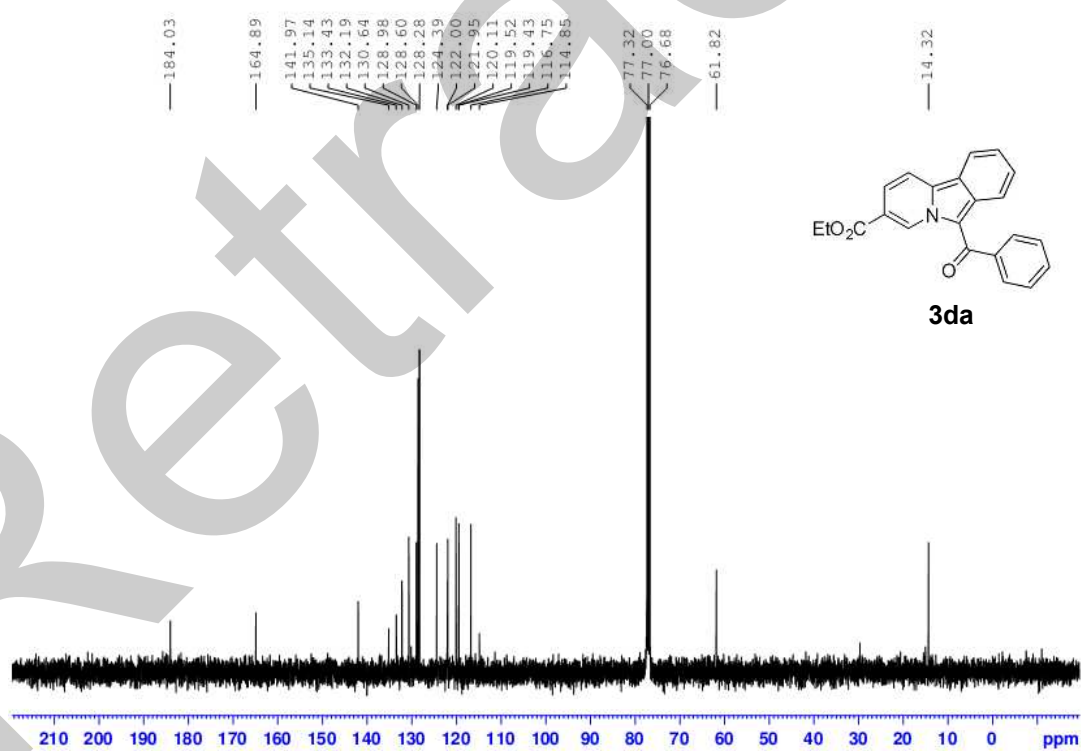
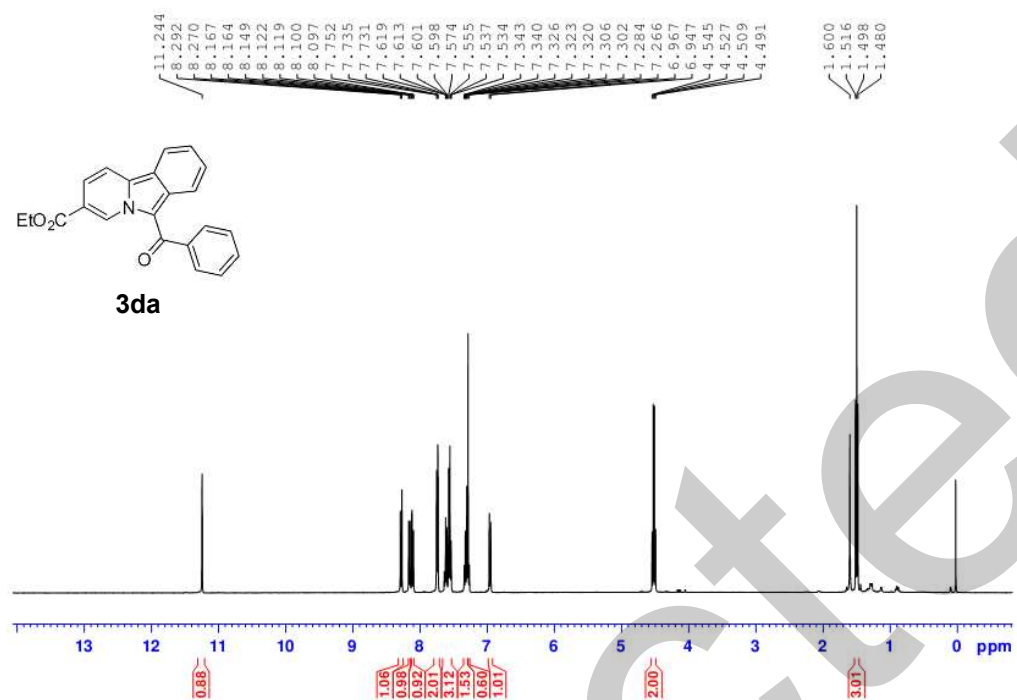
VI. Copies of ^1H and ^{13}C NMR spectra:

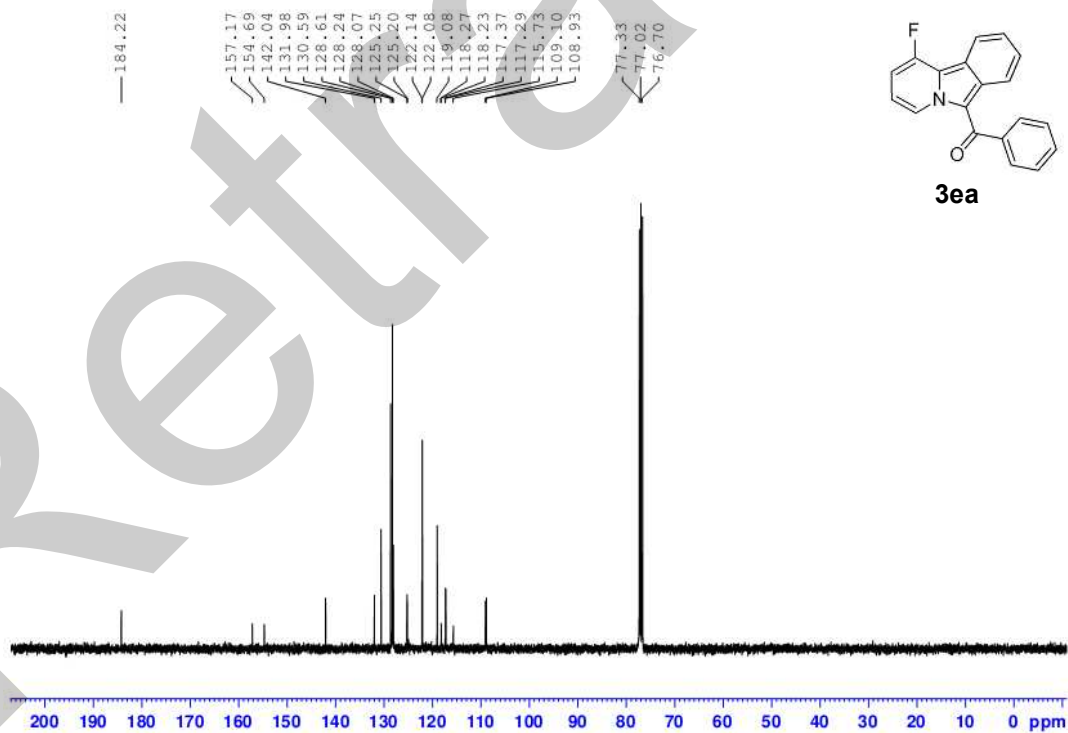
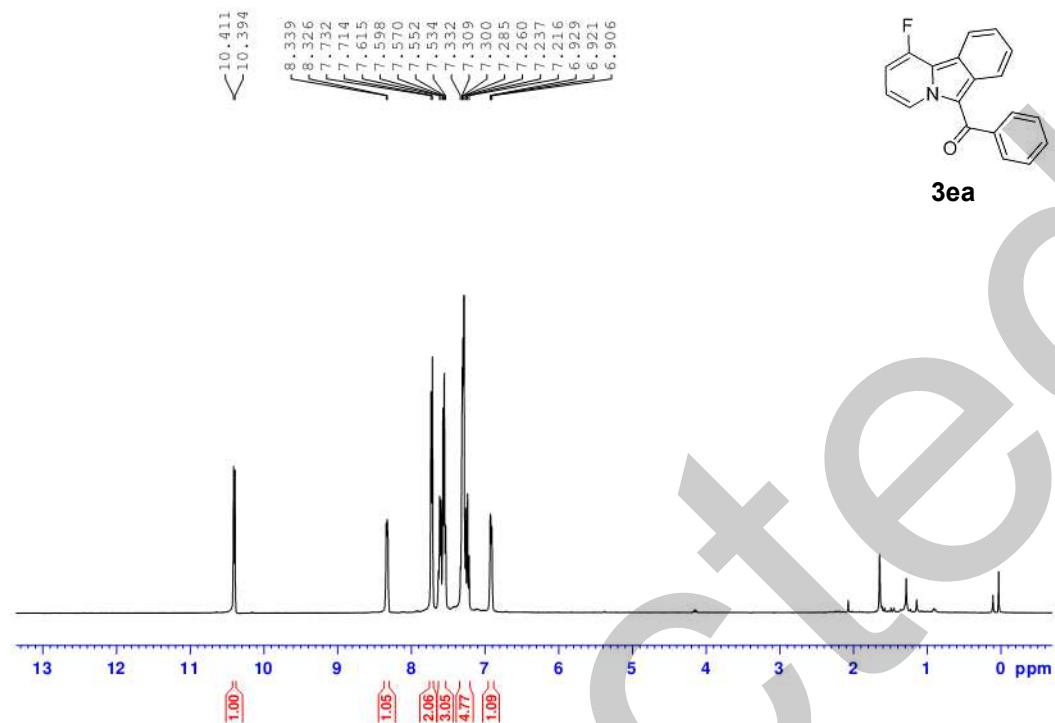


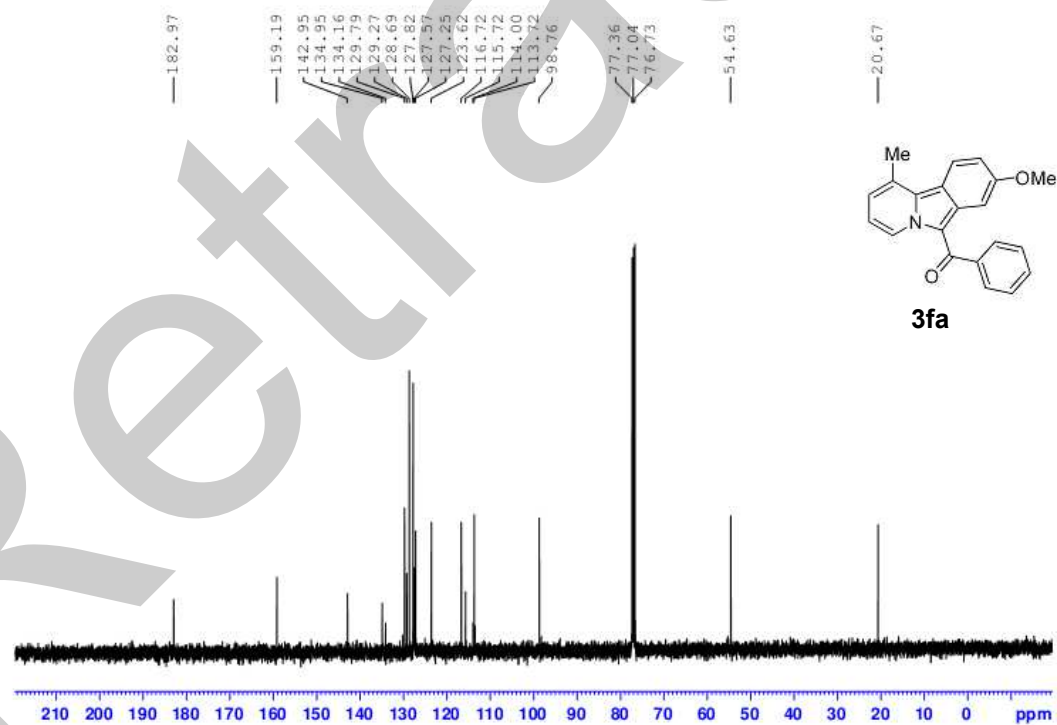
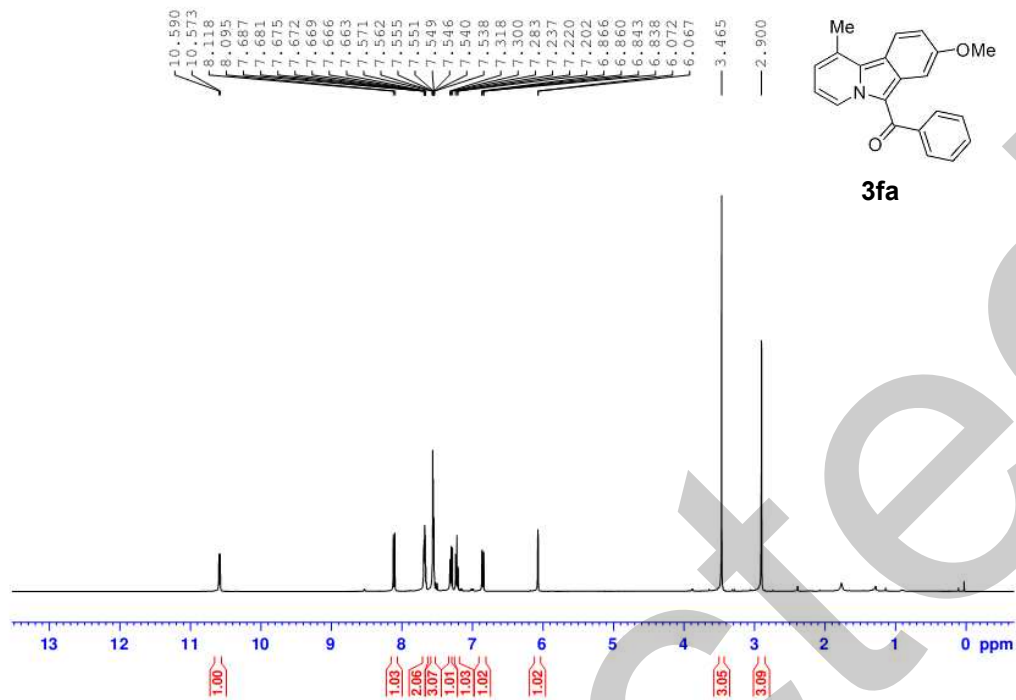


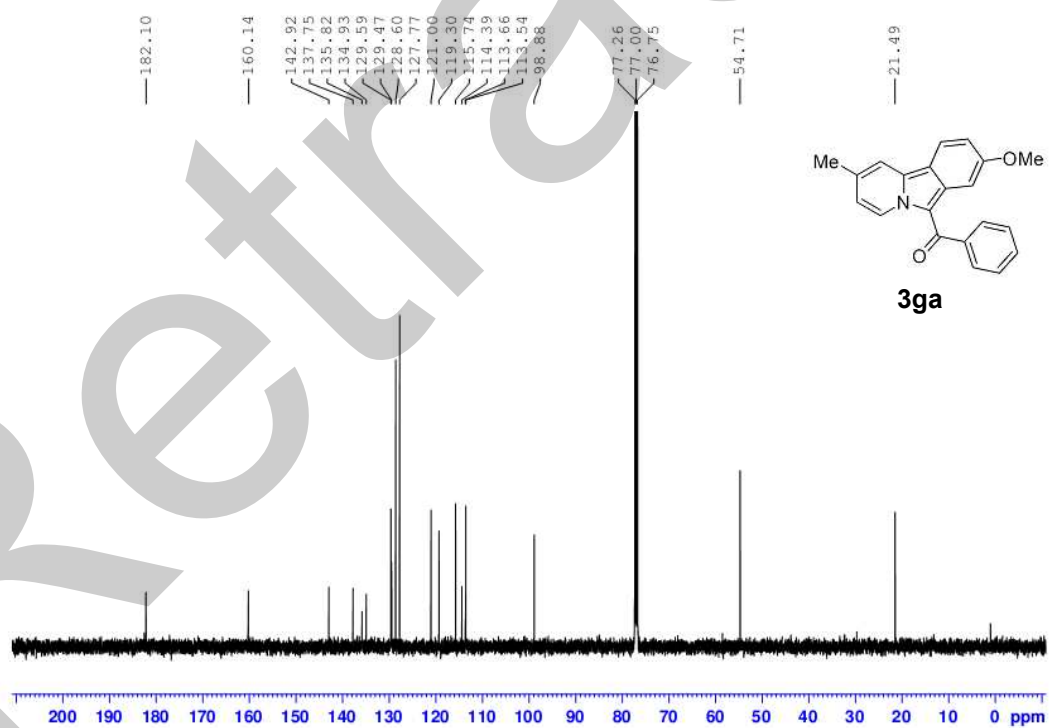
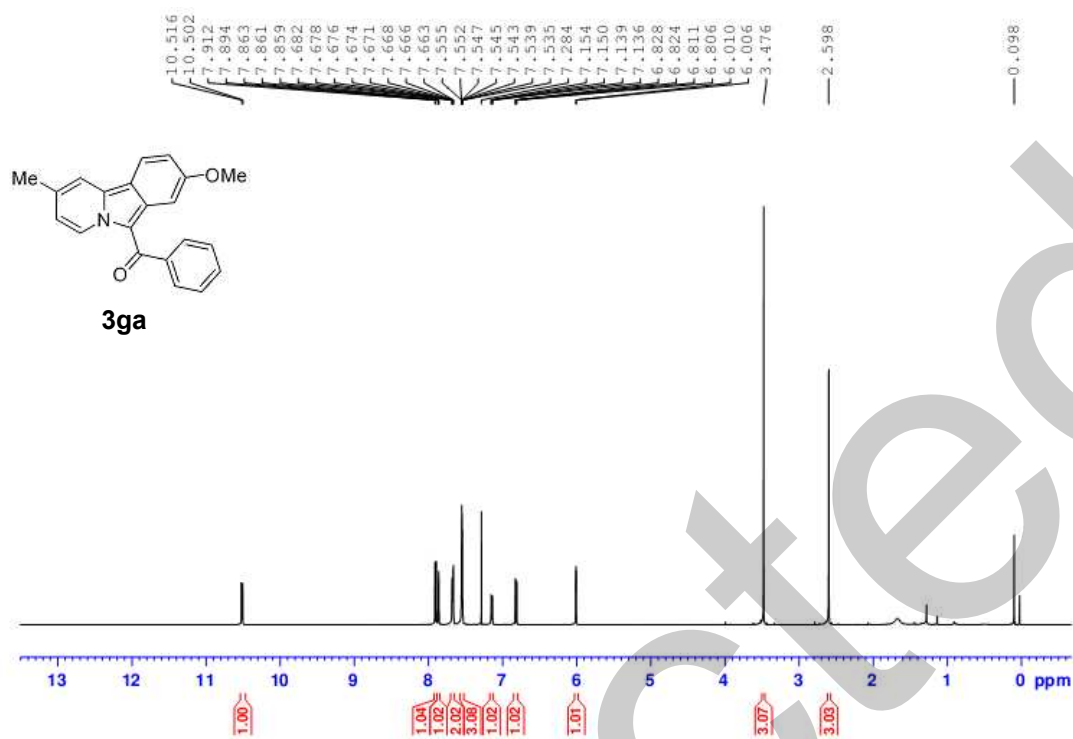


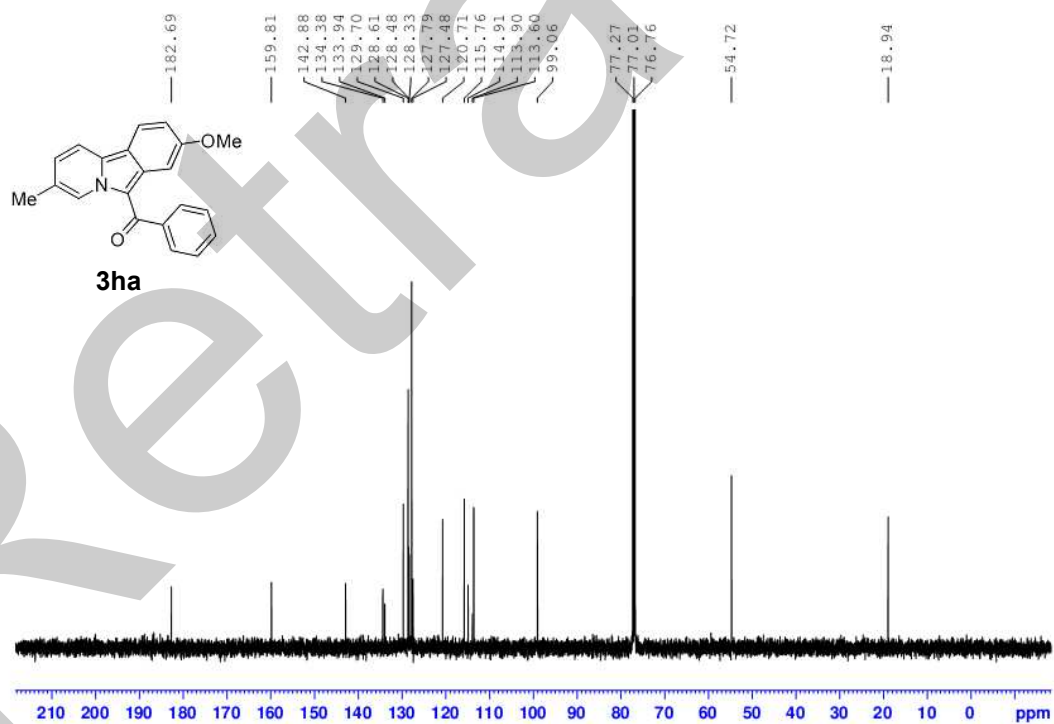
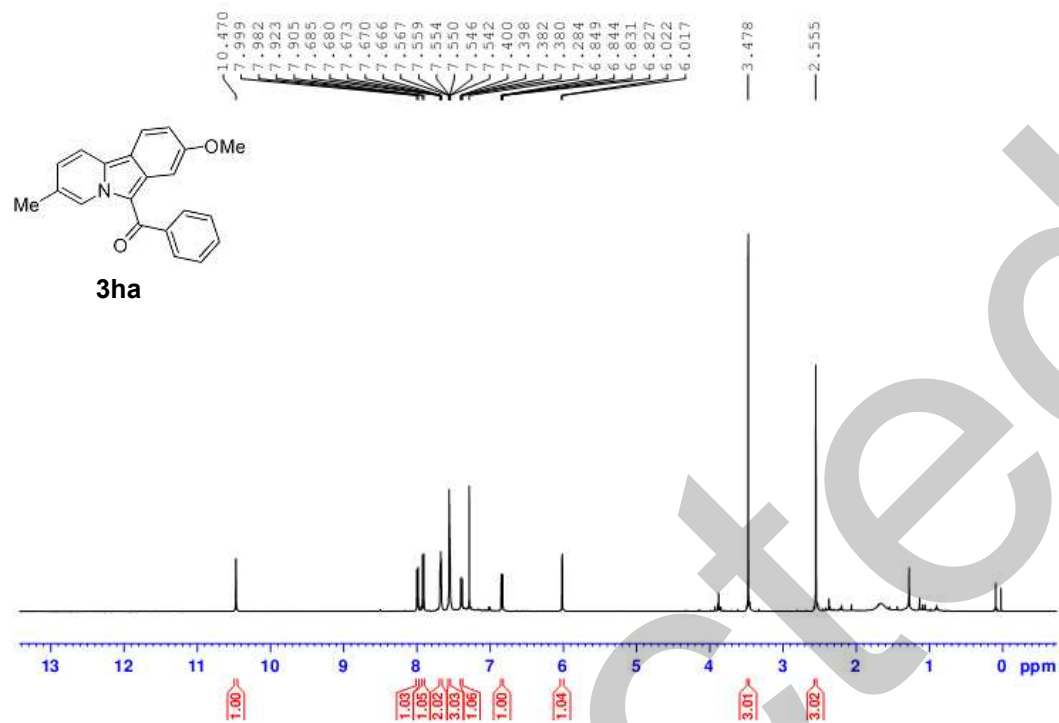


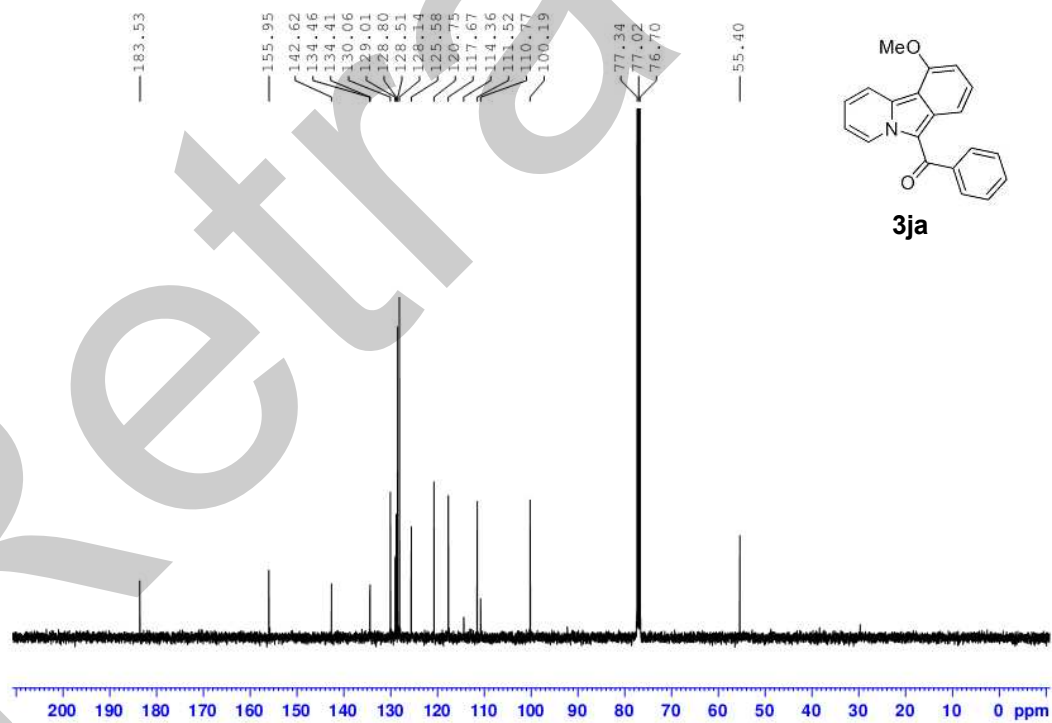
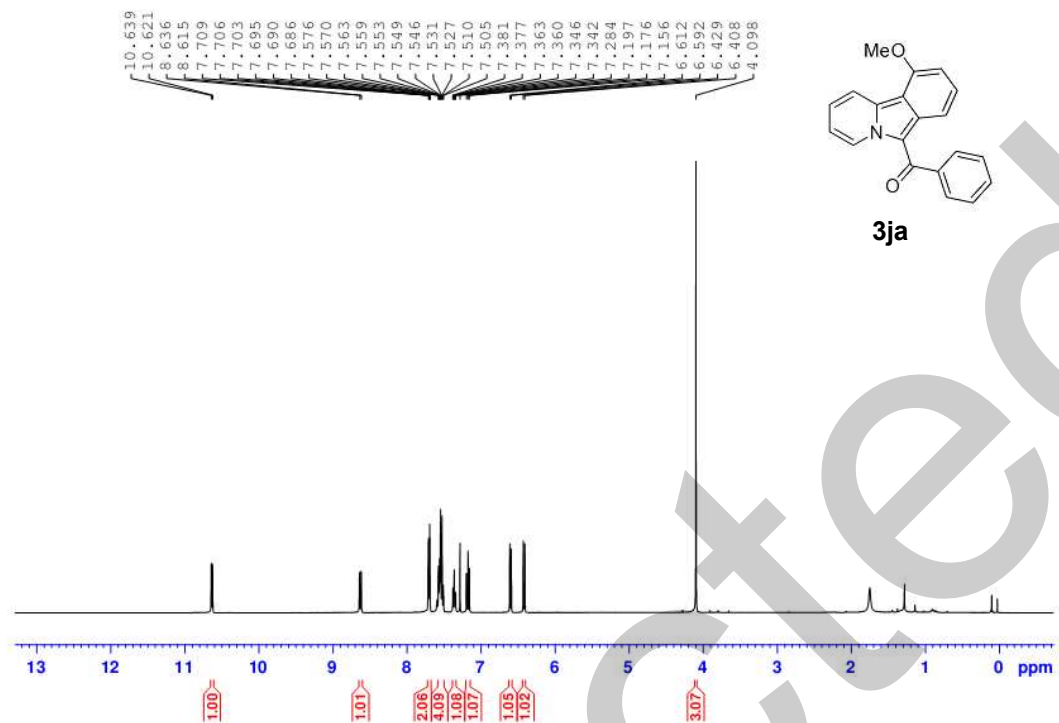


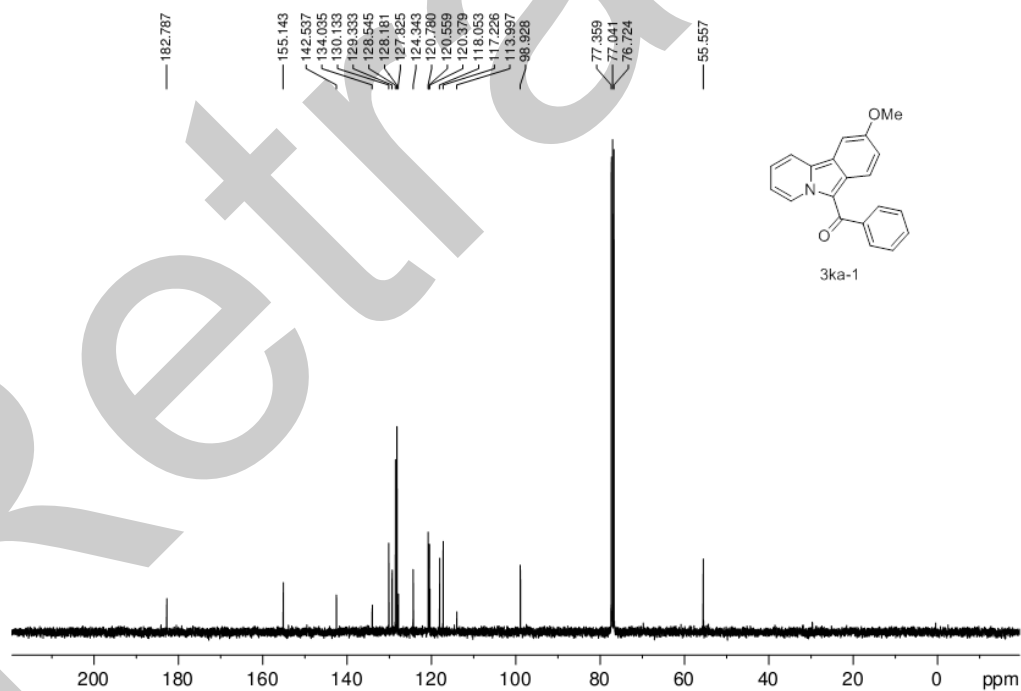
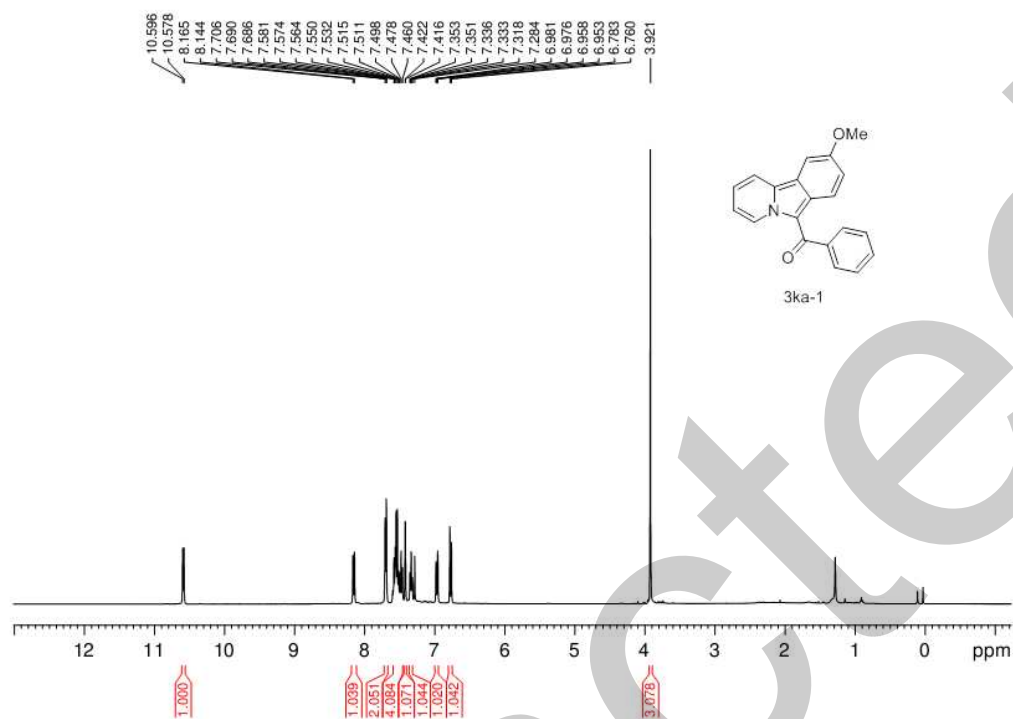


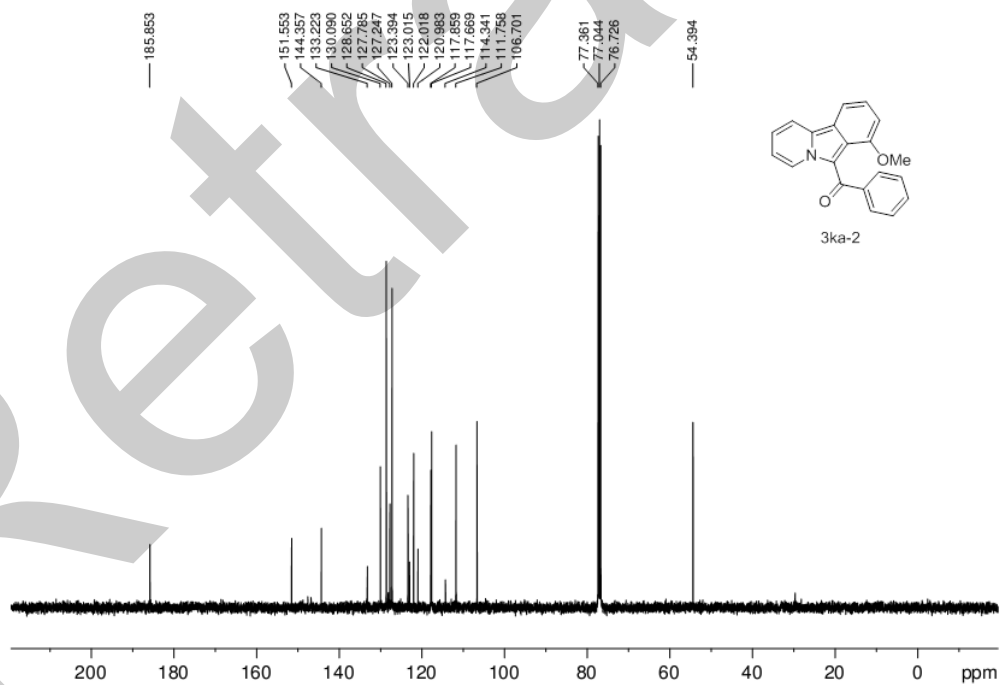
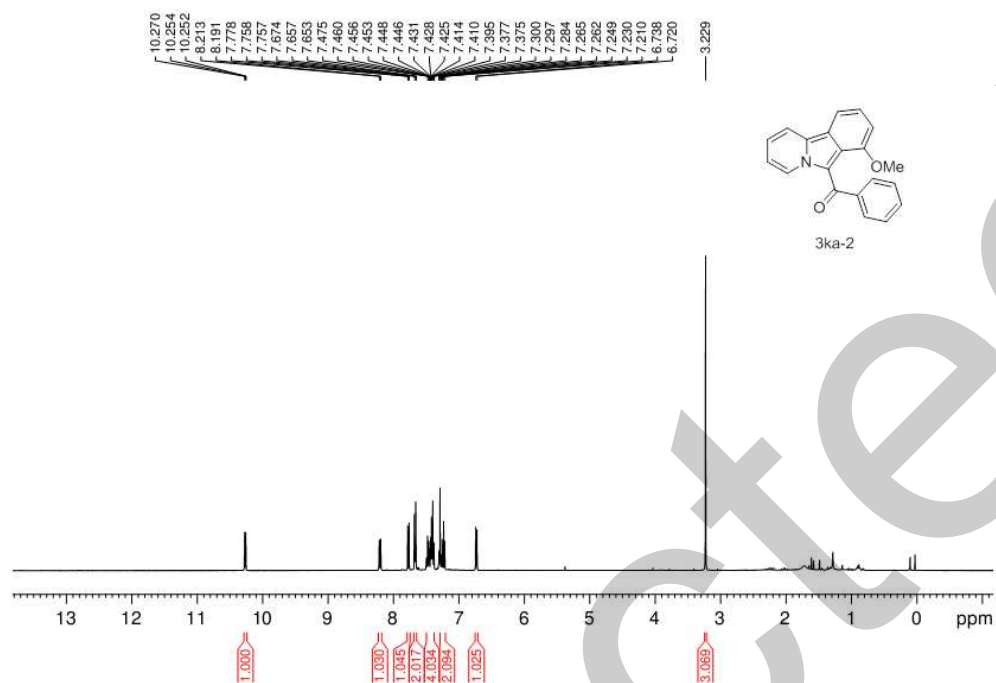


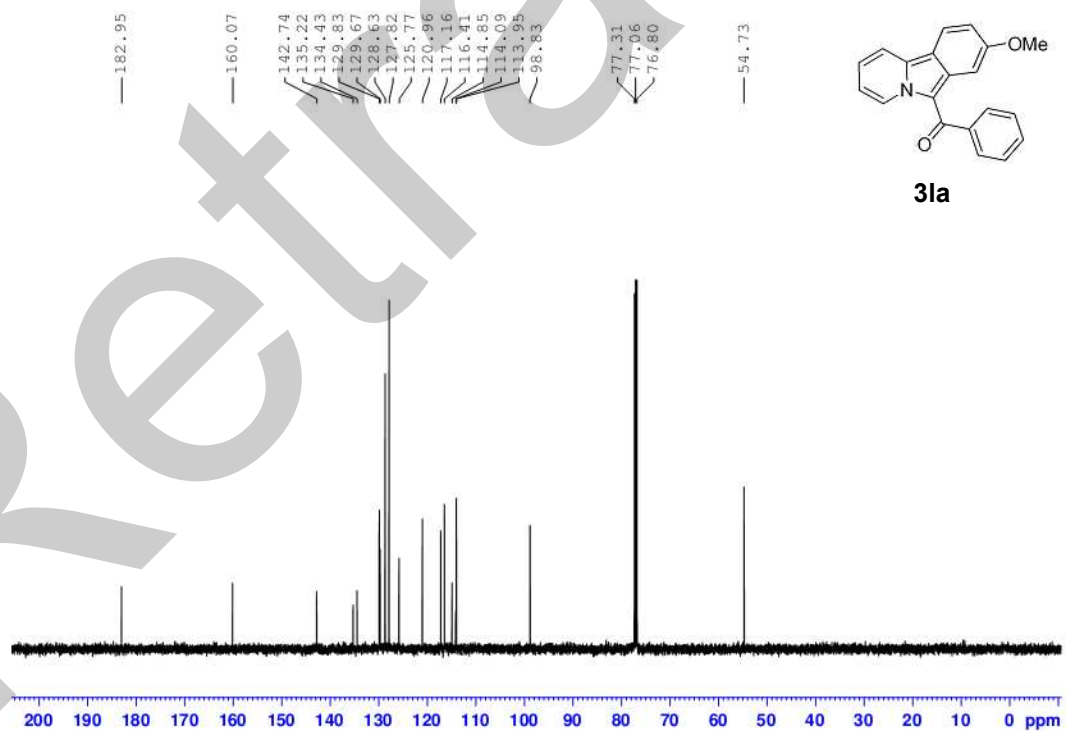
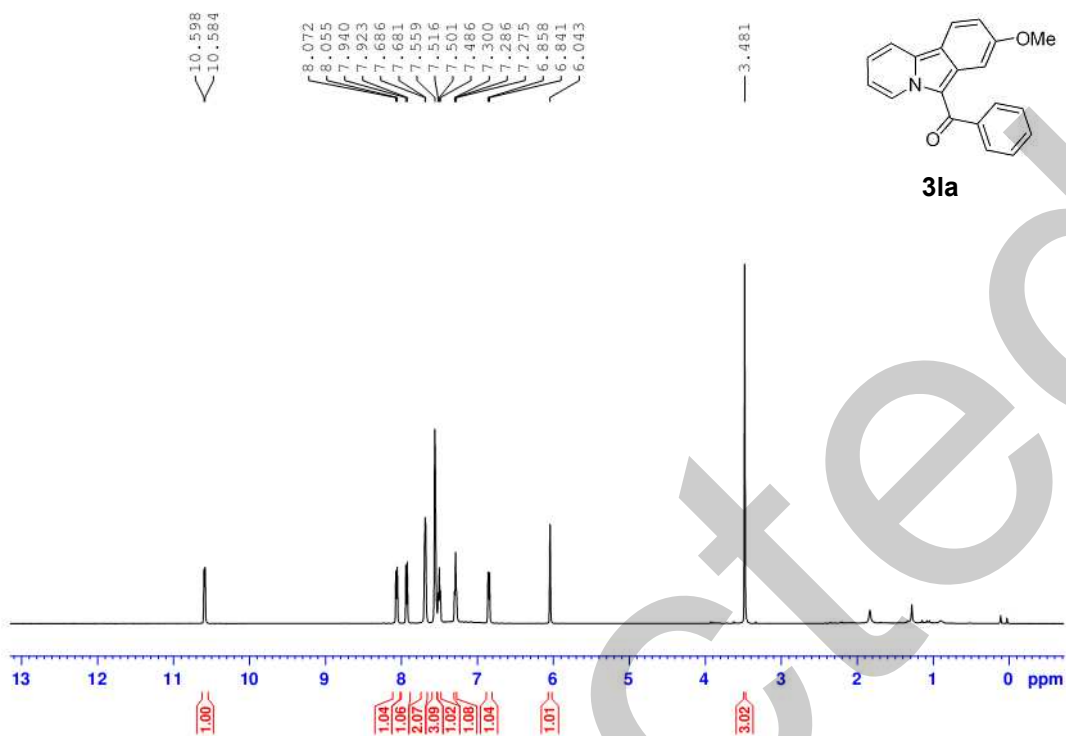


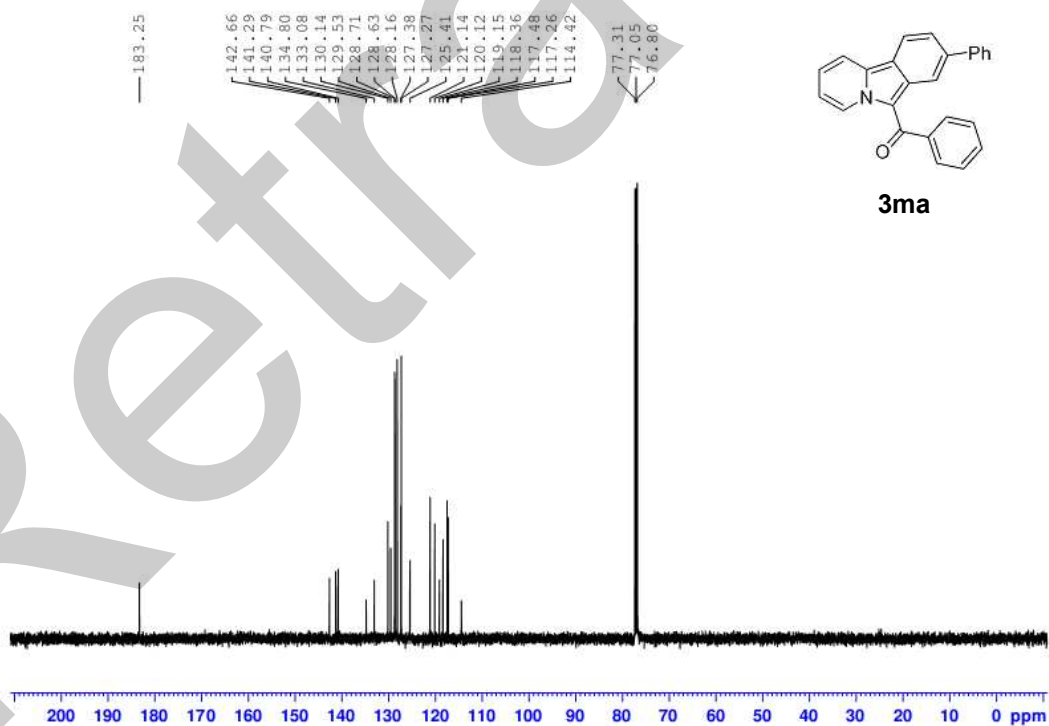
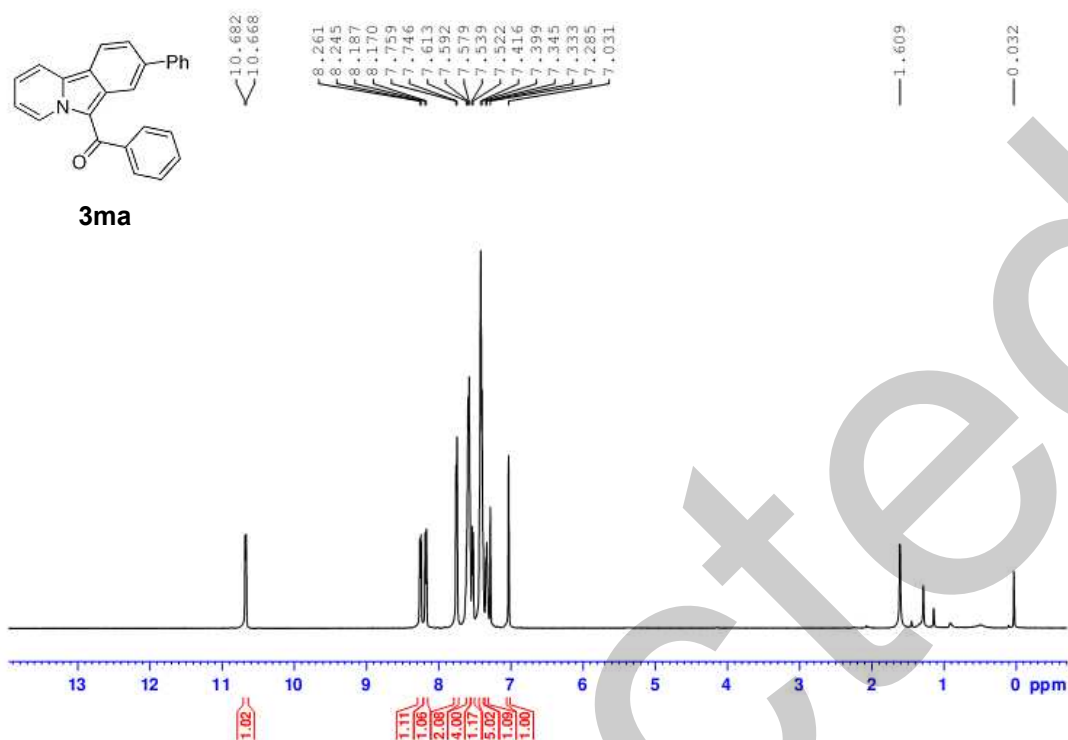


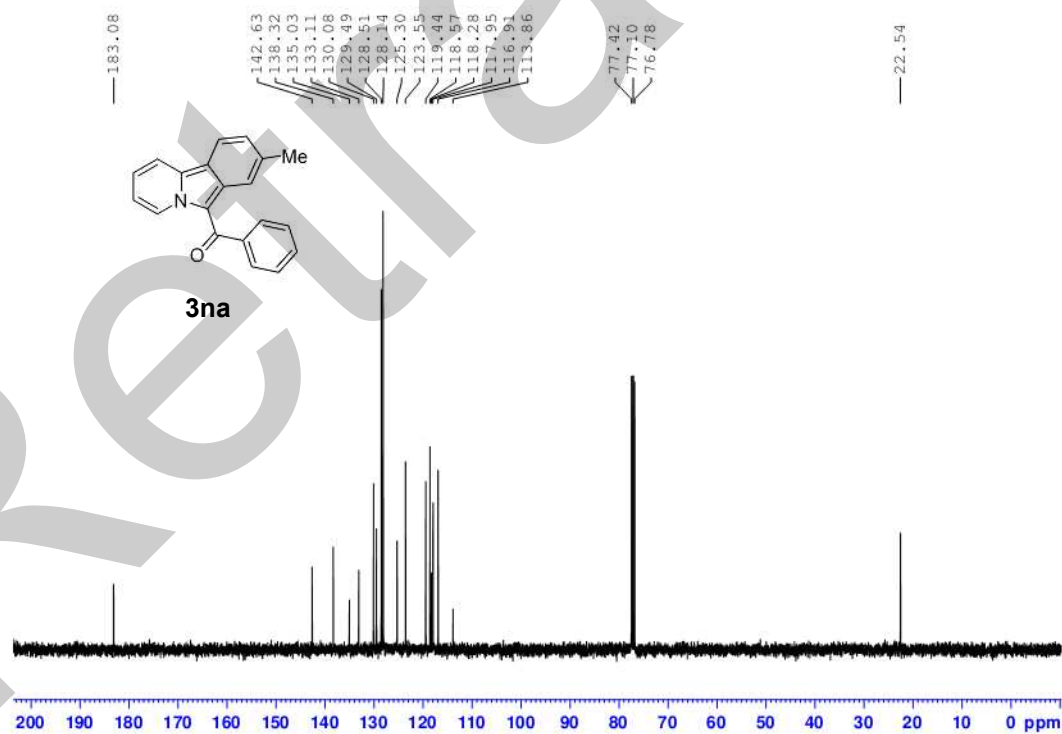
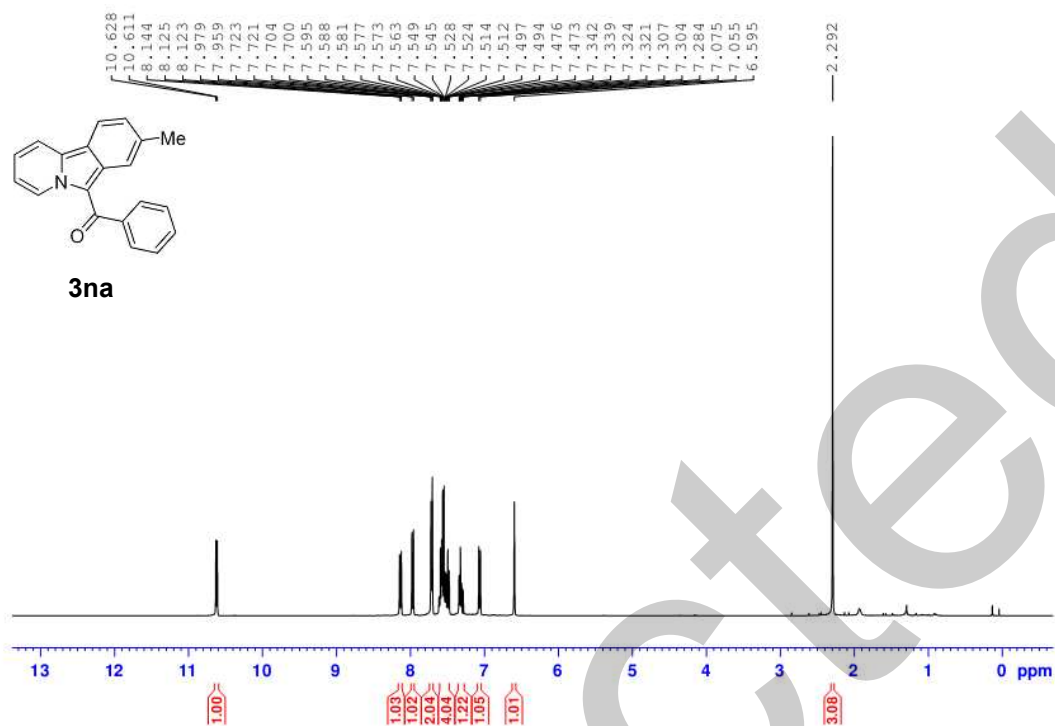


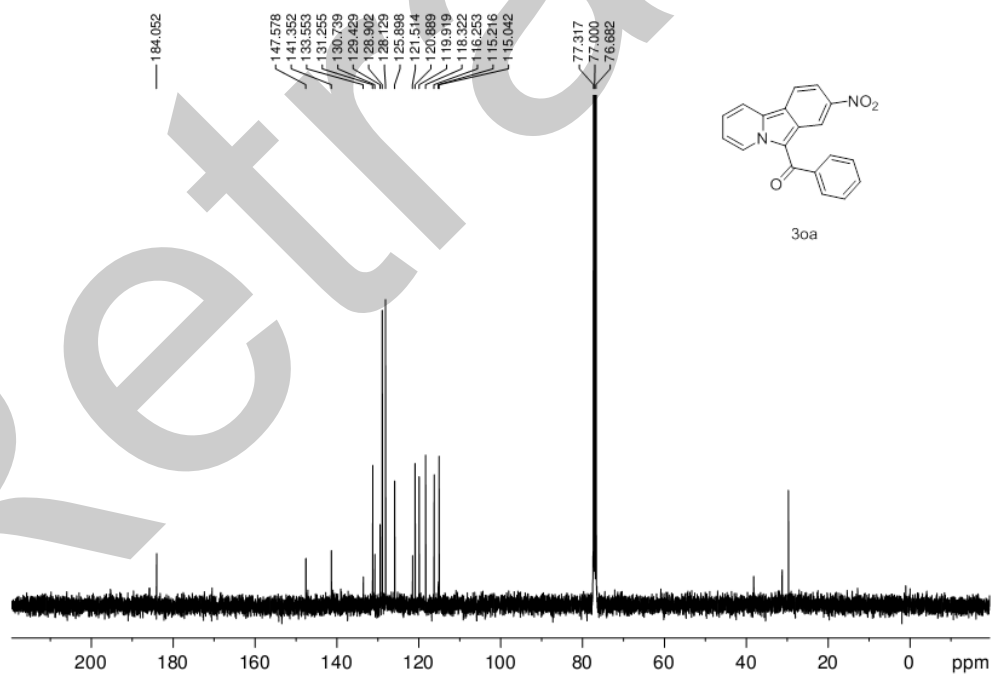
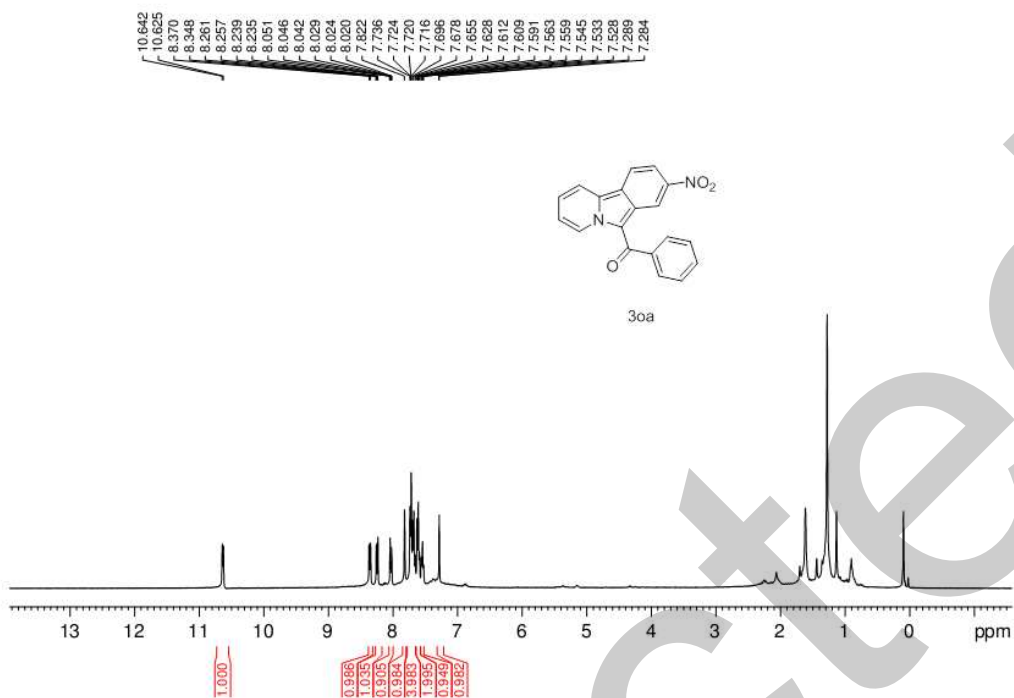


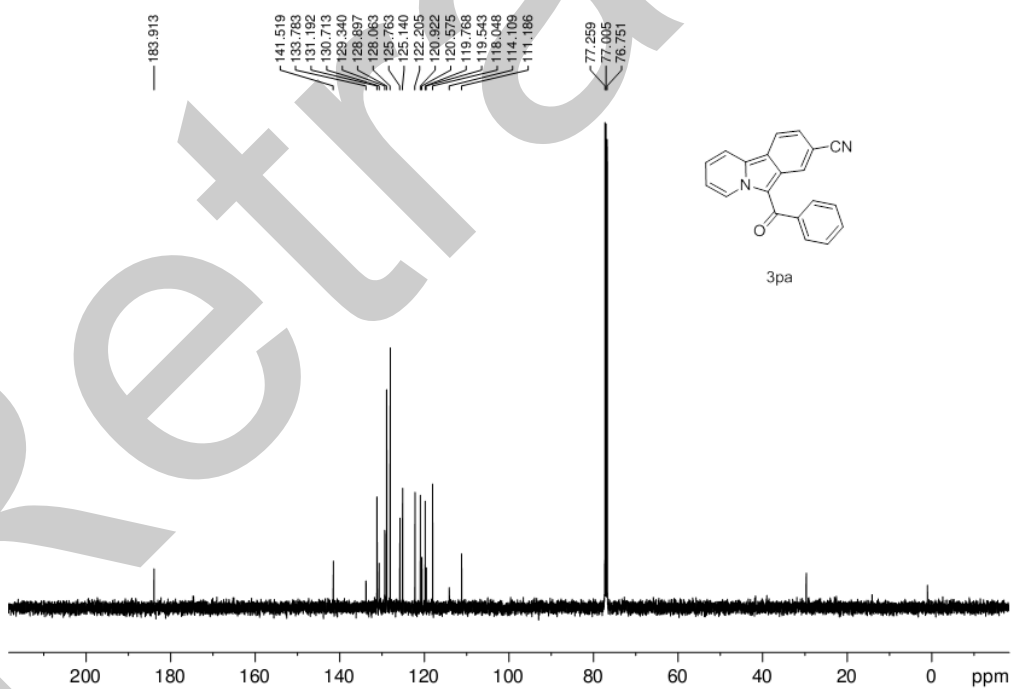
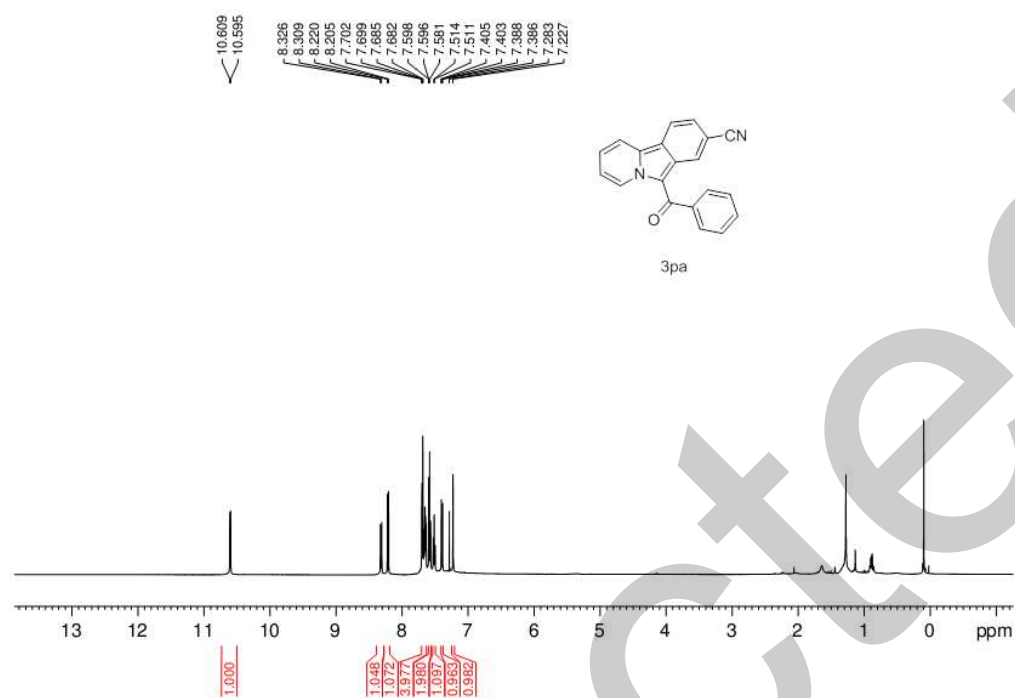


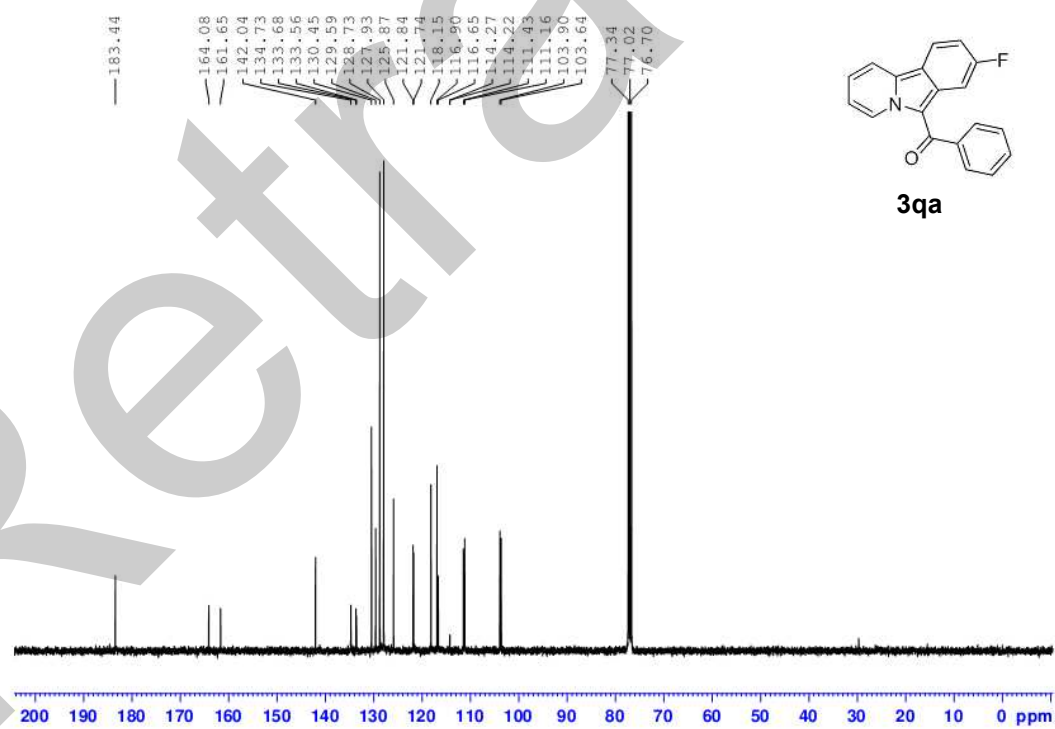
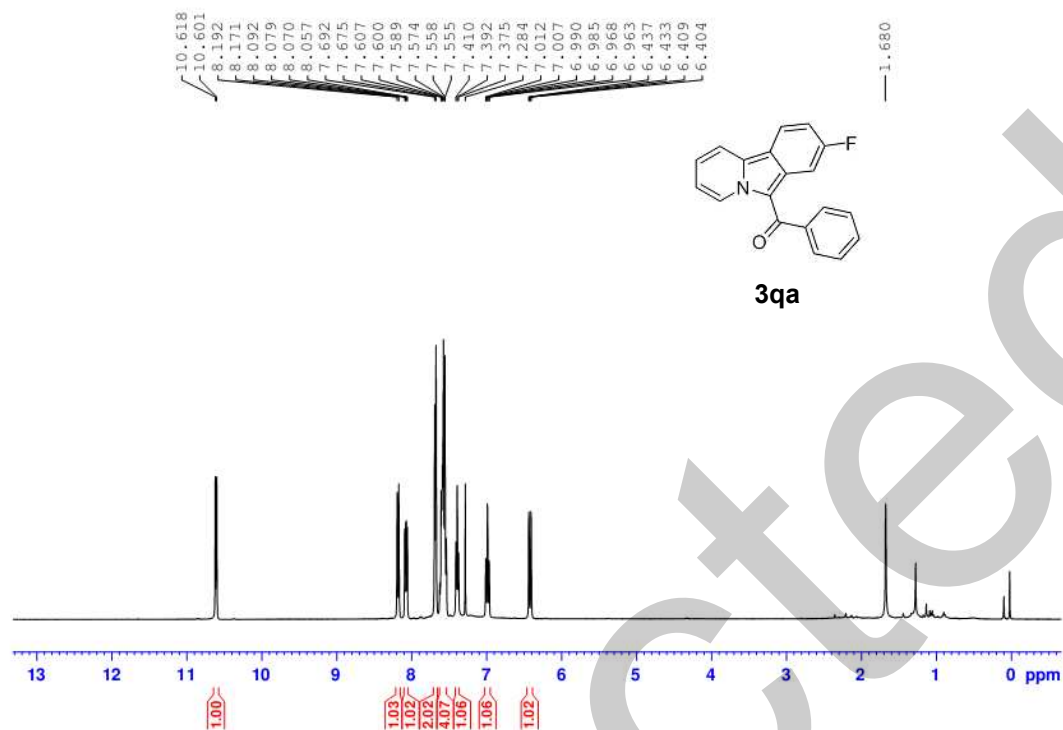


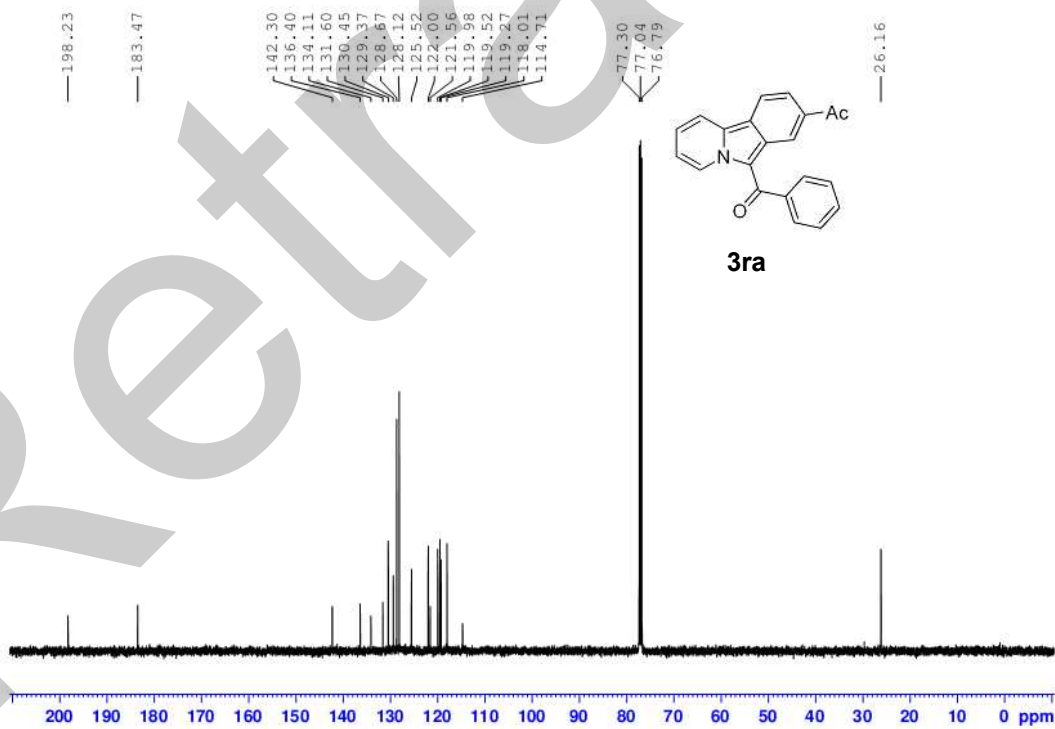
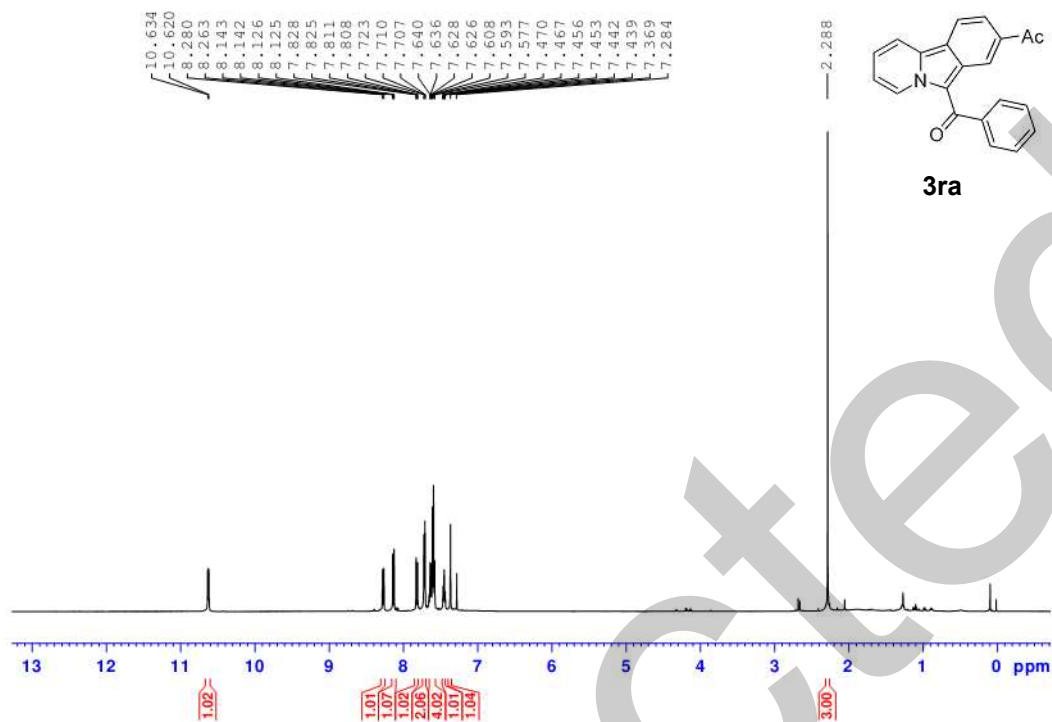


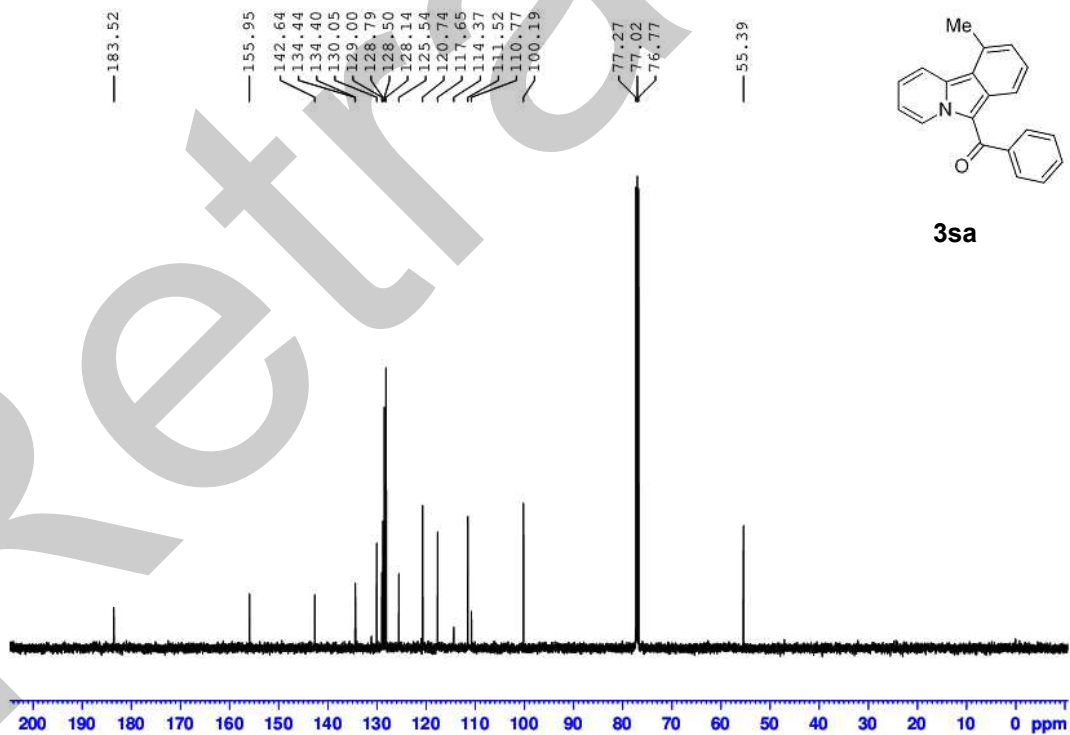
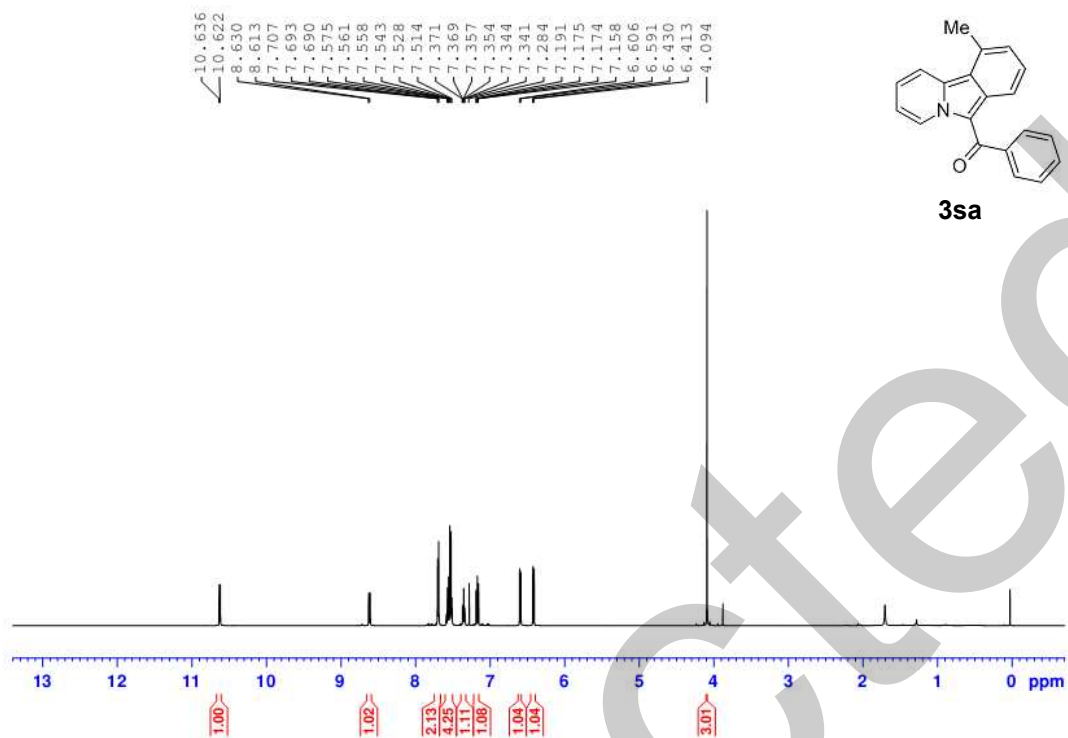


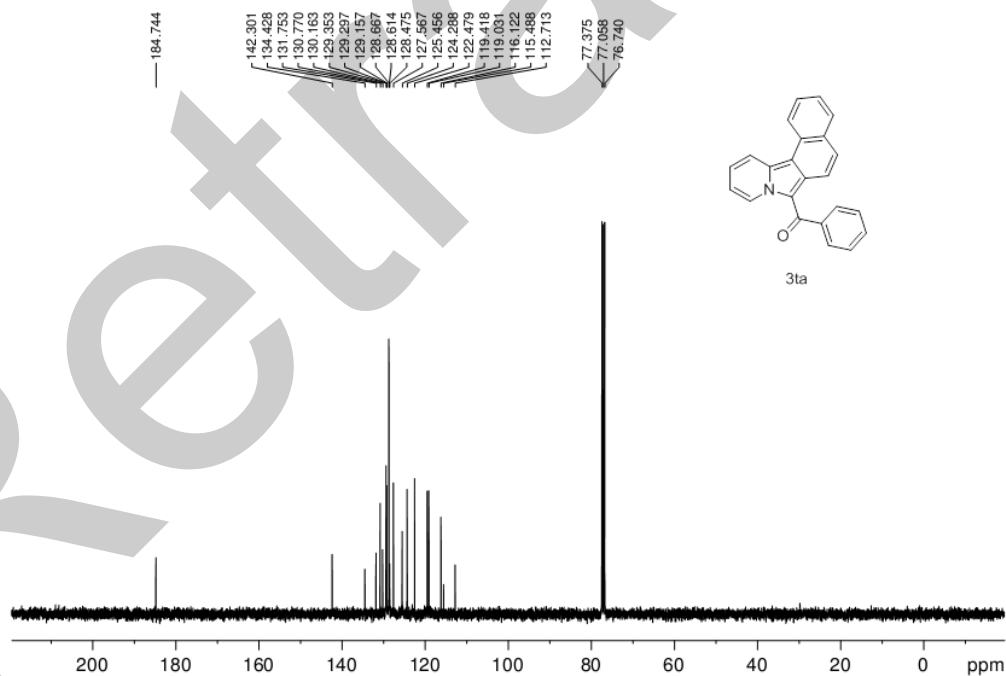
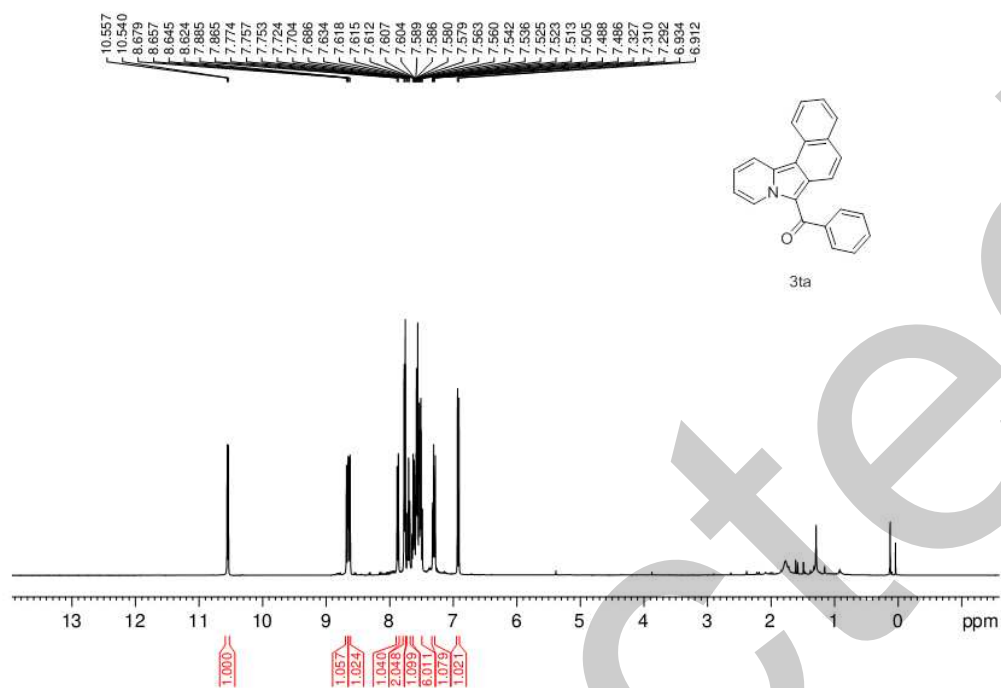


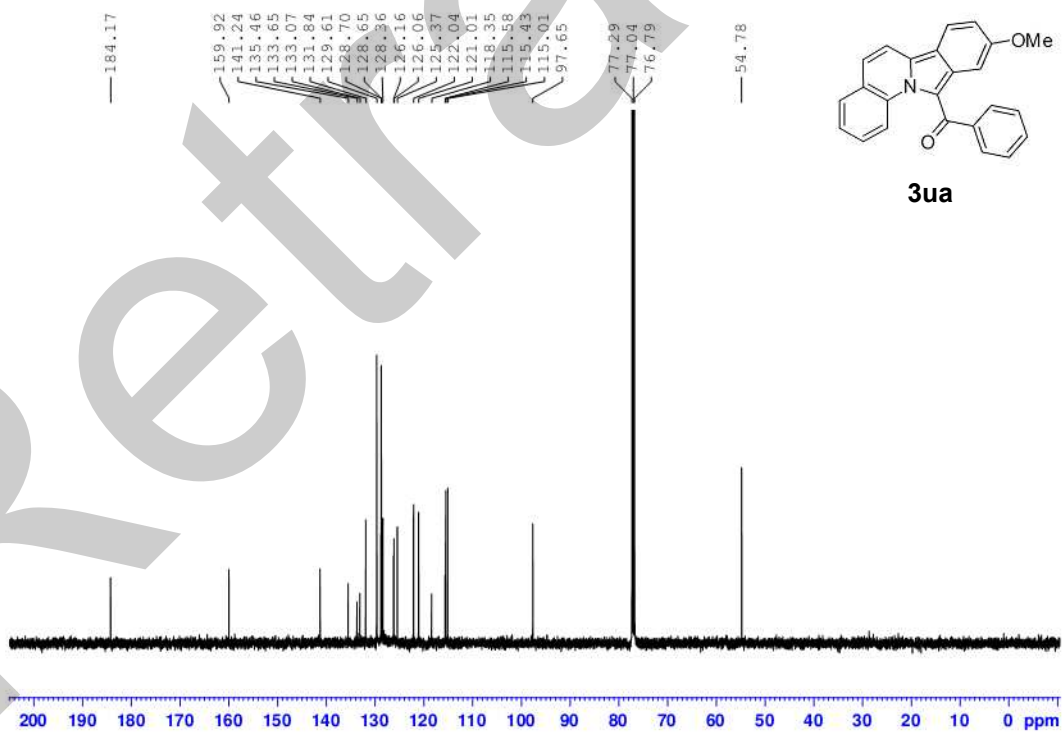
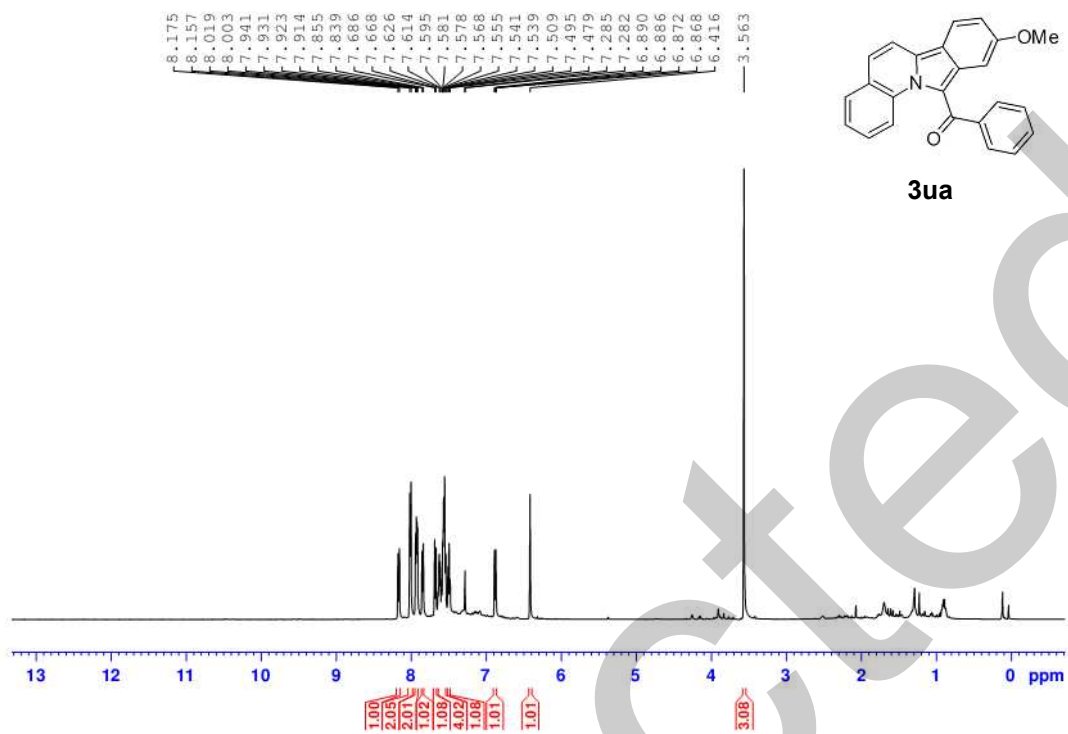


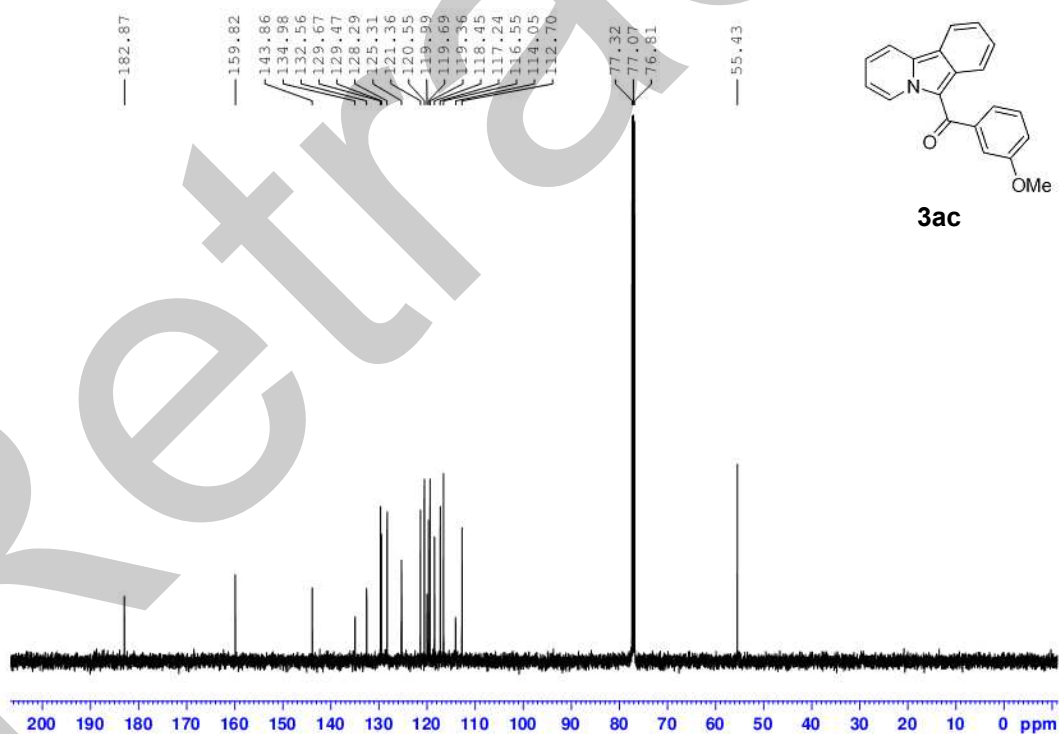
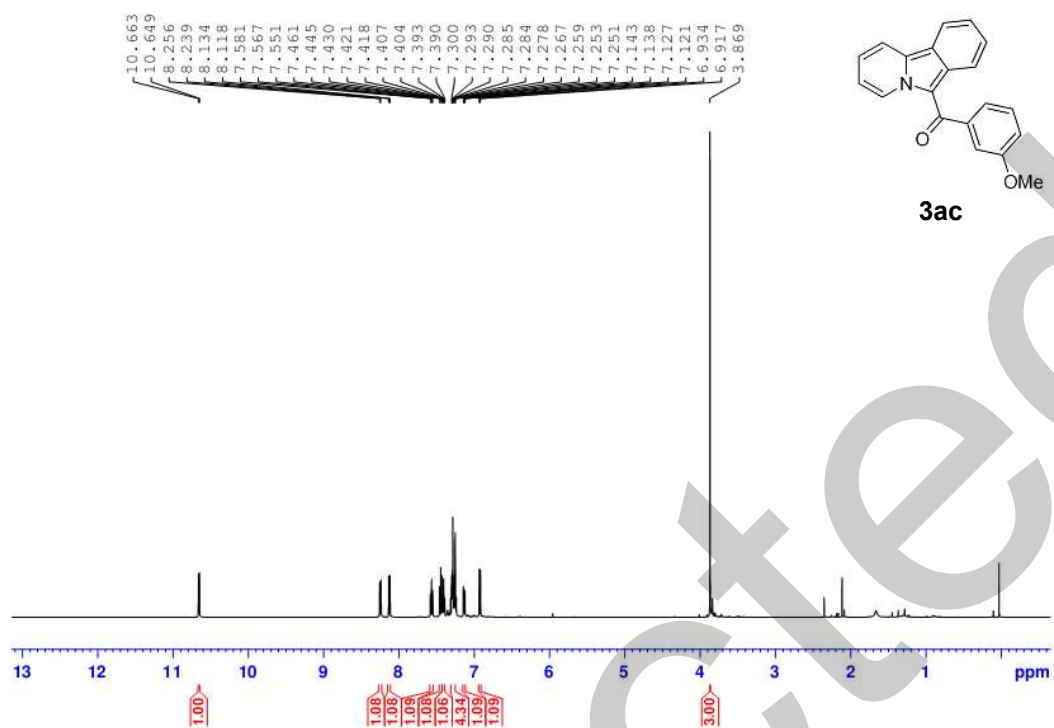


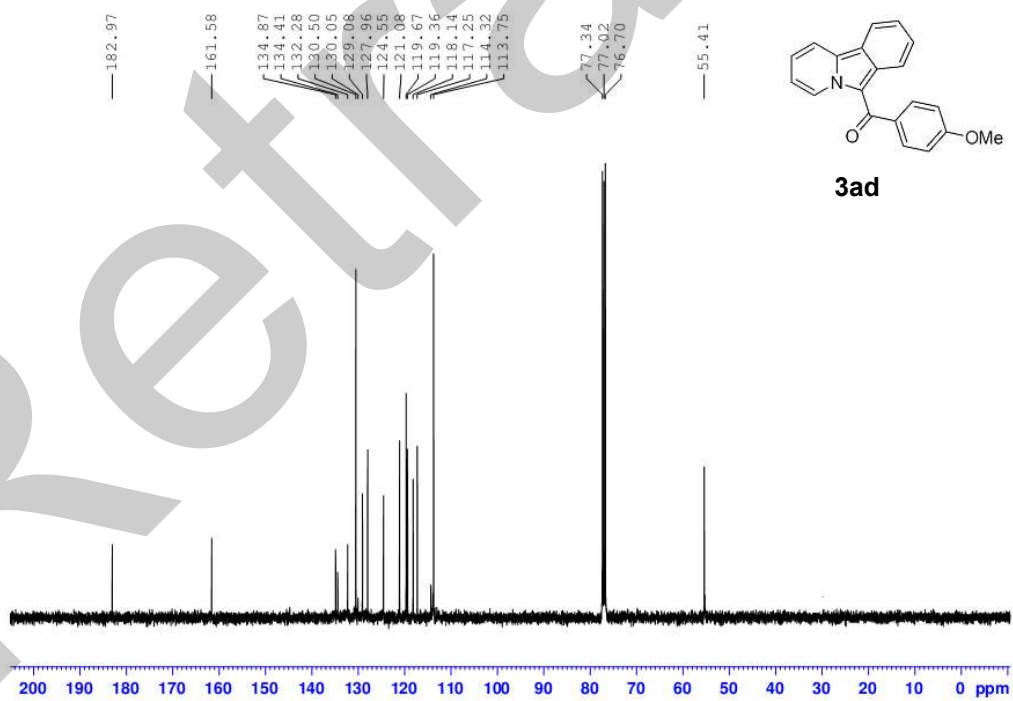
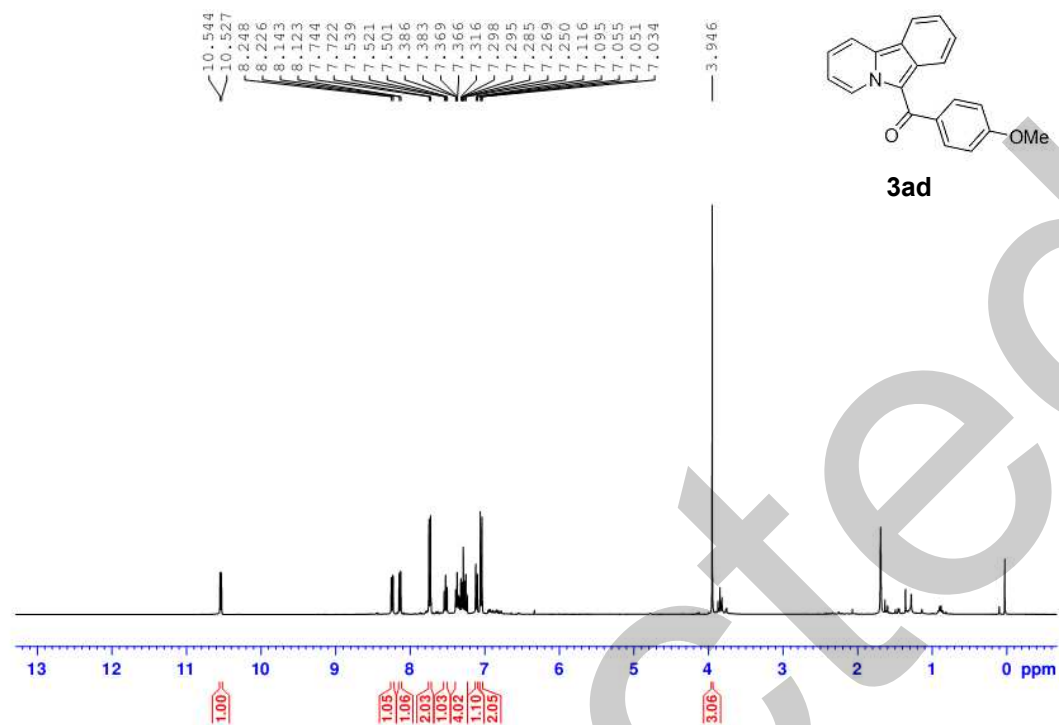


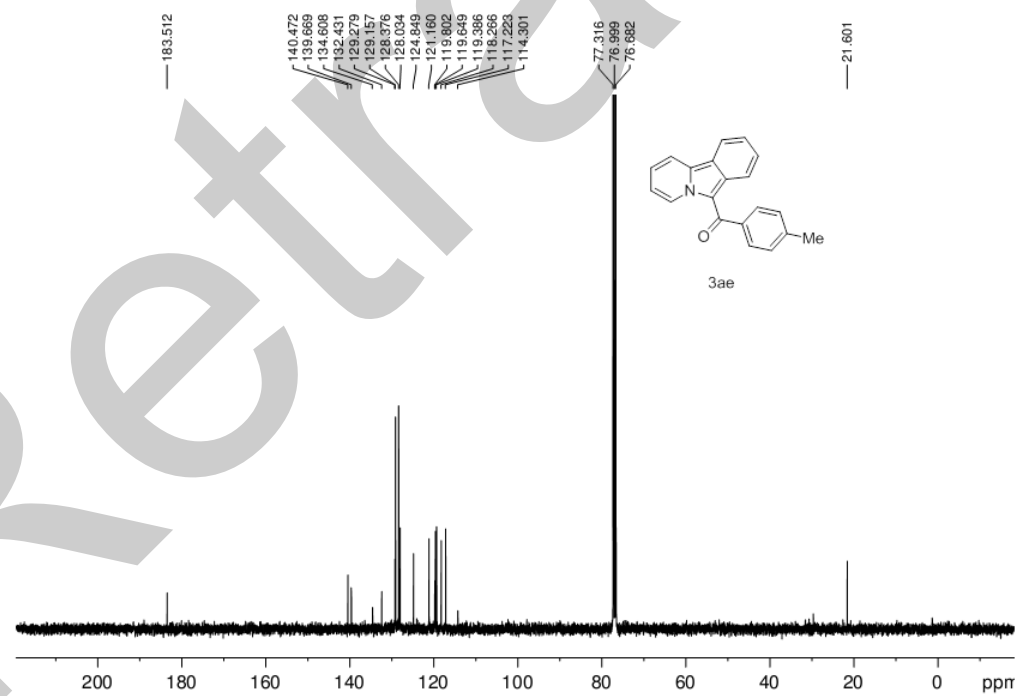
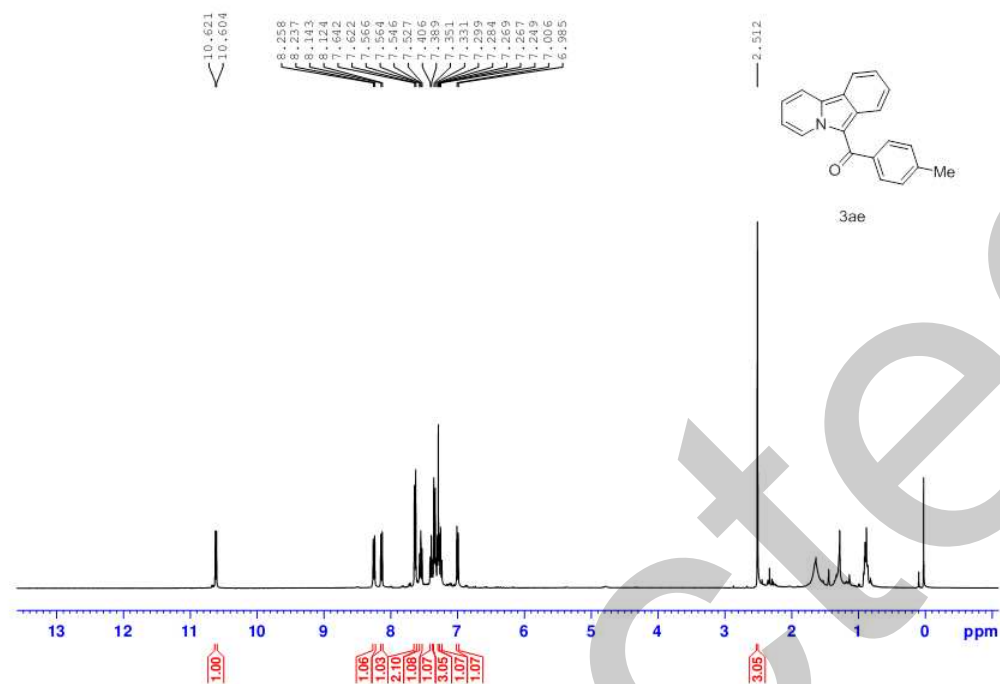


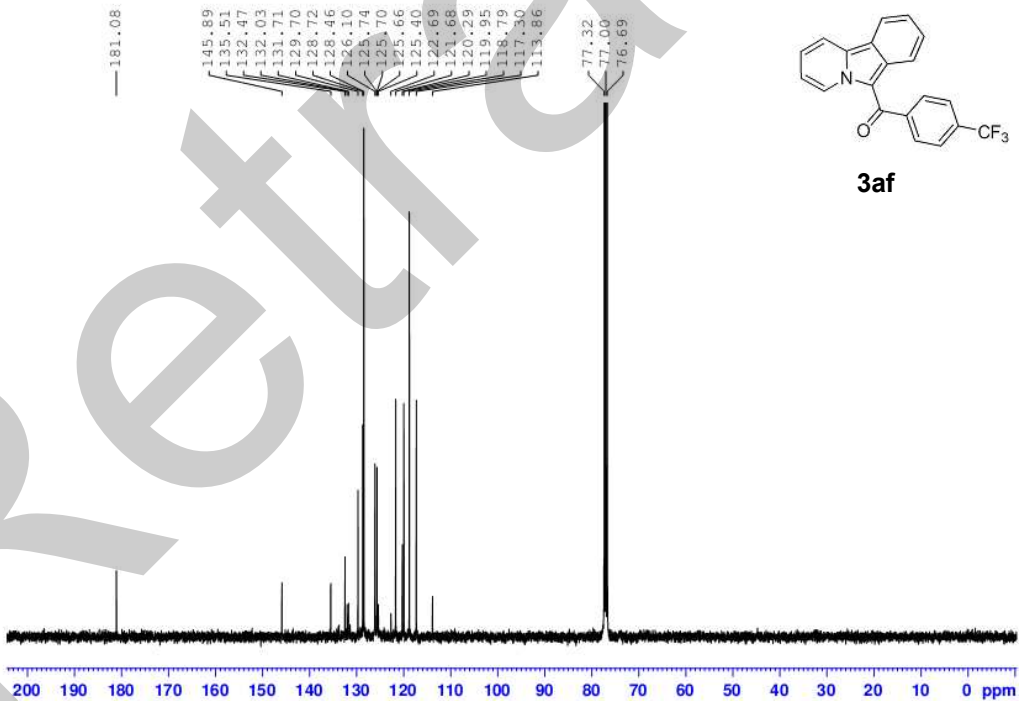
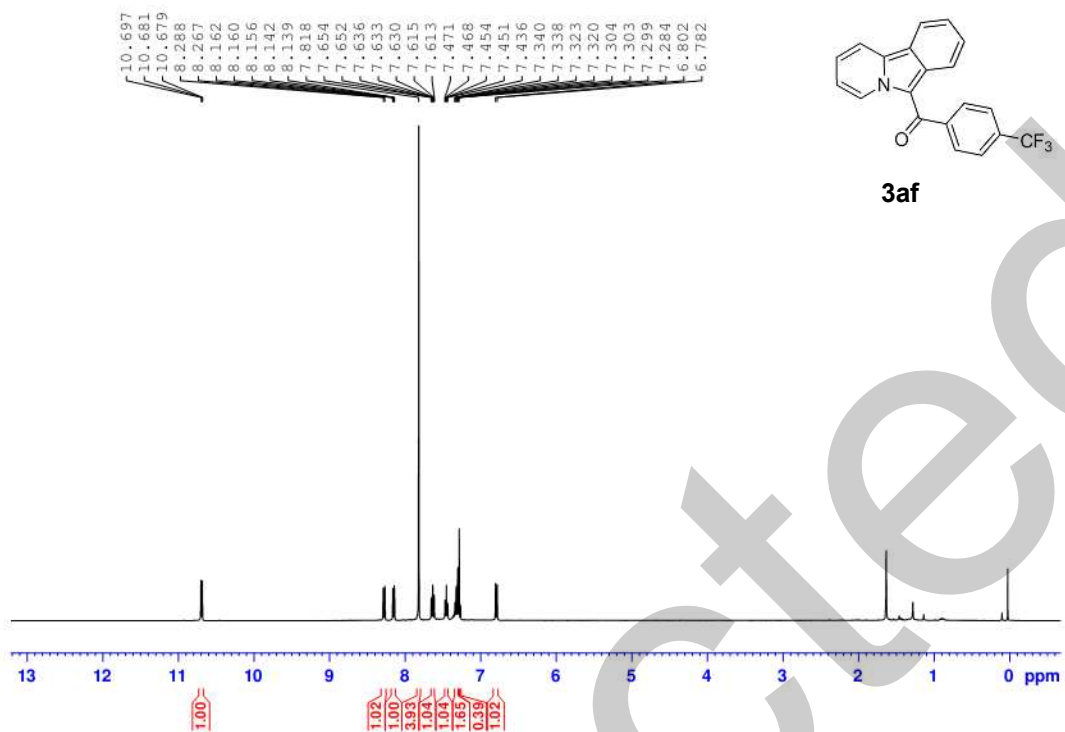


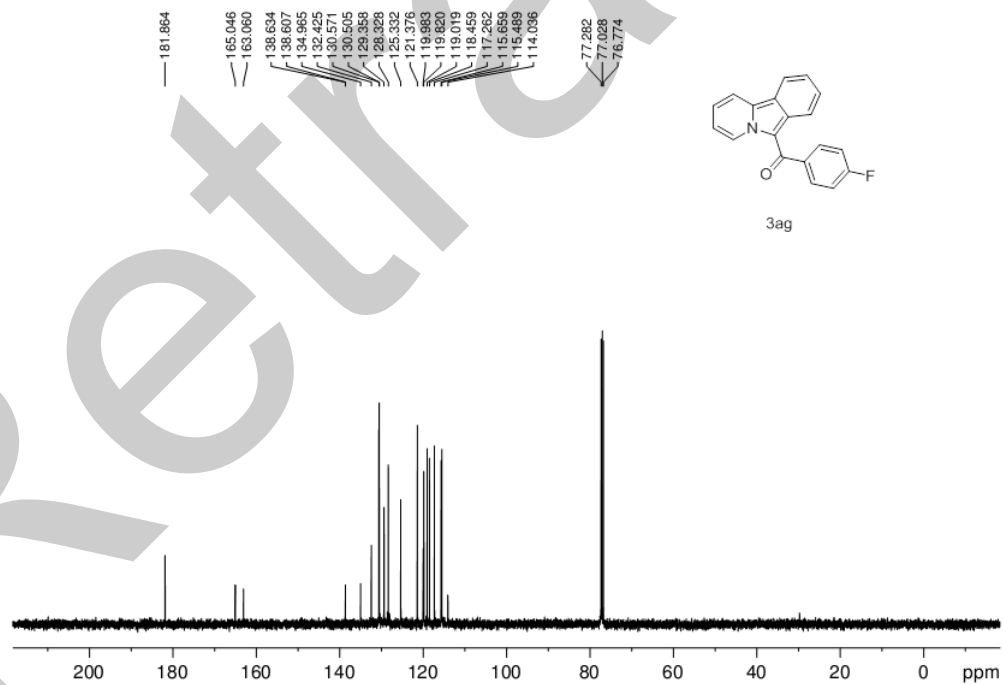
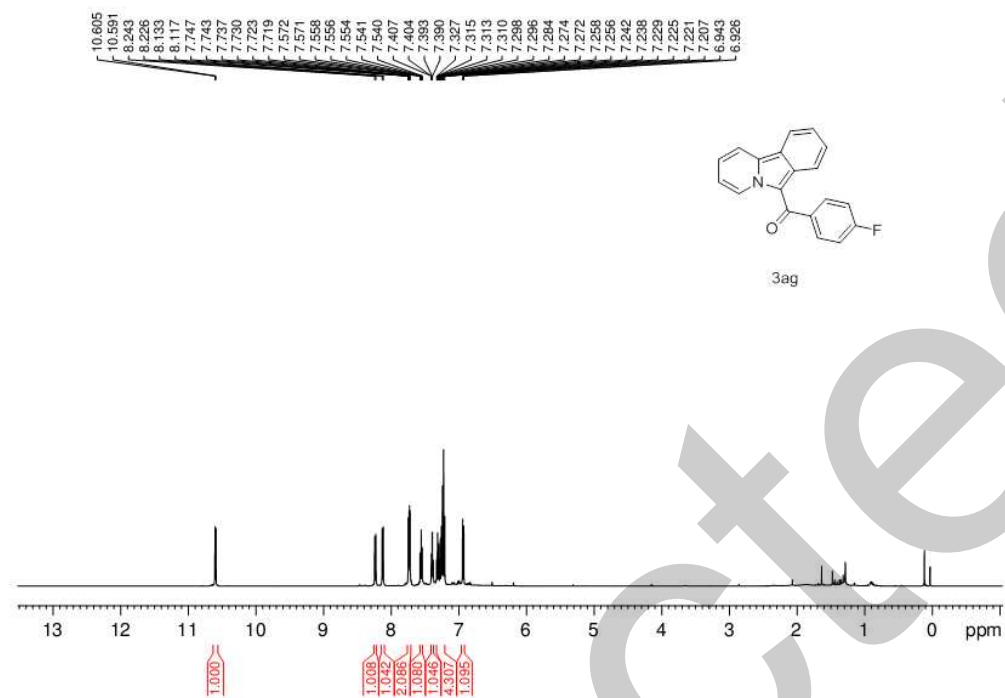


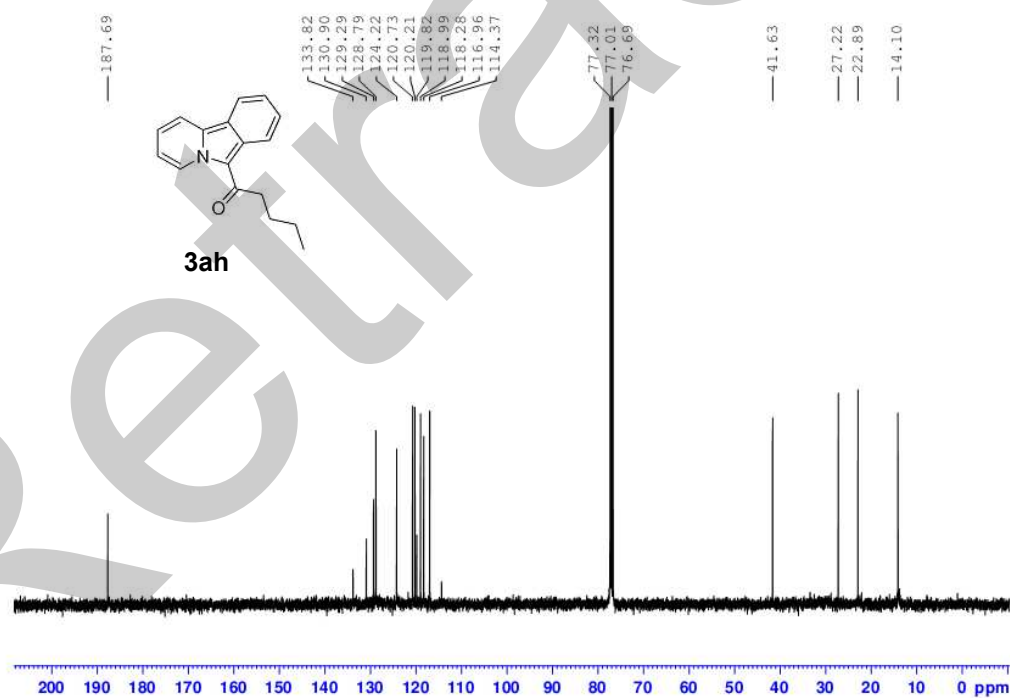
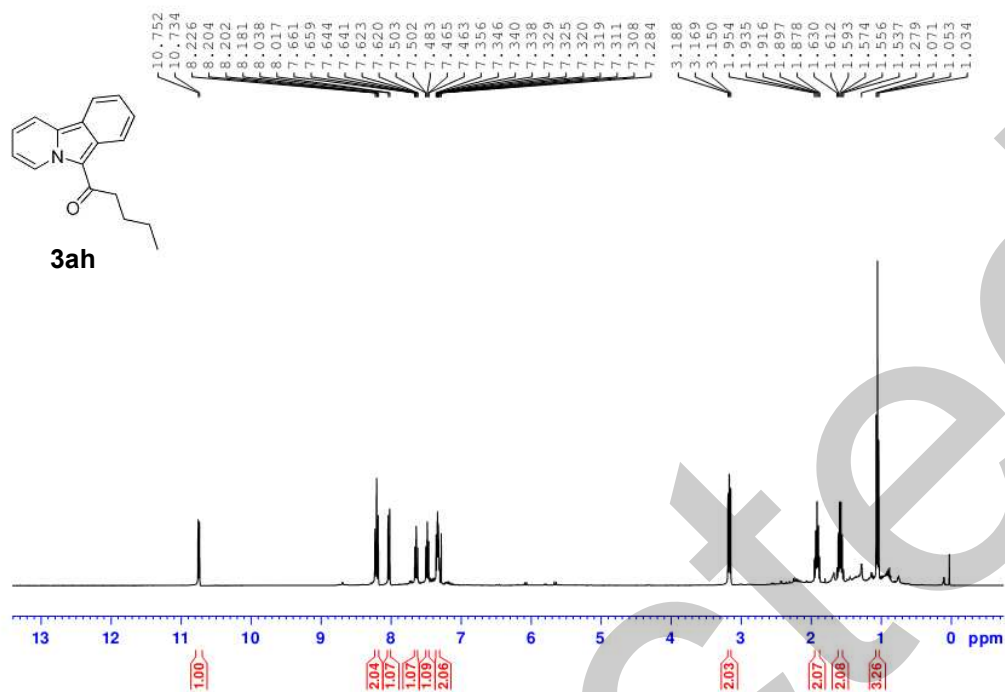










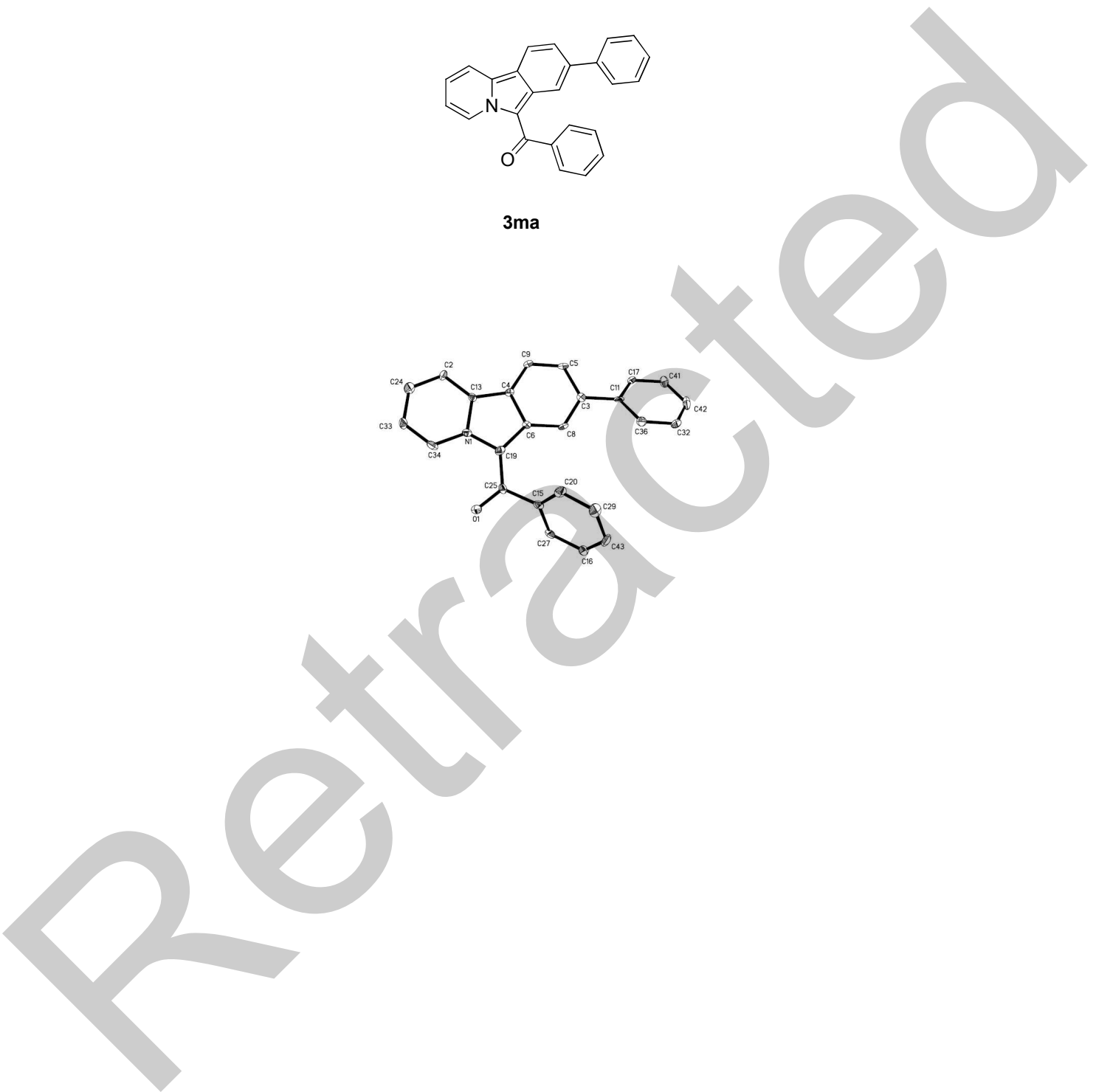


3ma

The ORTEP diagram shows the molecular structure of compound 3ma. The molecule consists of a central indole ring system. The indole ring is substituted at the 2-position with a benzoyl group (C15-C16-C17) and at the 3-position with a phenyl group (C18-C19-C20). The benzoyl group is further substituted at the carbonyl carbon (C15) with a phenyl group (C21-C22-C23). The phenyl group at the 3-position is further substituted at the para position (C24) with a phenyl group (C25-C26-C27). The structure is shown with thermal ellipsoids at the 50% probability level. The atoms are labeled with their respective element symbols and numbers: C1-C20 for carbon, N1 for nitrogen, and O1 for oxygen.

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