Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

DBU-catalyzed dearomative annulation of 2-pyridylacetates with *α,β*-unsaturated pyrazolamides for the synthesis of multisubstituted 2,3-dihydro-4*H*-quinolizin-4-ones

Yao-Bin Shen,[a,b,c] Jian-Qiang Zhao,[b] Zhen-Hua Wang,[b] Yong You,[b] Ming-Qiang Zhou,[a]* and Wei-Cheng Yuan[a,b]*

[a] National Engineering Research Center of Chiral Drugs, Chengdu Institute of Organic Chemistry, Chinese Academy of Sciences, Chengdu, 610041, China

[b] Innovation Research Center of Chiral Drugs, Institute for Advanced Study, Chengdu University, Chengdu, 610106, China

[c] University of Chinese Academy of Sciences, Beijing, 100049, China

E-mail: yuanwc@cioc.ac.cn
screenfilm@foxmail.com

Supporting Information

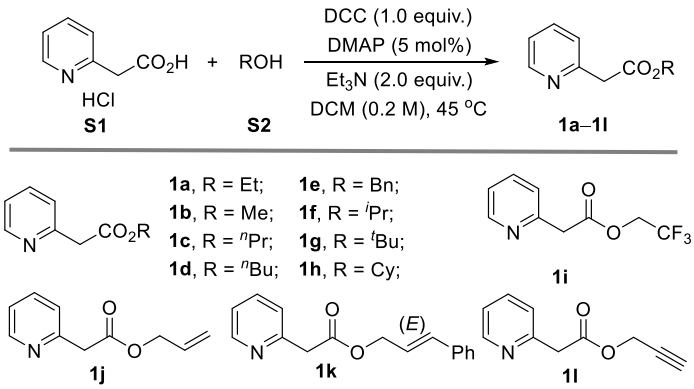
Table of Contents

1. General Information

Unless otherwise noted, all commercial available reagents were used as received without further purification. Reactions were monitored by thin layer chromatography (TLC) with 0.2 mm silica gel-coated HSGF 254 plates visualized by UV light at 254 or 365 nm. Products were isolated and purified by column chromatography on silica gel (200−300 mesh). ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker 300, 400, or 600 MHz NMR spectrometer using $CDCl_3$ as the solvent. The chemical shifts (δ) were reported in ppm relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$, ^{1}H: δ = 7.26 ppm, ^{13}C: δ = 77.16 ppm). Coupling constants (J) were given in Hertz (Hz). Splitting patterns of apparent multiplets associated with an averaged coupling constants were designated as s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). All ^{13}C spectra were recorded with broadband proton decoupling. HRMS were performed on a Bruker Q-TOF mass spectrometer. Melting points were recorded on a Büchi Melting Point B-545 unit.

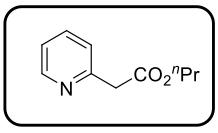
2. General Procedure for the Synthesis of α-Picoline Derivatives

2.1 General Procedure for the Synthesis of 2 -Pyridylacetates 1a–l[1]



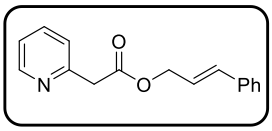
An oven-dried 100 mL of round-bottomed flask was charged with 2-pyridylacetic acid hydrochloride **S1** (6.0 mmol, 1.0 equiv., 1.04 g), DCC (6.0 mmol, 1.0 equiv., 1.24 g), DMAP (0.3 mmol, 5 mol%, 36.7 mg), Et_3N (12.0 mmol, 2.0 equiv. 1.62 mL), alcohol **S2** (9.0 mmol, 1.5 equiv.), and DCM (30 mL) at room temperature. The reaction mixture was stirred at 45 ^{o}C in an oil bath for about 12 h. Then the reaction mixture was cooled to room temperature and filtered to remove 1,3-dicyclohexylurea. The filtrate was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. And the residue was purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc) to afford 2−pyridylacetates **1a**–**l**. **1a** is commercial available, and **1c** and **1k** are new compounds.

Propyl 2-(pyridin-2-yl)acetate (1c).



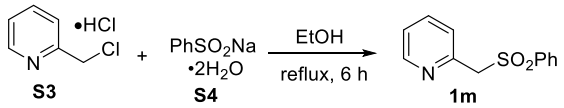
Light yellow oil; 612.2 mg, 57% yield; R_f = 0.37 (petroleum ether/EtOAc = 3/1); column chromatography eluent, petroleum ether/EtOAc = 6/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.55 (d, J = 4.7 Hz, 1H), 7.65 (td, J = 7.7, 1.8 Hz, 1H), 7.29 (d, J = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 6.7 Hz, 2H), 3.84 (s, 2H), 1.64 (h, J = 7.2 Hz, 2H), 0.90 (t, J = 7.4 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.7, 154.6, 149.5, 136.6, 123.9, 122.1, 66.6, 44.0, 21.9, 10.3; **HRMS** (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{10}H_{13}NNaO_2$, 202.0838; found, 202.0838.

Cinnamyl 2-(pyridin-2-yl)acetate (1k).



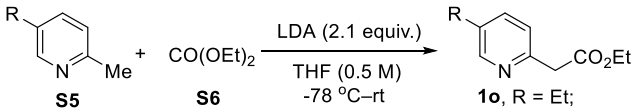
Light yellow oil; 895.6 mg, 59% yield; R_f = 0.16 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc = 8/1; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.56 (ddd, *J* = 5.0, 1.9, 0.9 Hz, 1H), 7.65 (td, *J* = 7.7, 1.6 Hz, 1H), 7.39–7.33 (m, 2H), 7.33–7.27 (m, 3H), 7.27–7.21 (m, 1H), 7.18 (ddd, *J* = 7.7, 4.9, 1.2 Hz, 1H), 6.61 (dt, *J* = 16.0, 1.4 Hz, 1H), 6.27 (dt, *J* = 15.9, 6.4 Hz, 1H), 4.79 (dd, *J* = 6.4, 1.4 Hz, 2H), 3.90 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.5, 154.3, 149.6, 136.7, 136.2, 134.3, 128.6, 128.1, 126.7, 124.0, 123.0, 122.2, 65.6, 44.0; **HRMS** (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{15}NNaO_2$, 276.0995; found, 276.1001.

2.2 General Procedure for the Synthesis of 1m[2]



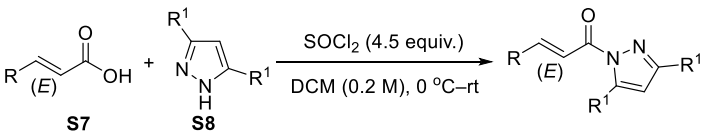
An oven-dried 100 mL of round-bottomed flask was charged with 2-(chloromethyl)pyridine hydrochloride **S3** (10.0 mmol, 1.0 equiv., 1.64 g), $PhSO_2Na·2H_2O$ **S4** (15.0 mmol, 1.5 equiv., 3.0 g), and EtOH (30 mL) at room temperature. The reaction mixture was refluxed in an oil bath for about 6 h. Then the reaction mixture was cooled to room temperature, neutralized by saturated $NaHCO_3$ (aq.), and extracted with DCM (50 mL × 3). Afterward, the combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. And the residue was purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc = 1/1, R_f = 0.50) to afford **1m** as a white solid in 47% yield (1.1 g).

2.3 General Procedure for the Synthesis of 2-Pyridylacetates 1o and 1p[3]



Under Ar atmosphere, LDA (2.0 M in THF, 12.6 mmol, 2.1 equiv., 6.3 mL) was added dropwise to a stirred solution of **S5** (6 mmol, 1.0 equiv.) and diethyl carbonate **S6** (6.6 mmol, 1.1 equiv., 0.8 mL) in THF (30 mL) at –78 °C for 1 h. Then the reaction mixture was stirred at room temperature and monitored by TLC analysis. Upon completion, the reaction mixture was quenched by brine, and extracted with EtOAc (50 mL × 3). Afterward, the combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. And the residue was purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc) to afford **1o** and **1p**.

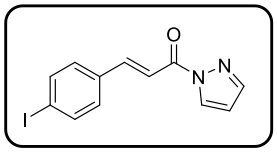
3. General Procedure for the Synthesis of α,β-Unsaturated Pyrazolamides 2a–l and 11[4]



2a, R = Ph;	**2f**, R = 4-I-C_6H_4;	**2j**, R = 4-MeO-C_6H_4;
2b, R = 3-Cl-C_6H_4;	**2g**, R = 4-CN-C_6H_4;	**2k**, R = 2-naphthyl;
2c, R = 4-Cl-C_6H_4;	**2h**, R = 4-CF_3-C_6H_4;	**2l**, R = 2-thienyl;
2d, R = 4-F-C_6H_4;	**2i**, R = 4-Me-C_6H_4;	**11**, R = Ph.
2e, R = 4-Br-C_6H_4;		

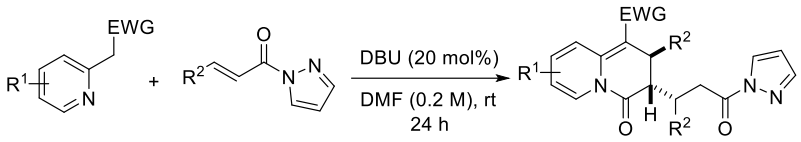
An oven-dried 100 mL of round-bottomed flask was charged with pyrazole **S8** (30 mmol, 3.0 equiv.) and DCM (50 mL) at 0 ℃ in an ice bath, and $SOCl_2$ (45 mmol, 4.5 equiv., 3.3 mL) was injected dropwise. Then the reaction mixture was brought to room temperature and stirred for 1 h. Afterward, *trans-α,β*-unsaturated carboxylic acid **S7** (10 mmol, 1.0 equiv.) was added in one portion. And the reaction mixture was further stirred for another 3 h, which was monitored by TLC analysis. Upon completion, the reaction mixture was added DCM (50 mL), washed with NaOH (0.5 M, 50 mL × 3) and brine (50 mL × 3), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. And the residue was purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc/DCM) to afford **2a–l** and **11**. **2f** is a new compound.

(E)-3-(4-iodophenyl)-1-(1H-pyrazol-1-yl)prop-2-en-1-one (2f).



White solid; 2.68 g, 83% yield; mp 121.8–123.4 ℃; R_f = 0.17 (petroleum ether/EtOAc = 10/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 1/10/1; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 2.9 Hz, 1H), 7.96–7.85 (m, 2H), 7.82–7.71 (m, 3H), 7.39 (d, *J* = 8.2 Hz, 2H), 6.49 (dd, *J* = 2.8, 1.5 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.5, 146.6, 144.1, 138.3, 134.0, 130.3, 128.9, 116.6, 110.1, 97.7; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{12}H_{10}IN_2O$, 324.9832; found, 324.9832.

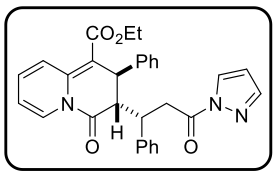
4. General Procedure for the Synthesis of Products 3



1 **2** **3**

An oven-dried 15 mL of reaction tube was charged with *α*-picoline derivatives **1** (0.4 mmol, 1.0 equiv.), *α,β*-unsaturated pyrazolamides **2** (1.4 mmol, 3.5 equiv.), DBU (0.08 mmol, 20 mol%, 12.2 mg), and DMF (2 mL). And the reaction mixture was stirred at room temperature for 24 h. Then the reaction mixture was added DCM (20 mL), washed with brine (20 mL × 4), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. And the residue was purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc/DCM) to afford products **3**.

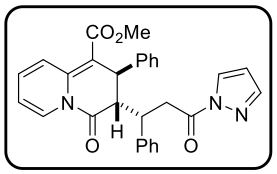
Ethyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine -1-carboxylate (3aa).



Orange solid; 155.8 mg, 79% yield; >20:1 dr; mp 180.2–181.7 ℃; R_f = 0.33 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.47 (d, *J* = 9.9 Hz, 1H), 8.06 (d, *J* = 2.8 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.62 (s, 1H), 7.41–7.27 (m, 5H), 7.23–7.11 (m, 3H), 6.97–6.89 (m, 2H), 6.72 (ddd, *J* = 10.1, 6.1, 1.4 Hz, 1H), 6.35 (dd, *J* = 2.7, 1.4 Hz, 1H), 5.96 (ddd, *J* = 7.5, 6.0, 1.3 Hz, 1H), 4.05 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.85 (dq, *J* = 10.7, 7.0 Hz, 1H), 3.79–3.68 (m, 2H), 3.68–3.60 (m, 2H), 3.04 (dd, *J* = 11.2, 1.5 Hz, 1H), 0.98 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.3, 170.1, 166.8, 146.6, 144.1, 140.5, 140.4, 130.5, 129.0, 128.9, 128.2, 128.1, 127.7, 127.1, 126.6, 123.4, 109.7, 108.6, 96.3, 59.6, 54.1, 40.4, 39.5, 38.9, 14.2; **HRMS** (ESI-TOF) *m/z*:

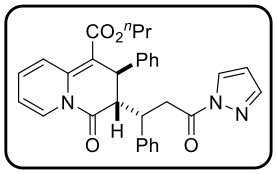
$[M + H]^+$ calcd for $C_{30}H_{28}N_3O_4$, 494.2074; found, 494.2079.

Methyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3ba).



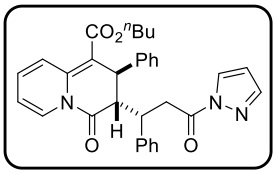
Orange solid; 162.8 mg, 85% yield; >20:1 dr; mp 192.4–193.9 ℃; R_f = 0.22 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 9.9 Hz, 1H), 8.06 (d, *J* = 2.9 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.61 (d, *J* = 1.4 Hz, 1H), 7.40–7.34 (m, 2H), 7.33–7.27 (m, 3H), 7.21–7.11 (m, 3H), 6.95 (d, *J* = 7.2 Hz, 2H), 6.73 (ddd, *J* = 10.0, 6.1, 1.4 Hz, 1H), 6.34 (dd, *J* = 2.8, 1.5 Hz, 1H), 5.97 (ddd, *J* = 7.5, 6.0, 1.3 Hz, 1H), 3.78–3.70 (m, 2H), 3.69–3.61 (m, 2H), 3.48 (s, 3H), 3.06 (dd, *J* = 11.3, 1.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.3, 170.1, 167.3, 146.8, 144.0, 140.4, 140.2, 130.7, 129.01, 128.98, 128.2, 128.1, 127.8, 127.2, 126.7, 123.4, 109.7, 108.7, 95.9, 54.3, 51.0, 40.5, 39.5, 39.0; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{29}H_{26}N_3O_4$, 480.1918; found, 480.1925.

Propyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3ca).



Orange solid; 152.1 mg, 75% yield; >20:1 dr; mp 142.4–143.3 ℃; R_f = 0.27 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.47 (dt, *J* = 9.9, 1.2 Hz, 1H), 8.06 (dd, *J* = 2.9, 0.7 Hz, 1H), 7.75 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.68–7.54 (m, 1H), 7.42–7.26 (m, 5H), 7.22–7.10 (m, 3H), 6.99–6.85 (m, 2H), 6.71 (ddd, *J* = 9.9, 6.0, 1.4 Hz, 1H), 6.34 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.96 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 3.90 (dt, *J* = 10.7, 6.5 Hz, 1H), 3.85–3.69 (m, 3H), 3.69–3.55 (m, 2H), 3.05 (dd, *J* = 11.3, 1.7 Hz, 1H), 1.34 (h, *J* = 7.0 Hz, 2H), 0.60 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.3, 170.1, 166.9, 146.5, 144.0, 140.6, 140.5, 130.5, 129.1, 128.9, 128.2, 128.1, 127.8, 127.1, 126.6, 123.4, 109.7, 108.6, 96.5, 65.3, 54.2, 40.6, 39.8, 39.1, 22.0, 10.4; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{31}H_{30}N_3O_4$, 508.2231; found, 508.2241.

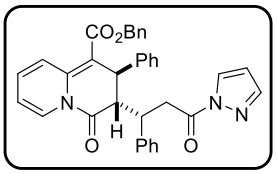
Butyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3da).



Orange solid; 152.1 mg, 73% yield; >20:1 dr; mp 126.4–127.5 ℃; R_f = 0.30 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.47 (dt, *J* = 10.0, 1.2 Hz, 1H), 8.10–8.00 (m, 1H), 7.75 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.65–7.57 (m, 1H), 7.41–7.27 (m, 5H), 7.22–7.09 (m, 3H), 6.97–6.86 (m, 2H), 6.71 (ddd, *J* = 10.0, 6.1, 1.5 Hz, 1H), 6.34 (dd, *J* = 2.8, 1.5 Hz, 1H), 5.96 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 3.94 (dt, *J* = 10.8, 6.5 Hz, 1H), 3.83 (dt, *J* = 11.0, 6.6 Hz, 1H), 3.79–3.69 (m, 2H), 3.68–3.55 (m, 2H), 3.05 (dd, *J* = 11.3, 1.7 Hz, 1H), 1.29 (dq, *J* = 8.2, 6.5 Hz, 2H), 1.07–0.93 (m, 2H), 0.73 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.3, 170.1, 166.9, 146.5, 144.1, 140.7, 140.5, 130.5, 129.1, 128.9, 128.3, 128.2, 127.7, 127.1, 126.6, 123.5, 109.7, 108.6, 96.5, 63.5, 54.2, 40.6, 39.9, 39.1, 30.7, 19.1, 13.7; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{32}H_{32}N_3O_4$, 522.2387; found, 522.2401.

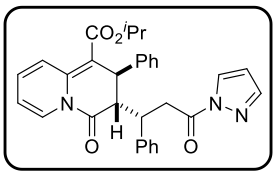
Benzyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-

quinolizine-1-carboxylate (3ea).



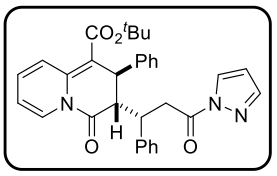
Yellow solid; 208.7 mg, 94% yield; >20:1 dr; mp 109.8–111.4 ℃; R_f = 0.29 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 9.9 Hz, 1H), 8.04 (d, *J* = 2.9 Hz, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.59 (s, 1H), 7.27–7.13 (m, 11H), 6.94–6.88 (m, 4H), 6.77–6.68 (m, 1H), 6.35–6.30 (m, 1H), 6.02–5.92 (m, 1H), 5.01 (d, *J* = 12.9 Hz, 1H), 4.91 (d, *J* = 12.9 Hz, 1H), 3.85 (s, 1H), 3.74 (ddd, *J* = 11.3, 8.1, 5.6 Hz, 1H), 3.68–3.54 (m, 2H), 3.06 (dd, *J* = 11.4, 1.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.3, 170.0, 166.5, 147.0, 144.1, 140.6, 140.3, 136.8, 130.9, 129.1, 129.0, 128.3, 128.2, 128.1, 127.8, 127.6, 127.4, 127.2, 127.1, 126.7, 123.4, 109.7, 108.7, 95.8, 65.2, 54.3, 40.6, 39.8, 39.0.; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{35}H_{30}N_3O_4$, 556.2231; found, 556.2238.

Isopropyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3fa).



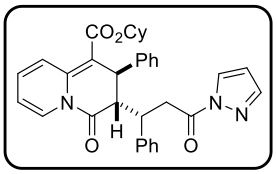
Orange solid; 146.0 mg, 72% yield; >20:1 dr; mp 170.8–171.9 ℃; R_f = 0.33 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.44 (dt, *J* = 10.0, 1.2 Hz, 1H), 8.06 (dd, *J* = 2.9, 0.8 Hz, 1H), 7.74 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.61 (dd, *J* = 1.5, 0.7 Hz, 1H), 7.41–7.28 (m, 5H), 7.21–7.11 (m, 3H), 6.91 (dt, *J* = 7.8, 1.3 Hz, 2H), 6.69 (ddd, *J* = 10.0, 6.1, 1.4 Hz, 1H), 6.34 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.94 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 4.87 (hept, *J* = 6.2 Hz, 1H), 3.79–3.69 (m, 2H), 3.68–3.60 (m, 2H), 3.04 (dd, *J* = 11.3, 1.4 Hz, 1H), 1.05 (d, *J* = 6.2 Hz, 3H), 0.86 (d, *J* = 6.2 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.3, 170.1, 166.3, 146.2, 144.1, 140.8, 140.5, 130.2, 129.1, 128.8, 128.24, 128.19, 127.7, 127.0, 126.6, 123.5, 109.7, 108.5, 97.0, 66.7, 54.1, 40.5, 39.8, 39.0, 22.0, 21.7; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{31}H_{30}N_3O_4$, 508.2231; found, 508.2235.

tert-Butyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3ga).



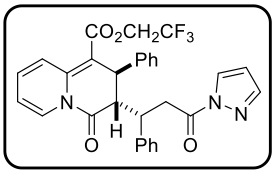
Yellow solid; 95.9 mg, 46% yield; >20:1 dr; mp 169.5–170.7 ℃; R_f = 0.38 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.42 (dt, *J* = 10.0, 1.2 Hz, 1H), 8.06 (dd, *J* = 2.9, 0.7 Hz, 1H), 7.73 (dt, *J* = 7.7, 1.2 Hz, 1H), 7.61 (dd, *J* = 1.5, 0.7 Hz, 1H), 7.44–7.27 (m, 5H), 7.21–7.08 (m, 3H), 6.90 (dd, *J* = 7.9, 1.7 Hz, 2H), 6.65 (ddd, *J* = 10.0, 6.1, 1.4 Hz, 1H), 6.34 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.92 (ddd, *J* = 7.5, 6.0, 1.3 Hz, 1H), 3.80–3.68 (m, 2H), 3.67–3.60 (m, 2H), 3.01 (dd, *J* = 11.3, 1.4 Hz, 1H), 1.20 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.3, 170.1, 166.1, 145.8, 144.0, 140.9, 140.6, 129.9, 129.1, 128.8, 128.2, 127.7, 126.9, 126.6, 123.5, 109.7, 108.4, 98.3, 79.5, 54.1, 40.5, 40.2, 39.0, 28.1; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{32}H_{32}N_3O_4$, 522.2387; found, 522.2393.

Cyclohexyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3ha).



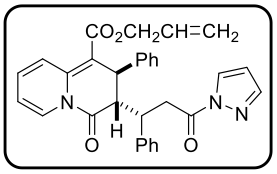
Yellow solid; 72.2 mg, 33% yield; >20:1 dr; mp 165.7–166.9 ℃; R_f = 0.36 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/4/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.46 (dt, *J* = 9.9, 1.2 Hz, 1H), 8.06 (d, *J* = 2.8 Hz, 1H), 7.74 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.64–7.58 (m, 1H), 7.41–7.27 (m, 5H), 7.20–7.10 (m, 3H), 6.94–6.87 (m, 2H), 6.69 (ddd, *J* = 10.0, 6.1, 1.5 Hz, 1H), 6.34 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.94 (ddd, *J* = 7.5, 6.0, 1.3 Hz, 1H), 4.70 (tt, *J* = 7.2, 3.8 Hz, 1H), 3.82–3.70 (m, 2H), 3.67–3.59 (m, 2H), 3.04 (dd, *J* = 11.3, 1.6 Hz, 1H), 1.64–1.55 (m, 1H), 1.42–1.20 (m, 5H), 1.15–0.99 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.3, 170.1, 166.1, 146.3, 144.1, 140.8, 140.5, 130.2, 129.1, 128.9, 128.3, 128.2, 127.7, 127.04, 127.02, 126.6, 123.5, 109.7, 108.5, 97.0, 71.0, 54.3, 40.6, 40.0, 39.0, 31.4, 31.1, 25.5, 23.1, 22.7; **HRMS** (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{34}H_{33}N_3NaO_4$, 570.2363; found, 570.2365.

2,2,2-Trifluoroethyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3ia).



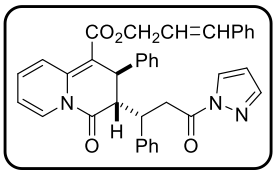
Orange solid; 144.4 mg, 66% yield; >20:1 dr; mp 134.3–135.8 ℃; R_f = 0.31 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.47 (dt, *J* = 9.9, 1.1 Hz, 1H), 8.13–8.01 (m, 1H), 7.84 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.68–7.57 (m, 1H), 7.44–7.27 (m, 5H), 7.22–7.11 (m, 3H), 6.93–6.82 (m, 3H), 6.35 (dd, *J* = 2.8, 1.5 Hz, 1H), 6.08 (ddd, *J* = 7.5, 6.2, 1.3 Hz, 1H), 4.47 (dq, *J* = 12.7, 8.7 Hz, 1H), 4.11 (dq, *J* = 12.6, 8.6 Hz, 1H), 3.85–3.55 (m, 4H), 3.09 (dd, *J* = 11.1, 1.3 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.3, 170.1, 164.8, 148.5, 144.1, 140.5, 140.1, 132.3, 129.2, 129.1, 128.3, 128.0, 127.9, 127.7, 127.3, 126.5, 123.3 (q, *J* = 276.0 Hz), 123.2, 109.7, 109.1, 93.6, 59.6 (q, *J* = 36.1 Hz), 54.4, 40.7, 39.8, 39.0; **^{19}F NMR** (565 MHz, $CDCl_3$) δ –73.7; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{25}F_3N_3O_4$, 548.1792; found, 548.1796.

Allyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3ja).



Orange solid; 153.5 mg, 76% yield; >20:1 dr; mp 159.3–160.9 ℃; R_f = 0.28 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.49 (dt, *J* = 10.0, 1.2 Hz, 1H), 8.06 (d, *J* = 2.9 Hz, 1H), 7.82–7.71 (m, 1H), 7.61 (s, 1H), 7.41–7.26 (m, 5H), 7.23–7.11 (m, 3H), 6.98–6.90 (m, 2H), 6.74 (ddd, *J* = 10.0, 6.1, 1.5 Hz, 1H), 6.35 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.98 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 5.66 (ddt, *J* = 17.0, 10.5, 5.2 Hz, 1H), 5.06–4.84 (m, 2H), 4.42 (qdt, *J* = 13.8, 5.4, 1.6 Hz, 2H), 3.85–3.59 (m, 4H), 3.06 (dd, *J* = 11.3, 1.7 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.3, 170.1, 166.4, 147.0, 144.1, 140.4, 132.7, 130.8, 129.1, 129.0, 128.2, 128.1, 127.8, 127.2, 127.1, 126.7, 123.4, 116.8, 109.7, 108.7, 95.8, 64.2, 54.3, 40.5, 39.6, 39.0; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{31}H_{28}N_3O_4$, 506.2074; found, 506.2081.

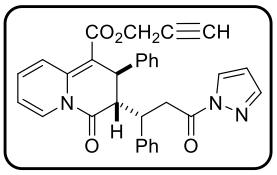
Cinnamyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3ka).



Orange solid; 162.7 mg, 70% yield; >20:1 dr; mp 162.2–164.3 ℃; R_f = 0.22 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (400 MHz, $CDCl_3$) δ

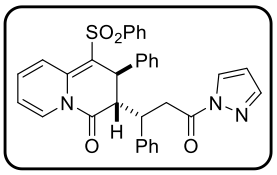
8.51 (dt, *J* = 9.9, 1.2 Hz, 1H), 8.05 (d, *J* = 2.9 Hz, 1H), 7.76 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.60 (d, *J* = 1.4 Hz, 1H), 7.32–7.27 (m, 6H), 7.25–7.21 (m, 3H), 7.21–7.12 (m, 4H), 6.98–6.93 (m, 2H), 6.75 (ddd, *J* = 9.9, 6.1, 1.4 Hz, 1H), 6.33 (dd, *J* = 2.9, 1.5 Hz, 1H), 6.25 (dt, *J* = 16.1, 1.6 Hz, 1H), 6.06–5.95 (m, 2H), 4.63 (ddd, *J* = 13.6, 5.6, 1.6 Hz, 1H), 4.52 (ddd, *J* = 13.6, 6.0, 1.5 Hz, 1H), 3.84 (d, *J* = 1.7 Hz, 1H), 3.75 (ddd, *J* = 11.4, 8.1, 5.7 Hz, 1H), 3.69–3.57 (m, 2H), 3.06 (dd, *J* = 11.4, 1.7 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.3, 170.1, 166.4, 147.1, 144.1, 140.38, 140.37, 136.6, 132.4, 130.9, 129.1, 129.0, 128.6, 128.3, 128.1, 127.84, 127.80, 127.23, 127.20, 126.7, 126.6, 124.1, 123.5, 109.7, 108.8, 95.8, 64.0, 54.4, 40.5, 39.7, 39.0; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{37}H_{32}N_3O_4$, 582.2387; found, 582.2396.

Prop-2-yn-1-yl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3la).



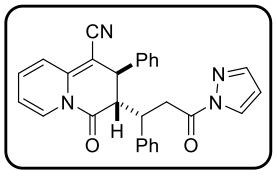
Orange solid; 161.0 mg, 80% yield; >20:1 dr; mp 170.4–171.9 ℃; R_f = 0.24 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.52 (dt, *J* = 9.9, 1.2 Hz, 1H), 8.06 (dd, *J* = 2.9, 0.7 Hz, 1H), 7.78 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.62 (dd, *J* = 1.5, 0.7 Hz, 1H), 7.44–7.28 (m, 5H), 7.22–7.13 (m, 3H), 6.93 (dd, *J* = 7.9, 1.8 Hz, 2H), 6.79 (ddd, *J* = 9.9, 6.1, 1.4 Hz, 1H), 6.35 (dd, *J* = 2.9, 1.5 Hz, 1H), 6.02 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 4.64 (dd, *J* = 15.6, 2.4 Hz, 1H), 4.39 (dd, *J* = 15.6, 2.5 Hz, 1H), 3.85–3.70 (m, 2H), 3.69–3.62 (m, 2H), 3.07 (dd, *J* = 11.2, 1.7 Hz, 1H), 2.37 (t, *J* = 2.4 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.3, 170.1, 165.9, 147.6, 144.1, 140.3, 140.2, 131.4, 129.2, 129.0, 128.2, 128.1, 127.8, 127.3, 127.2, 126.7, 123.5, 109.7, 108.9, 94.8, 78.7, 73.9, 54.4, 51.1, 40.3, 39.4, 38.8; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{31}H_{26}N_3O_4$, 504.1918; found, 504.1928.

3-(3-Oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-1-(phenylsulfonyl)-2,3-dihydro-4H-quinolizin-4-one (3ma).



Yellow solid; 44.9 mg, 20% yield; >20:1 dr; mp 193.1–194.8 ℃; R_f = 0.38 (petroleum ether/EtOAc = 3/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 30/6/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.11–8.02 (m, 2H), 7.72 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.63–7.58 (m, 1H), 7.46–7.29 (m, 8H), 7.18 (t, *J* = 7.1 Hz, 2H), 7.12–7.00 (m, 3H), 6.78 (ddd, *J* = 9.9, 6.2, 1.4 Hz, 1H), 6.69–6.60 (m, 2H), 6.36 (dd, *J* = 2.8, 1.5 Hz, 1H), 5.98 (ddd, *J* = 7.5, 6.2, 1.2 Hz, 1H), 3.96 (s, 1H), 3.81 (dt, *J* = 11.4, 6.8 Hz, 1H), 3.64 (dd, *J* = 17.4, 6.3 Hz, 1H), 3.50 (dd, *J* = 17.4, 7.4 Hz, 1H), 3.06 (dd, *J* = 11.5, 1.6 Hz, 1H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.9, 169.5, 144.6, 144.1, 142.6, 139.6, 138.9, 132.4, 131.3, 129.3, 129.1, 128.5, 128.4, 128.2, 128.1, 127.6, 127.5, 126.79, 126.76, 120.6, 109.7, 108.3, 105.5, 55.2, 41.1, 40.2, 39.2; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{33}H_{28}N_3O_4S$, 562.1795; found, 562.1803.

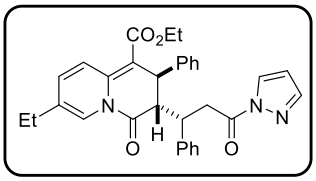
4-Oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carbonitrile (3na).



Yellow solid; 119.5 mg, 67% yield; >20:1 dr; mp 184.3–185.7 ℃; R_f = 0.17 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 50/10/1; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 2.9, 0.7 Hz, 1H), 7.69–7.59 (m, 2H), 7.46–7.40 (m, 2H), 7.40–7.36 (m, 2H), 7.36–7.31 (m, 1H), 7.26–7.17 (m, 3H), 7.05 (dt, *J* =

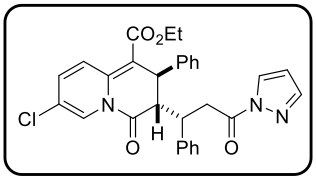
9.6, 1.1 Hz, 1H), 6.97–6.93 (m, 2H), 6.70 (ddd, *J* = 9.6, 6.2, 1.3 Hz, 1H), 6.37 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.93 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 3.79 (ddd, *J* = 11.2, 7.5, 6.0 Hz, 1H), 3.70 (dd, *J* = 17.5, 6.1 Hz, 1H), 3.60 (dd, *J* = 17.5, 7.5 Hz, 1H), 3.33–3.29 (m, 1H), 3.11 (dd, *J* = 11.3, 1.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 169.9, 168.8, 147.9, 144.2, 139.7, 138.4, 131.0, 129.5, 129.3, 128.3, 128.2, 128.0, 127.9, 127.2, 126.4, 122.6, 119.6, 109.8, 108.5, 76.8, 54.1, 40.7, 40.5, 38.8; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{28}H_{23}N_4O_2$, 447.1816; found, 447.1816.

Ethyl 7-ethyl-4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3oa).



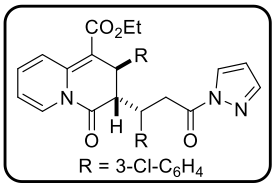
Orange solid; 79.2 mg, 38% yield; >20:1 dr; mp 143.9–145.6 ℃; R_f = 0.43 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.46 (d, *J* = 10.1 Hz, 1H), 8.04 (d, *J* = 2.8 Hz, 1H), 7.58 (d, *J* = 9.8 Hz, 2H), 7.41–7.27 (m, 5H), 7.21–7.12 (m, 3H), 6.95–6.89 (m, 2H), 6.66 (dd, *J* = 10.1, 1.9 Hz, 1H), 6.34 (dd, *J* = 2.9, 1.5 Hz, 1H), 4.05 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.86 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.78–3.52 (m, 4H), 3.10–3.00 (m, 1H), 2.31 (q, *J* = 7.5 Hz, 2H), 1.17 (t, *J* = 7.5 Hz, 3H), 0.99 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.2, 170.1, 166.9, 146.1, 144.0, 140.8, 140.6, 133.2, 129.0, 128.9, 128.3, 128.2, 127.7, 127.0, 126.7, 123.6, 123.3, 122.5, 109.6, 96.3, 59.6, 54.1, 40.6, 39.6, 38.9, 25.3, 14.3, 13.4; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{32}H_{32}N_3O_4$, 522.2387; found, 522.2394.

Ethyl 7-chloro-4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3pa).



Orange solid; 73.8 mg, 35% yield; >20:1 dr; mp 187.5–189.2 ℃; R_f = 0.20 (petroleum ether/EtOAc = 10/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/4/1; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.48 (dd, *J* = 10.5, 0.8 Hz, 1H), 8.08 (dd, *J* = 2.9, 0.7 Hz, 1H), 7.81 (dd, *J* = 2.1, 0.8 Hz, 1H), 7.62 (dd, *J* = 1.5, 0.7 Hz, 1H), 7.40–7.34 (m, 2H), 7.33–7.28 (m, 3H), 7.22–7.13 (m, 3H), 6.96–6.89 (m, 2H), 6.63 (dd, *J* = 10.4, 2.1 Hz, 1H), 6.37 (dd, *J* = 2.9, 1.5 Hz, 1H), 4.06 (dq, *J* = 10.8, 7.0 Hz, 1H), 3.87 (dq, *J* = 10.9, 7.1 Hz, 1H), 3.79 (d, *J* = 1.7 Hz, 1H), 3.75–3.54 (m, 3H), 3.11–3.03 (m, 1H), 0.99 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.0, 169.2, 166.4, 144.3, 144.2, 140.3, 139.9, 131.7, 129.14, 129.06, 128.3, 128.1, 127.9, 127.3, 126.6, 124.8, 124.1, 117.2, 109.8, 98.6, 60.0, 53.9, 40.5, 39.6, 39.0, 14.2; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{27}ClN_3O_4$, 528.1685; found, 528.1693.

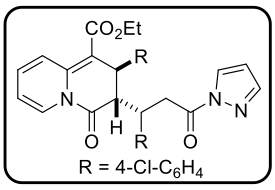
Ethyl 2-(3-chlorophenyl)-3-(1-(3-chlorophenyl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3ab).



Yellow solid; 179.5 mg, 80% yield; >20:1 dr; mp 217.1–218.7 ℃; R_f = 0.30 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.48 (d, *J* = 10.0 Hz, 1H), 8.07 (d, *J* = 2.8 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.63 (s, 1H), 7.38–7.20 (m, 4H), 7.17–7.11 (m, 2H), 6.90 (s, 1H), 6.87–6.80 (m, 1H), 6.75 (ddd, *J* = 10.0, 6.2, 1.5 Hz, 1H), 6.37 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.99 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 4.09 (dq, *J* = 10.6, 7.1 Hz, 1H), 3.94 (dq, *J* = 10.6, 7.1 Hz, 1H), 3.76–3.54 (m, 4H), 2.99 (dd, *J* = 11.1, 1.7 Hz, 1H), 1.04 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.7, 169.6, 166.4, 146.8, 144.3, 142.44, 142.36, 135.0, 134.7, 131.0, 130.5, 130.3, 128.7,

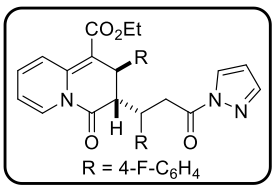
128.3, 128.2, 127.5, 127.1, 127.0, 125.8, 124.8, 123.4, 109.9, 109.0, 95.3, 60.0, 53.7, 40.1, 39.4, 38.6, 14.3; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{26}Cl_2N_3O_4$, 562.1295; found, 562.1297.

Ethyl 2-(4-chlorophenyl)-3-(1-(4-chlorophenyl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3ac).



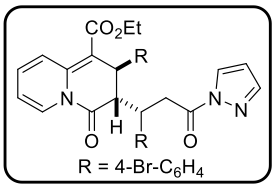
Yellow solid; 190.8 mg, 85% yield; >20:1 dr; mp 181.4–183.1 ℃; R_f = 0.29 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.44 (dt, *J* = 10.0, 1.2 Hz, 1H), 8.05 (d, *J* = 2.9 Hz, 1H), 7.74 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.64–7.58 (m, 1H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 6.73 (ddd, *J* = 9.9, 6.1, 1.2 Hz, 1H), 6.35 (dd, *J* = 2.8, 1.4 Hz, 1H), 5.98 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 4.06 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.89 (dq, *J* = 10.9, 7.1 Hz, 1H), 3.76–3.56 (m, 4H), 2.95 (dd, *J* = 11.0, 1.5 Hz, 1H), 1.02 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.8, 166.5, 146.7, 144.2, 138.8, 138.7, 133.7, 133.0, 130.9, 129.5, 129.4, 129.3, 129.2, 128.3, 128.1, 127.0, 123.3, 109.9, 108.9, 95.6, 59.8, 53.9, 39.9, 39.1, 38.8, 14.3; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{26}Cl_2N_3O_4$, 562.1295; found, 562.1303.

Ethyl 2-(4-fluorophenyl)-3-(1-(4-fluorophenyl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3ad).



Orange solid; 179.9 mg, 85% yield; >20:1 dr; mp 150.6–152.3 ℃; R_f = 0.30 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.44 (dt, *J* = 10.0, 1.2 Hz, 1H), 8.11–8.00 (m, 1H), 7.75 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.67–7.55 (m, 1H), 7.35–7.23 (m, 2H), 7.06 (t, *J* = 8.6 Hz, 2H), 6.95–6.84 (m, 4H), 6.73 (ddd, *J* = 9.9, 6.1, 1.5 Hz, 1H), 6.35 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.98 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 4.06 (dq, *J* = 10.6, 7.0 Hz, 1H), 3.90 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.79–3.66 (m, 2H), 3.66–3.56 (m, 2H), 2.96 (dd, *J* = 11.2, 1.8 Hz, 1H), 1.01 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.0, 169.9, 166.6, 162.2 (d, *J* = 245.0 Hz), 162.0 (d, *J* = 243.9 Hz), 146.6, 144.2, 136.1 (d, *J* = 3.2 Hz), 135.9 (d, *J* = 3.0 Hz), 130.8, 129.7 (d, *J* = 8.0 Hz), 128.3, 128.2 (d, *J* = 7.3 Hz), 127.1, 123.4, 116.0 (d, *J* = 21.3 Hz), 115.9 (d, *J* = 21.1 Hz), 109.9, 108.9, 96.1, 59.8, 54.3, 39.8, 38.99, 38.96, 14.3; **^{19}F NMR** (376 MHz, $CDCl_3$) δ –114.4, –115.7; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{26}F_2N_3O_4$, 530.1886; found,530.1895.

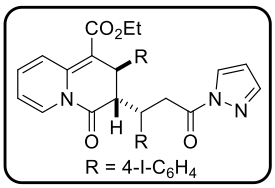
Ethyl 2-(4-bromophenyl)-3-(1-(4-bromophenyl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3ae).



Yellow solid; 203.1 mg, 78% yield; >20:1 dr; mp 190.6–192.1 ℃; R_f = 0.29 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.45 (dt, *J* = 9.9, 1.2 Hz, 1H), 8.05 (d, *J* = 2.8 Hz, 1H), 7.77–7.70 (m, 1H), 7.61 (d, *J* = 1.6 Hz, 1H), 7.49 (d, *J* = 8.3 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 6.81 (d, *J* = 8.4 Hz, 2H), 6.74 (ddd, *J* = 9.9, 6.1, 1.4 Hz, 1H), 6.36 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.98 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 4.06 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.89 (dq, *J* = 10.9, 7.1 Hz, 1H), 3.75–3.54 (m, 4H), 2.95 (dd, *J* = 11.2, 1.8 Hz, 1H), 1.02 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.74, 169.70, 166.4, 146.7, 144.2, 139.4, 139.2, 132.2,

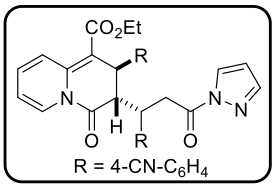
132.1, 130.9, 129.8, 128.5, 128.3, 127.0, 123.3, 121.8, 121.1, 109.9, 108.9, 95.6, 59.9, 53.7, 40.0, 39.2, 38.7, 14.3; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{26}Br_2N_3O_4$, 650.0285; found, 650.0293.

Ethyl 2-(4-iodophenyl)-3-(1-(4-iodophenyl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3af).



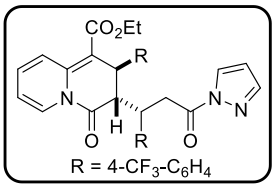
Yellow solid; 238.4 mg, 80% yield; >20:1 dr; mp 210.7–212.2 ℃; R_f = 0.29 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.44 (dt, *J* = 9.9, 1.1 Hz, 1H), 8.05 (dd, *J* = 2.9, 0.8 Hz, 1H), 7.73 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.62–7.59 (m, 1H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.3 Hz, 2H), 6.77–6.65 (m, 3H), 6.35 (dt, *J* = 2.8, 1.3 Hz, 1H), 5.97 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 4.06 (dq, *J* = 10.9, 7.1 Hz, 1H), 3.88 (dq, *J* = 10.9, 7.1 Hz, 1H), 3.71–3.54 (m, 4H), 2.95 (dd, *J* = 10.9, 1.7 Hz, 1H), 1.02 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.72, 169.66, 166.4, 146.7, 144.2, 140.0, 139.9, 138.2, 138.0, 130.9, 130.1, 128.8, 128.3, 127.0, 123.3, 109.9, 108.9, 95.5, 93.4, 92.6, 59.9, 53.6, 40.1, 39.3, 38.6, 14.3; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{26}I_2N_3O_4$, 746.0007; found, 745.9942.

Ethyl 2-(4-cyanophenyl)-3-(1-(4-cyanophenyl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3ag).



Orange solid; 102.1 mg, 47% yield; >20:1 dr; mp 200.5–201.1 ℃; R_f = 0.24 (petroleum ether/EtOAc = 2/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 32/8/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.43 (dt, *J* = 9.9, 1.2 Hz, 1H), 8.04 (d, *J* = 2.9 Hz, 1H), 7.74 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.64–7.60 (m, 1H), 7.50 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.3 Hz, 2H), 7.02 (d, *J* = 8.3 Hz, 2H), 6.79 (ddd, *J* = 10.0, 6.1, 1.4 Hz, 1H), 6.38 (dd, *J* = 2.9, 1.5 Hz, 1H), 6.03 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 4.05 (dq, *J* = 11.0, 7.1 Hz, 1H), 3.92 (dq, *J* = 11.0, 7.2 Hz, 1H), 3.81 (dt, *J* = 11.4, 7.1 Hz, 1H), 3.71–3.58 (m, 3H), 3.02 (dd, *J* = 11.3, 1.5 Hz, 1H), 1.01 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.3, 168.9, 166.0, 147.0, 145.7, 145.6, 144.5, 133.0, 131.5, 129.0, 128.3, 127.6, 127.0, 123.2, 118.6, 118.3, 112.2, 111.5, 110.2, 109.4, 94.5, 60.0, 53.1, 40.6, 40.0, 38.4, 14.4; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{32}H_{26}N_5O_4$, 544.1979; found, 544.1972.

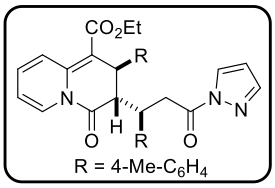
Ethyl 4-oxo-3-(3-oxo-3-(1H-pyrazol-1-yl)-1-(4-(trifluoromethyl)phenyl)propyl)-2-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2H-quinolizine-1-carboxylate (3ah).



Yellow solid; 186.2 mg, 74% yield; >20:1 dr; mp 199.7–200.9 ℃; R_f = 0.33 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.47 (d, *J* = 9.9 Hz, 1H), 8.06 (d, *J* = 2.6 Hz, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.70–7.58 (m, 3H), 7.53–7.40 (m, 4H), 7.05 (d, *J* = 7.9 Hz, 2H), 6.77 (ddd, *J* = 9.8, 6.2, 1.5 Hz, 1H), 6.37 (dd, *J* = 3.0, 1.5 Hz, 1H), 6.02 (td, *J* = 6.3, 3.2 Hz, 1H), 4.04 (dq, *J* = 10.7, 7.2 Hz, 1H), 3.94–3.78 (m, 2H), 3.76–3.62 (m, 3H), 3.06 (dd, *J* = 11.3, 1.7 Hz, 1H), 0.97 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.6, 169.4, 166.3, 146.9, 144.5, 144.4, 144.3, 131.2, 130.3 (q, *J* = 32.4 Hz), 129.7 (q, *J* = 32.3 Hz), 128.6, 128.3, 127.2, 127.1, 126.3–126.0 (difficult assigned multiplet, 126.21, 126.16, 126.11, 126.06, 126.01), 124.1 (q, *J* = 270.4 Hz), 124.0 (q, *J* = 270.4 Hz), 123.3, 110.0, 109.1, 95.2, 59.9, 53.4, 40.4, 39.6, 38.7, 14.1;

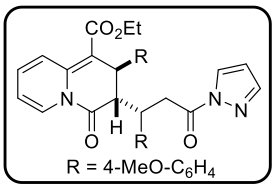
^{19}F NMR (376 MHz, $CDCl_3$) δ –62.58, –62.63; **HRMS** (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{32}H_{25}F_6N_3NaO_4$, 652.1641; found, 652.1640.

Ethyl 4-oxo-3-(3-oxo-3-(1H-pyrazol-1-yl)-1-(p-tolyl)propyl)-2-(p-tolyl)-3,4-dihydro-2H-quinolizine-1-carboxylate (3ai).



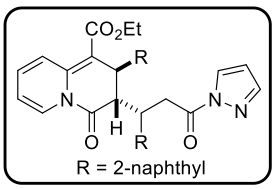
Yellow solid; 150.1 mg, 72% yield; >20:1 dr; mp 159.5–160.9 ℃; R_f = 0.41 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.45 (dt, *J* = 10.0, 1.2 Hz, 1H), 8.06 (dd, *J* = 2.9, 0.7 Hz, 1H), 7.75 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.64–7.58 (m, 1H), 7.22–7.13 (m, 4H), 6.99 (d, *J* = 7.9 Hz, 2H), 6.84 (d, *J* = 8.0 Hz, 2H), 6.70 (ddd, *J* = 10.0, 6.1, 1.3 Hz, 1H), 6.34 (dd, *J* = 2.8, 1.5 Hz, 1H), 5.94 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 4.08 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.86 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.78–3.58 (m, 4H), 3.00 (dd, *J* = 11.1, 1.5 Hz, 1H), 2.34 (s, 3H), 2.24 (s, 3H), 1.01 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.5, 170.2, 166.9, 146.5, 144.0, 137.4, 137.2, 136.6, 130.4, 129.7, 129.6, 128.2, 128.0, 127.1, 126.6, 123.5, 109.6, 108.5, 96.7, 59.6, 54.2, 40.0, 39.1, 39.0, 21.2, 21.1, 14.2; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{32}H_{32}N_3O_4$, 522.2387; found, 522.2391.

Ethyl 2-(4-methoxyphenyl)-3-(1-(4-methoxyphenyl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3aj).



Orange solid; 154.9 mg, 70% yield; >20:1 dr; mp 147.5–149.6 ℃; R_f = 0.19 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 50/10/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.44 (d, *J* = 9.9 Hz, 1H), 8.05 (d, *J* = 2.8 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.65–7.55 (m, 1H), 7.21 (d, *J* = 8.6 Hz, 2H), 6.93–6.81 (m, 4H), 6.77–6.64 (m, 3H), 6.34 (dd, *J* = 2.8, 1.4 Hz, 1H), 5.94 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 4.07 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.88 (dq, *J* = 10.9, 7.1 Hz, 1H), 3.79 (s, 3H), 3.76–3.56 (m, 7H), 2.96 (dd, *J* = 11.0, 1.7 Hz, 1H), 1.02 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.6, 170.2, 166.9, 159.0, 158.6, 146.4, 144.0, 132.3, 130.4, 129.1, 128.2, 127.7, 127.1, 123.5, 114.34, 114.28, 109.7, 108.6, 96.8, 59.6, 55.33, 55.26, 54.5, 39.7, 39.1, 38.8, 14.3; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{32}H_{32}N_3O_6$, 554.2286; found, 554.2290.

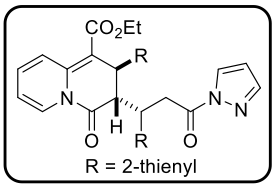
Ethyl 2-(naphthalen-2-yl)-3-(1-(naphthalen-2-yl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3ak).



Yellow solid; 158.9 mg, 67% yield; >20:1 dr; mp 183.7–185.1 ℃; R_f = 0.22 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.60 (dt, *J* = 9.9, 1.2 Hz, 1H), 8.06 (dd, *J* = 2.9, 0.7 Hz, 1H), 7.95 (d, *J* = 8.5 Hz, 1H), 7.89–7.83 (m, 2H), 7.81 (d, *J* = 1.7 Hz, 1H), 7.79 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.75–7.71 (m, 1H), 7.70–7.66 (m, 2H), 7.63 (d, *J* = 1.4 Hz, 1H), 7.57 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.54–7.47 (m, 2H), 7.42–7.37 (m, 3H), 7.04 (dd, *J* = 8.6, 1.9 Hz, 1H), 6.79 (ddd, *J* = 10.0, 6.1, 1.4 Hz, 1H), 6.34 (dd, *J* = 2.9, 1.5 Hz, 1H), 6.01 (ddd, *J* = 7.5, 6.0, 1.3 Hz, 1H), 4.01 (ddd, *J* = 11.4, 7.7, 6.1 Hz, 1H), 3.94–3.70 (m, 5H), 3.30 (dd, *J* = 11.4, 1.8 Hz, 1H), 0.66 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 170.3, 170.1, 166.9, 146.9, 144.1, 137.7, 137.5, 133.64, 133.57, 133.0, 132.7, 130.8, 129.2, 128.9, 128.3, 128.1, 127.93, 127.90, 127.8, 127.6, 127.2, 126.5, 126.2, 126.1, 125.7, 125.5, 125.0, 124.8, 123.5, 109.7, 108.8, 96.1, 59.7, 53.8, 40.7,

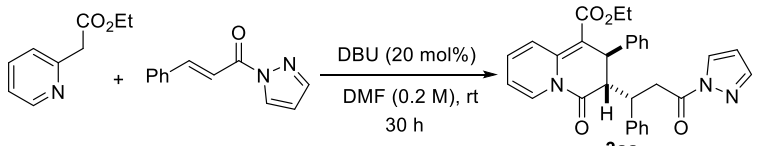
39.8, 38.9, 13.8; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{38}H_{32}N_3O_4$, 594.2387; found, 594.2397.

Ethyl 4-oxo-3-(3-oxo-3-(1H-pyrazol-1-yl)-1-(thiophen-2-yl)propyl)-2-(thiophen-2-yl)-3,4-dihydro-2H-quinolizine-1-carboxylate (3al).



Orange solid; 141.4 mg, 70% yield; >20:1 dr; mp 81.6–82.9 ℃; R_f = 0.22 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.41 (dt, *J* = 9.9, 1.1 Hz, 1H), 8.08 (dd, *J* = 2.9, 0.7 Hz, 1H), 7.75 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.62 (dd, *J* = 1.5, 0.7 Hz, 1H), 7.26–7.19 (m, 1H), 7.06 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.98–6.91 (m, 2H), 6.83 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.79–6.75 (m, 1H), 6.69 (ddd, *J* = 9.9, 6.1, 1.4 Hz, 1H), 6.36 (dd, *J* = 2.9, 1.5 Hz, 1H), 5.93 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 4.25–3.96 (m, 4H), 3.74 (dd, *J* = 17.4, 5.6 Hz, 1H), 3.62 (dd, *J* = 17.4, 8.0 Hz, 1H), 3.22 (dd, *J* = 11.4, 1.8 Hz, 1H), 1.13 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.8, 169.5, 166.3, 146.0, 144.4, 144.1, 143.2, 130.8, 128.2, 127.0, 126.92, 126.87, 126.5, 125.0, 124.1, 123.8, 123.4, 109.8, 108.9, 97.2, 59.8, 54.2, 40.1, 35.4, 35.3, 14.3; **HRMS** (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{26}H_{23}N_3NaO_4S_2$, 528.1022; found, 528.1029.

5. Gram-Scale Synthesis and Transformations of Product 3aa

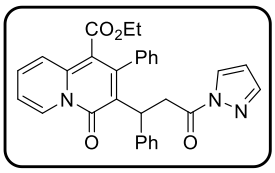


An oven-dried 50 mL of round-bottomed flask was charged with ethyl 2-(pyridin-2-yl)acetate **1a** (3.2 mmol, 1.0 equiv., 528.6 mg), (*E*)-3-phenyl-1-(*1H*-pyrazol-1-yl)prop-2-en-1-one **2a** (11.2 mmol, 3.5 equiv., 2.22 g), DBU (0.64 mmol, 5 mol%, 97.4 mg), and DMF (16 mL). And the reaction mixture was stirred at room temperature for 30 h. Then the reaction mixture was added DCM (100 mL), washed with brine (100 mL × 4), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. And the residue was purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1) to afford product **3aa** as an orange solid in 71% yield (1.12 g) with good diastereoselectivity (>20:1 dr).

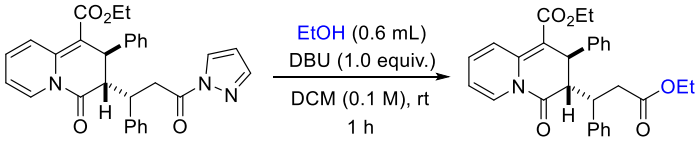
An oven-dried 15 mL of reaction tube was charged with **3aa** (0.2 mmol, 1.0 equiv., 98.6 mg), DDQ (0.24 mmol, 1.2 equiv., 54.5 mg), and DCM (2 mL) under Ar atmosphere. And the reaction mixture was stirred at room temperature for 48 h. Then the reaction mixture was concentrated under reduced pressure and directly purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc = 3/1) to afford product **4** as a light yellow oil in 54% yield (53.0 mg).

Ethyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-4H-quinolizine-1-

carboxylate (4).



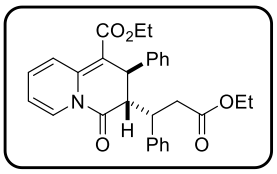
Light yellow oil; 53.0 mg, 54% yield; R_f = 0.25 (petroleum ether/EtOAc = 3/1); column chromatography eluent, petroleum ether/EtOAc = 3/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.21 (dt, *J* = 7.4, 1.2 Hz, 1H), 8.21–8.08 (m, 1H), 7.85 (dt, *J* = 9.1, 1.2 Hz, 1H), 7.65–7.58 (m, 1H), 7.47–7.26 (m, 7H), 7.23–7.09 (m, 4H), 7.01 (ddd, *J* = 7.6, 6.6, 1.4 Hz, 1H), 6.37 (dd, *J* = 2.8, 1.5 Hz, 1H), 4.66 (dd, *J* = 8.7, 6.1 Hz, 1H), 4.49 (dd, *J* = 16.6, 8.8 Hz, 1H), 4.15 (dd, *J* = 16.6, 6.1, 1H), 3.83 (q, *J* = 7.2 Hz, 2H), 0.79 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.2, 167.4, 156.9, 149.9, 143.8, 142.6, 139.9, 138.3, 131.4, 128.6, 128.5, 128.2, 128.1, 128.0, 127.94, 127.89, 127.6, 126.4, 123.1, 119.9, 115.4, 109.4, 109.3, 61.3, 41.7, 36.9, 13.5; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{28}H_{26}N_3O_4$, 492.1918; found, 492.1914.



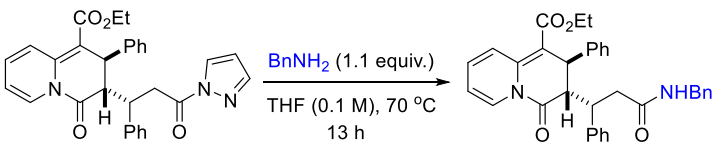
3aa, >20:1 dr　　**5**, 90% yield, >20:1 dr

An oven-dried 15 mL of reaction tube was charged with **3aa** (0.2 mmol, 1.0 equiv., 98.6 mg), EtOH (0.6 mL), DBU (0.2 mmol, 1.0 equiv., 30.4 mg), and DCM (2 mL). And the reaction mixture was stirred at room temperature for about 1 h. Then the reaction mixture was concentrated under reduced pressure and directly purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1) to afford product **5** as an orange oil in 90% yield (84.8 mg) with good diastereoselectivity (>20:1 dr).

Ethyl 3-(3-ethoxy-3-oxo-1-phenylpropyl)-4-oxo-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (5).



Orange oil; 84.8 mg, 90% yield; >20:1 dr; R_f = 0.40 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.44 (dt, *J* = 10.0, 1.2 Hz, 1H), 7.75 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.41–7.34 (m, 2H), 7.32–7.25 (m, 3H), 7.21–7.11 (m, 3H), 6.95–6.89 (m, 2H), 6.68 (ddd, *J* = 10.0, 6.1, 1.4 Hz, 1H), 5.94 (ddd, *J* = 7.5, 6.0, 1.3 Hz, 1H), 4.11–4.00 (m, 1H), 4.00–3.80 (m, 3H), 3.75 (d, *J* = 1.6 Hz, 1H), 3.49 (ddd, *J* = 11.4, 8.1, 6.7 Hz, 1H), 2.94 (dd, *J* = 11.4, 1.7 Hz, 1H), 2.81–2.72 (m, 2H), 1.04 (t, *J* = 7.2 Hz, 3H), 0.99 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.5, 170.1, 166.7, 146.4, 140.5, 130.4, 128.92, 128.90, 128.1, 127.6, 127.0, 126.8, 126.6, 123.5, 108.7, 96.6, 60.5, 59.6, 54.1, 41.0, 39.6, 39.3, 14.2, 14.1; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{29}H_{30}NO_5$, 472.2118; found, 472.2124.

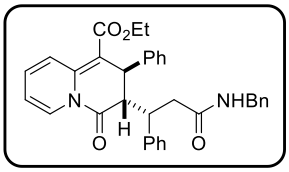


3aa, >20:1 dr　　**6**, 60% yield, >20:1 dr

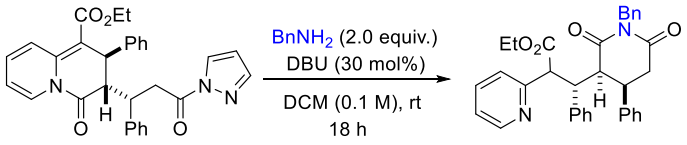
An oven-dried 15 mL of sealed tube was charged with **3aa** (0.2 mmol, 1.0 equiv., 98.6 mg), $BnNH_2$ (0.22 mmol, 1.1 equiv., 23.6 mg), and THF (2 mL). And the reaction mixture was stirred at 70 °C in an oil bath for about 13 h. Then the reaction mixture was concentrated under reduced

pressure and directly purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc = 3/1) to afford product **6** as an orange oil in 60% yield (63.8 mg) with good diastereoselectivity (>20:1 dr).

Ethyl 3-(3-(benzylamino)-3-oxo-1-phenylpropyl)-4-oxo-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (6).



Orange oil; 63.8 mg, 60% yield; >20:1 dr; R_f = 0.17 (petroleum ether/EtOAc = 3/1); column chromatography eluent, petroleum ether/EtOAc = 3/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.41 (dt, *J* = 10.0, 1.2 Hz, 1H), 7.72 (dt, *J* = 7.7, 1.2 Hz, 1H), 7.41–7.32 (m, 3H), 7.26 (dt, *J* = 5.5, 1.6 Hz, 2H), 7.23–7.12 (m, 6H), 6.95–6.89 (m, 2H), 6.88–6.82 (m, 2H), 6.66 (ddd, *J* = 10.0, 6.1, 1.4 Hz, 1H), 5.92 (ddd, *J* = 7.6, 6.1, 1.3 Hz, 1H), 5.65 (s, 1H), 4.32 (dd, *J* = 14.9, 6.4 Hz, 1H), 4.12–3.98 (m, 2H), 3.84 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.76 (d, *J* = 1.6 Hz, 1H), 3.61 (ddd, *J* = 11.5, 9.5, 5.3 Hz, 1H), 2.96 (dd, *J* = 11.6, 1.7 Hz, 1H), 2.66 (dd, *J* = 14.6, 5.3 Hz, 1H), 2.53 (dd, *J* = 14.7, 9.5 Hz, 1H), 0.98 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.3, 170.2, 166.7, 146.4, 140.7, 140.6, 138.1, 130.4, 129.1, 128.9, 128.6, 128.1, 127.6, 127.5, 127.3, 127.1, 126.7, 126.6, 123.6, 108.9, 96.8, 59.6, 54.1, 43.4, 41.7, 41.4, 39.7, 14.2; **HRMS** (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{34}H_{32}N_2NaO_4$, 555.2254; found, 555.2261.

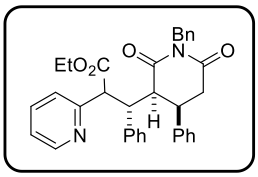


3aa, >20:1 dr

7, 77% yield, 53:47 dr

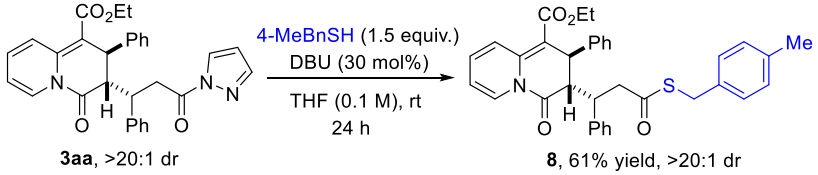
An oven-dried 15 mL of reaction tube was charged with **3aa** (0.1 mmol, 1.0 equiv., 49.3 mg), $BnNH_2$ (0.2 mmol, 2.0 equiv., 21.4 mg), DBU (30 mol%, 4.6 mg), and DCM (1 mL). And the reaction mixture was stirred at room temperature for about 18 h. Then the reaction mixture was concentrated under reduced pressure and directly purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc = 5/1) to afford product **7** as a colorless oil in 77% yield (41.0 mg) with low diastereoselectivity (53:47 dr).

Ethyl 3-(1-benzyl-2,6-dioxo-4-phenylpiperidin-3-yl)-3-phenyl-2-(pyridin-2-yl)propanoate (7).



Colorless oil; 41.0 mg, 77% yield; 53:47 dr; the diastereomers could be seperated by column chromatography; column chromatography eluent, petroleum ether/EtOAc = 5/1. **For the major diastereomer**, R_f = 0.19 (petroleum ether/EtOAc = 5/1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.41–8.32 (m, 1H), 7.31 (td, *J* = 7.8, 1.8 Hz, 1H), 7.26–7.18 (m, 5H), 7.15–7.01 (m, 8H), 6.90 (dd, *J* = 7.6, 4.3 Hz, 2H), 6.82 (d, *J* = 6.6 Hz, 2H), 5.01 (d, *J* = 14.0 Hz, 1H), 4.91 (d, *J* = 14.0 Hz, 1H), 4.44 (d, *J* = 11.0 Hz, 1H), 4.27 (dd, *J* = 11.0, 8.4 Hz, 1H), 4.10–3.92 (m, 2H), 3.42 (dd, *J* = 8.6, 3.1 Hz, 1H), 3.19–3.06 (m, 2H), 2.83 (dd, *J* = 19.1, 5.6 Hz, 1H), 1.11 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.7, 172.1, 171.3, 157.4, 149.2, 141.4, 139.4, 137.0, 136.3, 129.0, 128.90, 128.86, 128.6, 128.2, 127.3, 127.2, 127.1, 126.9, 124.4, 121.8, 61.2, 56.7, 53.9, 48.6, 43.6, 36.7, 34.7, 14.1; **HRMS** (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{34}H_{32}N_2NaO_4$, 555.2254; found, 555.2265. **For the minor diastereomer**, R_f = 0.22 (petroleum ether/EtOAc = 5/1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.58 (d, *J* = 5.0 Hz, 1H), 7.60 (td, *J* = 7.7, 1.9 Hz, 1H), 7.36–7.31 (m, 3H), 7.30–7.24 (m, 3H), 7.22–7.06 (m, 9H), 6.76–6.69 (m, 2H), 4.60 (t, *J* = 6.7 Hz, 3H),

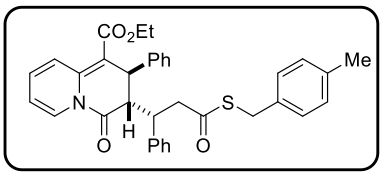
4.40 (d, *J* = 13.9 Hz, 1H), 3.76 (q, *J* = 7.1 Hz, 2H), 3.16 (t, *J* = 4.6 Hz, 1H), 2.99 (q, *J* = 5.1 Hz, 1H), 2.89 (dd, *J* = 17.4, 5.5 Hz, 1H), 2.67 (dd, *J* = 17.3, 5.2 Hz, 1H), 0.82 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ173.1, 171.2, 171.0, 155.9, 149.4, 141.4, 140.1, 136.9, 136.7, 129.1, 128.9, 128.8, 128.3, 127.7, 127.4, 127.2, 127.0, 124.6, 122.9, 60.9, 56.5, 52.6, 47.0, 43.0, 36.5, 36.0, 13.7; **HRMS** (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{34}H_{32}N_2NaO_4$, 555.2254; found, 555.2267.



3aa, >20:1 dr **8**, 61% yield, >20:1 dr

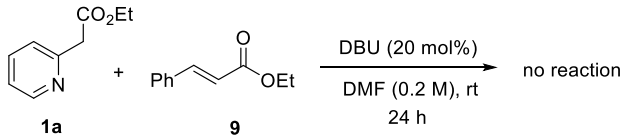
An oven-dried 15 mL of reaction tube was charged with **3aa** (0.1 mmol, 1.0 equiv., 49.3 mg), 4-methylbenzyl mercaptan (0.15 mmol, 1.5 equiv., 20.7 mg), DBU (30 mol%, 4.6 mg), and THF (1 mL). And the reaction mixture was stirred at room temperature for about 24 h. Then the reaction mixture was concentrated under reduced pressure and directly purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1) to afford product **8** as an orange oil in 61% yield (34.3 mg) with good diastereoselectivity (>20:1 dr).

Ethyl 3-(3-((4-methylbenzyl)thio)-3-oxo-1-phenylpropyl)-4-oxo-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (8).



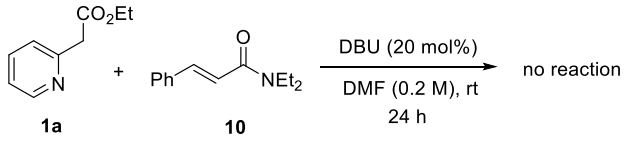
Orange oil; 34.3 mg, 61% yield; >20:1 dr; R_f = 0.55 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.44 (dt, *J* = 10.0, 1.2 Hz, 1H), 7.71 (dt, *J* = 7.6, 1.3 Hz, 1H), 7.45–7.31 (m, 3H), 7.25 (dt, *J* = 6.7, 1.5 Hz, 2H), 7.21–7.11 (m, 3H), 7.03 (d, *J* = 7.9 Hz, 2H), 6.99–6.89 (m, 4H), 6.69 (ddd, *J* = 10.0, 6.1, 1.4 Hz, 1H), 5.93 (ddd, *J* = 7.5, 6.1, 1.3 Hz, 1H), 4.06 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.96–3.81 (m, 3H), 3.76 (d, *J* = 1.6 Hz, 1H), 3.60 (ddd, *J* = 11.3, 8.8, 5.8 Hz, 1H), 3.14–2.91 (m, 3H), 2.30 (s, 3H), 1.00 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 196.6, 170.0, 166.7, 146.4, 140.5, 139.9, 136.9, 134.3, 130.5, 130.4, 129.3, 129.0, 128.9, 128.7, 128.2, 127.7, 127.1, 126.8, 126.6, 123.5, 108.8, 96.7, 59.6, 54.0, 48.1, 41.3, 39.6, 33.0, 21.2, 14.2; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{35}H_{34}NO_4S$, 564.2203; found, 564.2218.

6. Control Experiments

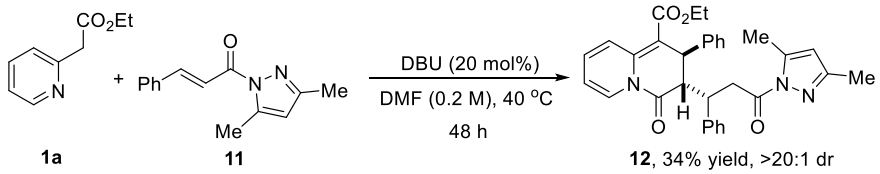


1a **9**

An oven-dried 15 mL of reaction tube was charged with ethyl 2-(pyridin-2-yl)acetate **1a** (0.4 mmol, 1.0 equiv., 66.0 mg), ethyl cinnamate **9** (1.4 mmol, 3.5 equiv., 246.4 mg), DBU (0.08 mmol, 20 mol%, 12.2 mg), and DMF (2 mL). And the reaction mixture was stirred at room temperature for 24 h. However, no reaction occurred.

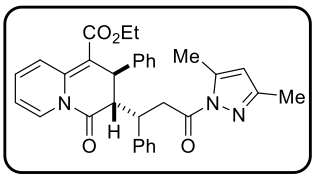


An oven-dried 15 mL of reaction tube was charged with ethyl 2-(pyridin-2-yl)acetate **1a** (0.4 mmol, 1.0 equiv., 66.0 mg), *N*,*N*-diethylcinnamamide **10** (1.4 mmol, 3.5 equiv., 284.2 mg), DBU (0.08 mmol, 20 mol%, 12.2 mg), and DMF (2 mL). And the reaction mixture was stirred at room temperature for 24 h. However, no reaction occurred.



An oven-dried 15 mL of sealed tube was charged with ethyl 2-(pyridin-2-yl)acetate **1a** (0.4 mmol, 1.0 equiv., 66.0 mg), (*E*)-1-(3,5-dimethyl-*1H*-pyrazol-1-yl)-3-phenylprop-2-en-1-one **11** (1.4 mmol, 3.5 equiv., 316.4 mg), DBU (0.08 mmol, 20 mol%, 12.2 mg), and DMF (2 mL). And the reaction mixture was stirred at 40 ^{o}C in an oil bath for 48 h. Then the reaction mixture was added DCM (20 mL), washed with brine (20 mL × 4), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. And the residue was purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc/DCM = 40/8/1) to afford product **12** as an orange solid in 34% yield (70.8 mg) with good diastereoselectivity (>20:1 dr).

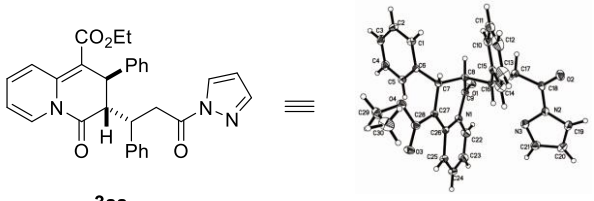
ethyl 3-(3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-oxo-1-phenylpropyl)-4-oxo-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (12).



Orange solid; 70.8 mg, 34% yield; >20:1 dr; mp 146.5–147.9 ℃; R_f = 0.38 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 40/8/1; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.47 (dt, *J* = 9.9, 1.1 Hz, 1H), 7.74 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.39–7.34 (m, 2H), 7.33–7.26 (m, 3H), 7.21–7.10 (m, 3H), 6.95–6.91 (m, 2H), 6.70 (ddd, *J* = 10.0, 6.1, 1.5 Hz, 1H), 5.94 (ddd, *J* = 7.6, 6.1, 1.3 Hz, 1H), 5.86 (d, *J* = 1.2 Hz, 1H), 4.05 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.86 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.79–3.69 (m, 2H), 3.65 (dd, *J* = 17.1, 5.8 Hz, 1H), 3.50 (dd, *J* = 17.1, 8.0 Hz, 1H), 3.03 (dd, *J* = 11.3, 1.8 Hz, 1H), 2.34 (d, *J* = 1.0 Hz, 3H), 2.16 (s, 3H), 0.98 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 171.7, 170.5, 166.8, 152.1, 146.6, 144.0, 140.9, 140.6, 130.5, 129.0, 128.9, 128.3, 127.6, 127.1, 127.0, 126.7, 123.5, 111.1, 108.5, 96.5, 59.6, 54.1, 40.6, 40.3, 39.6, 14.4, 14.3, 13.9; **HRMS** (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{32}H_{32}N_3O_4$, 522.2387; found, 522.2386.

7. X-ray Crystallography of 3aa

Single crystal of compound **3aa** was obtained via slow evaporation in the solution of ethanol and DCM at room temperature.



ORTEP diagram of compound **3aa**, thermal ellipsoids are drawn on 50% probability level.

Crystal data and structure refinement for **3aa**.

Identification code	3**aa**
Empirical formula	$C_{30}H_{27}N_3O_4$
Formula weight	493.54
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	10.9633(4)
b/Å	16.4739(5)
c/Å	14.0175(5)
α/°	90
β/°	98.379(4)
γ/°	90
Volume/Å^3	2504.65(15)
Z	4
ρ_{calc}g/cm^3	1.309
μ/mm^{-1}	0.711
F(000)	1040.0
Crystal size/mm^3	0.17 × 0.15 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.334 to 134.13
Index ranges	$-12 \le h \le 13$, $-19 \le k \le 19$, $-16 \le l \le 16$
Reflections collected	9689
Independent reflections	4461 [R_{int}= 0.0298, R_{sigma}= 0.0367]
Data/restraints/parameters	4461/3/350
Goodness-of-fit on F^2	1.021
Final R indexes [I>=2σ (I)]	R_1= 0.0416, wR_2 = 0.0988
Final R indexes [all data]	R_1= 0.0568, wR_2 = 0.1098
Largest diff. peak/hole / e Å^{-3}	0.19/-0.15

1. Z. Chen, P. Liang, X. Ma, H. Luo, G. Xu, T. Liu, X. Wen, J. Zheng and H. Ye. *J. Org. Chem*., 2019, **84**, 1630.

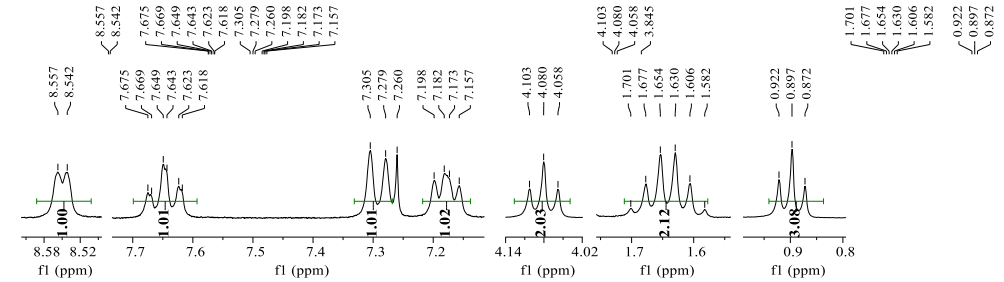
2. A, Hossan. *Chemistry of Heterocyclic Compounds*, 2016, **52**, 570.

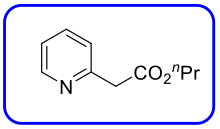
3. D. Yang, Y. Yu, Y. Wu, H. Feng, X. Li and H. Cao. *Org. Lett.*, 2018, **20**, 2477.

4. S. K. Ray, R. G. Biswas, A. Suneja, M. M. Sadhu and V. K. Singh. *J. Org. Chem*., 2018, **83**, 2293.

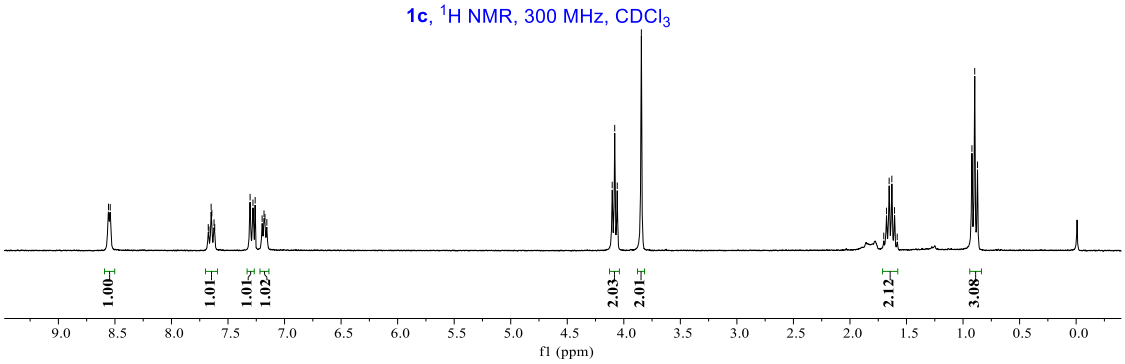
8. Copies of ^{1}H, ^{13}C, and ^{19}F NMR Spectra

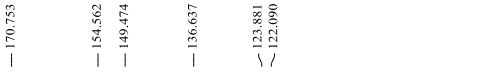
propyl 2-(pyridin-2-yl)acetate (1c).

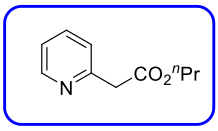




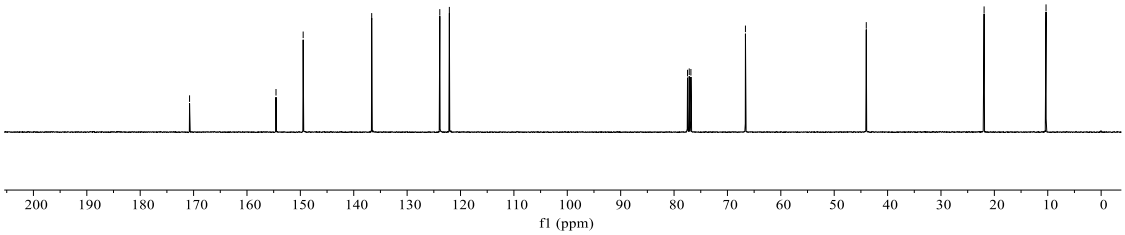
1c, ^{1}H NMR, 300 MHz, $CDCl_3$



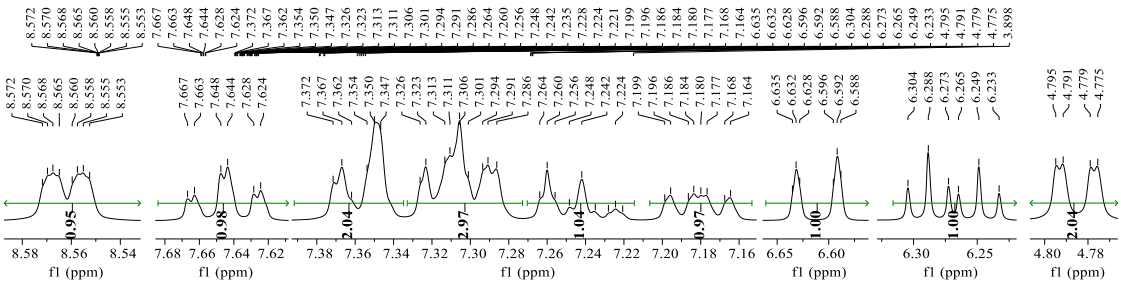


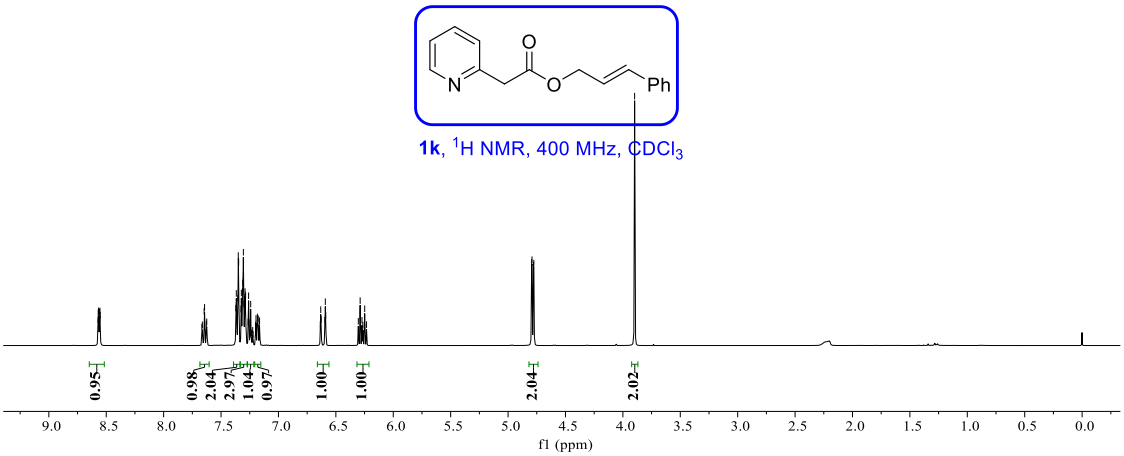


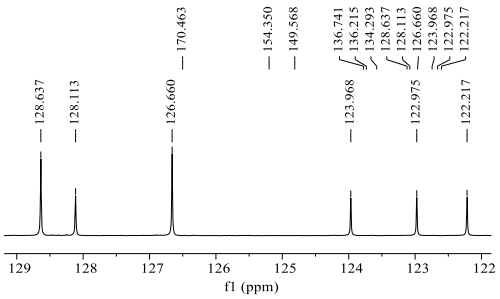
1c, ^{13}C NMR, 100 MHz, $CDCl_3$

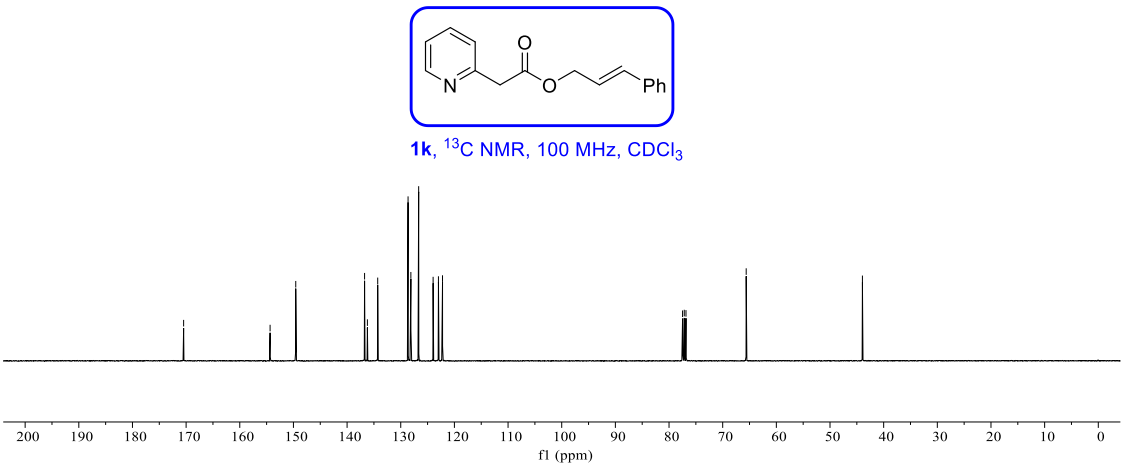


cinnamyl 2-(pyridin-2-yl)acetate (1k).

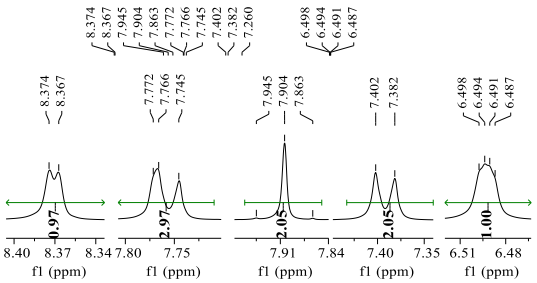


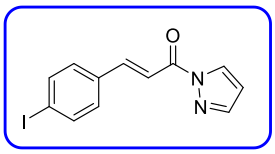




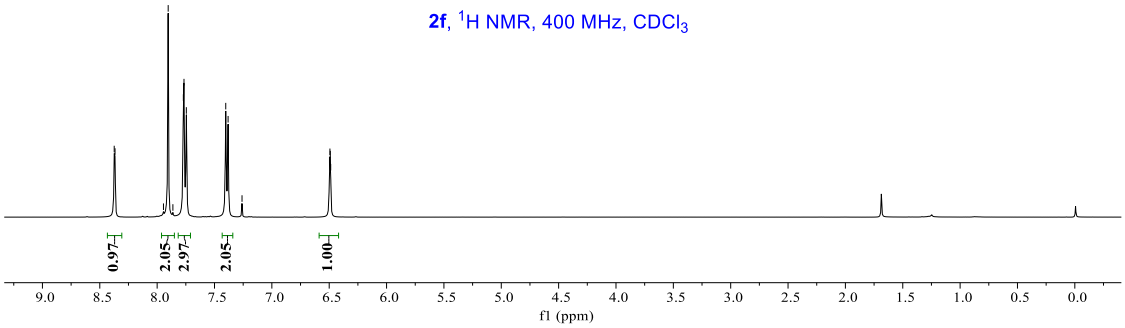


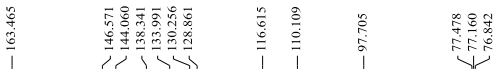
(E)-3-(4-iodophenyl)-1-(1H-pyrazol-1-yl)prop-2-en-1-one (2f).

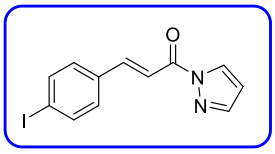




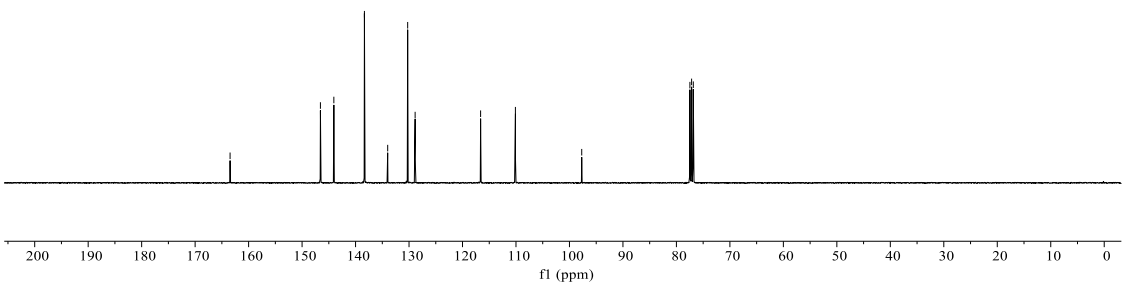
2f, ^{1}H NMR, 400 MHz, $CDCl_3$



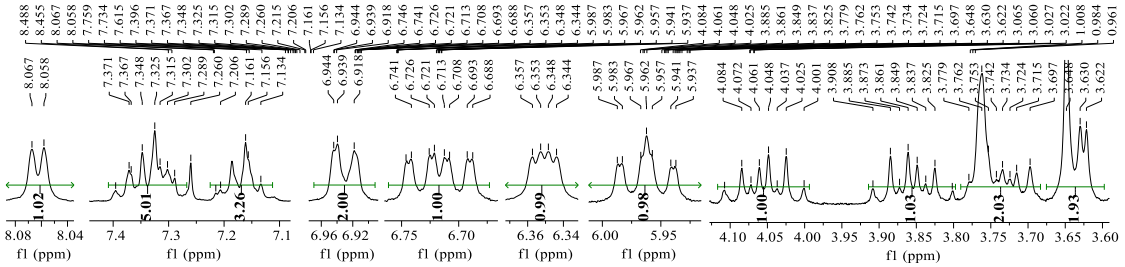


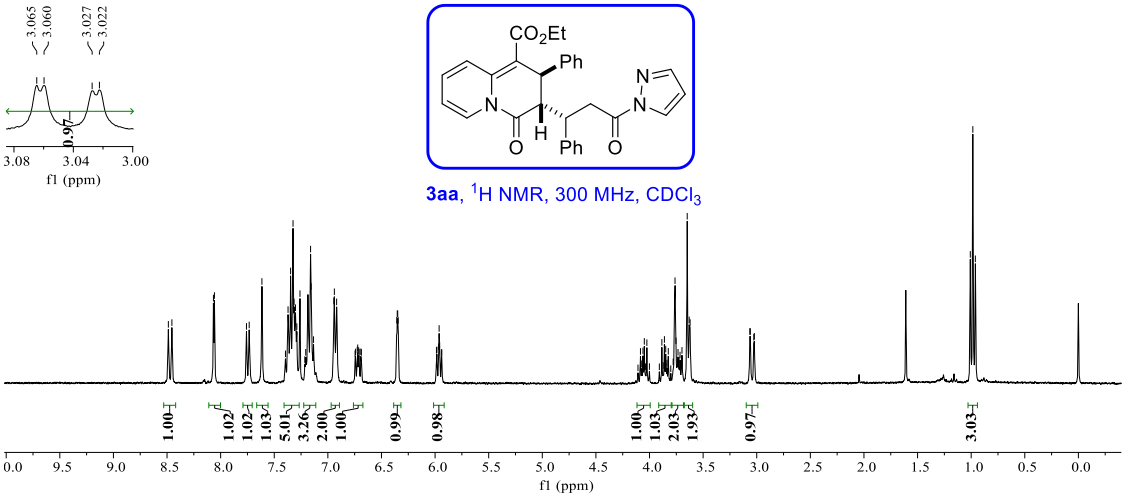


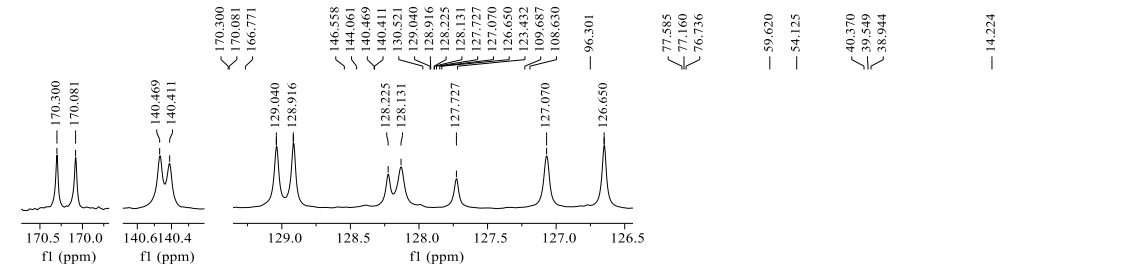
2f, ^{13}C NMR, 100 MHz, $CDCl_3$

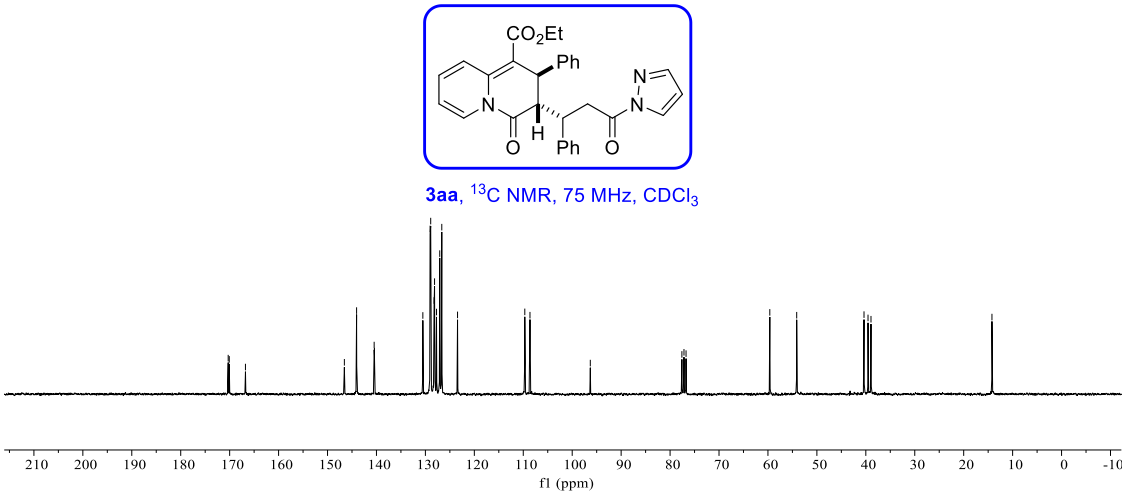


ethyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine -1-carboxylate (3aa).

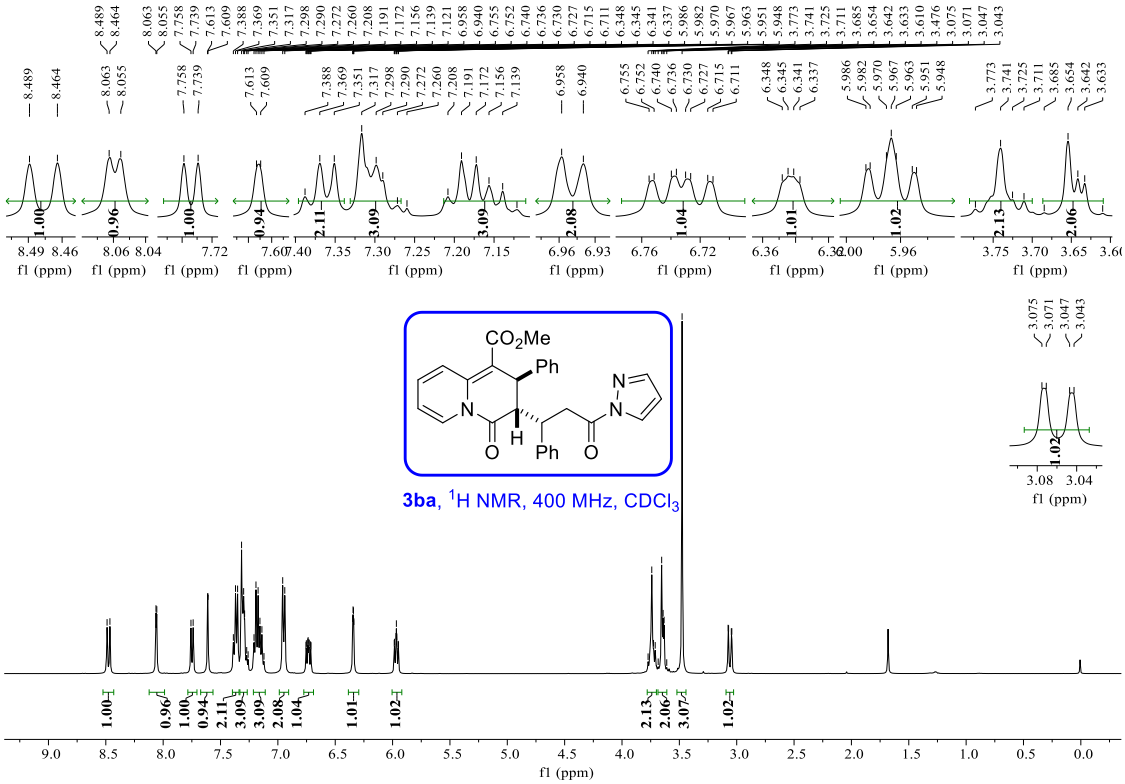


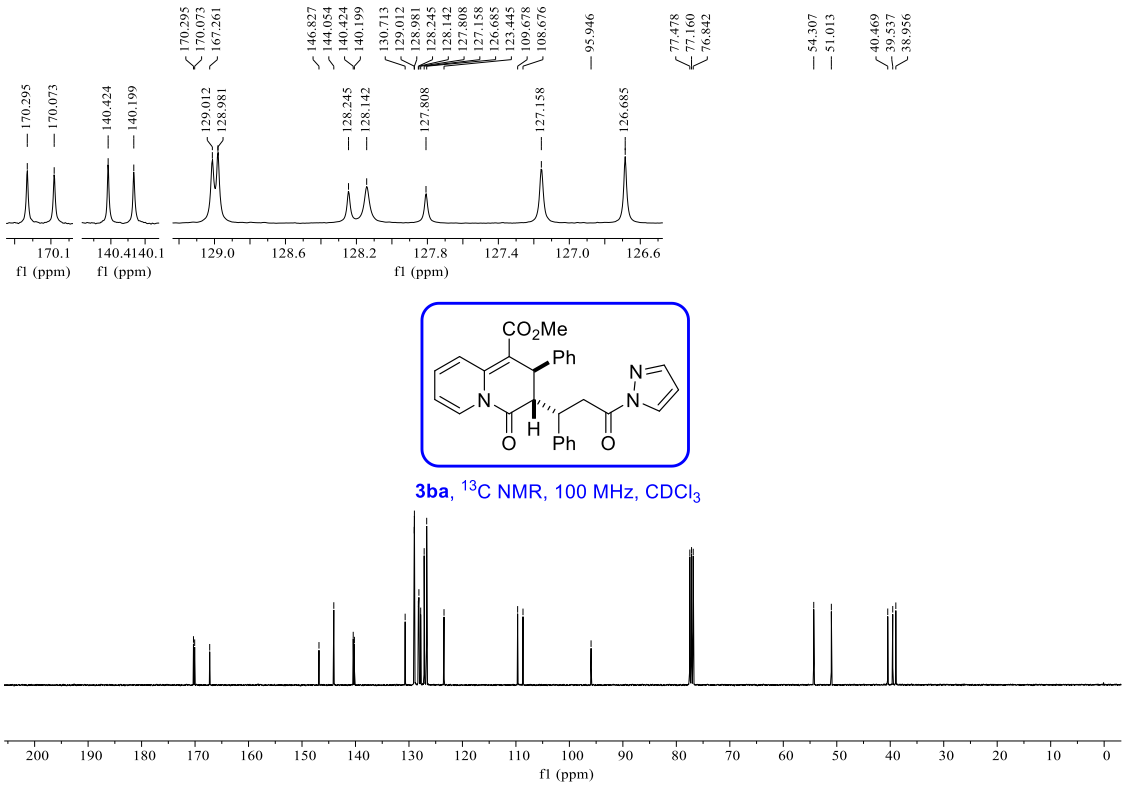




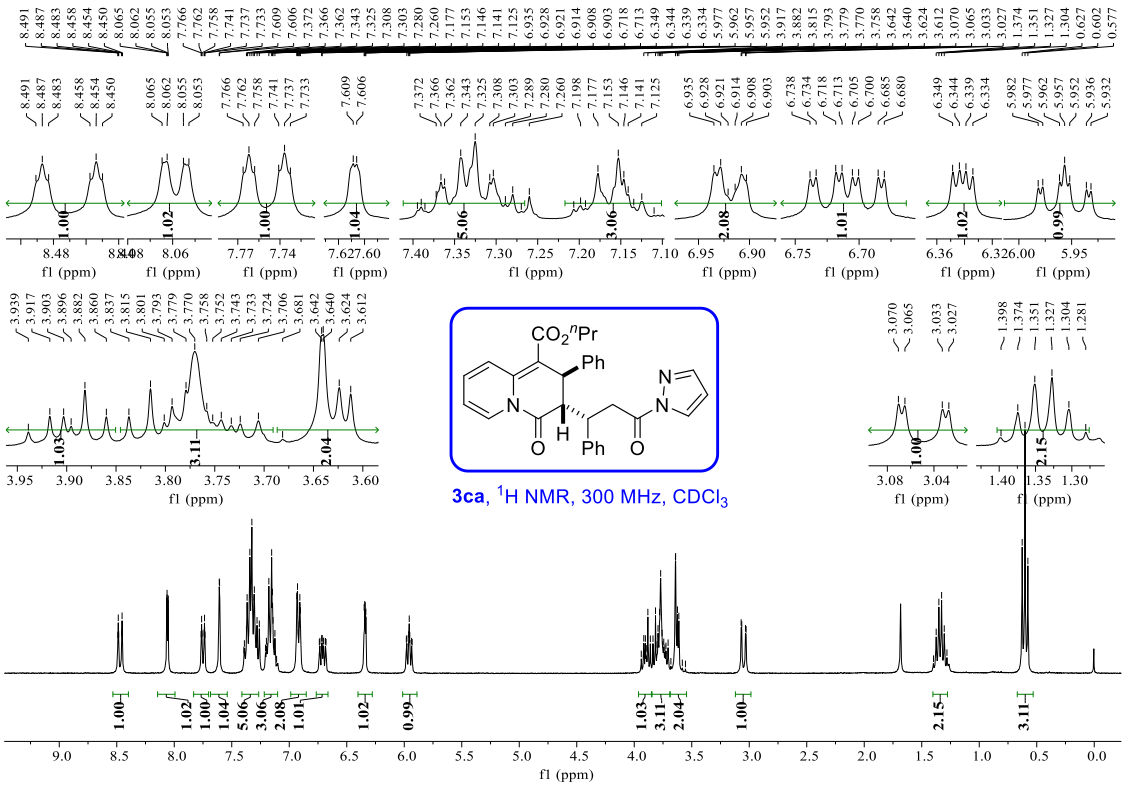


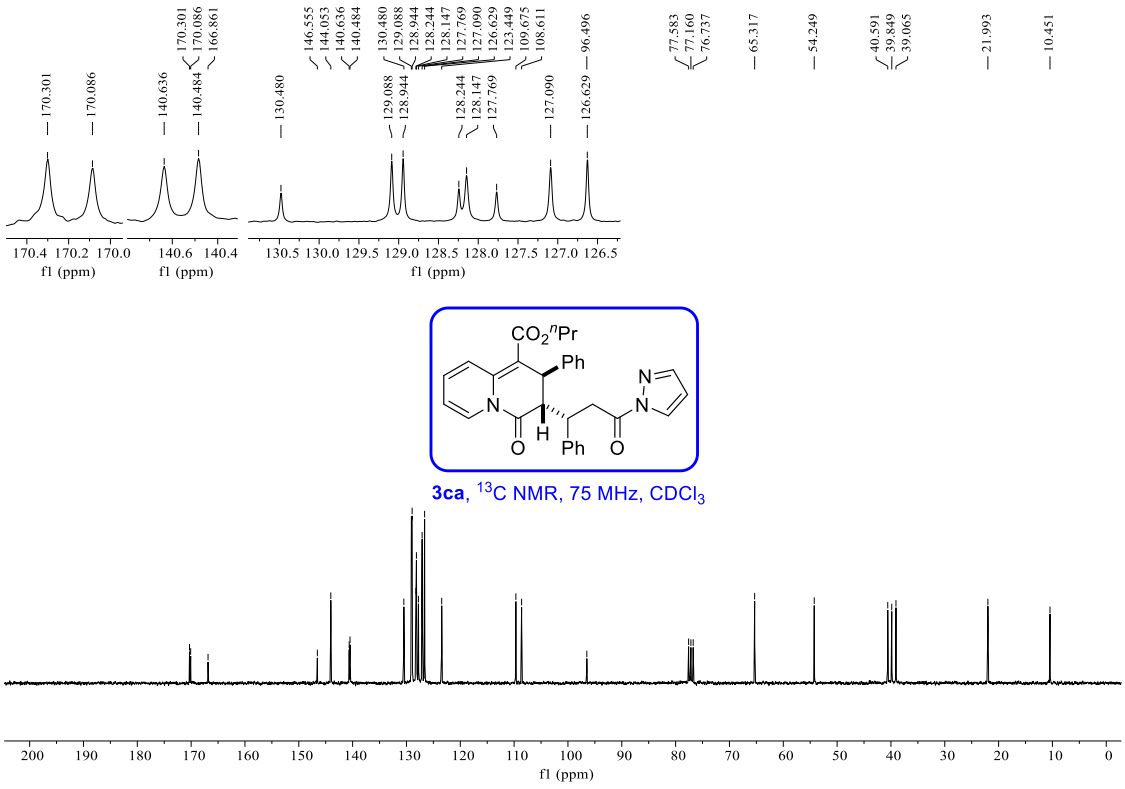
methyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3ba).



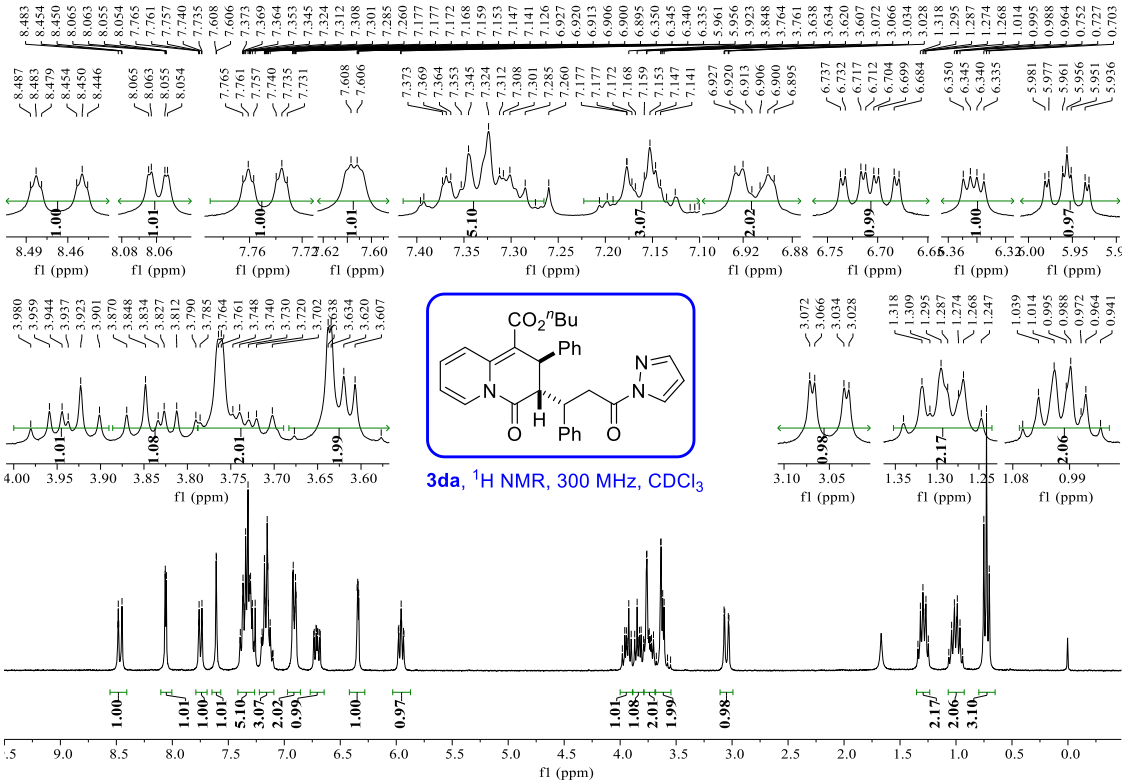


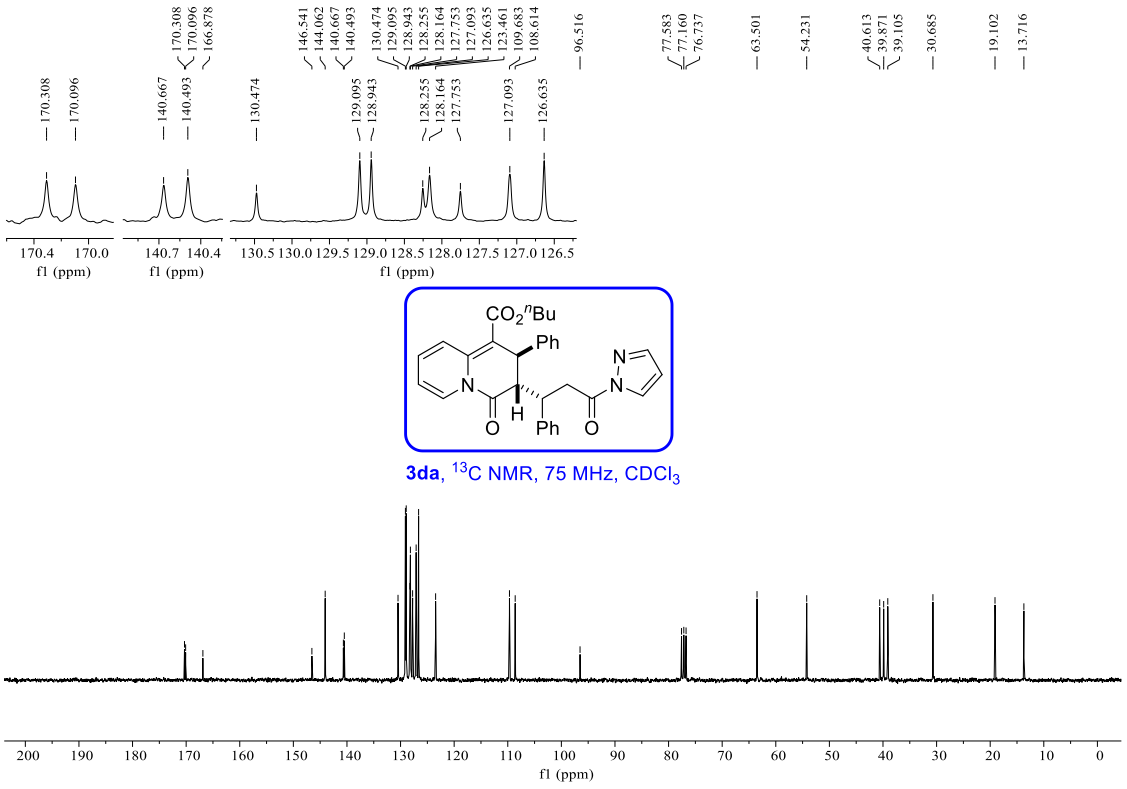
propyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3ca).



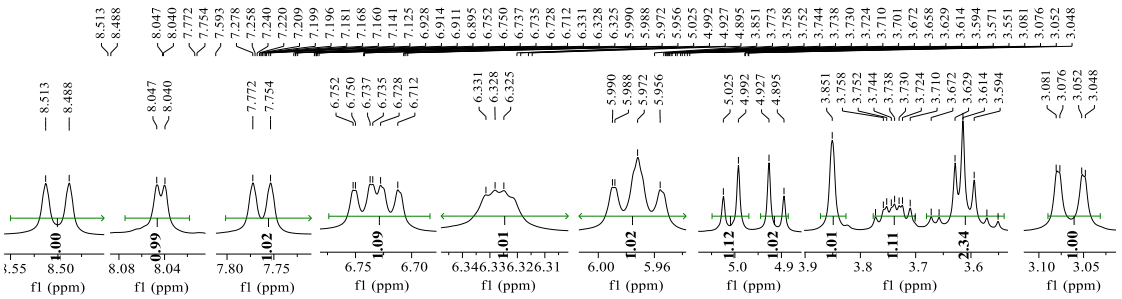


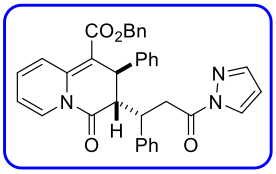
butyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3da).



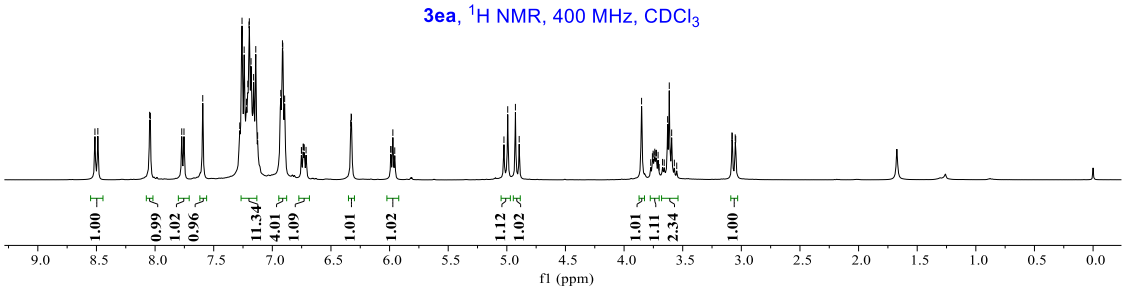


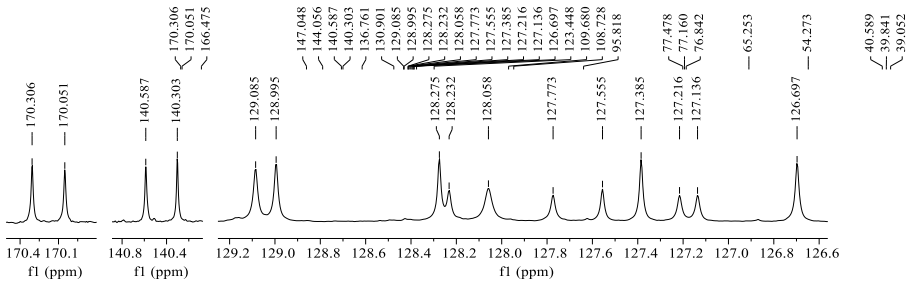
benzyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3ea).

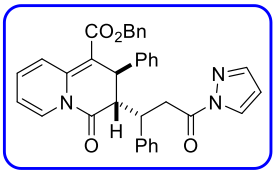




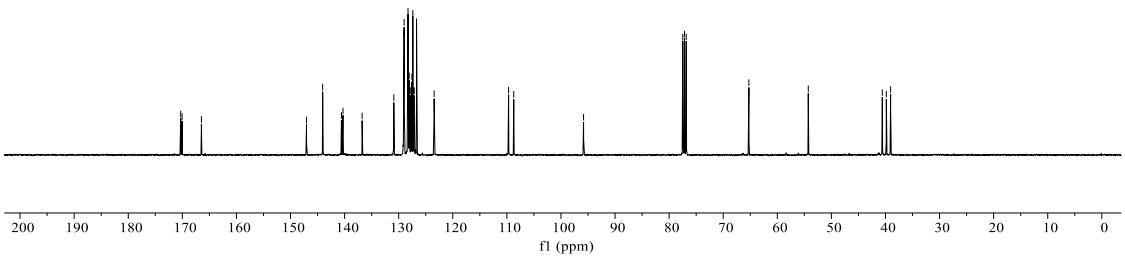
3ea, ^{1}H NMR, 400 MHz, $CDCl_3$



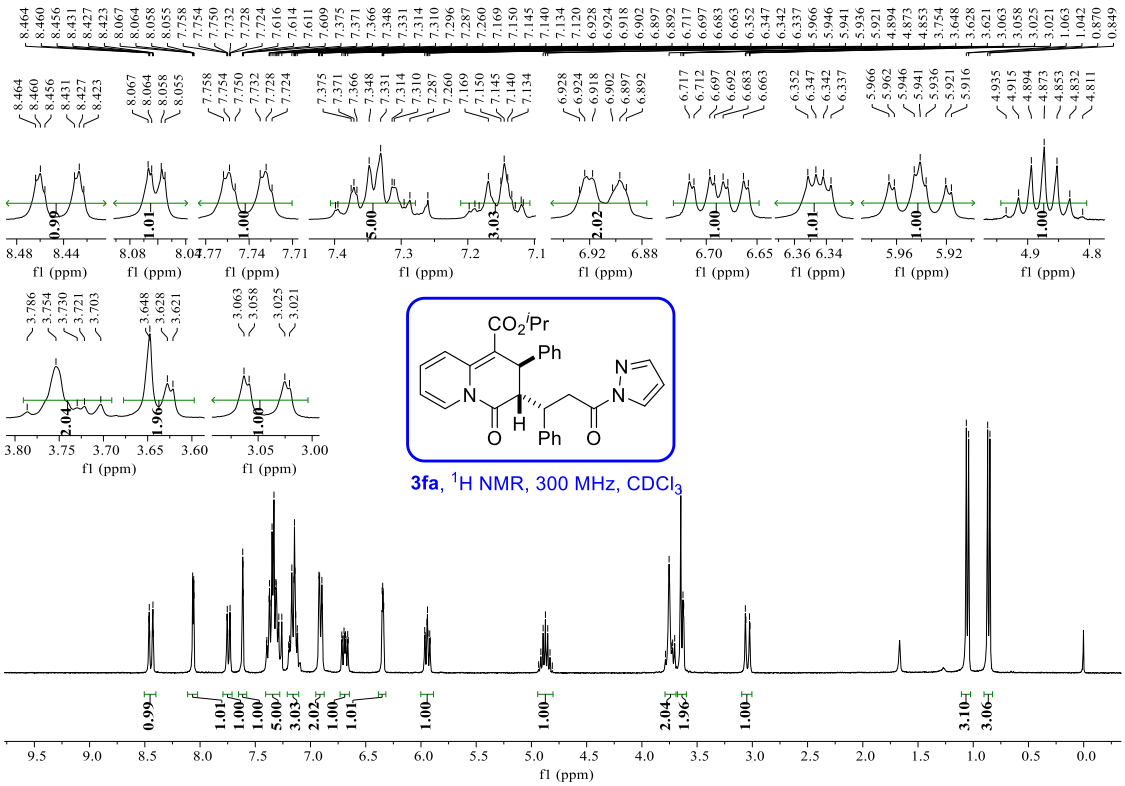


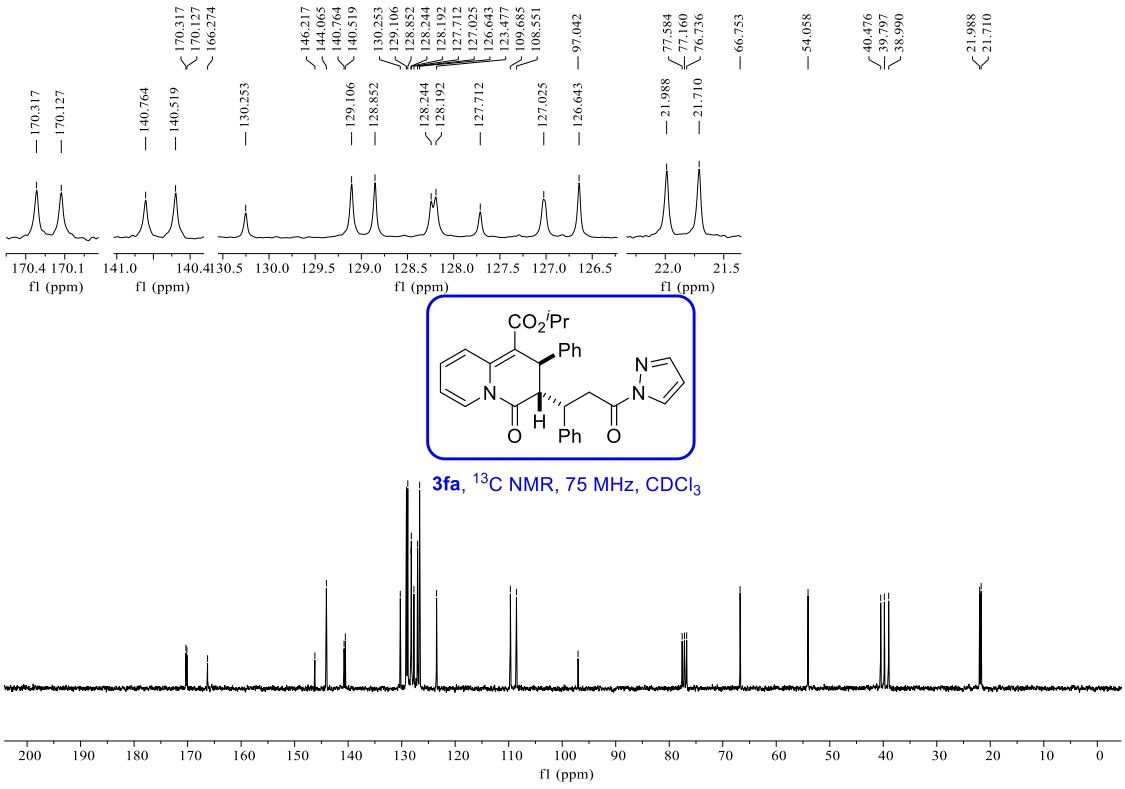


3ea, ^{13}C NMR, 100 MHz, $CDCl_3$

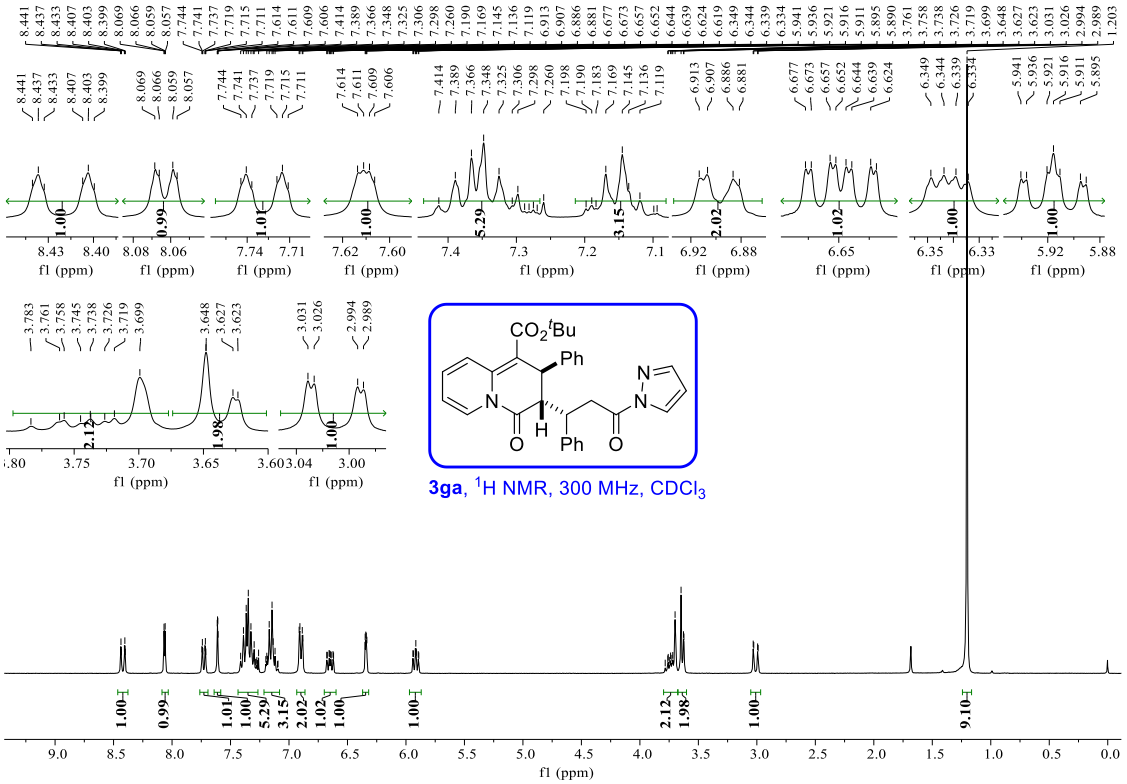


isopropyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3fa).

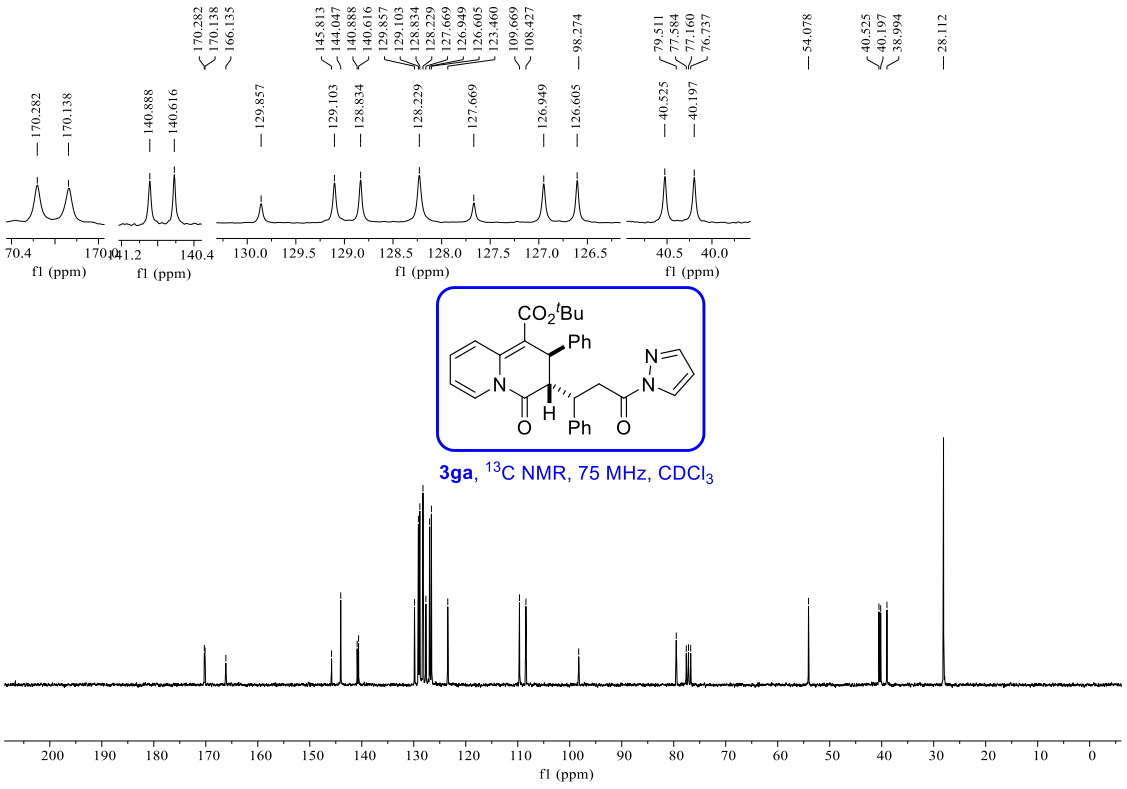




tert-butyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3ga).

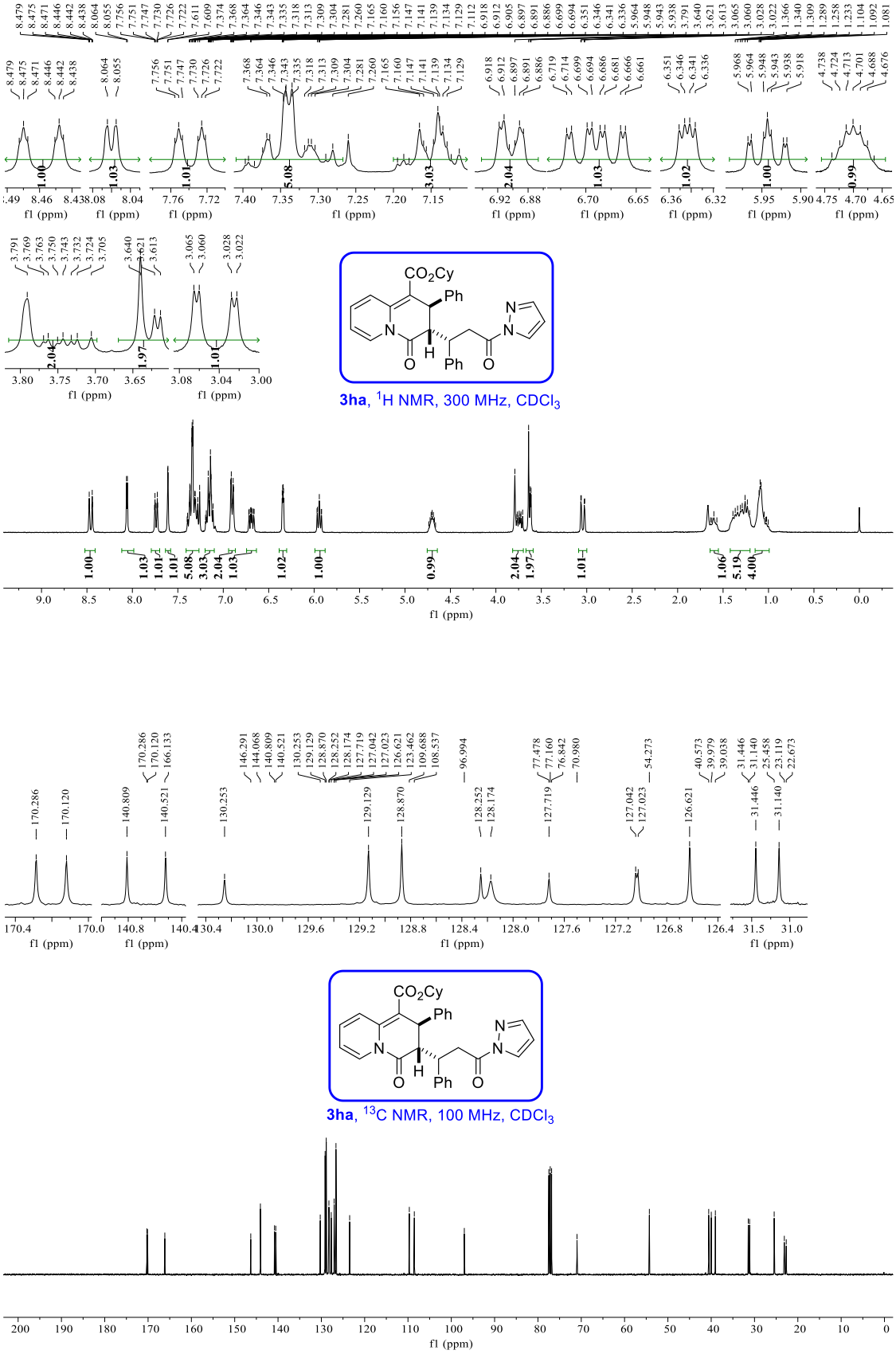


3ga, ^{1}H NMR, 300 MHz, $CDCl_3$

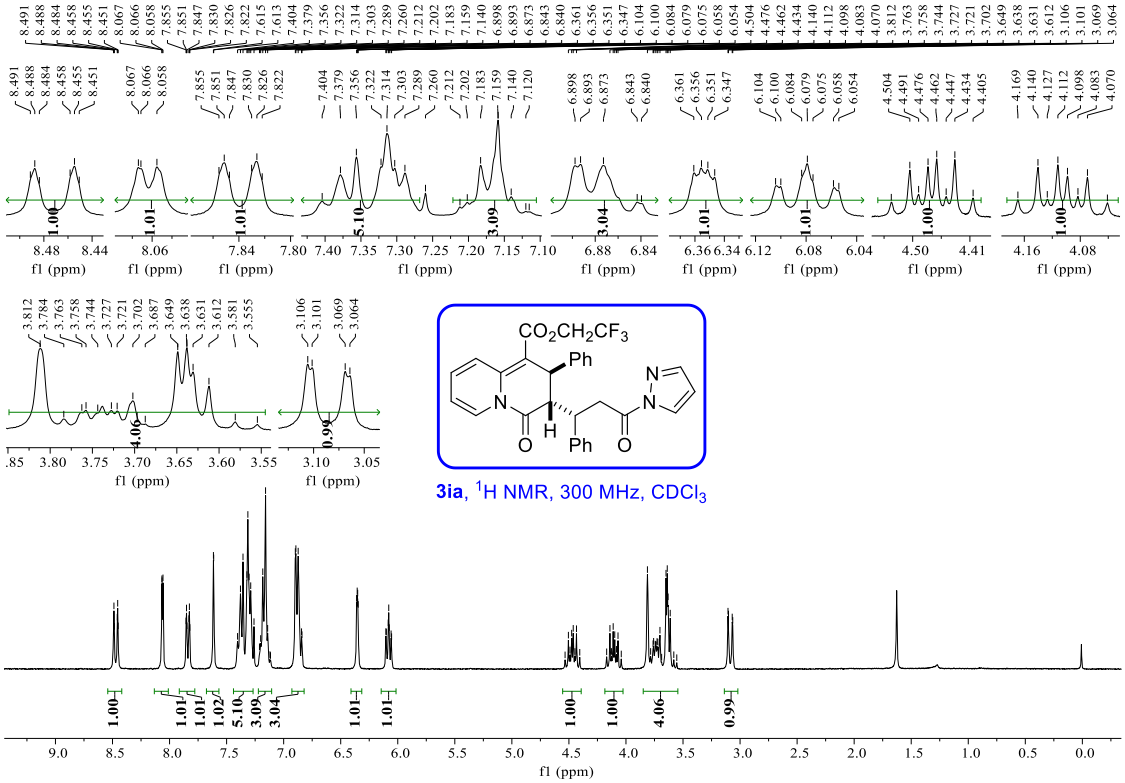


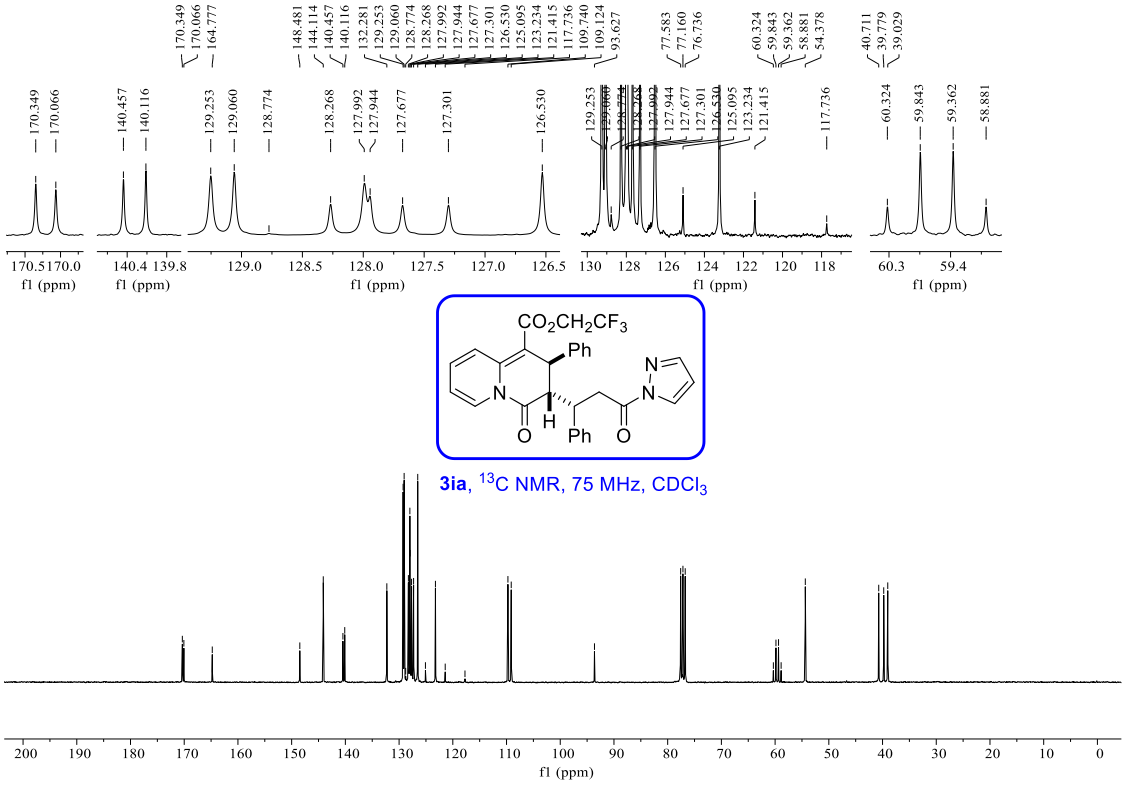
3ga, ^{13}C NMR, 75 MHz, $CDCl_3$

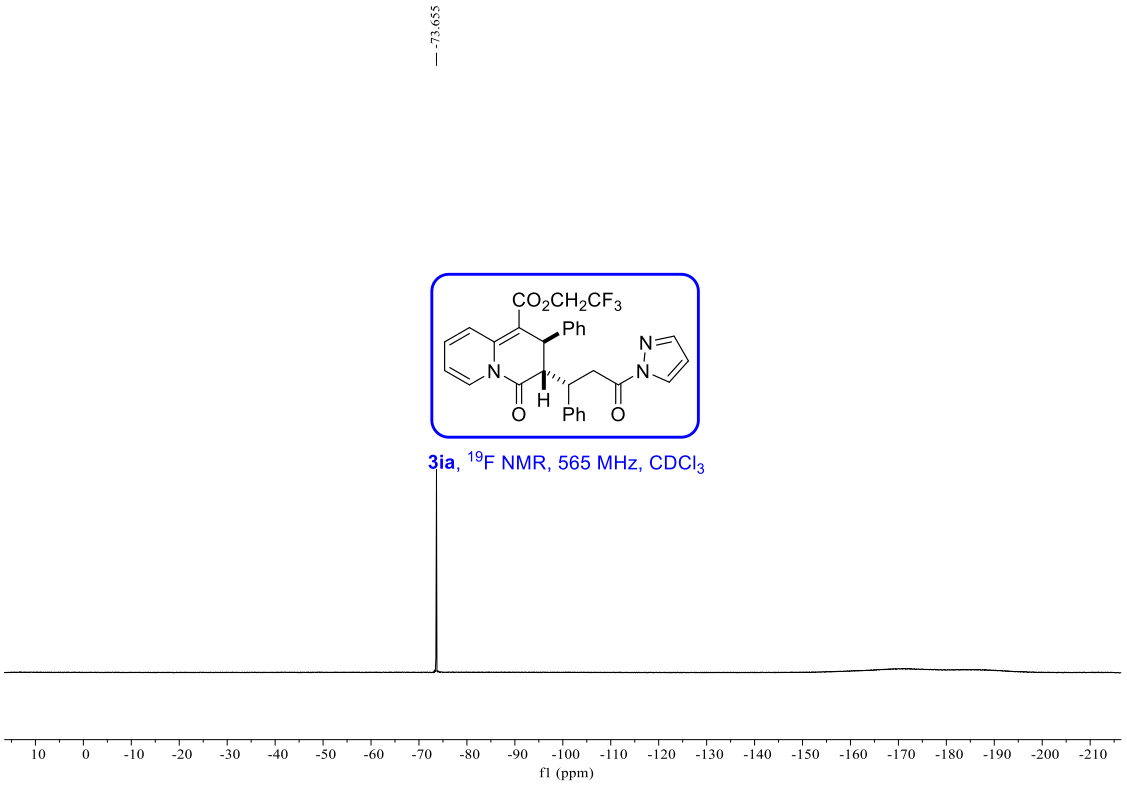
cyclohexyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3ha).



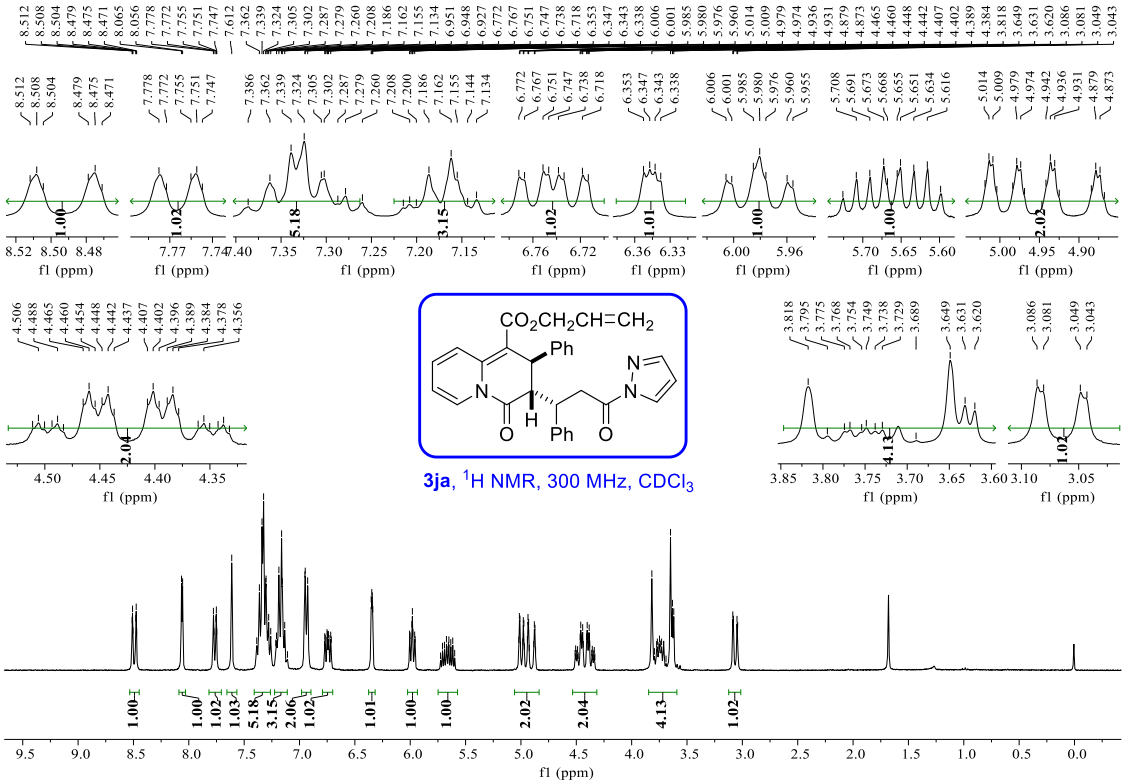
2,2,2-trifluoroethyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3ia).

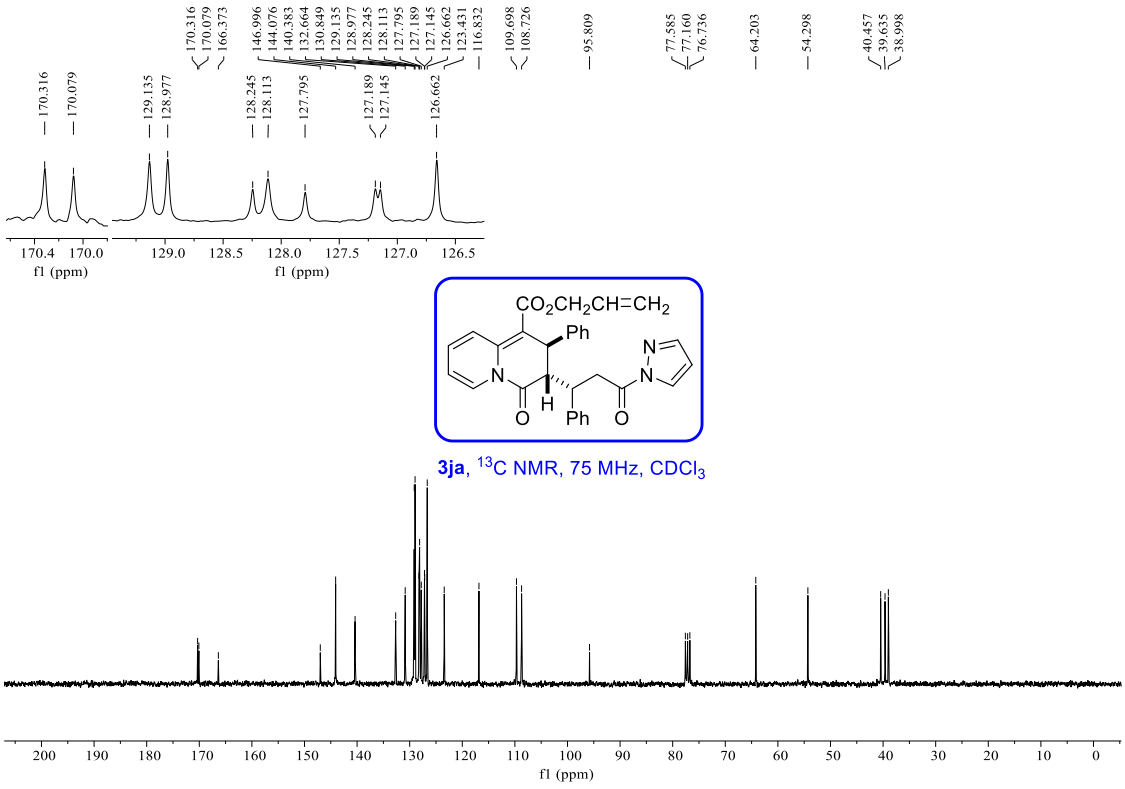




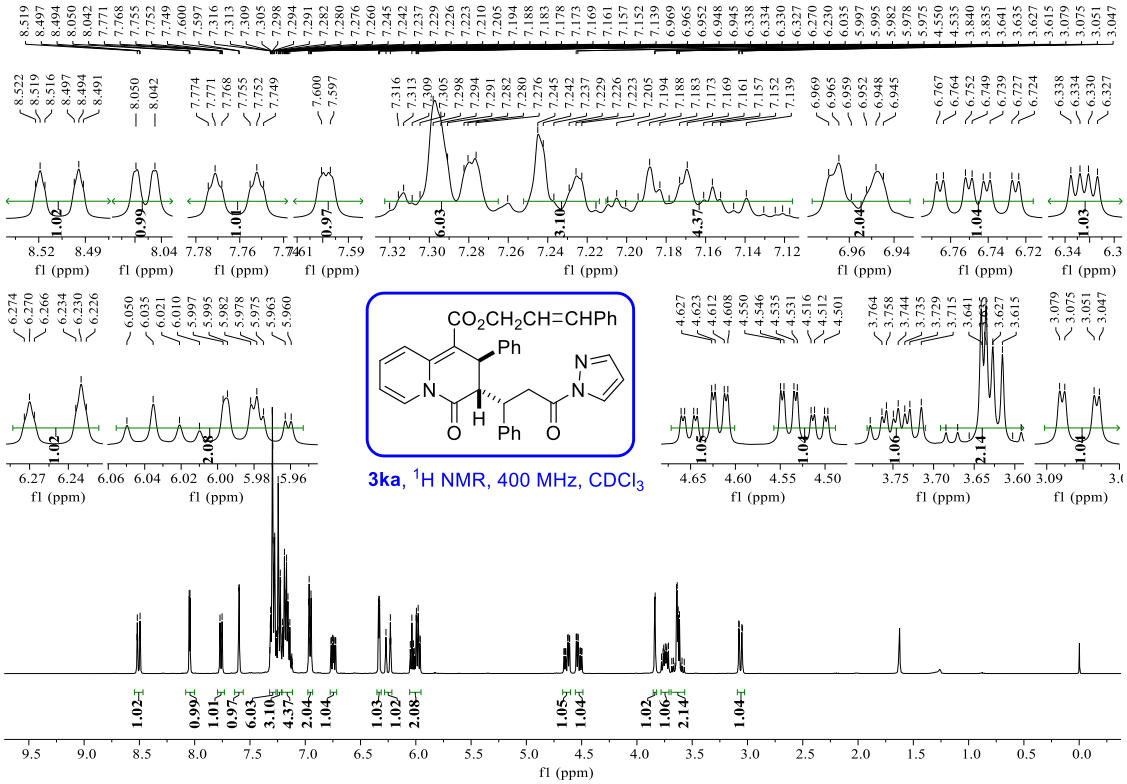

-73.655
CO2CH2CF3
Ph
N
N
N
H
O
Ph
O
3ia, 19F NMR, 565 MHz, CDCl3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

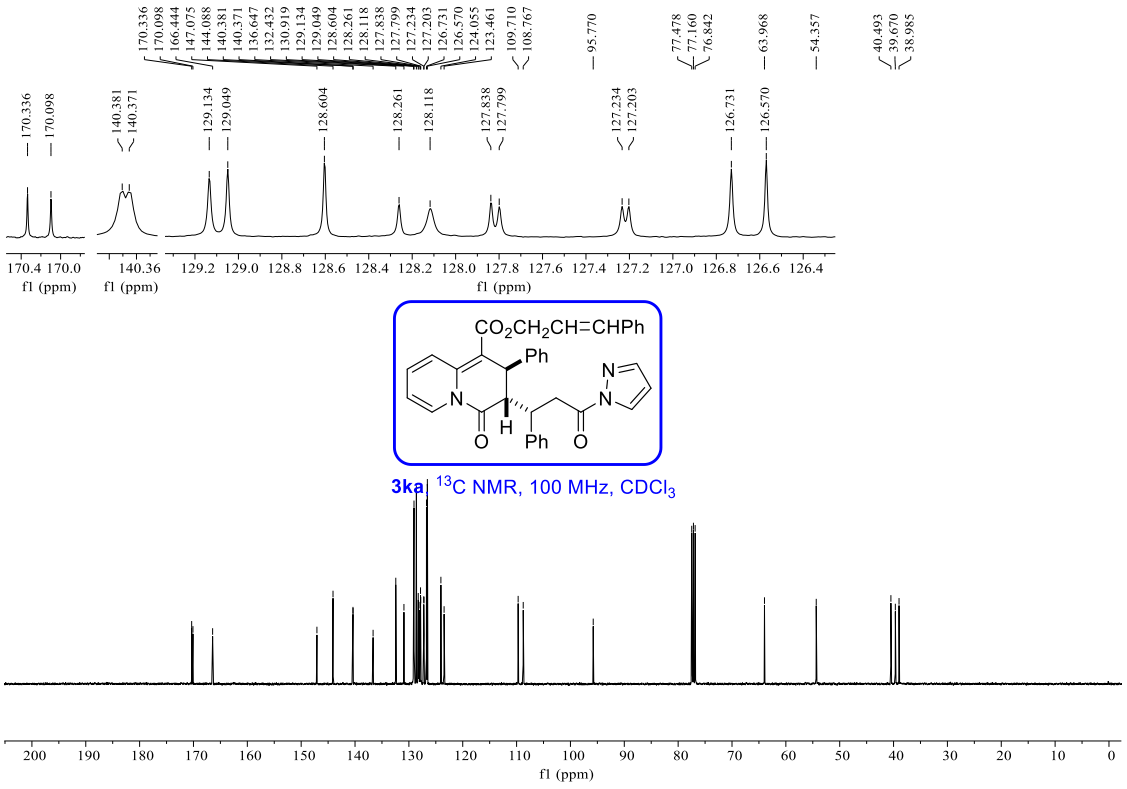
allyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine -1-carboxylate (3ja).



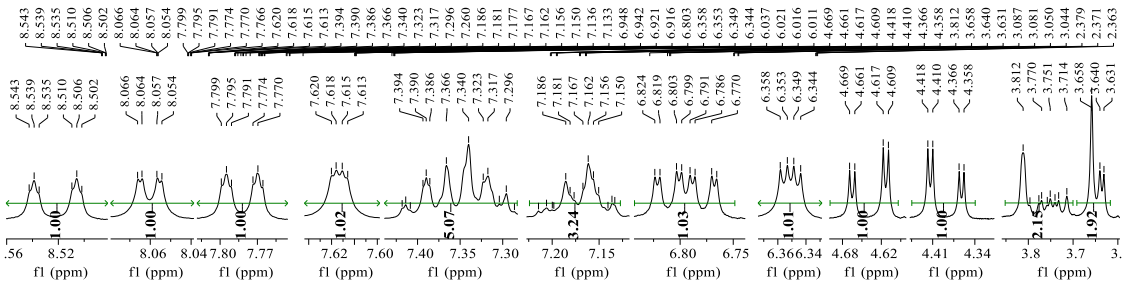


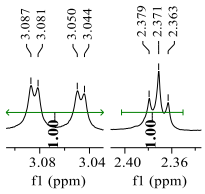
cinnamyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3ka).

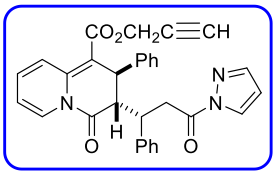




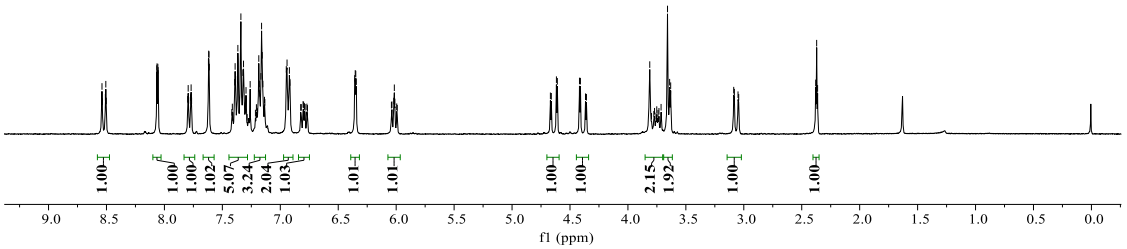
prop-2-yn-1-yl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H -quinolizine-1-carboxylate (3la).

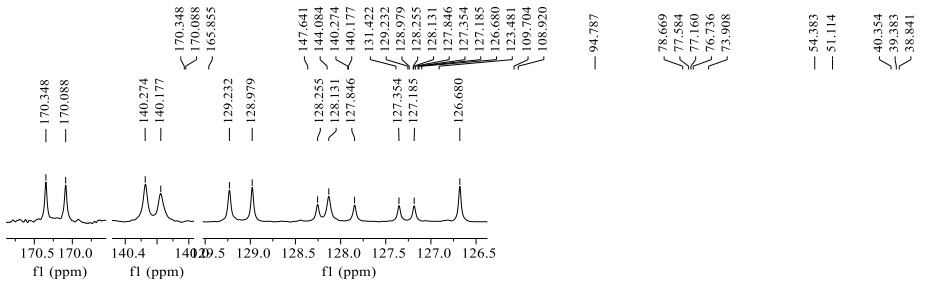


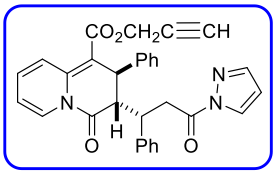




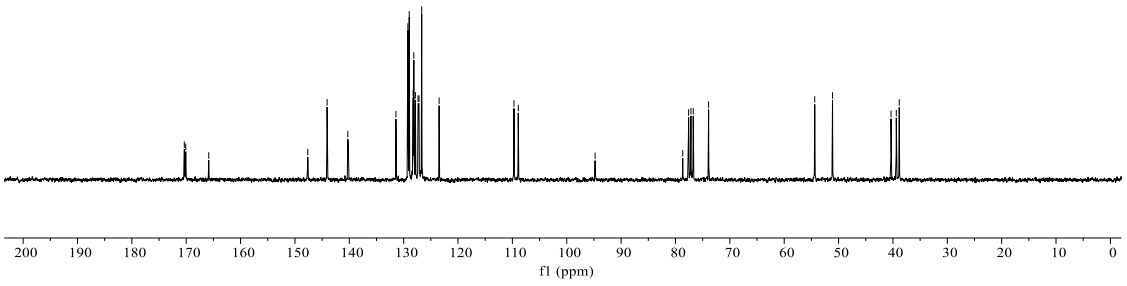
3la, ^{1}H NMR, 300 MHz, $CDCl_3$



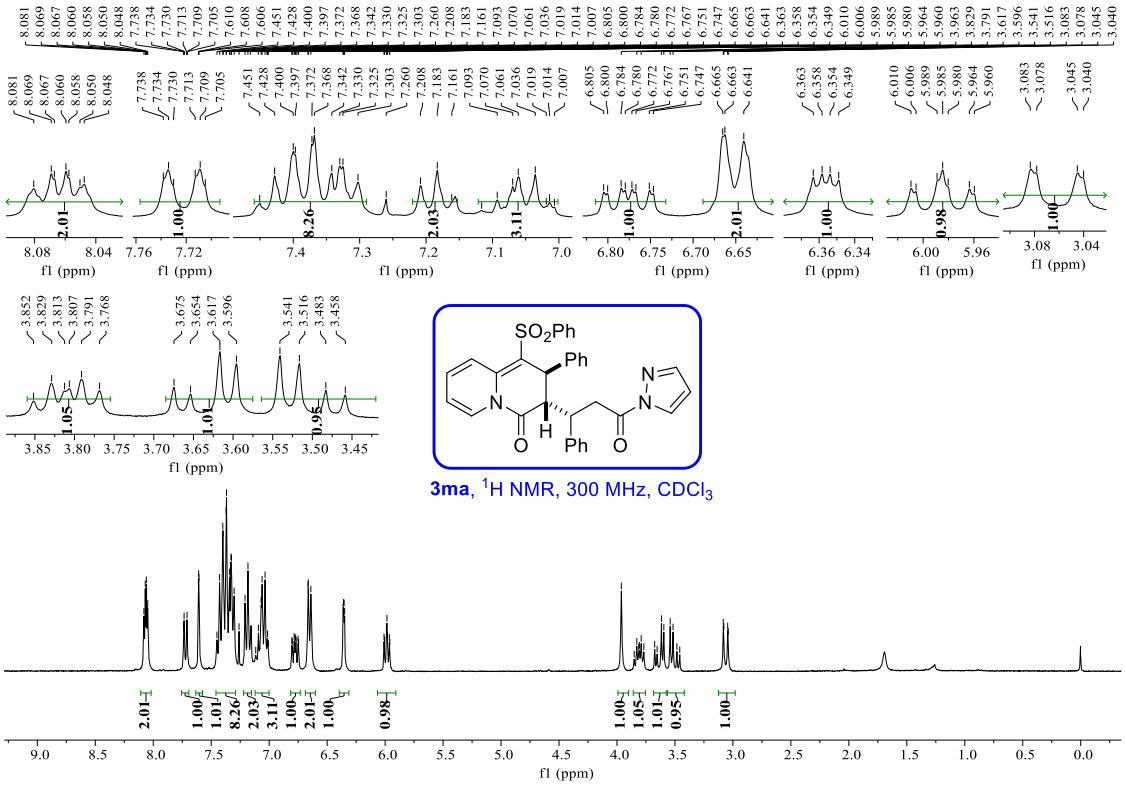


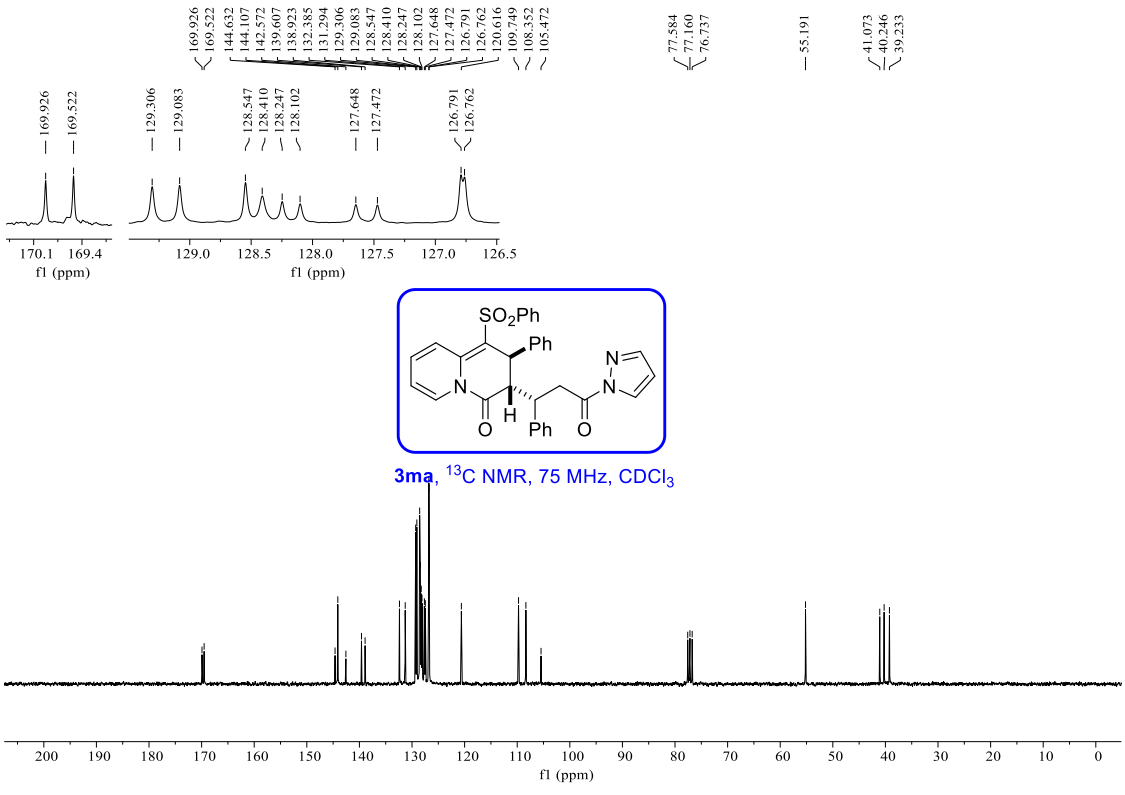


3la, ^{13}C NMR, 75 MHz, $CDCl_3$

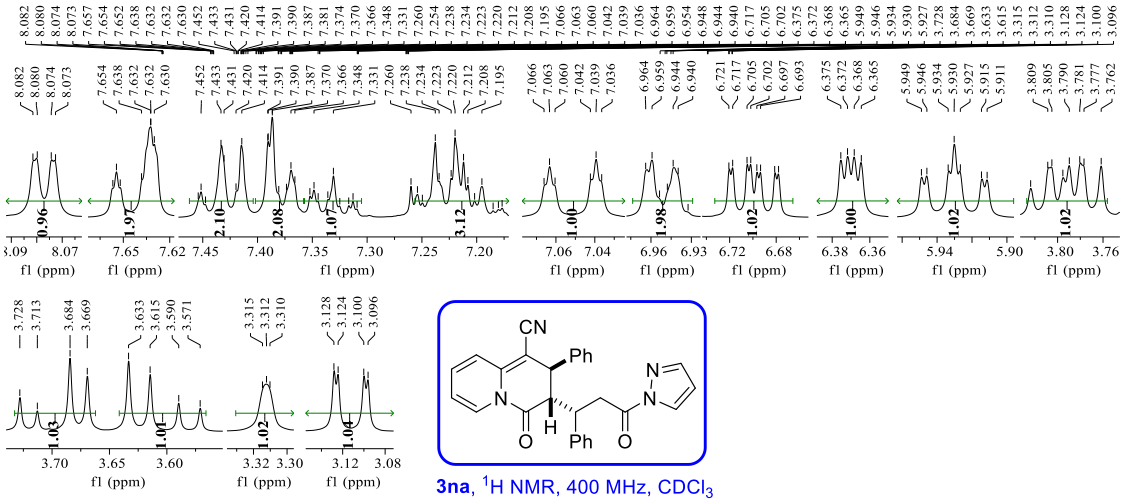


3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-1-(phenylsulfonyl)-2,3-dihydro-4H-quinolizin-4-one (3ma).

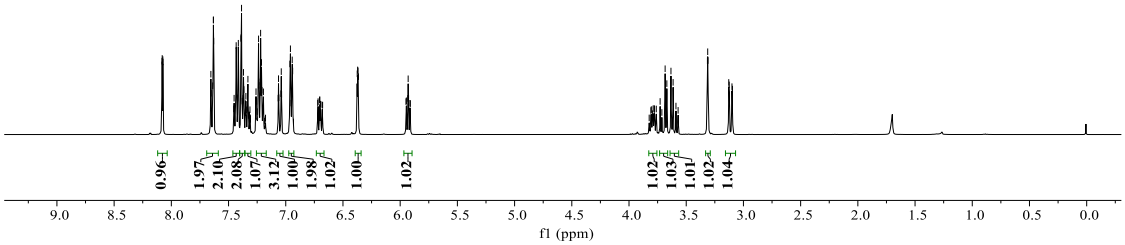


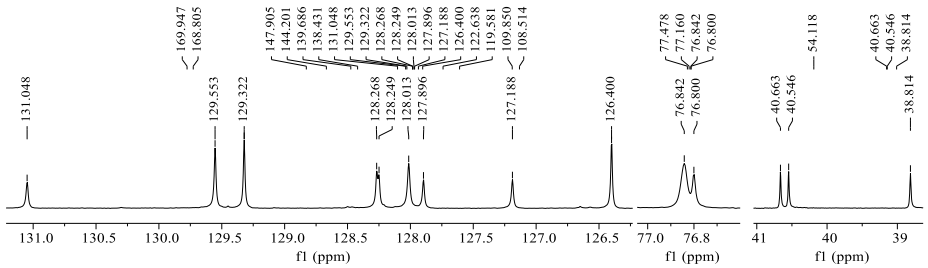


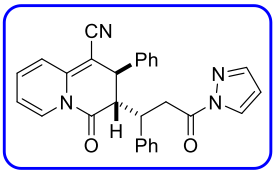
4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carbonitrile (3na).



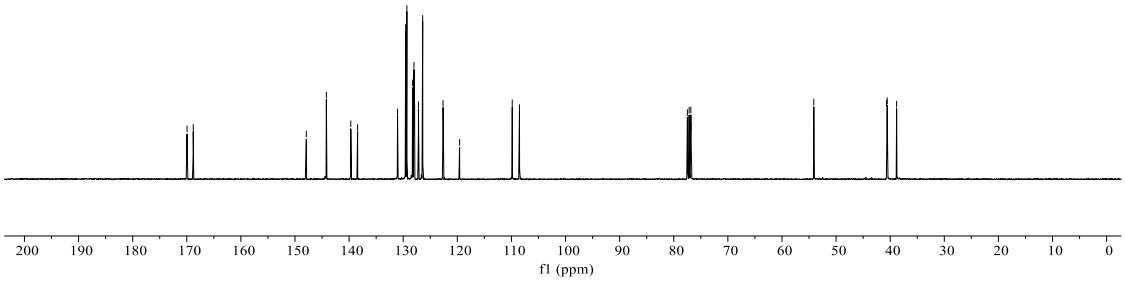
3na, ^{1}H NMR, 400 MHz, $CDCl_3$



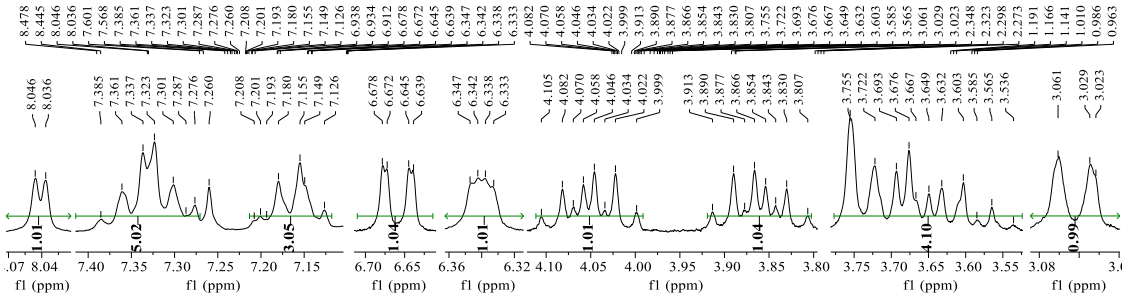


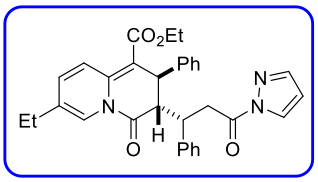


3na, ^{13}C NMR, 100 MHz, $CDCl_3$

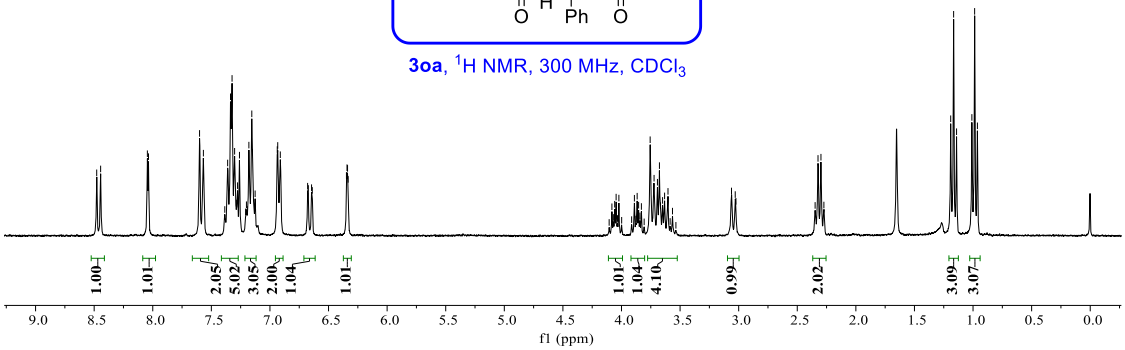


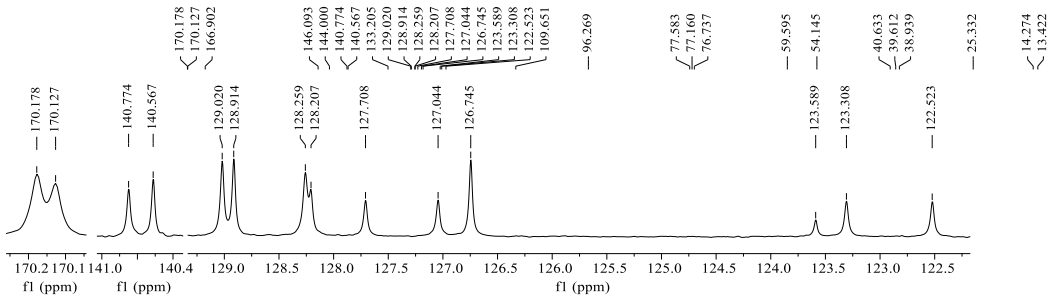
ethyl 7-ethyl-4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3oa).

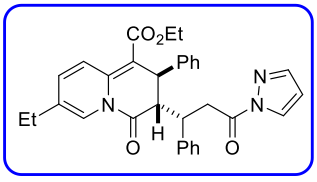




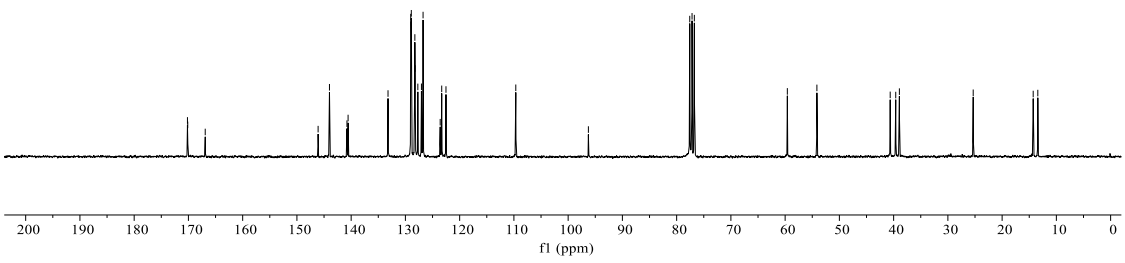
3oa, ^{1}H NMR, 300 MHz, $CDCl_3$



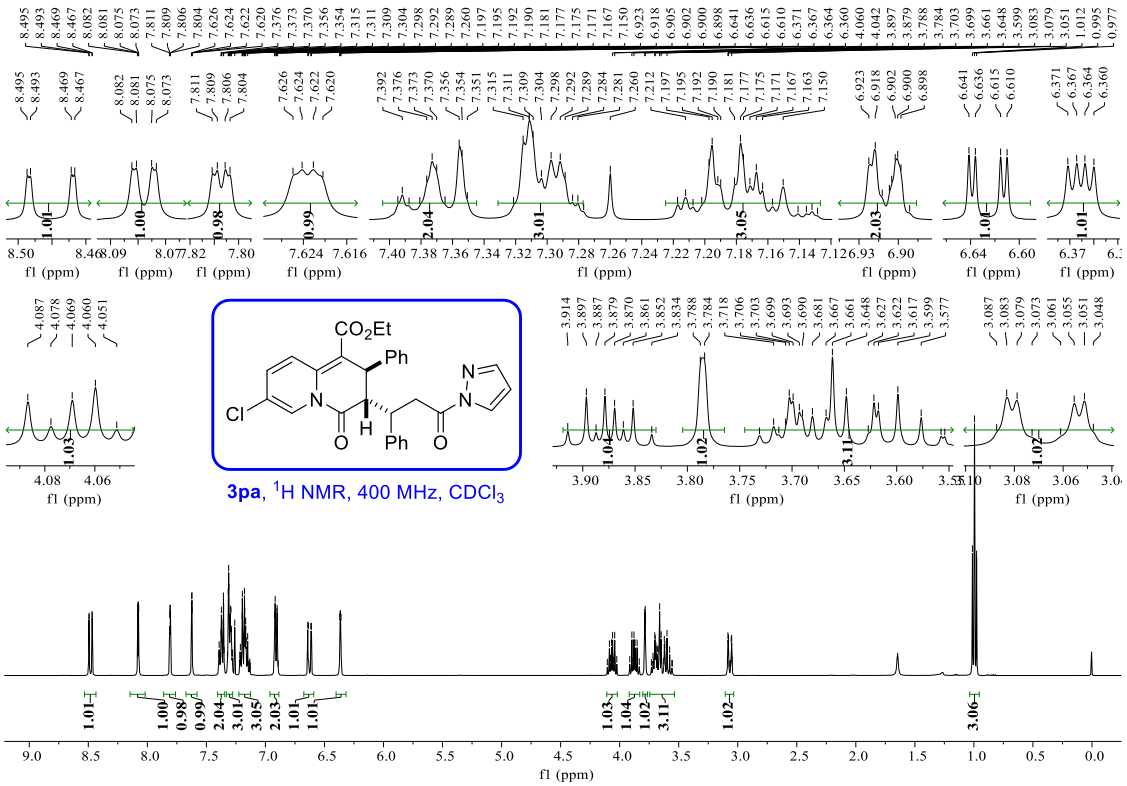


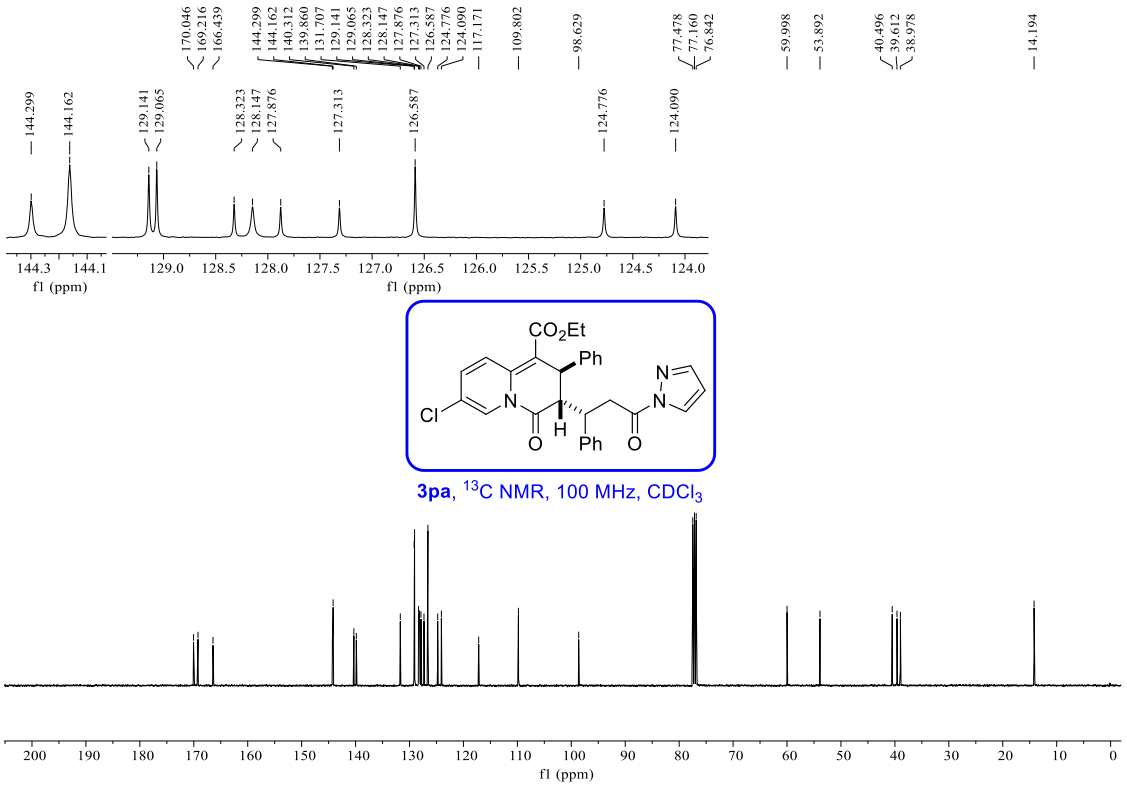


3oa, ^{13}C NMR, 75 MHz, $CDCl_3$

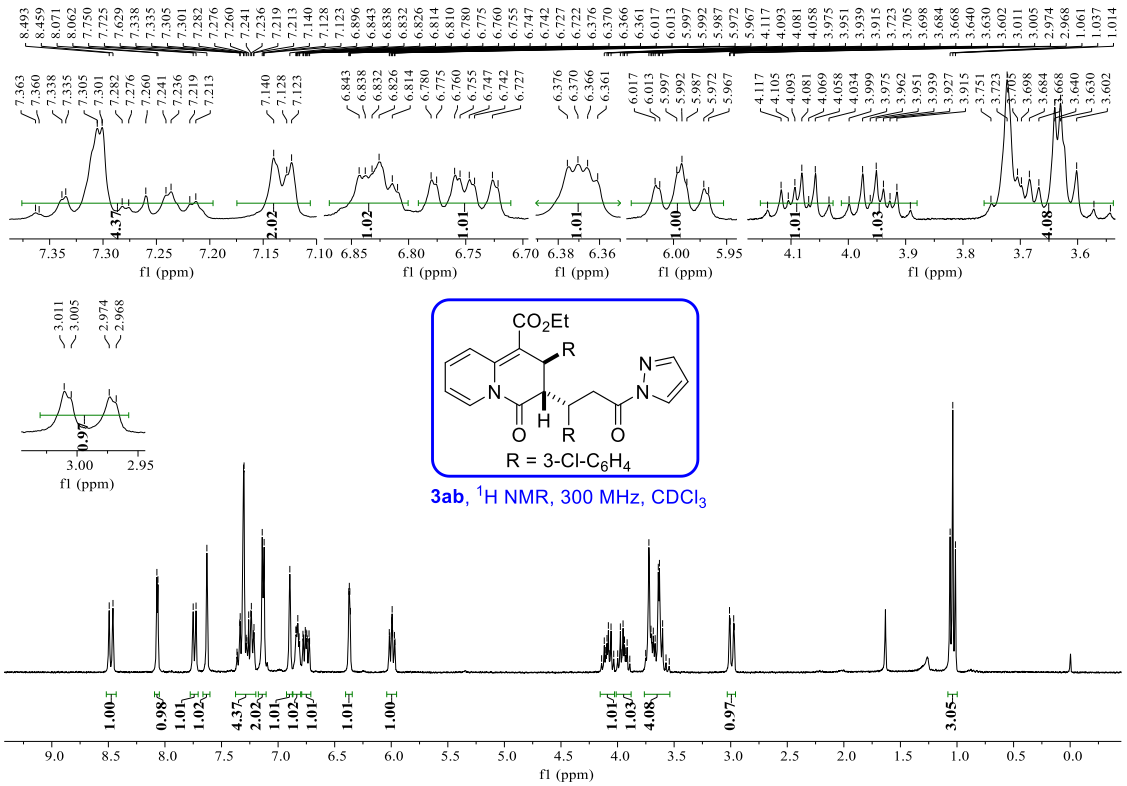


ethyl 7-chloro-4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (3pa).

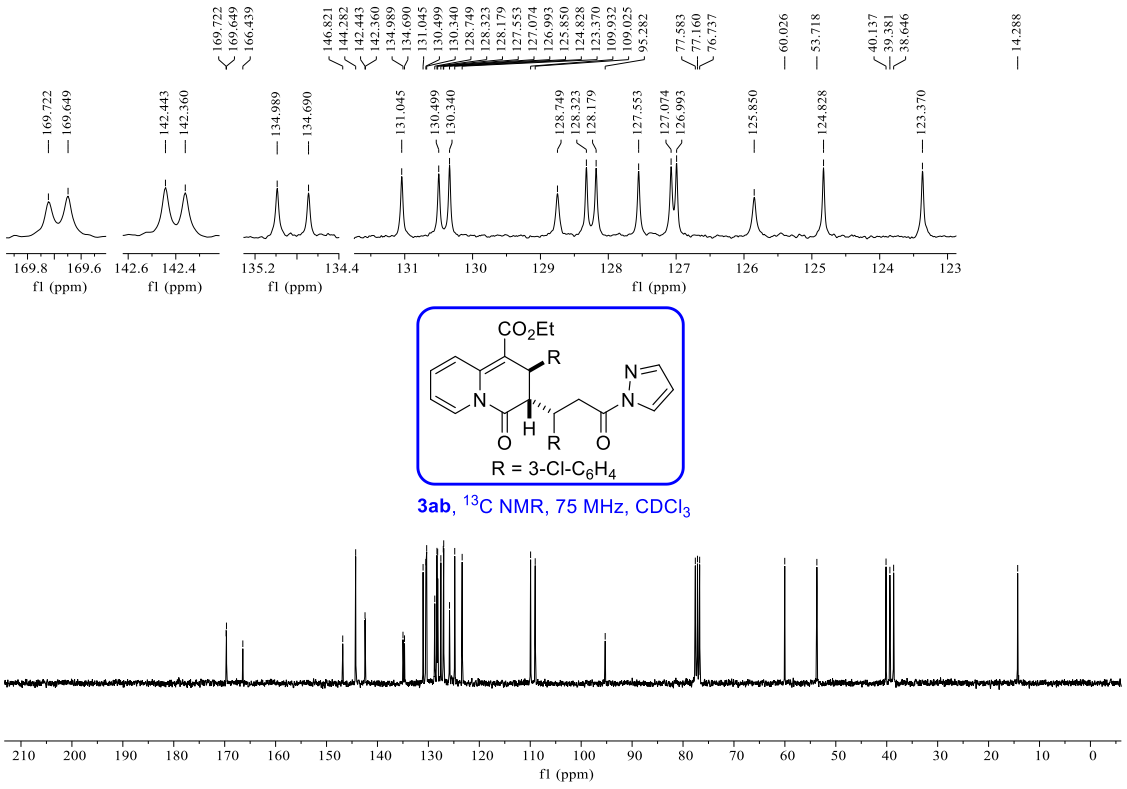




ethyl 2-(3-chlorophenyl)-3-(1-(3-chlorophenyl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3ab).

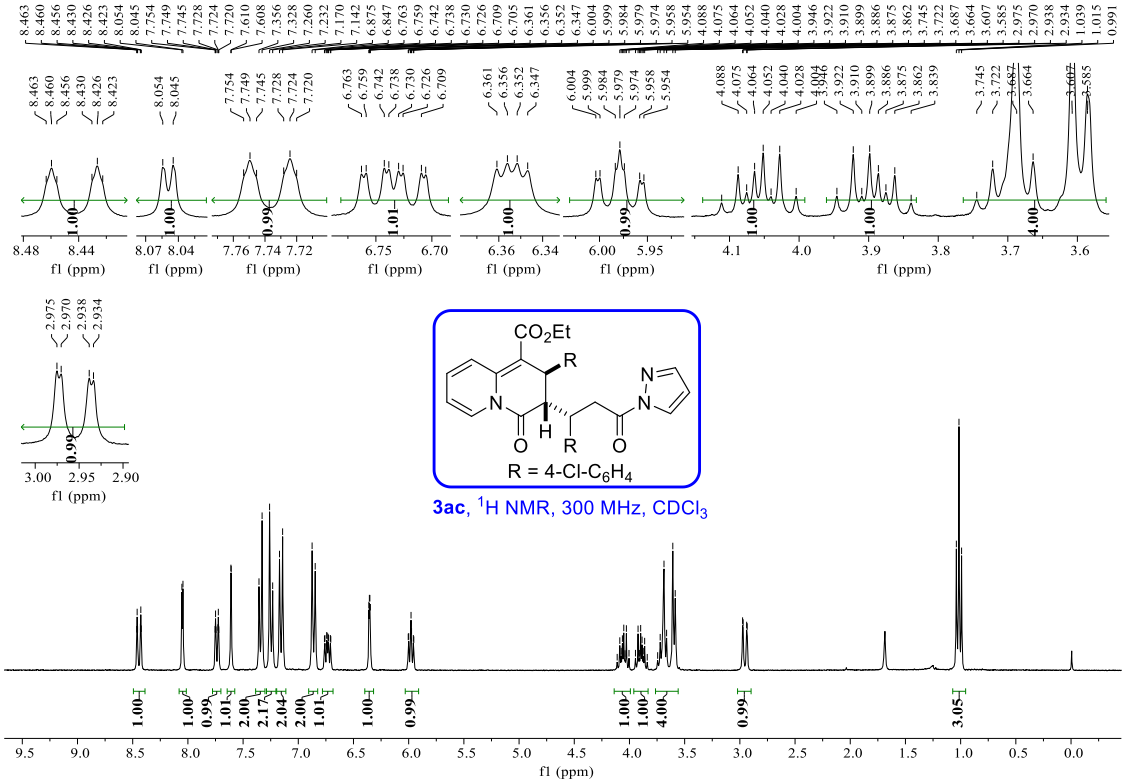


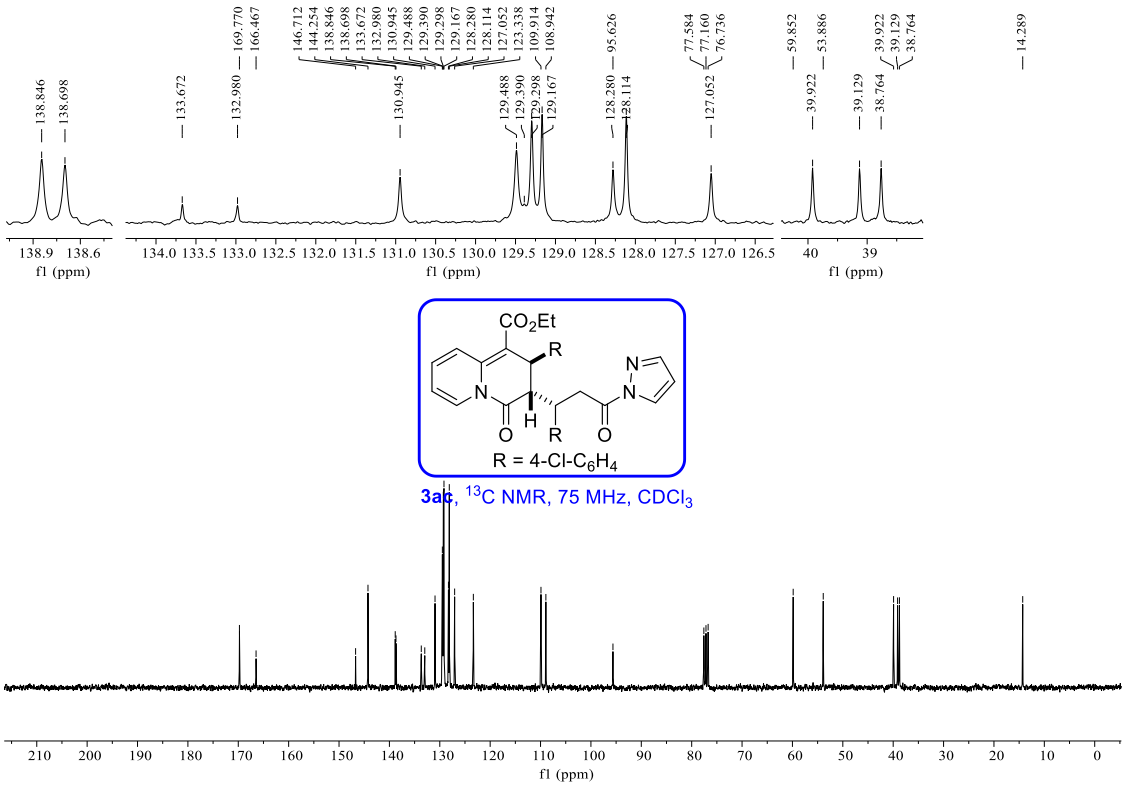
3ab, ^{1}H NMR, 300 MHz, $CDCl_3$



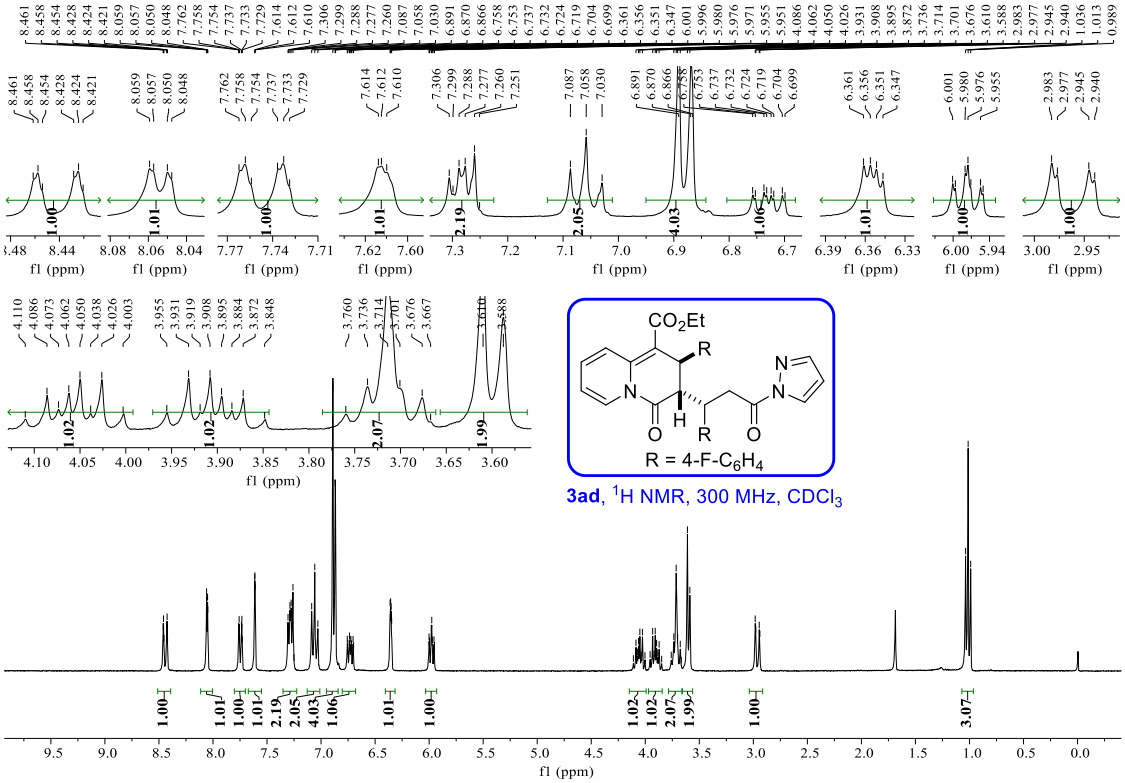
3ab, ^{13}C NMR, 75 MHz, $CDCl_3$

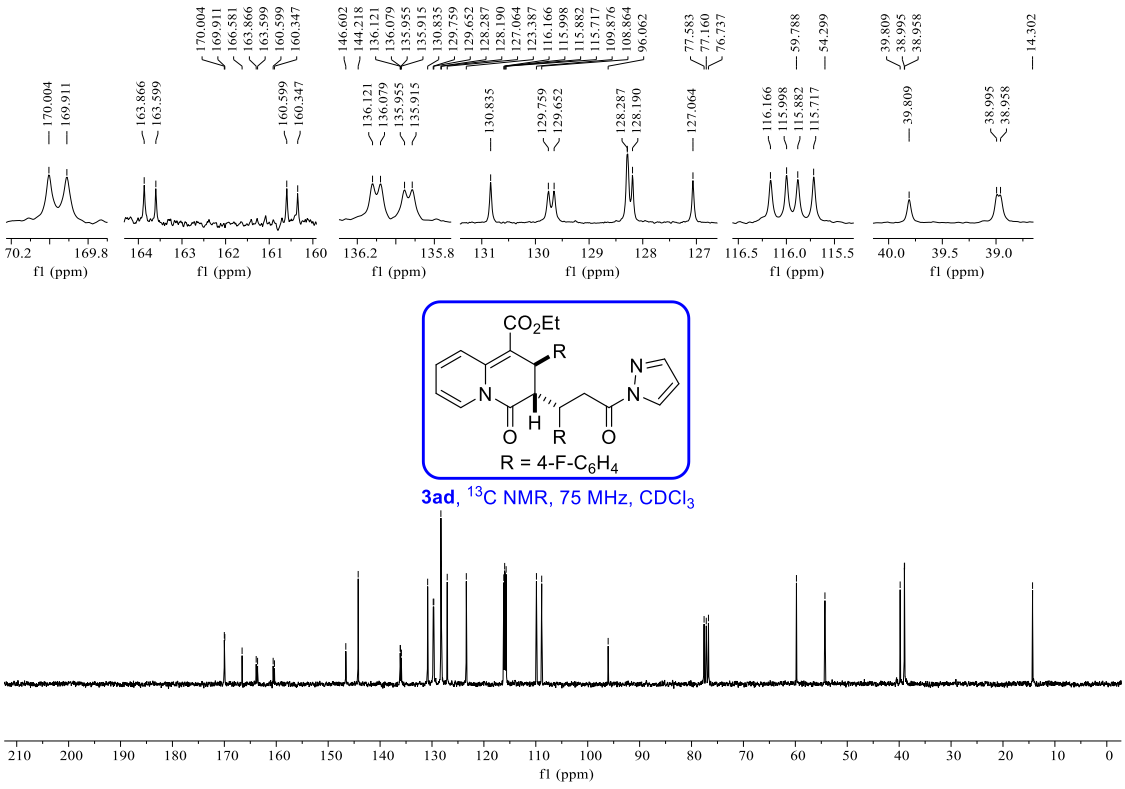
ethyl 2-(4-chlorophenyl)-3-(1-(4-chlorophenyl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3ac).

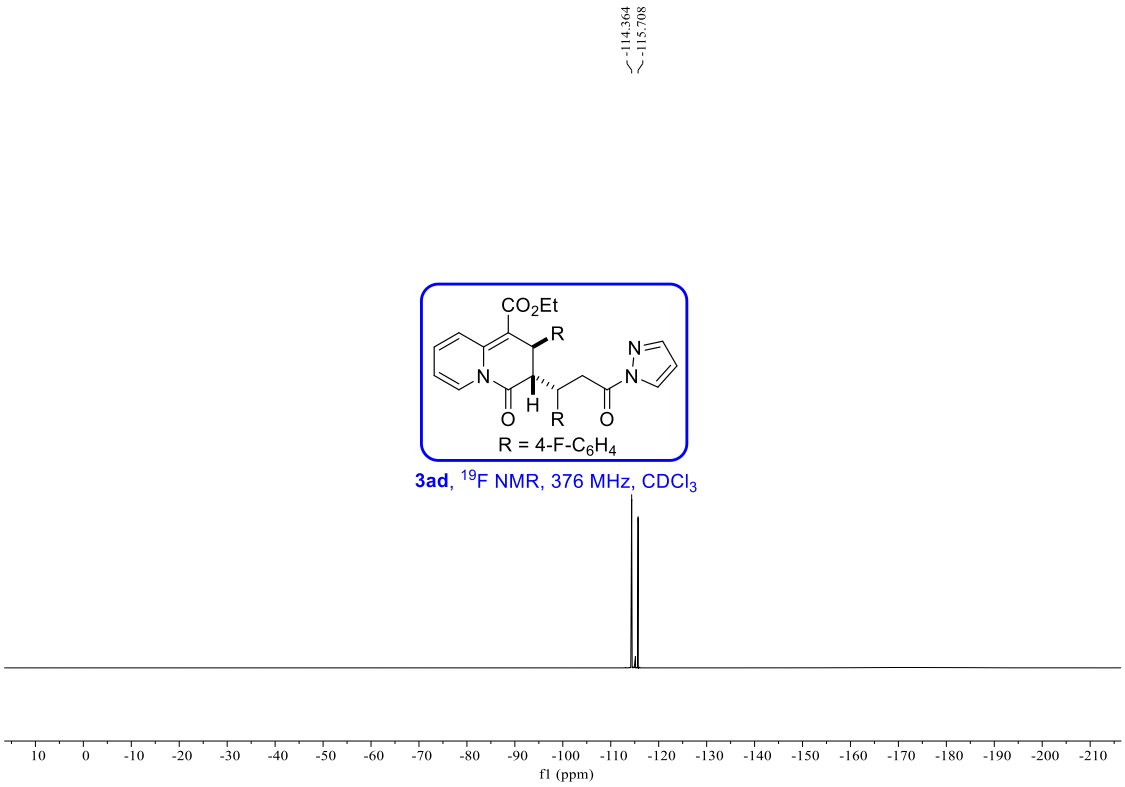




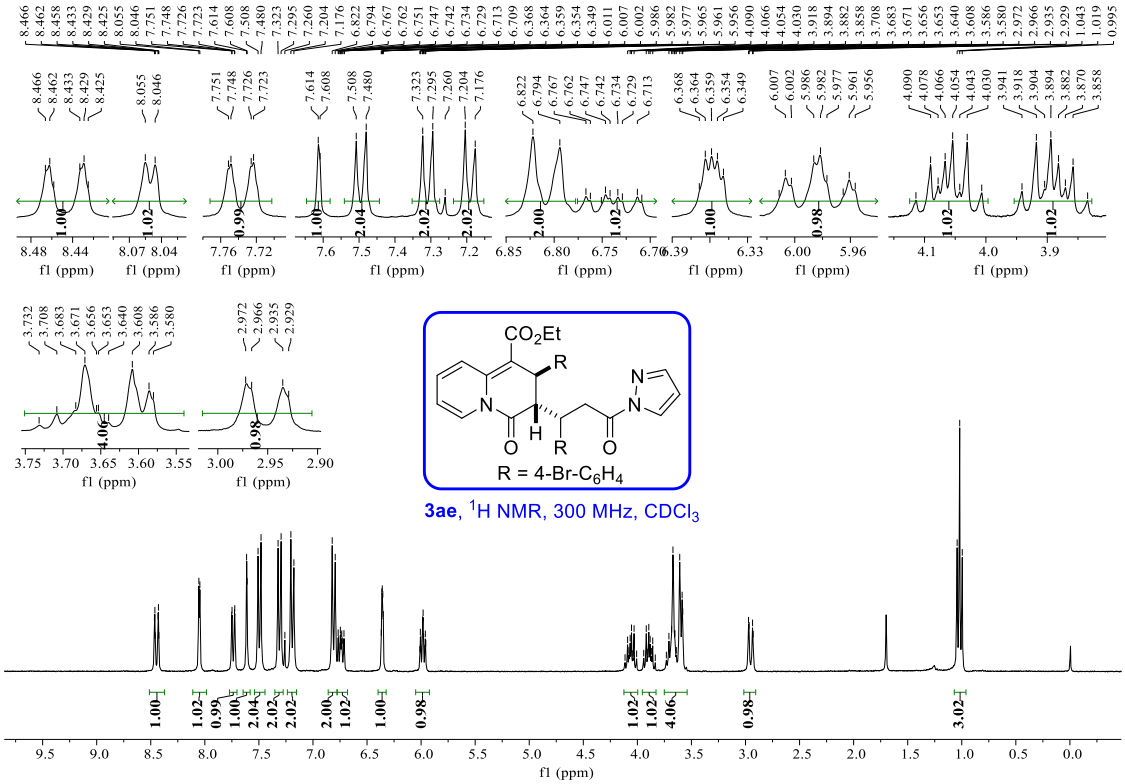
ethyl 2-(4-fluorophenyl)-3-(1-(4-fluorophenyl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3ad).

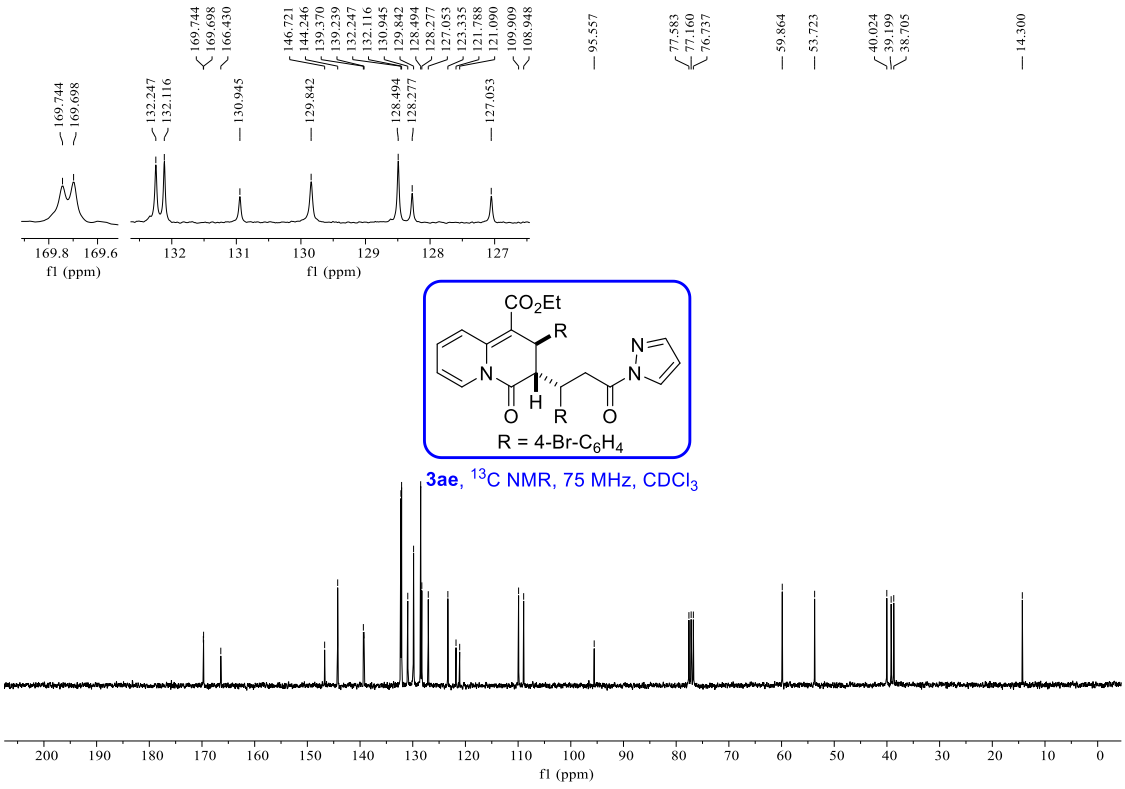




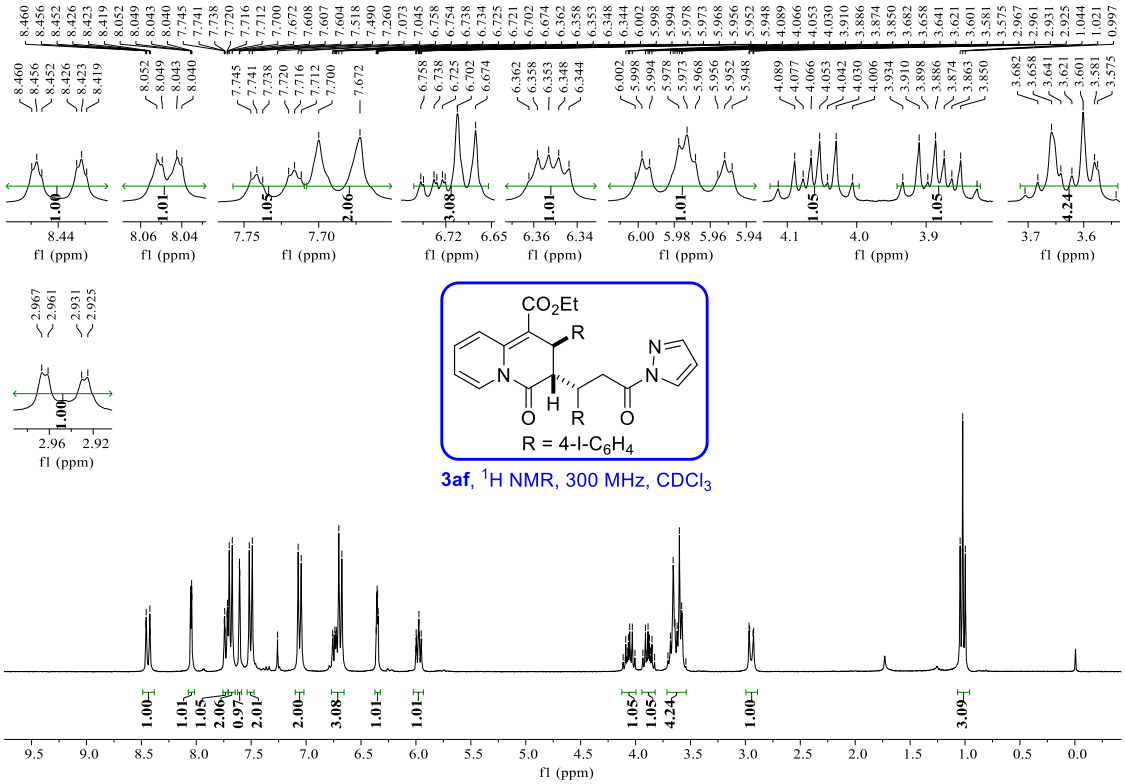

-114.364
-115.708
CO2Et
R
N
N
N
H
O
R
O
R = 4-F-C6H4
3ad, 19F NMR, 376 MHz, CDCl3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

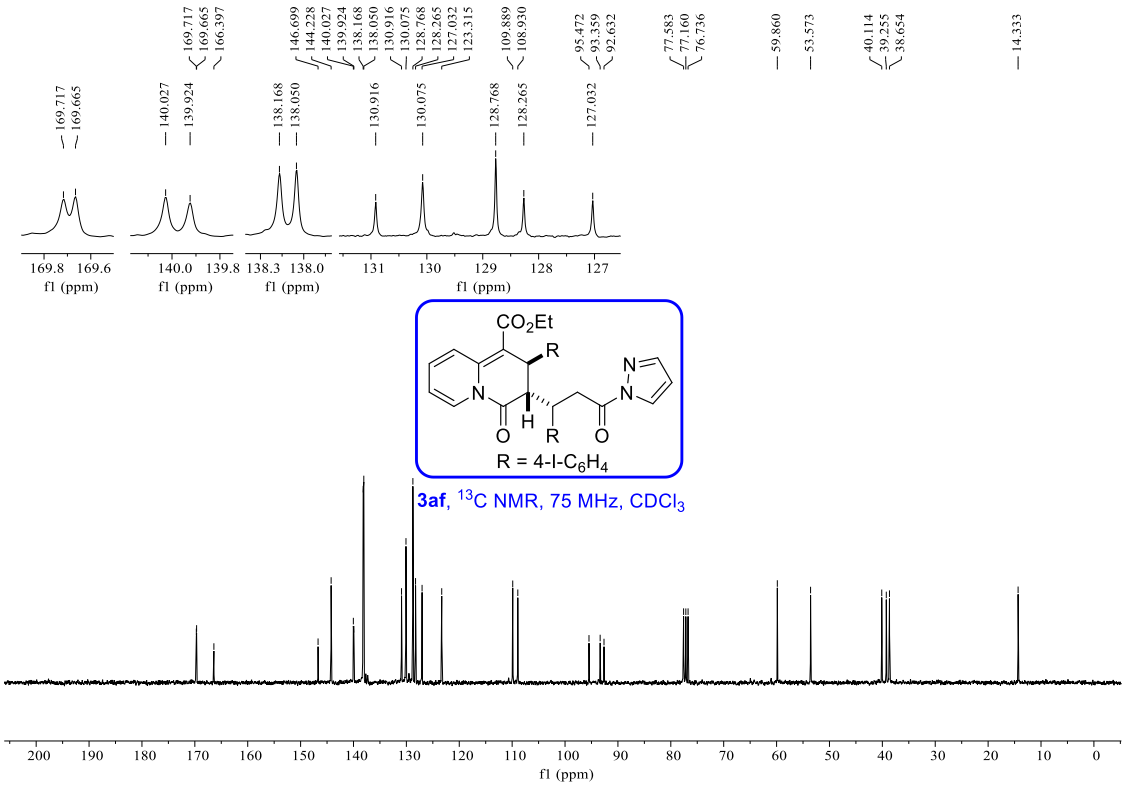
ethyl 2-(4-bromophenyl)-3-(1-(4-bromophenyl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3ae).



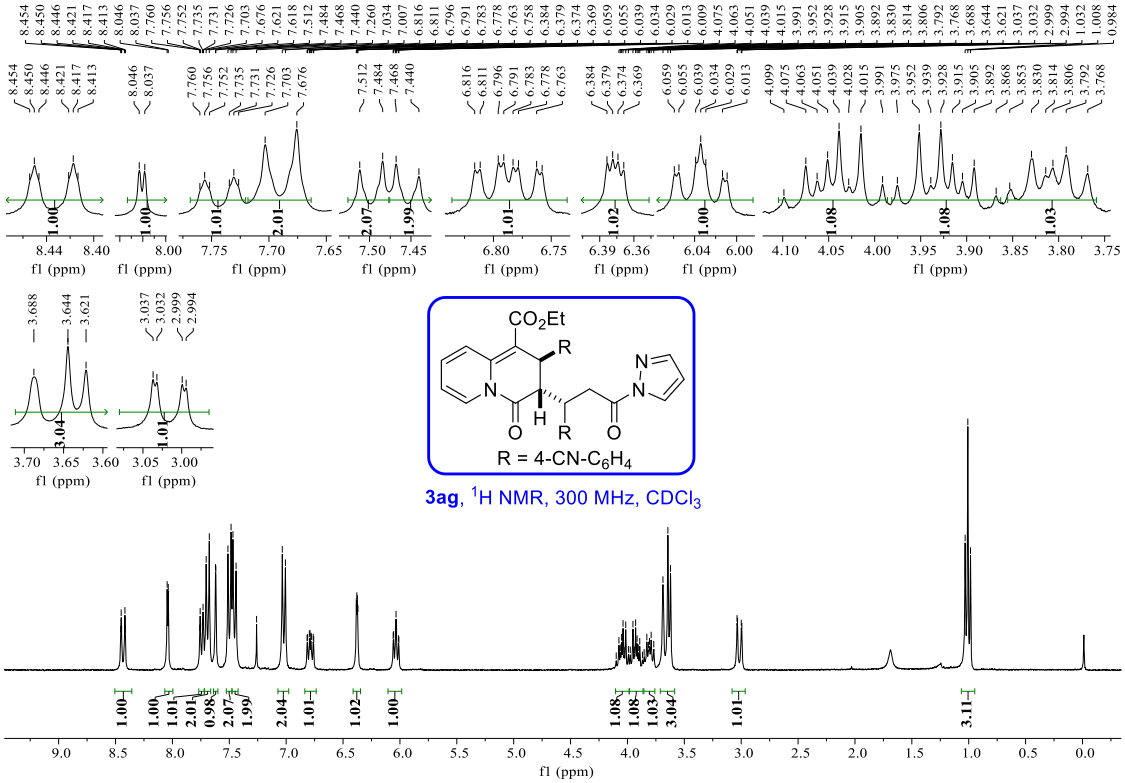


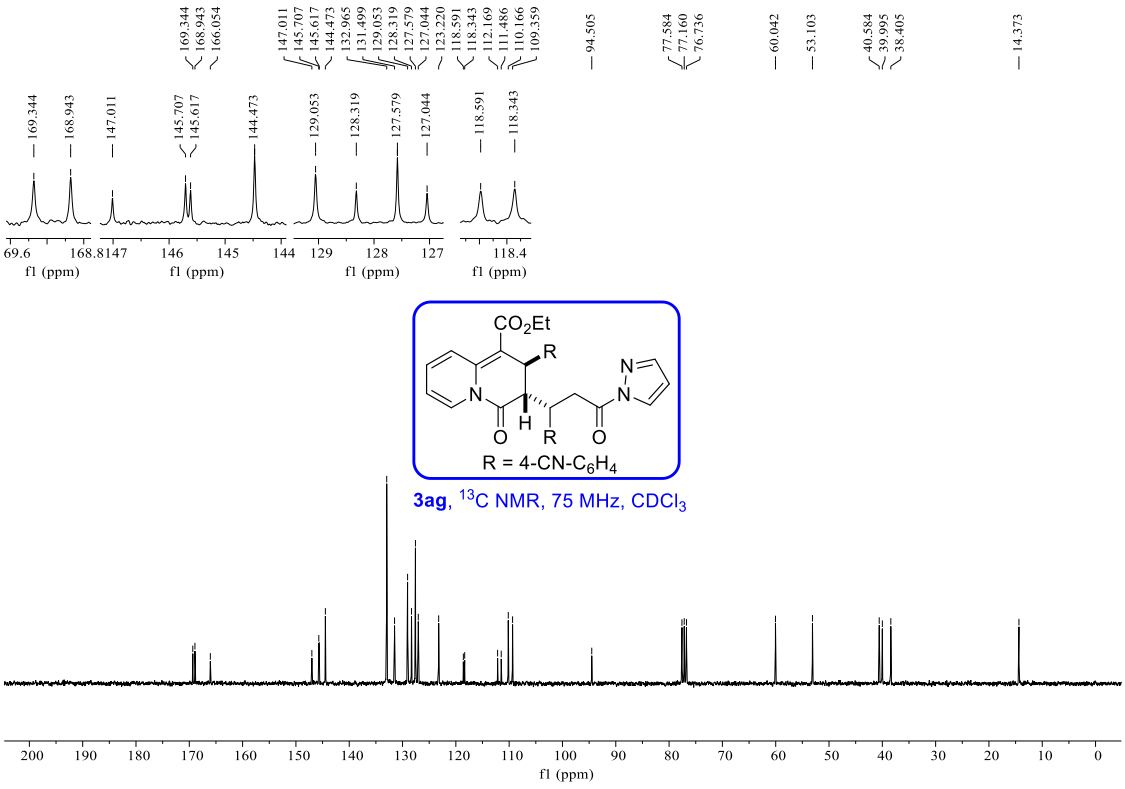
ethyl 2-(4-iodophenyl)-3-(1-(4-iodophenyl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3af).



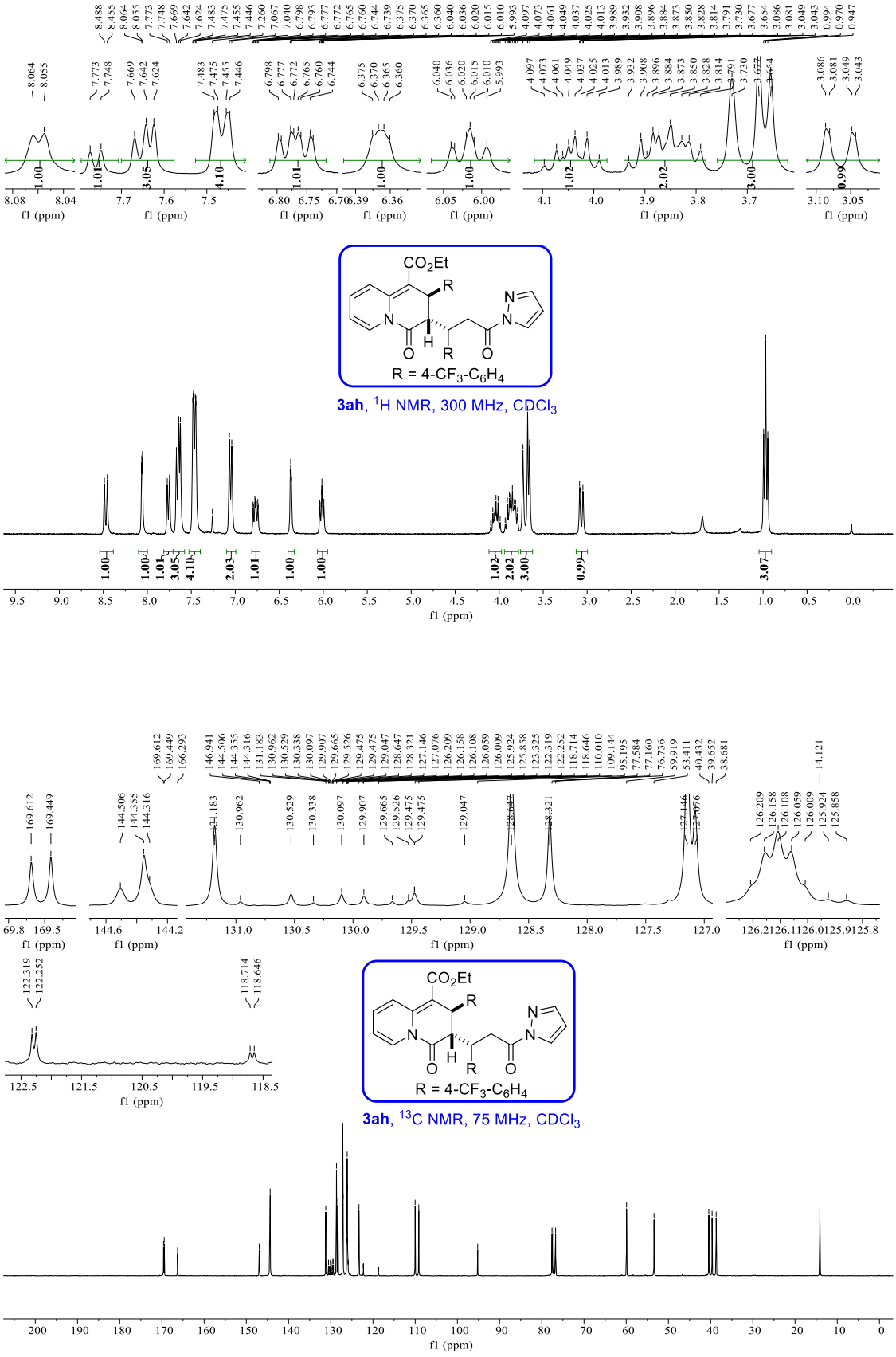


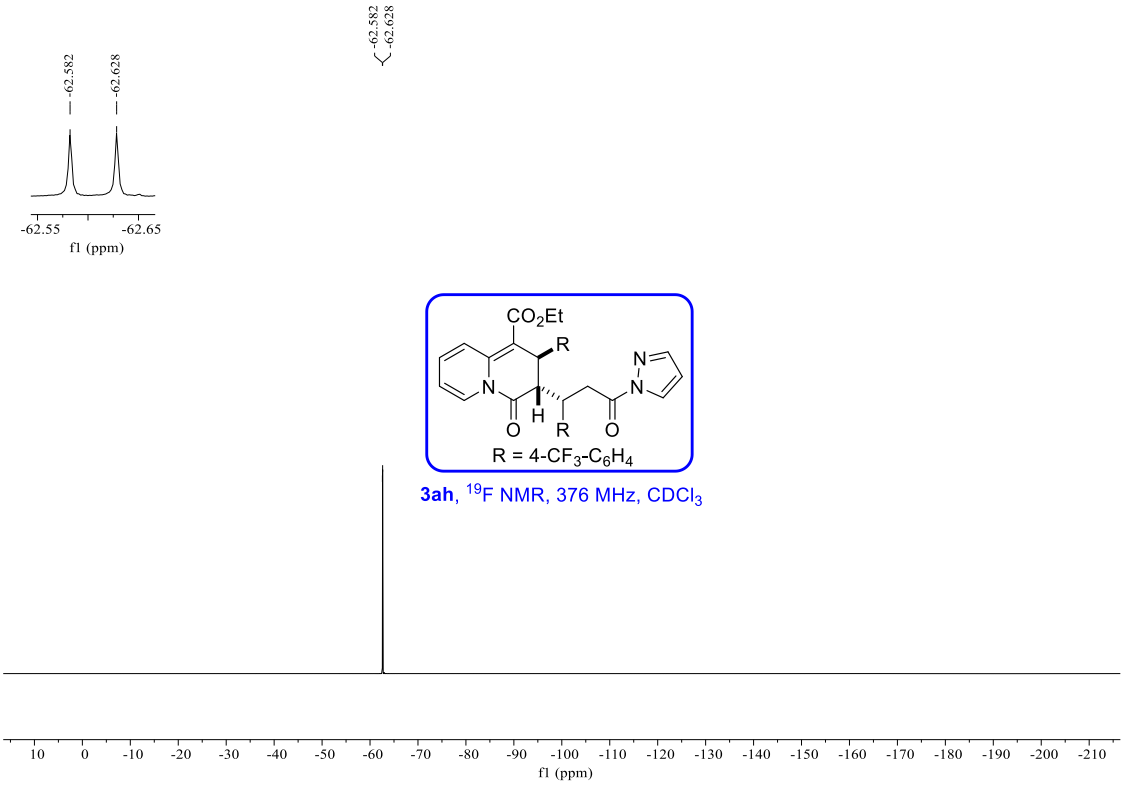
ethyl 2-(4-cyanophenyl)-3-(1-(4-cyanophenyl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3ag).



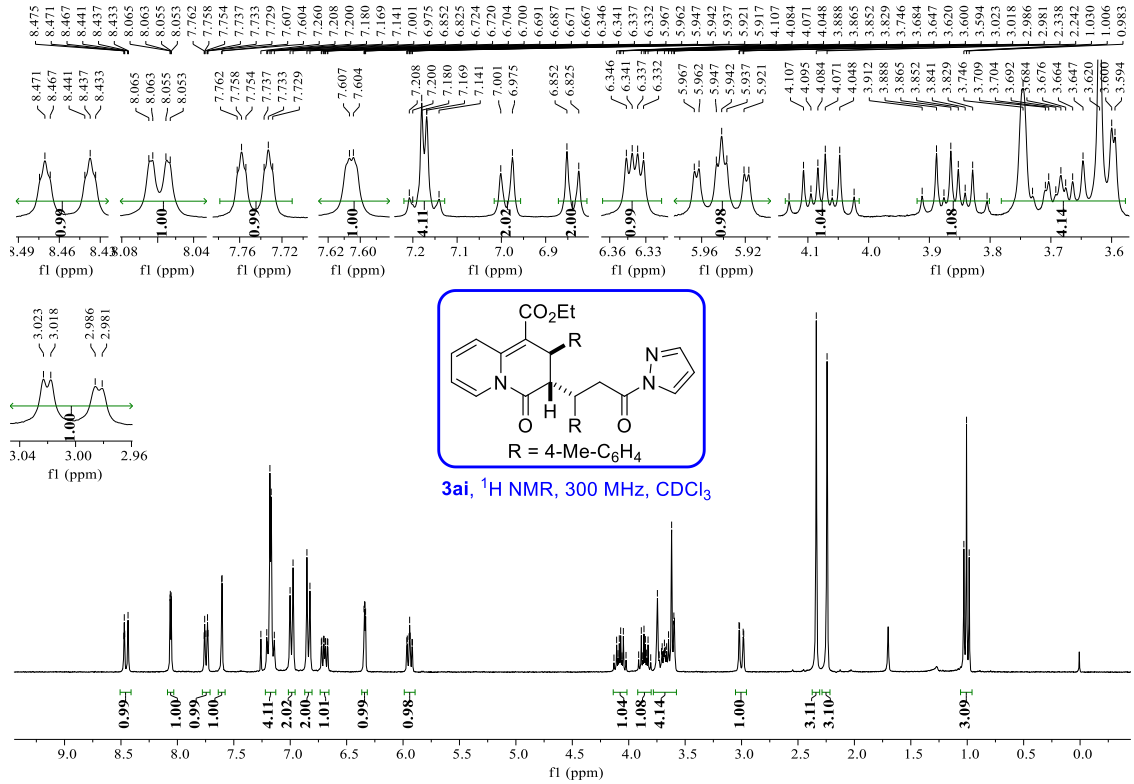


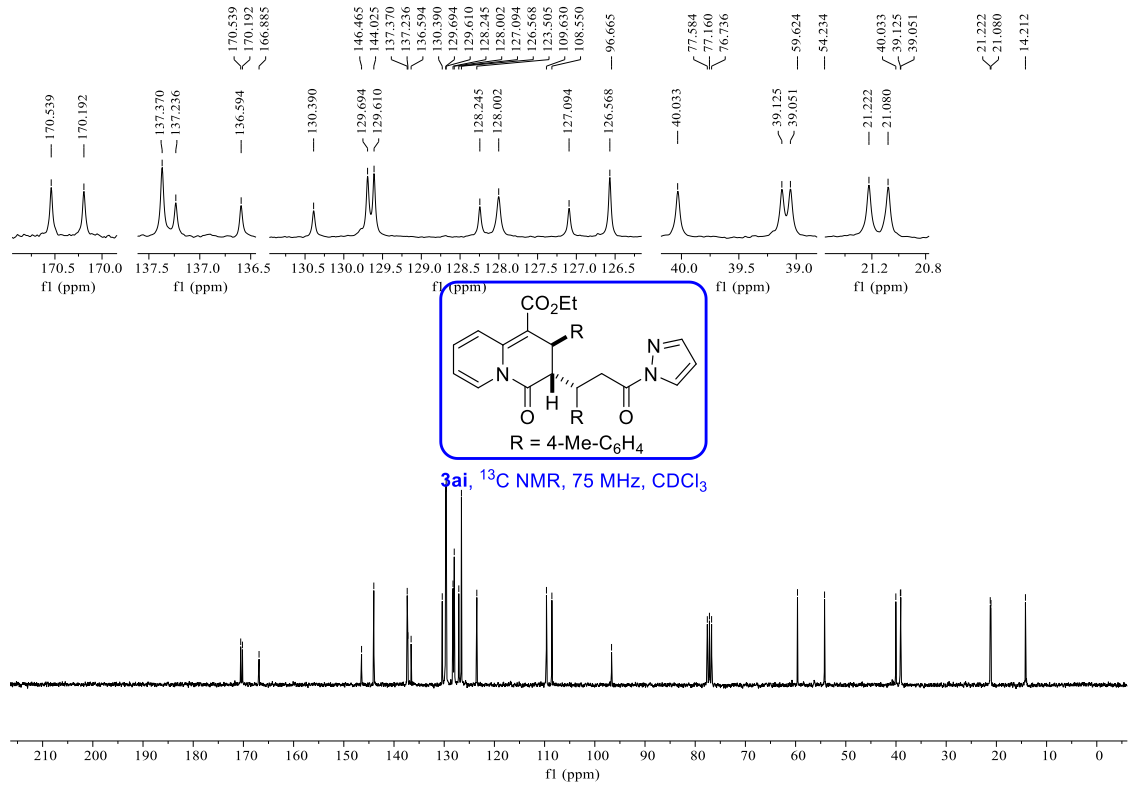
ethyl 4-oxo-3-(3-oxo-3-(1H-pyrazol-1-yl)-1-(4-(trifluoromethyl)phenyl)propyl)-2-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2H-quinolizine-1-carboxylate (3ah).



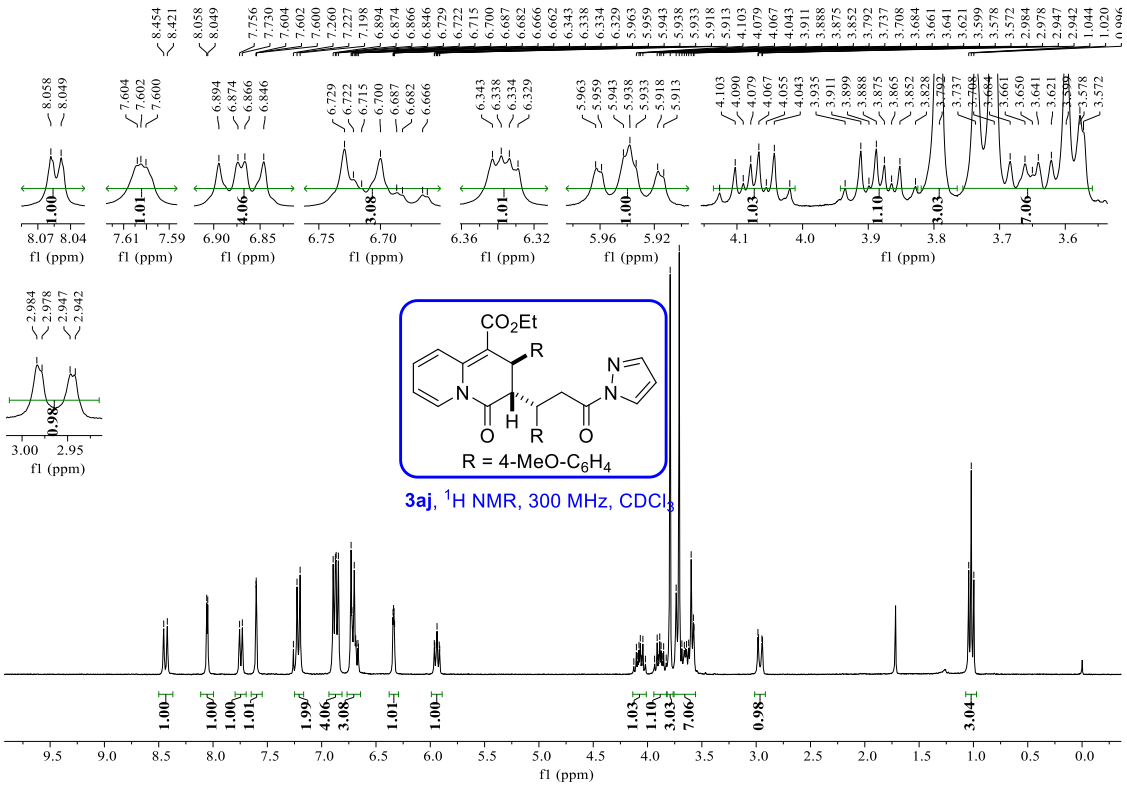

-62.582
-62.628
-62.582
-62.628
-62.55
-62.65
f1 (ppm)
CO2Et
R
N
N
N
H
R
O
O
R = 4-CF3-C6H4
3ah, 19F NMR, 376 MHz, CDCl3
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

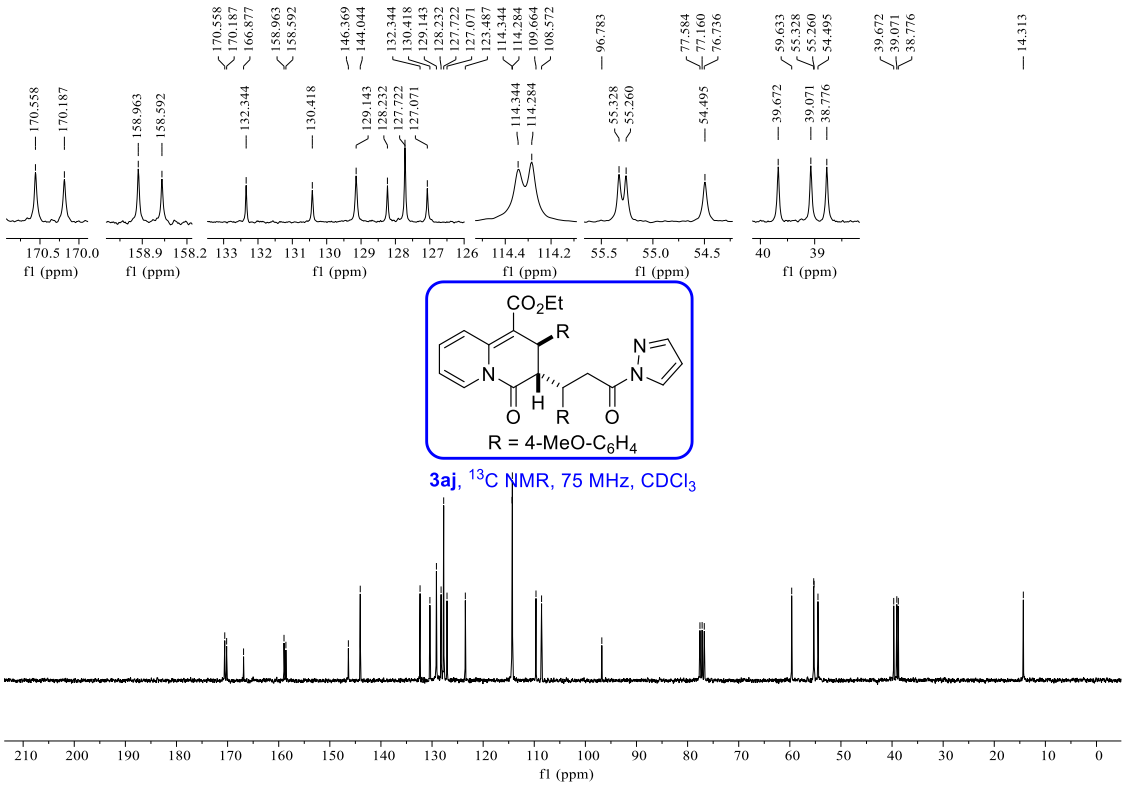
ethyl 4-oxo-3-(3-oxo-3-(1H-pyrazol-1-yl)-1-(p-tolyl)propyl)-2-(p-tolyl)-3,4-dihydro-2H-quinolizine-1-carboxylate (3ai).



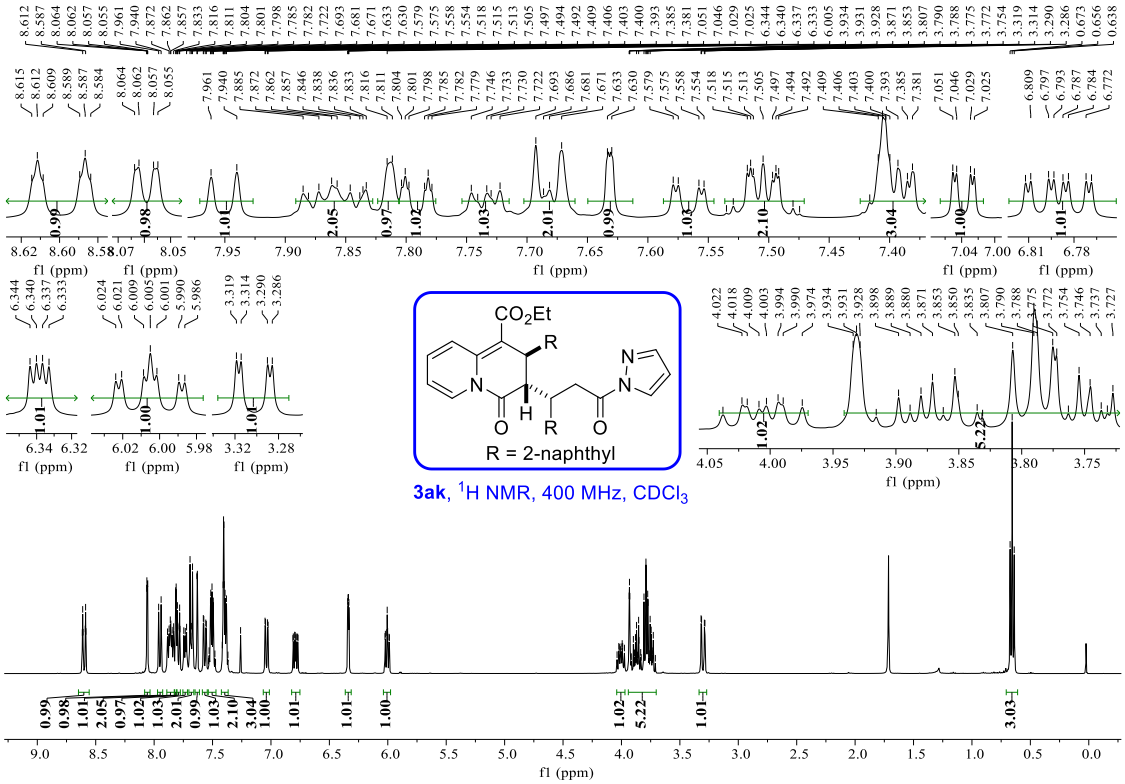


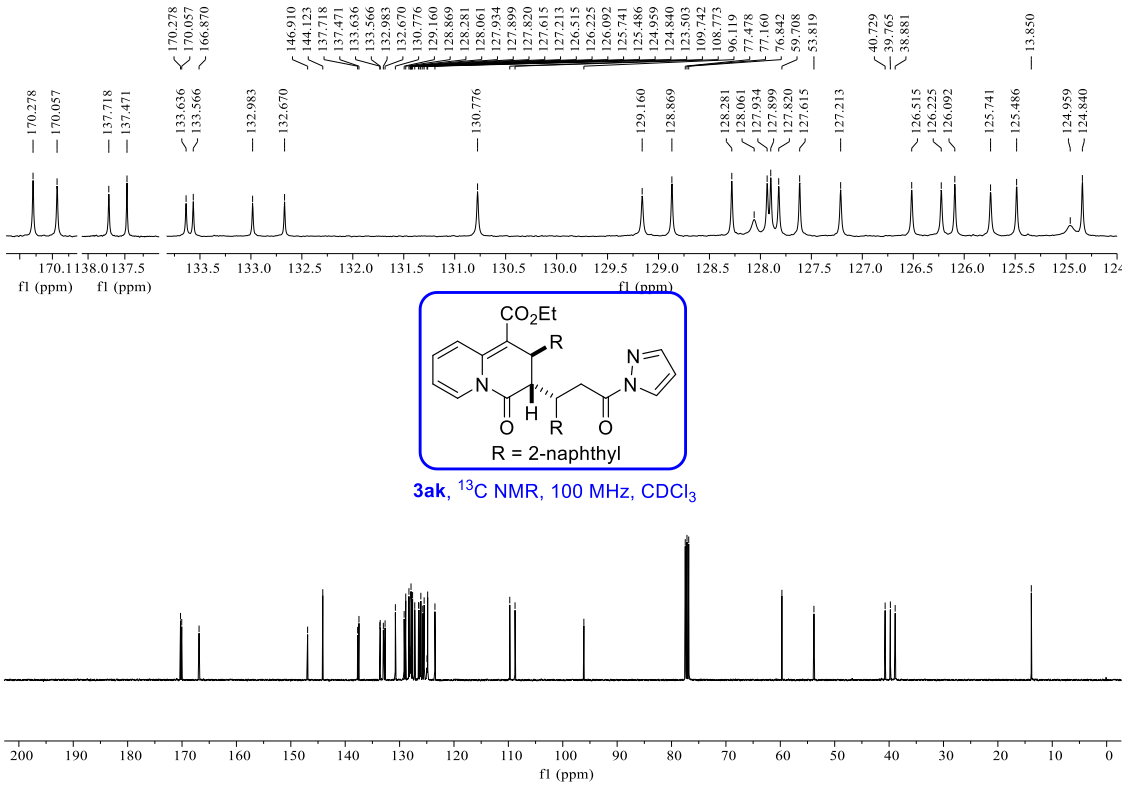
ethyl 2-(4-methoxyphenyl)-3-(1-(4-methoxyphenyl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3aj).



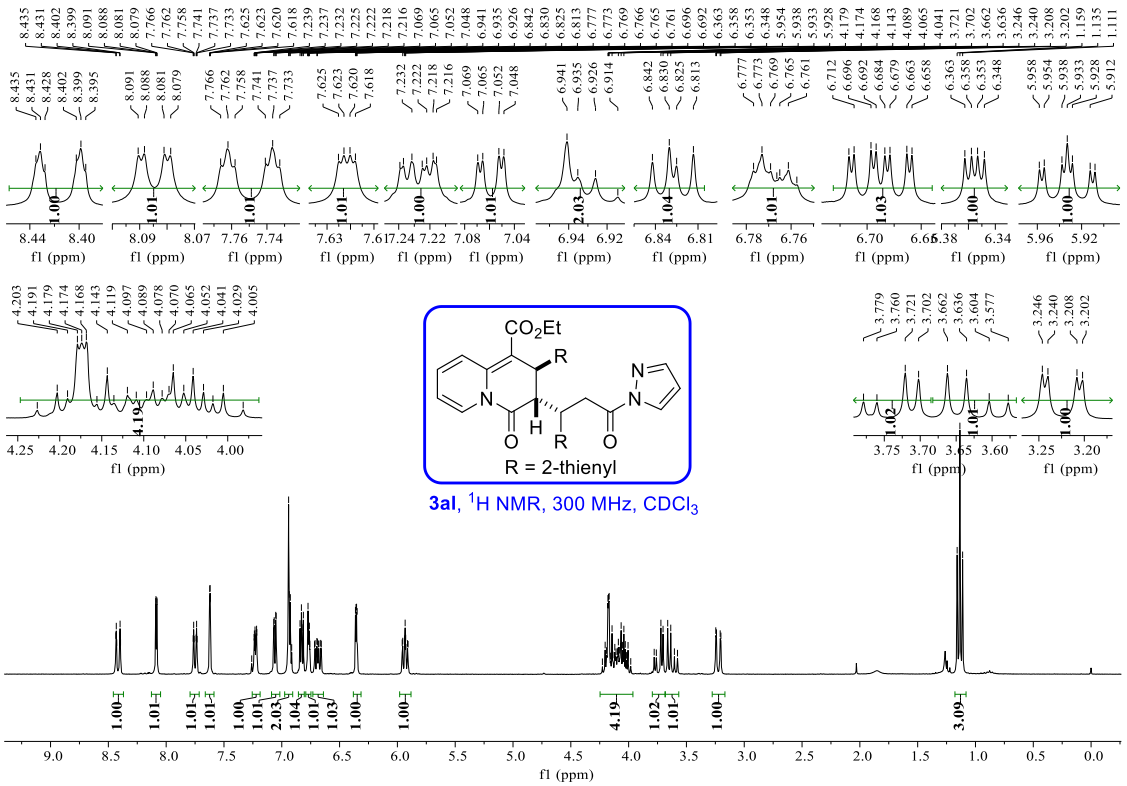


ethyl 2-(naphthalen-2-yl)-3-(1-(naphthalen-2-yl)-3-oxo-3-(1H-pyrazol-1-yl)propyl)-4-oxo-3,4-dihydro-2H-quinolizine-1-carboxylate (3ak).

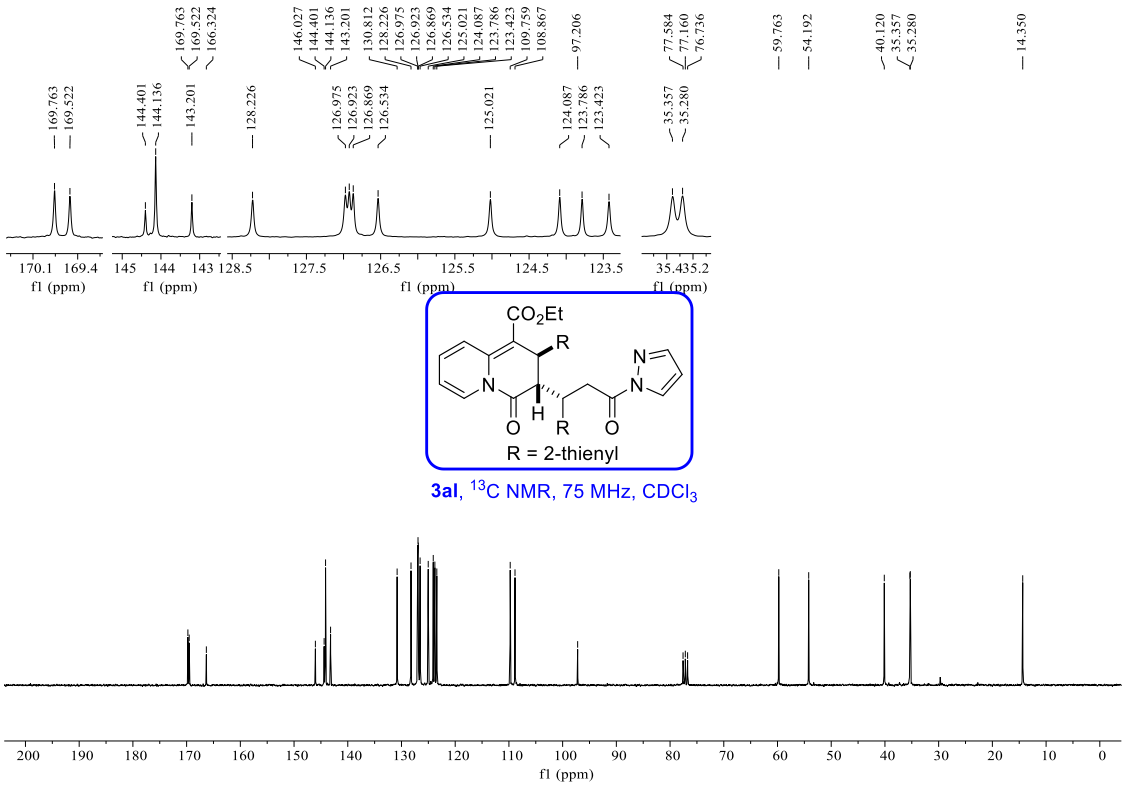




ethyl 4-oxo-3-(3-oxo-3-(1H-pyrazol-1-yl)-1-(thiophen-2-yl)propyl)-2-(thiophen-2-yl)-3,4-dihydro-2H-quinolizine-1-carboxylate (3al).

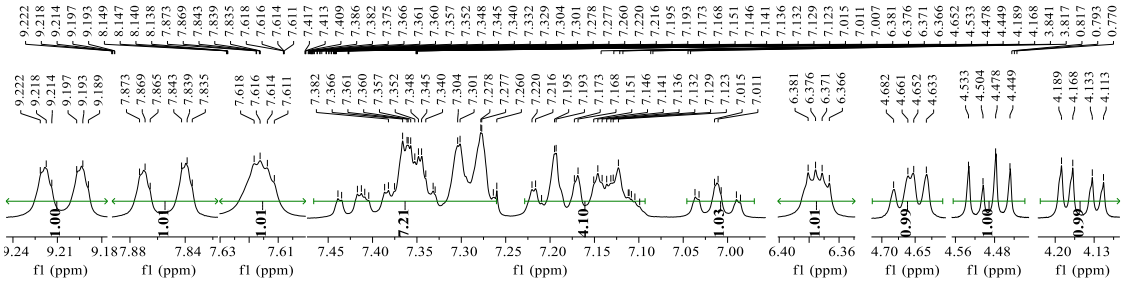


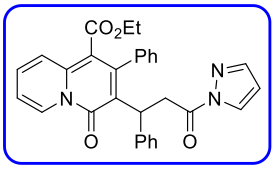
3al, ^{1}H NMR, 300 MHz, $CDCl_3$



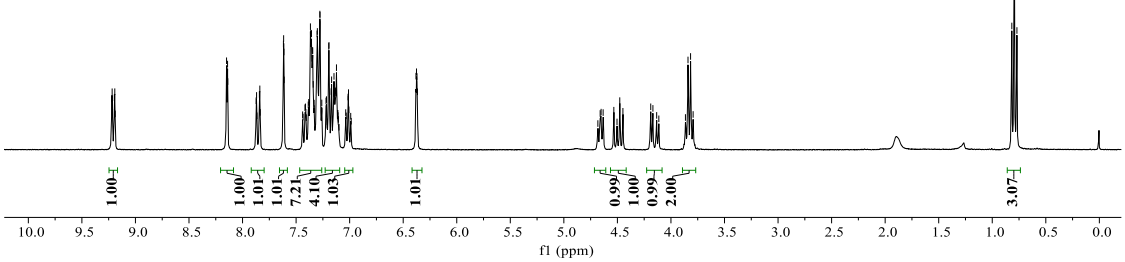
3al, ^{13}C NMR, 75 MHz, $CDCl_3$

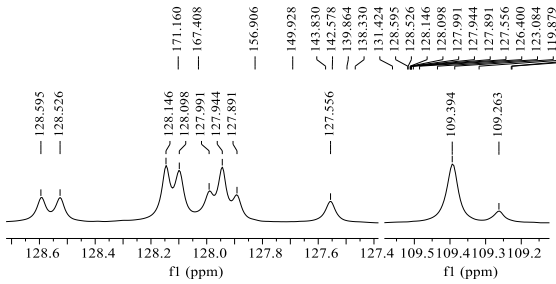
ethyl 4-oxo-3-(3-oxo-1-phenyl-3-(1H-pyrazol-1-yl)propyl)-2-phenyl-4H-quinolizine-1-carboxylate (4).

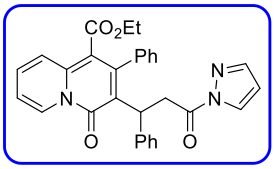




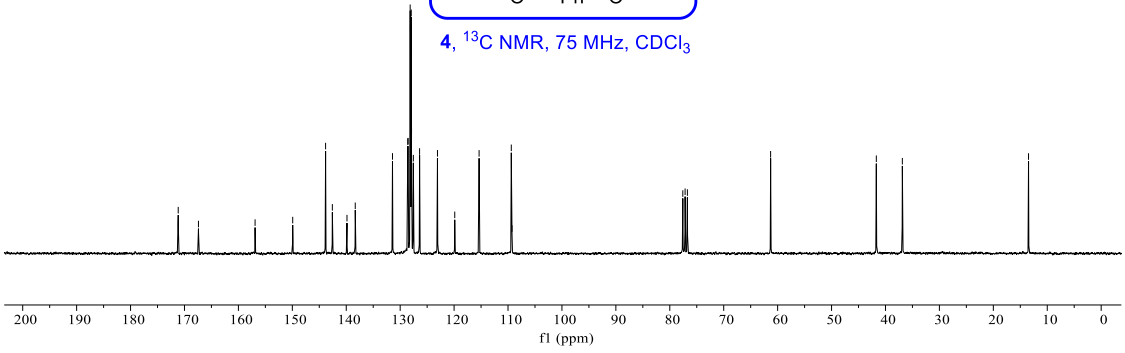
4, ^{1}H NMR, 300 MHz, $CDCl_3$



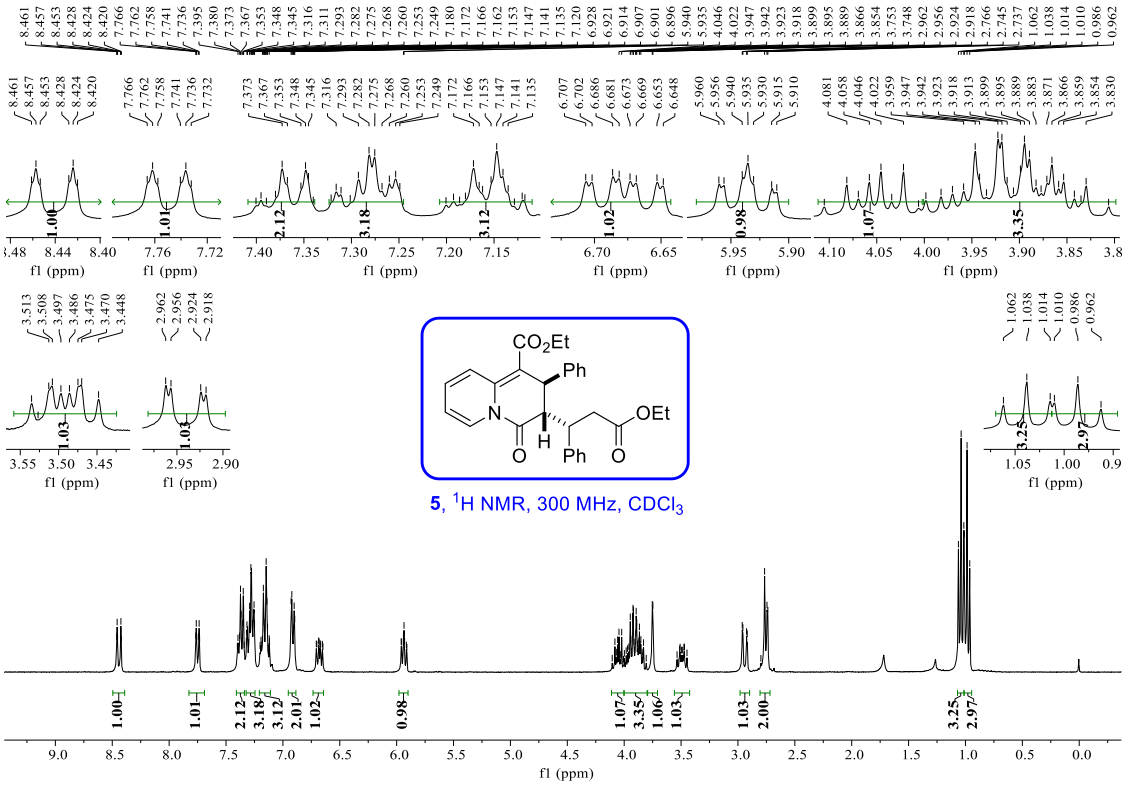


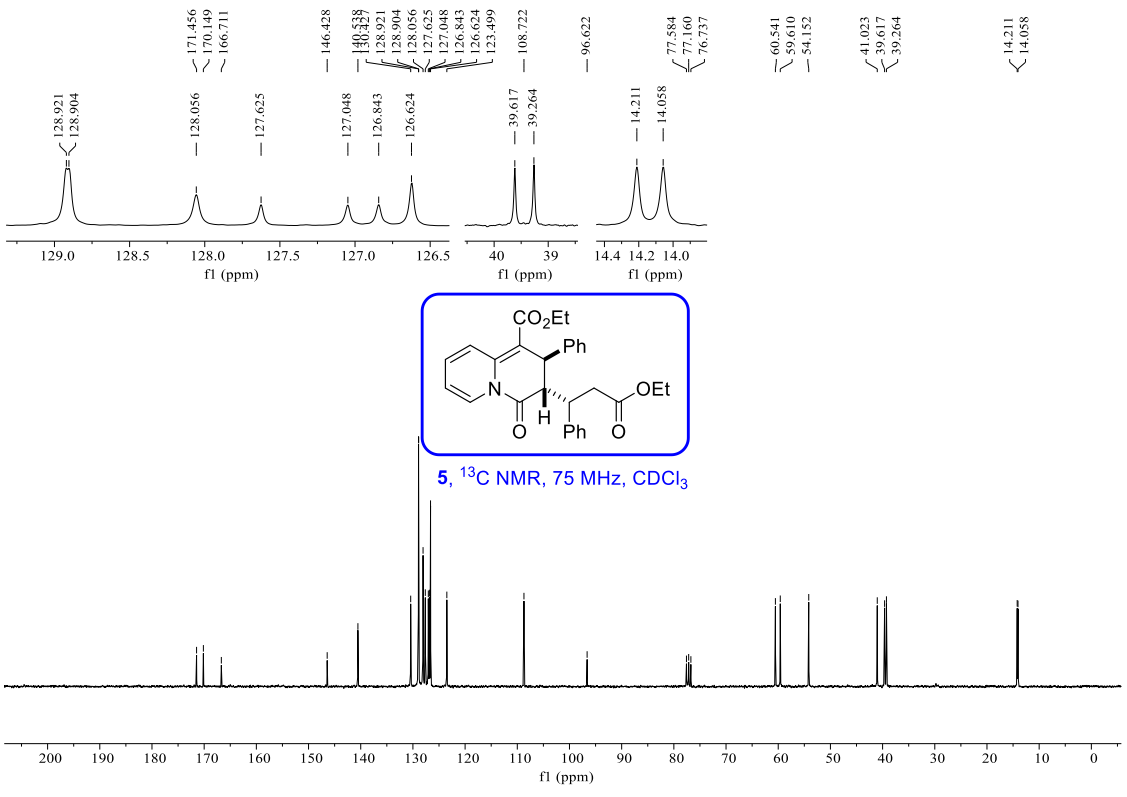


4, ^{13}C NMR, 75 MHz, $CDCl_3$

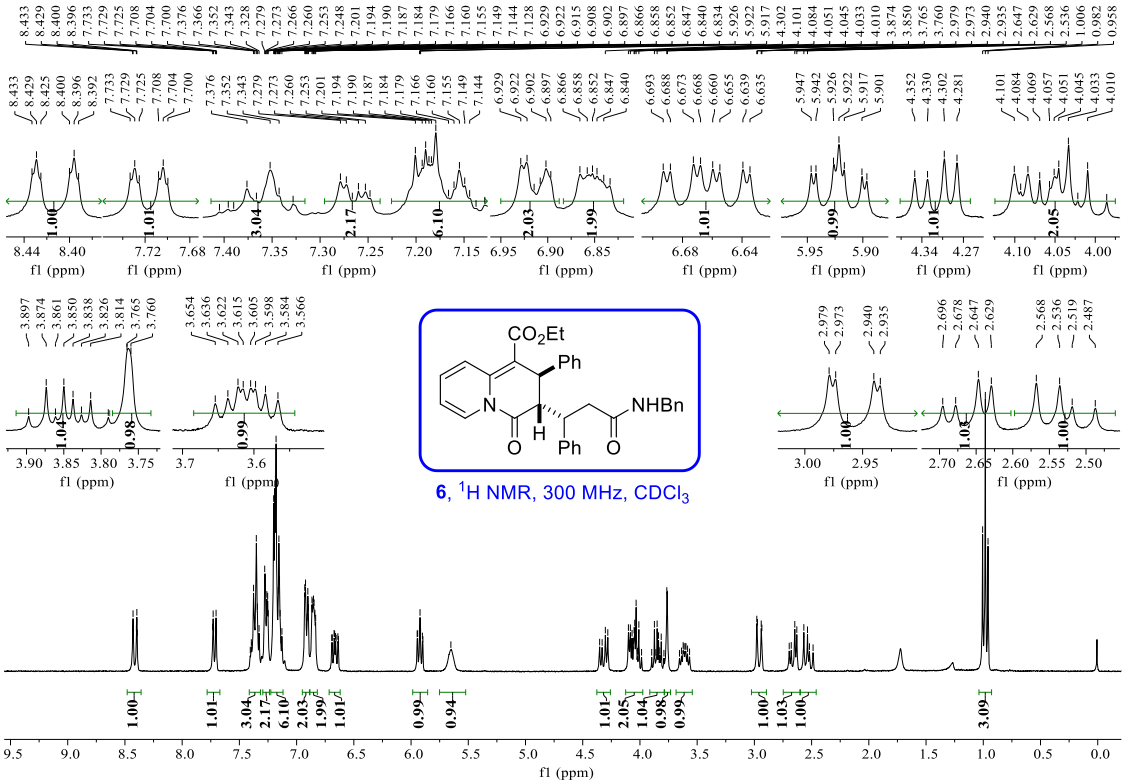


ethyl 3-(3-ethoxy-3-oxo-1-phenylpropyl)-4-oxo-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (5).

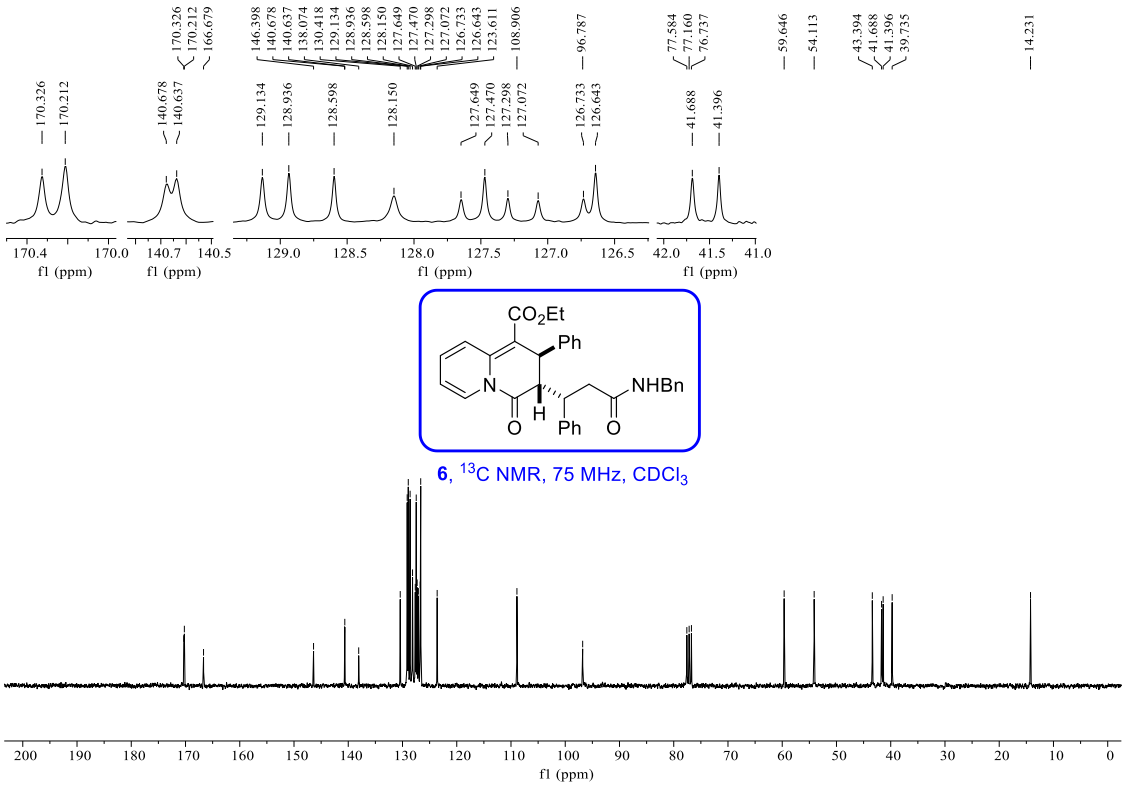




ethyl 3-(3-(benzylamino)-3-oxo-1-phenylpropyl)-4-oxo-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (6).

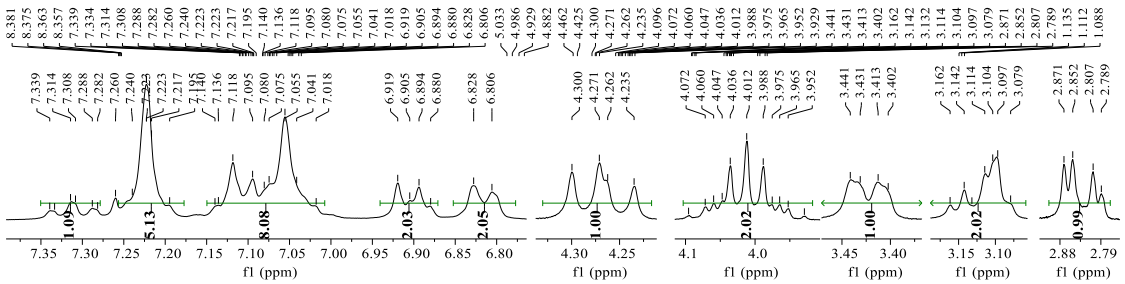


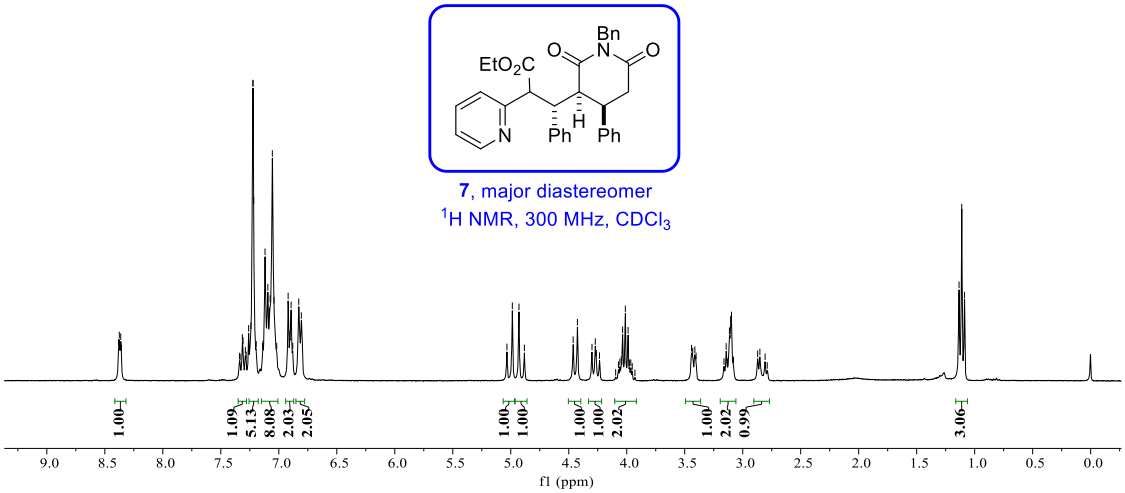
6, ^{1}H NMR, 300 MHz, $CDCl_3$

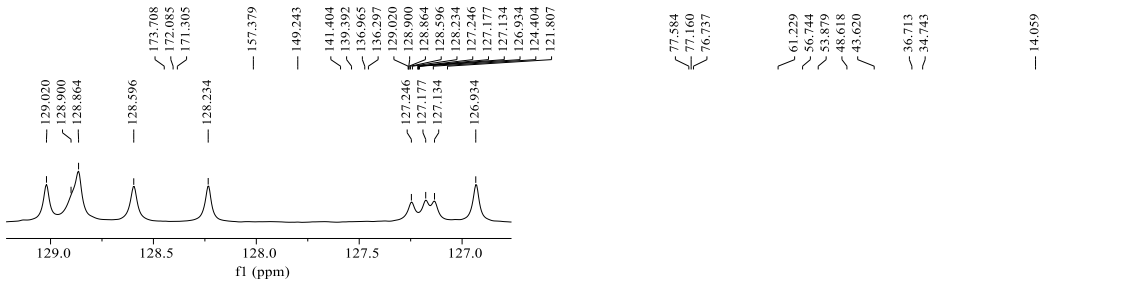


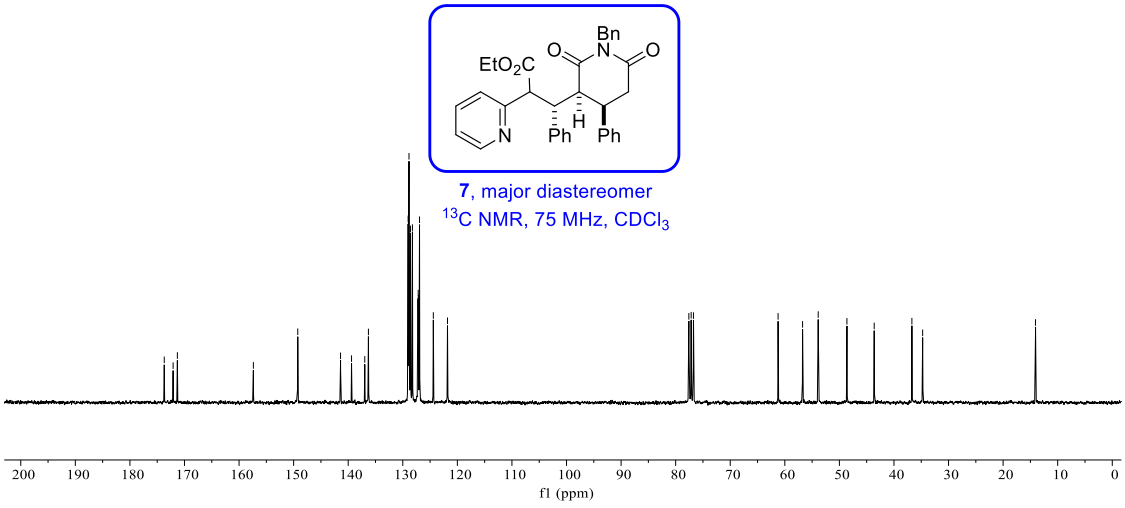
6, ^{13}C NMR, 75 MHz, $CDCl_3$

ethyl 3-(1-benzyl-2,6-dioxo-4-phenylpiperidin-3-yl)-3-phenyl-2-(pyridin-2-yl)propanoate (7, major diastereomer).

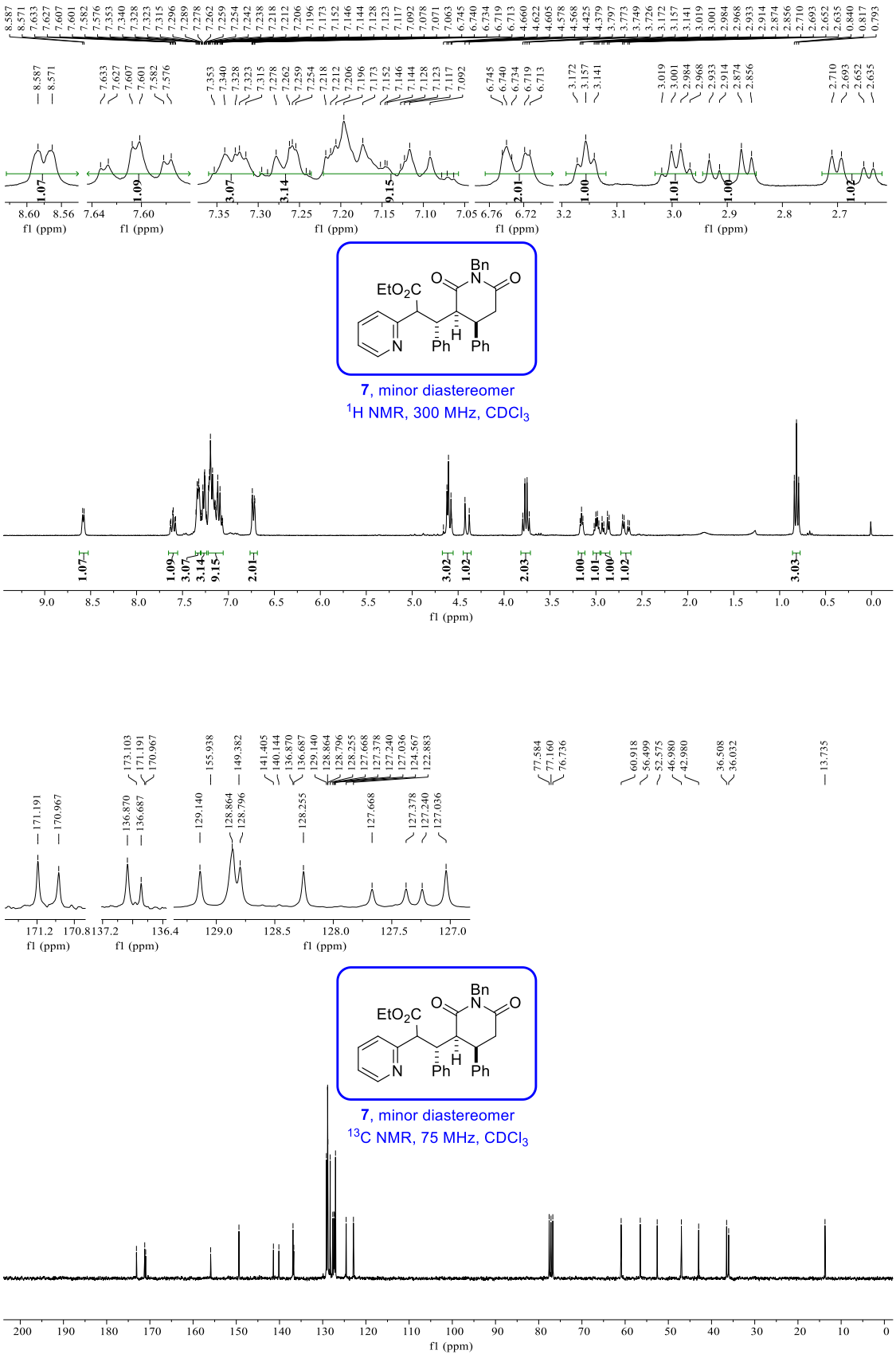




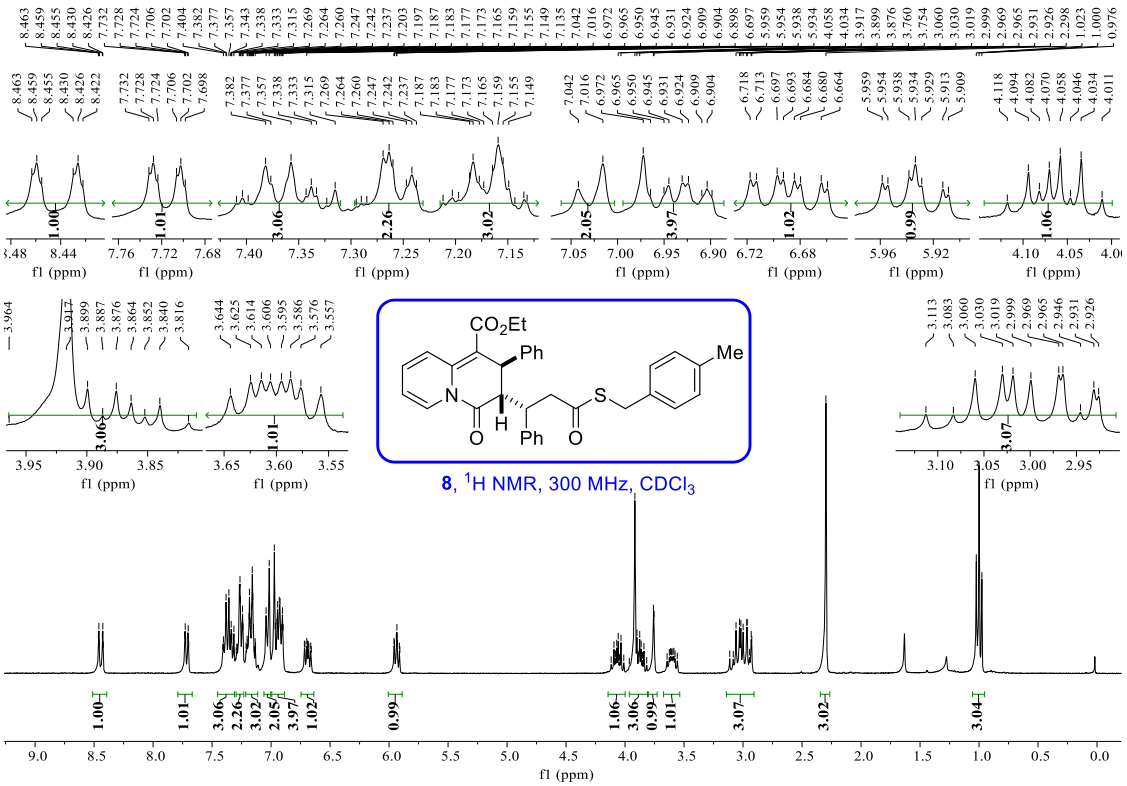


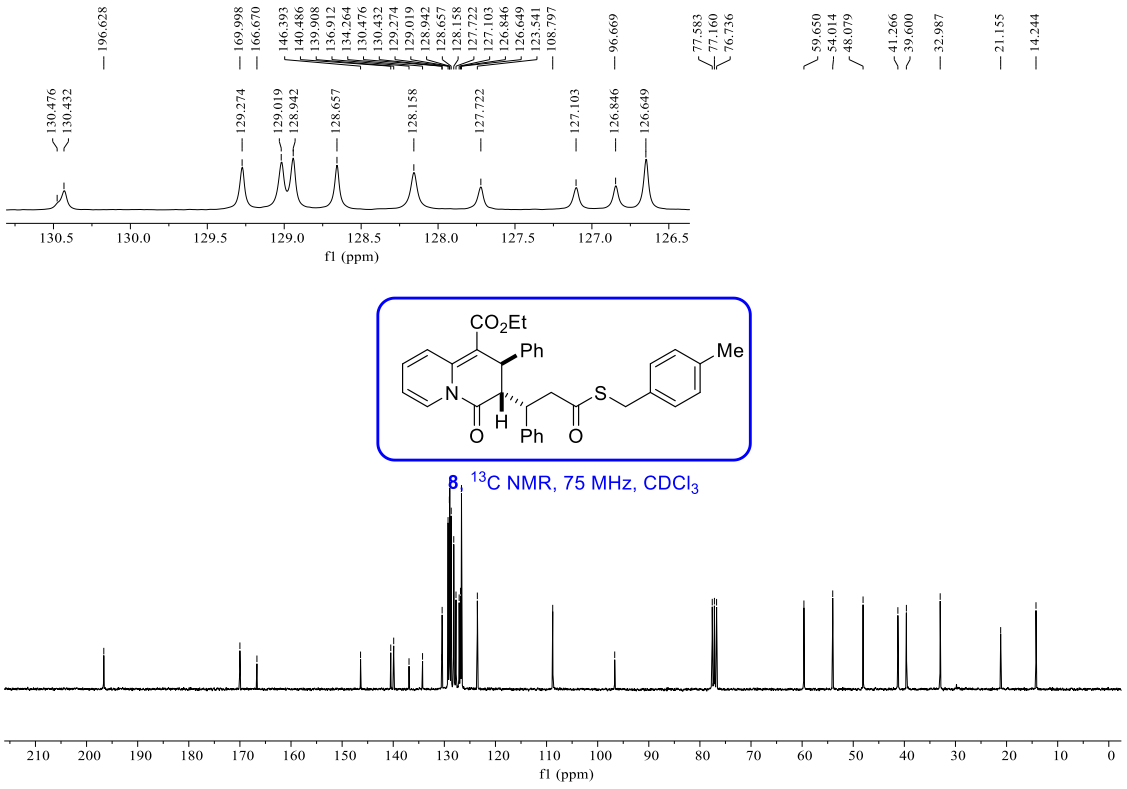


ethyl 3-(1-benzyl-2,6-dioxo-4-phenylpiperidin-3-yl)-3-phenyl-2-(pyridin-2-yl)propanoate (7, minor diastereomer).

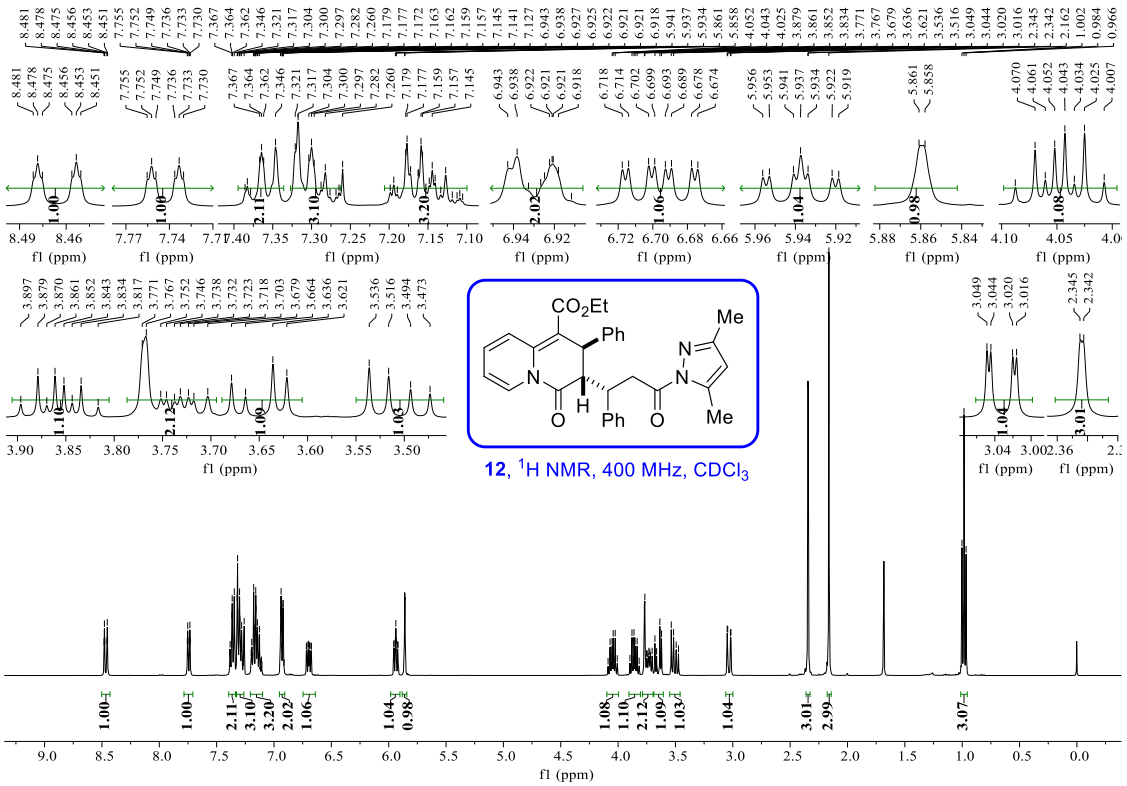


ethyl 3-(3-((4-methylbenzyl)thio)-3-oxo-1-phenylpropyl)-4-oxo-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (8).

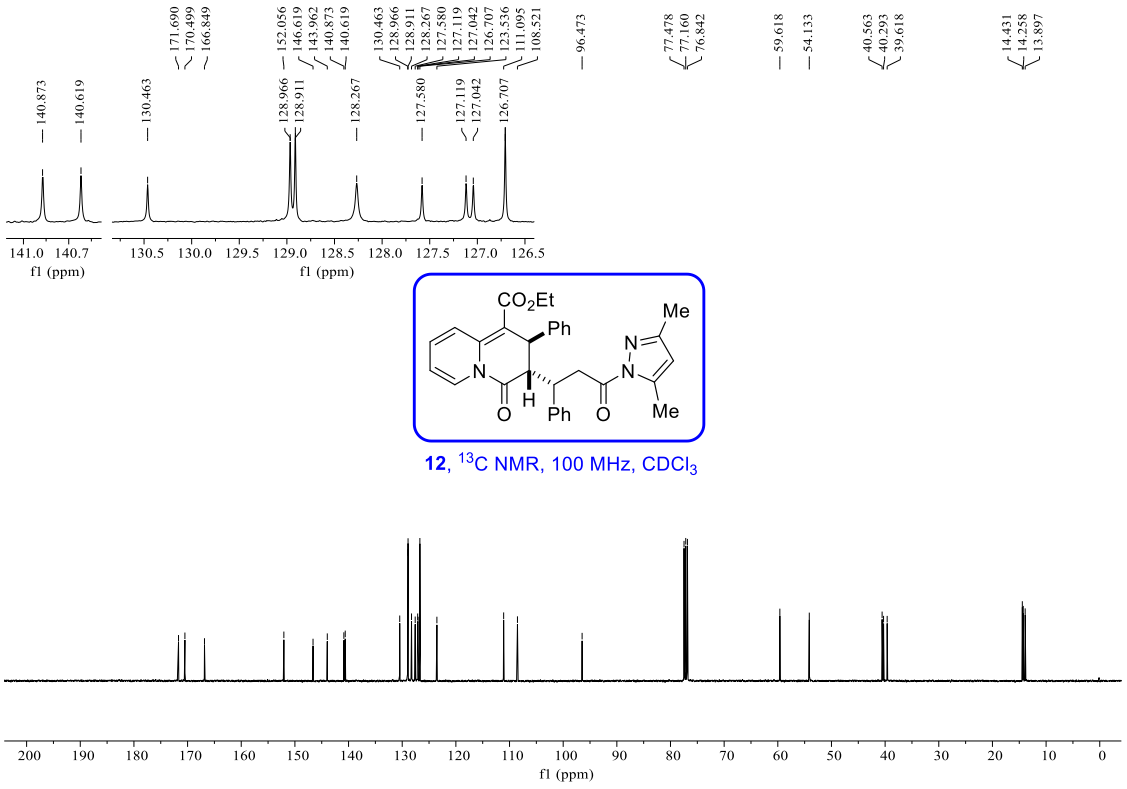




ethyl 3-(3-(3,5-dimethyl-1H-pyrazol-1-yl)-3-oxo-1-phenylpropyl)-4-oxo-2-phenyl-3,4-dihydro-2H-quinolizine-1-carboxylate (12).



12, ^{1}H NMR, 400 MHz, $CDCl_3$



12, ^{13}C NMR, 100 MHz, $CDCl_3$