DBU-catalyzed dearomative annulation of 2-pyridylacetates with

α,β -unsaturated pyrazolamides for the synthesis of

multisubstituted 2,3-dihydro-4H-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	S1
2. General Procedure for the Synthesis of α -Picoline Derivatives	S1
3. General Procedure for the Synthesis of α,β -Unsaturated Pyrazolamides 2a–l and 11	S2
4. General Procedure for the Synthesis of Products 3	S3
5. Gram-Scale Synthesis and Transformations of Product 3aa	S12
6. Control Experiments	S15
7. X-ray Crystallography of 3aa	S16
8. Copies of ¹ H, ¹³ C, and ¹⁹ F NMR Spectra	S18

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). ¹H, ¹³C, and ¹⁹F NMR spectra were recorded on a Bruker 300, 400, or 600 MHz NMR spectrometer using CDCl₃ as the solvent. The chemical shifts (δ) were reported in ppm relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard (CDCl₃, ¹H: δ = 7.26 ppm, ¹³C: 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 ¹³C 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 a-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), Et₃N (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 °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 Na₂SO₄, 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–1. 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; ¹H NMR (300 MHz, CDCl₃) 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 = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 7.7 Hz, 1H), 7.29 (d, J = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 7.7 Hz, 1H), 7.29 (d, J = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 7.7 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 4.08 (t, J = 7.6, 5.0 Hz, 1H), 7.18 (dd, J = 7.6, 5.0 Hz, 1H), 7.08 (dd, J = 7.6 (dd, J = 7.6), 7.08 (dd, J = 7.6 (dd, J = 7.6), 8.08 (dd, J = 7.6 (dd, J = 7.6), 8.08 (dd, J = 7.6 (dd, J = 7.6), 8.08 (dd, J = 7.6 (dd, J = 7.6), 8.08 (dd, J = 7.6 (dd, J = 7.6), 8.08 (dd, J = 7.6 (dd, J = 7.6), 8.08 (dd, J = 7.6 (dd, J = 7.6), 8.08 (dd, J = 7.6 (dd, J = 7.6), 8.08 (dd, J = 7.6 (dd, J = 7.6), 8.08 (dd, J = 7.6 (dd, J = 7.6), 8.08 (dd, J = 7.6 (dd, J = 7.6), 8.08 (dd, J = 7.6 (dd, J = 7.6), 8.08 (dd, J = 7.6 (dd, J = 7.6), 8.08 (dd, J = 7.6 (dd, J = 7.6), 8.08 (dd, J = 7.6 (dd, J = 7

6.7 Hz, 2H), 3.84 (s, 2H), 1.64 (h, J = 7.2 Hz, 2H), 0.90 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₀H₁₃NNaO₂, 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; ¹H NMR (400 MHz, CDCl₃) 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, CDCl₃) 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 C₁₆H₁₅NNaO₂, 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), PhSO₂Na 2H₂O **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 NaHCO₃ (aq.), and extracted with DCM (50 mL × 3). Afterward, the combined organic phase was washed with brine, dried over anhydrous Na₂SO₄, 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 10 and 1p³

$$\begin{array}{c|c} & & LDA (2.1 \text{ equiv.}) \\ \hline & & \\ N & Me^{+} & CO(OEt)_{2} & \\ \hline & THF (0.5 \text{ M}) \\ \hline & & \\ S5 & S6 & -78 \text{ }^{\circ}\text{C}-\text{rt} \\ \hline & & 10, \text{ R} = \text{Et}; \\ \hline & & 1p, \text{ R} = \text{CI}. \end{array}$$

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 Na₂SO₄, and concentrated under reduced pressure. And the residue was purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc) to afford **10** and **1p**.

3. General Procedure for the Synthesis of α , β -Unsaturated Pyrazolamides 2a–l and 11⁴

0 R (E) S7 S1	R ¹ SOCI ₂ (4.5 equiv.) DCM (0.2 M), 0 °C-rt	$R \xrightarrow{(E)} N \xrightarrow{N} R^{1}$
2a , R = Ph;	2f , R = 4-I-C ₆ H ₄ ;	2j , R = 4-MeO-C ₆ H ₄ ;
2b , R = 3-CI-C ₆ H ₄ ;	2g , R = 4-CN-C ₆ H ₄ ;	2k, R = 2-naphthyl;
2c , R = 4-CI-C ₆ H ₄ ;	2h , R = 4-CF ₃ -C ₆ H ₄ ;	2I , R = 2-thienyl;
2d , R = 4-F-C ₆ H ₄ ;	2i , R = 4-Me-C ₆ H ₄ ;	11 , R = Ph.
2e , R = 4-Br-C ₆ H 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 °C in an ice bath, and SOCl₂ (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-\alpha,\beta*-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 Na₂SO₄, and concentrated under reduced pressure. And the residue was purified by flash column chromatography (column chromatography eluent, petroleum ether/EtOAc/DCM) to afford **2a–1** 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 °C; $R_f = 0.17$ (petroleum ether/EtOAc = 10/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 1/10/1; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₁₂H₁₀IN₂O, 324.9832; found, 324.9832.

4. General Procedure for the Synthesis of Products 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 Na₂SO₄, 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 °C; R_f = 0.33 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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-2Hquinolizine-1-carboxylate (3ba).



Orange solid; 162.8 mg, 85% yield; >20:1 dr; mp 192.4–193.9 °C; R_f = 0.22 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹**H NMR** (400 MHz, CDCl₃) 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, CDCl₃) 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 C₂₉H₂₆N₃O₄, 480.1918; found, 480.1925.

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



Orange solid; 152.1 mg, 75% yield; >20:1 dr; mp 142.4–143.3 °C; $R_f = 0.27$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C **NMR** (75 MHz, CDCl₃) 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 C₃₁H₃₀N₃O₄, 508.2231; found, 508.2241.

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



Orange solid; 152.1 mg, 73% yield; >20:1 dr; mp 126.4–127.5 °C; R_f = 0.30 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹**H NMR** (300 MHz, CDCl₃) 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, CDCl₃) 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 C₃₂H₃₂N₃O₄, 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 °C; $R_f = 0.29$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (400 MHz, CDCl₃) 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, CDCl₃) 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 C₃₅H₃₀N₃O₄, 556.2231; found, 556.2238.

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



Orange solid; 146.0 mg, 72% yield; >20:1 dr; mp 170.8–171.9 °C; $R_f = 0.33$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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 C₃₁H₃₀N₃O₄, 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-2Hquinolizine-1-carboxylate (3ga).



Yellow solid; 95.9 mg, 46% yield; >20:1 dr; mp 169.5–170.7 °C; $R_f = 0.38$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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 C₃₂H₃₂N₃O₄, 522.2387; found, 522.2393.

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



Yellow solid; 72.2 mg, 33% yield; >20:1 dr; mp 165.7–166.9 °C; $R_f = 0.36$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/4/1; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C **NMR** (100 MHz, CDCl₃) 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 C₃₄H₃₃N₃NaO₄, 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 °C; $R_f = 0.31$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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, CDCl₃) 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, CDCl₃) δ –73.7; **HRMS** (ESI-TOF) m/z: [M + H]⁺ calcd for C₃₀H₂₅F₃N₃O₄, 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 °C; $R_f = 0.28$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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 C₃₁H₂₈N₃O₄, 506.2074; found, 506.2081.

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



Orange solid; 162.7 mg, 70% yield; >20:1 dr; mp 162.2–164.3 °C; $R_f = 0.22$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₃₇H₃₂N₃O₄, 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 °C; $R_f = 0.24$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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, CDCl₃) 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 C₃₁H₂₆N₃O₄, 504.1918; found, 504.1928.

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



Yellow solid; 44.9 mg, 20% yield; >20:1 dr; mp 193.1–194.8 °C; $R_f = 0.38$ (petroleum ether/EtOAc = 3/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 30/6/1; ¹H NMR (300 MHz, CDCl₃) 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, CDCl₃) 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 C₃₃H₂₈N₃O₄S, 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-ca rbonitrile (3na).



Yellow solid; 119.5 mg, 67% yield; >20:1 dr; mp 184.3–185.7 °C; $R_f = 0.17$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 50/10/1; ¹H NMR (400 MHz, CDCl₃) 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 = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 3H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.05 (dt, J = 2.9, 0.7 Hz, 1H), 7.26–7.17 (m, 2H), 7.26–7.17 (m, 2H), 7.26–7.17 (m, 2H), 7.26–7.17 (m, 2H), 7.26–7.19 (m, 2H), 7.26–7.19

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); ¹³C NMR (100 MHz, CDCl₃) 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 C₂₈H₂₃N₄O₂, 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 °C; R_f = 0.43 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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 C₃₂H₃₂N₃O₄, 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 °C; R_f = 0.20 (petroleum ether/EtOAc = 10/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/4/1; ¹**H NMR** (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₃₀H₂₇ClN₃O₄, 528.1685; found, 528.1693.

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



Yellow solid; 179.5 mg, 80% yield; >20:1 dr; mp 217.1–218.7 °C; $R_f = 0.30$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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, CDCl₃) 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-3,4dihydro-2H-quinolizine-1-carboxylate (3ac).



Yellow solid; 190.8 mg, 85% yield; >20:1 dr; mp 181.4–183.1 °C; $R_f = 0.29$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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 C₃₀H₂₆Cl₂N₃O₄, 562.1295; found, 562.1303.

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



Orange solid; 179.9 mg, 85% yield; >20:1 dr; mp 150.6–152.3 °C; $R_f = 0.30$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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; ¹⁹F NMR (376 MHz, CDCl₃) δ –114.4, –115.7; HRMS (ESI-TOF) m/z: [M + H]⁺ calcd for C₃₀H₂₆F₂N₃O₄, 530.1886; found, 530.1895.

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



Yellow solid; 203.1 mg, 78% yield; >20:1 dr; mp 190.6–192.1 °C; $R_f = 0.29$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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-3,4dihydro-2H-quinolizine-1-carboxylate (3af).



Yellow solid; 238.4 mg, 80% yield; >20:1 dr; mp 210.7–212.2 °C; $R_f = 0.29$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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 C₃₀H₂₆I₂N₃O₄, 746.0007; found, 745.9942.

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



Orange solid; 102.1 mg, 47% yield; >20:1 dr; mp 200.5–201.1 °C; $R_f = 0.24$ (petroleum ether/EtOAc = 2/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 32/8/1; ¹**H NMR** (300 MHz, CDCl₃) 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 = 1.2 Hz, 1H), 7.50 (d, J = 1.2

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); ¹³C NMR (75 MHz, CDCl₃) 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 C₃₂H₂₆N₅O₄, 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 °C; R_f = 0.33 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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, CDCl₃) δ –62.58, –62.63; **HRMS** (ESI-TOF) m/z: [M + Na]⁺ calcd for C₃₂H₂₅F₆N₃NaO₄, 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-2Hquinolizine-1-carboxylate (3ai).



Yellow solid; 150.1 mg, 72% yield; >20:1 dr; mp 159.5–160.9 °C; $R_f = 0.41$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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, CDCl₃) 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 C₃₂H₃₂N₃O₄, 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 °C; $R_f = 0.19$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 50/10/1; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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 C₃₂H₃₂N₃O₆, 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* (3*ak*).



Yellow solid; 158.9 mg, 67% yield; >20:1 dr; mp 183.7–185.1 °C; $R_f = 0.22$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₃₈H₃₂N₃O₄, 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)-3,4dihydro-2H-quinolizine-1-carboxylate (3al).



Orange solid; 141.4 mg, 70% yield; >20:1 dr; mp 81.6–82.9 °C; $R_f = 0.22$ (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 60/5/1; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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 C₂₆H₂₃N₃NaO₄S₂, 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 Na₂SO₄, and concentrated under reduced pressure. And the residue was purified by flash column chromatography cluent, 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 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; ¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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 C₂₈H₂₆N₃O₄, 492.1918; found, 492.1914.



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 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-1carboxylate (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; ¹H NMR (300 MHz, CDCl₃) 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, CDCl₃) 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 C₂₉H₃₀NO₅, 472.2118; found, 472.2124.



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, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) 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 C₃₄H₃₂N₂NaO₄, 555.2254; found, 555.2261.



An oven-dried 15 mL of reaction tube was charged with **3aa** (0.1 mmol, 1.0 equiv., 49.3 mg), BnNH₂ (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); ¹H NMR (300 MHz, CDCl₃) 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, CDCl₃) 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 C₃₄H₃₂N₂NaO₄, 555.2254; found, 555.2265. **For the minor diastereomer**, $R_f = 0.22$ (petroleum ether/EtOAc = 5/1); ¹**H NMR** (300 MHz, CDCl₃) 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); ¹³C NMR (75 MHz, CDCl₃) δ 173.1, 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 C₃₄H₃₂N₂NaO₄, 555.2254; found, 555.2267.



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-2Hquinolizine-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; ¹H NMR (300 MHz, CDCl₃) 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, CDCl₃) 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 C₃₅H₃₄NO₄S, 564.2203; found, 564.2218.

6. Control Experiments



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 °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 Na₂SO₄, 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 °C; R_f = 0.38 (petroleum ether/EtOAc = 5/1); column chromatography eluent, petroleum ether/EtOAc/DCM = 40/8/1; ¹**H NMR** (400 MHz, CDCl₃) 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); ¹³C NMR (100 MHz, CDCl₃) 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 C₃₂H₃₂N₃O₄, 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	$C_{30}H_{27}N_{3}O_{4}$		
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)		
$\alpha/^{\circ}$	90		
β/°	98.379(4)		
$\gamma^{\prime \circ}$	90		
Volume/Å ³	2504.65(15)		
Z	4		
$\rho_{calc}g/cm^3$	1.309		
μ/mm^{-1}	0.711		
F(000)	1040.0		
Crystal size/mm ³	0.17 imes 0.15 imes 0.1		
Radiation	$CuK\alpha$ ($\lambda = 1.54184$)		
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>=2 σ (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.



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





(Phil

-1-carboxylate (3aa). - 8.067 - 8.058 6.357 6.353 6.348 6.344 . 7.156 6.944 7.371 7.367 7.348 325 .302 6.939 6.721 - 6.708 - 6.693 - 6.688 5.987 5.983 5.967 5.962 5.957 5.957 $\sum_{3.622}^{3.630}$ 7.260 7.206 7.161 6.741 5.726 6.91 4.084 3.885 3.873 3.861 3.837 3.825 3.779 3.762 3.762 3.762 3.762 .734 5.937 4.072 4.048 4.025 1.001 908 697 1.06] 4.037 -66.0 96.0 2.03 8 ,ci 8.08 8.04 7.4 7.1 6.96 6.92 fl (ppm) 5 6.70 fl (ppm) 6.36 6.34 6.00 fl (ppm)) 5.95 fl (ppm) 4.10 4.05 4.00 3.95 3.90 3.85 3.80 3.75 3.70 3.65 3.60 fl (ppm) 7.3 7 fl (ppm) 7.2 6.75 fl (ppm) ~ 3.065 ~ 3.060 3.0273.022 ÇO₂Et Ph N= Ν IJ ∏ H O ö Ρh 3.08 3.04 3.00 fl (ppm) 3aa, ¹H NMR, 300 MHz, CDCl₃ 1.02 1.02 1.03 5.01 3.26 2.00 1.00 $1.00_{4}^{-1.00_{4}}$ H00.1 H60.0 H86.0 H70.0 3.03H 0.0 9.5 8.5 8.0 4.0 3.0 0.0 9.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 f1 (ppm) 3.5 2.5 2.0 1.5 1.0 0.5 146.558 144.061 140.469 140.469 130.521 130.521 130.520 128.954 128.151 128.151 127.777 128.151 127.777 123.452 123.452 123.452 109.656 123.452 109.656 100.656 100.65 $< rac{170.300}{170.081}$ ~ 166.771 — 59.620 — 54.125 77.585 77.160 76.736 $\frac{1}{2} \frac{40.370}{39.549}$ 38.944 - 96.301 - 14.224 170.300 — 140.469— 140.411 128.225 128.131 129.040 128.916 127.070 170.081 126.650 127.727 1 11 1 ٨٨ 170.5 170.0 140.6140.4 129.0 128.5 128.0 127.5 127.0 126.5 fl (ppm) fl (ppm) f1 (ppm) ÇO₂Et Ph N= ∥ Ĥ O 0 Ph 3aa, ¹³C NMR, 75 MHz, CDCl₃ 70 0 -10 210 200 190 180 170 160 150 140 130 120 110 100 90 80 60 50 40 30 20 10 fl (ppm)

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



S22



S23

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





S25



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





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

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).





10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 fl (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-

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).



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



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



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 (30a).*



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



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



S38

dihydro-2H-quinolizine-1-carboxylate (3ac). 8,8463 8,8463 8,8456 8,8426 8,8426 8,8426 8,8425 8,8425 8,8425 8,8425 8,8425 8,8425 8,8425 7,777 7,7745 8,8425 7,777 7,7745 8,8425 7,717 7,7745 7,775 ~3.745 ~3.722 <u>3.664</u> $\sum_{i=0.356}^{6.361}$ 6.356 $\sum_{i=0.352}^{6.352}$ 3.875 3.862 3.839 $\int_{6.726}^{6.763} 6.759 \\ 6.759 \\ 6.730 \\ 6.730 \\ 6.709 \\ 6.700 \\ 6.$ 3.607 $\sum_{\substack{7.754\\7.749\\7.728\\7.728\\7.728\\7.720}$ 6.004 5.999 5.984 5.979 5.974 5.958 4.088 4.075 4.064 t.052 t.040 4.028 -824 3.922 3.910 3.899 ~ 8.054 - 8.430 - 8.426 - 8.423 - 8.463 - 8.460 - 8.456 ΜÅ -10.1 -66.0 5 9 g 9 8.48 8.44 fl (ppm) 7.76 7.74 7.72 fl (ppm) 6.75 6 fl (ppm) 6.36 6.34 fl (ppm) 6.00 5.95 fl (ppm) 4.1 4.0 3.9 3 fl (ppm) 3.8 3.7 8.07 8.04 6.70 3.6 fl (ppm) 2.975 2.970 2.938 2.934 ÇO₂Et .R N= Ń ∥ Ĥ | O R ö $R = 4-CI-C_6H_4$ 3.00 2.95 2.90 fl (ppm) 3ac, ¹H NMR, 300 MHz, CDCl₃ 1.00⁴ 0.99 2.01⁴ 2.174 2.04 1.01⁴ 2.014 3.05H 1.004 1.004 4.004 H00.1 H60.0 166.0 1.00H 9.5 7.5 4.0 9.0 8.5 8.0 7.0 6.5 6.0 5.5 5.0 4.5 f1 (ppm) 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 146.712 144.254 138.846 138.648 138.648 133.672 133.672 133.672 132.946 132.945 132.945 132.945 122.167 122.167 122.167 122.167 122.333 122.3338 123.3338 122.3338 12 $\frac{-132.980}{-166.467} = 166.467$ 77.584 77.160 76.736 — 14.289 - 53.886 - 59.852 - 95.626 $\mathbf{\nabla}$ 129.488 129.390 129.298 129.167 39.922 — 39.129 - 38.764 128.280 -+28.114 -133.672127.052 - 138.698 30.945 138.9 138.6 134.0 133.5 133.0 132.5 132.0 131.5 131.0 130.5 130.0 129.5 129.0 128.5 128.0 127.5 127.0 126.5 40 39 fl (ppm) fl (ppm) fl (ppm) ÇO₂Et N= ∥ Ĥ | O R Ö R = 4-CI-C₆H₄ 3ac, ¹³C NMR, 75 MHz, CDCl₃ 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 fl (ppm)

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

dihydro-2H-quinolizine-1-carboxylate (3ad). $\begin{array}{c} 8,846 \\ 8,8456 \\ 8,8456 \\ 8,8456 \\ 8,842$ $\frac{\sum_{7.612}^{7.614}}{\sum_{7.610}^{7.610}}$ Z 7.299 7.299 7.288 7.277 7.260 6.891 6.870 6.876 6.737 6.737 6.737 6.737 6.737 6.732 6.732 6.719 6.719 $\frac{1}{2} \frac{8.059}{8.057} \\ \frac{1}{2} \frac{8.057}{8.048} \\ \frac{1}{2} \frac{1}{8.048} \\ \frac{1}{2} \frac{$ 7.758 7.758 7.754 7.737 7.733 7.733 -- 7.087 -- 7.058 -- 7.030 $\sum_{\substack{6.361\\6.356\\6.351\\6.347}$ - 6.001 - 5.980 - 5.976 5.955 ~ 2.983 ~ 2.977 ~ 2.945 ~ 2.940 $\overbrace{\begin{subarray}{c} 8.458\\ 8.458\\ 8.454\\ 8.428\\ 8.424\\ 8.421\\ 8.421\\ 8.421\\ \end{subarray}$ λŴ ₩\L 2.054 9 , di 7 7.74 7.71 fl (ppm) 3.48 8.44 8.08 8.06 8.04 7.77 fl (ppm) fl (ppm) f 7.62 7.60 fl (ppm) 7.3 7.2 7.0 fl (ppm) 6.7 6.39 6.36 6.33 fl (ppm) 6.00 5.94 fl (ppm) 0 2.95 fl (ppm) 7.1 6.9 6.8 3.00 4.110 4.086 4.073 4.073 4.073 4.050 4.038 4.038 4.038 4.038 ~ 3.760 3.714 3.714 3.676 3.667 3.667 3.955 3.931 3.919 3.908 3.895 3.884 3.872 3.872 ÇO₂Et R N= Ń_/ ∬ <mark>H</mark> í O R 8 2.07 96 ö 4.05 4.00 3.95 3.90 3.85 3.80 fl (ppm) 4.10 3.75 3.70 3.65 3.60 $R = 4-F-C_6H_4$ 3ad, ¹H NMR, 300 MHz, CDCl₃ 1.02 1.02 2.07 1.99 4 H00-1 1.01 1.01 1.01 2.19 2.05 4.03 4.03 1.06 1.06 1.06 H00.1 3.07H 1.01H 1.00-1 5.0 4.5 f1 (ppm) 9.5 8.5 4.0 3.5 3.0 1.0 9.0 8.0 7.5 7.0 6.5 6.0 5.5 2.5 2.0 1.5 0.5 0.0 $\int\limits_{160.347}^{170.004} [69.911] \\ \times [165.581] \\ \times [163.366] \\ 163.599 \\ 160.347 \\ 100.347 \\ 10$ 146.602 144.218 136.079 136.079 135.955 135.955 135.915 135.915 135.915 135.915 135.915 135.915 127.064 127.064 128.287 128.287 128.287 116.166 115.898 115.898 115.8987 115.9 77.583 77.160 76.737 - 54.299 $\underbrace{f_{38.995}^{39.809}}_{38.958}$ - 14.302 11 160.599 160.347 ~ 136.121 ~ 136.079 ~ 135.955 ~ 135.915 -170.004-169.911163.866 163.599 128.287 128.190 - 116.166 - 115.998 - 115.882 - 115.717 - 39.809 $< \frac{38.995}{38.958}$ 129.759 129.652 127.064 -130.83511 17 52 \sim T 70.2 162 161 160 135.8 131 128 127 116.5 116.0 115.5 40.0 169.8 164 163 136.2 130 129 39.5 39.0 f1 (ppm) fl (ppm) fl (ppm) fl (ppm) fl (ppm) fl (ppm) ÇO₂Et N= ∬ Ĥ [O R ö $R = 4 - F - C_6 H_4$ 3ad, ¹³C NMR, 75 MHz, CDCl₃ 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 fl (ppm)

ethyl



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



✓ -114.364
< -115.708</p>

ethyl dihydro-2H-quinolizine-1-carboxylate (3ae). 8,8466 8,8458 8,455 8,555 ~ 8.055 ~ 8.046 $\leq \frac{7.751}{7.748}$ $\leq \frac{7.726}{7.726}$ ~ 7.508 ~ 7.480 ~ 7.323 ~ 7.295 ~ 7.260 ~ 7.204 ~ 7.176 6.762
 6.747
 6.742
 6.734
 6.729
 √
 6.713
 √
 6.713
 √
 6.713 $\frac{\int_{0.364}^{0.368} 6.364}{6.359} = 0.354$ - 5.986 5.956 4.078 4.066 4.054 4.043 4.030 3.918 3.904 3.894 3.870 3.870 3.870 - 8.466 - 8.462 - 8.433 - 8.429 7.614 - 6.007 6.002 5 977 と5.961 4.090 3.941 5.822 5.794 7.4 7.3 7.2 6.85 Ę -07 1.02 7.6 7.5 7.4 7 fl (ppm) 5.96 7.76 7.72 fl (ppm) 6.80 6.75 fl (ppm) 6.00 5.9 f1 (ppm) 4.1 4.0 fl (ppm) 3.9 8.48 8.44 8.07 8.04 6.76.39 6.33 fl (ppm) fl (ppm) fl (ppm) 2.732 3.732 3.683 3.683 3.654 3.654 3.654 3.640 3.580 3.580 -2.972 -2.966 -2.935 -2.935 ÇO₂Et R N= Ń. 1 5 ∥ Ĥ O Ŕ ö 3.75 3.70 3.65 3.60 3.55 3.00 2.95 2.90 $R = 4-Br-C_6H_4$ fl (ppm) fl (ppm) 3ae, ¹H NMR, 300 MHz, CDCl₃ 1.02 0.99 1.00 2.04 2.02 1 2.02 1 -86.0 1.024 1.024 1.064 H86.0 3.02H H00.1 2.00 1.004 5.0 4.5 f1 (ppm) 9.5 9.0 4.0 3.0 2.5 8.5 8.0 7.5 7.0 6.5 6.0 5.5 3.5 2.0 1.5 1.0 0.5 0.0 $\underset{\sim}{\overset{169.744}{<}_{169.698}}$
 146.721

 144.246

 139.230

 139.237

 139.237

 132.2116

 132.247

 132.243

 122.3842

 128.277

 128.335

 121.783

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788

 121.788
 - 95.557 $\underbrace{ \int \frac{77.583}{77.160} \\ 76.737 }$ — 59.864 — 53.723 $\frac{1}{\sqrt{39.199}}$ - 14.300 51/-~ 132.247 ~ 132.116 130.945 129.842 169.744 169.698 - 127.053 ī 17 130 1 f1 (ppm) 169.8 169.6 131 127 132 129 128 fl (ppm) ÇO₂Et .R N= ∏ Ĥ ∏ O R ö $R = 4-Br-C_6H_4$ 3ae, ¹³C NMR, 75 MHz, CDCl₃ 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 fl (ppm)



dihydro-2H-quinolizine-1-carboxylate (3af). $\int_{3.575}^{3.682} 3.682$ $\int_{3.641}^{3.641} 3.641$ $\int_{3.575}^{3.575}$ - 6.758 - 6.738 6.725 6.702 6.674 $\sum_{\substack{8.052\\ 8.049}}^{8.052}$ $\sum_{n=0}^{6.362} \frac{6.362}{6.358} - \frac{6.353}{6.348} - \frac{6.348}{6.344}$ 5.968 5.952 4.030 4.006 3.934 3.910 3.886 3.874 3.863 3.850 8.452 8.426 8.423 8.419 8.419 7.710 6.002 5.998 5.994 5.978 5.973 5.956 080 4.066 4.053 4.042 898.8 4.077 7.745 7.700 7.672 7.741 6.00 5.98 5.96 5.94 fl (ppm) 1.01 8.44 fl (ppm) 8.06 8.04 fl (ppm) 6.36 6.34 fl (ppm) 4.0 f1 (ppm) 7.70 fl (ppm) 6.72 6.65 fl (ppm) 3.7 7 3.6 f1 (ppm) 7.75 4.1 3.9 2.967
 2.961
 2.931
 2.925
 2.925 ÇO₂Et .R N= Ń. ∥ Ĥ O Ŕ Ö 2.96 2.92 fl (ppm) $R = 4 - I - C_6 H_4$ 3af, ¹H NMR, 300 MHz, CDCl₃ 2.00H 3.09H 3.08H 1.01- $1.01 \pm$ 1.05d 1.05d 4.24q H00.1 5.0 4.5 f1 (ppm) 9.5 7.0 4.0 3.0 1.0 9.0 8.5 8.0 7.5 6.5 6.0 5.5 3.5 2.5 2.0 1.5 0.5 0.0 $< \frac{169.717}{169.665} \sim 166.397$ $\int_{128,09}^{146,699} 144.228$ $\int_{138,168}^{144,228} 138.168$ $\int_{138,168}^{138,168} 138.0916$ $\int_{130,916}^{138,168} 128.768$ $\int_{127,032}^{128,768} 128.758$ $\int_{127,032}^{127,032} 158.255$ $< 109.889 \\
< 108.930$ 55.472 593.359 592.632- 77.583 - 77.160 - 76.736 - 40.114 - 39.255 \ 38.654 - 14.333 - 138.168 - 138.050 -130.916128.768 - 128.265 - 169.717 - 169.665 130.075 -127.032ī 129 fl (ppm) 169.8 169.6 140.0 139.8 138.3 138.0 131 130 128 127 fl (ppm) fl (ppm) fl (ppm) ÇO₂Et Ņ= Ń ∥Ĥ | O R ö $R = 4 - I - C_6 H_4$ 3af, ¹³C NMR, 75 MHz, CDCl₃ 200 190 180 170 160 150 140 130 120 110 100 80 70 60 50 40 30 20 10 0 90 fl (ppm)

ethyl

dihydro-2H-quinolizine-1-carboxylate (3ag). 6.778 6.791 6.795 6.778 6.778 8.454 8.450 8.446 8.421 8.417 8.413 $< \frac{8.046}{8.037}$ - 7.484 - 7.468 - 7.440 3.975 3.975 3.975 3.975 3.975 3.975 3.928 3.915 3.915 3.892 3.892 3.888 3.882 3.853 3.853 ~ 7.512 6.384 6.379 6.374 6.369 6.059 6.055 6.039 6.034 6.029 6.013 4.099 4.075 4.063 4.051 4.039 4.028 3.830 3.814 3.806 3.792 3.768 7.760 7.756 7.755 7.752 7.735 7.731 7.731 7.703 7.703 Μж 1,Mi Ņ -10.1 02-80 -00.1 1.08 ğ ŝ 7.50 7.45 fl (ppm) 3.95 3.90 3.85 3.80 3.75 fl (ppm) 5 7.70 fl (ppm) 7.65 6.80 fl (ppm) 6.39 6.36 f1 (ppm) 6.04 6.00 4.10 4.05 4.00 fl (ppm) 8.44 8.40 8.00 7.75 6.75 fl (ppm) fl (ppm) 3.037 3.032 2.999 2.994 -3.6883.644 3.621 CO₂Et R N= N || **h** | O R 0 $R = 4-CN-C_6H_4$ 3.70 3.65 3.60 3.05 3.00 fl (ppm) fl (ppm) 3ag, ¹H NMR, 300 MHz, CDCl₃ 3.11H 2.04H 1.01H 1.00 - 1 - 00 - 1 - 00 - 1 - 00 - 1 - 00 - 0 1.02_{\pm} 1.00-1.08 1.03 3.04 4 1.01 8.5 7.5 7.0 4.5 f1 (ppm) 3.0 9.0 8.0 6.5 6.0 5.5 5.0 4.0 3.5 2.5 2.0 1.5 1.0 0.5 0.0 147.011 145.707 145.617 144.473 132.965 131.499 132.9053 131.499 127.579 127.5 169.344 168.943 166.054 - 77.584 - 77.160 - 76.736 -- 60.042 -- 53.103 $< \frac{40.584}{39.995}$ ~ 38.405 - 14.373 -- 94.505 \bigtriangledown) $\leq \frac{145.707}{145.617}$ 128.319 127.579 - 168.943 169.344 129.053 - 118.591 - 118.343 144.473 - 127.044 - 147.011 1 1 118.4 168.8147 144 129 128 127 69.6 146 145 fl (ppm) fl (ppm) fl (ppm) fl (ppm) ÇO₂Et R N= ∬ H ∫ O R 0 $R = 4-CN-C_6H_4$ 3ag, ¹³C NMR, 75 MHz, CDCl₃ 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 fl (ppm)

ethyl







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

S46

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





S50





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



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).



quinolizine-1-carboxylate (8). 8.430 8.426 8.422 7.728 7.724 7.706 6.697 6.697 6.693 6.684 6.680 5.954 5.938 5.934 5.929 5.913 5.913 7.732 7.698 7.382 7.357 7.357 7.357 7.357 7.358 7.338 7.338 7.338 7.269 7.7264 7.7264 7.7264 7.7264 7.127 7.127 7.127 7.1159 7.1155 7.1155 7.1155 7.1155 7.1155 6.950 - 6.718 5.959 -4.118 - 4.094 - 4.070 ~ 4.058 - 4.046 - 4.034 - 4.011 7.042 6.972 6.965 6.945 6.931 6.924 606.9 6.904 3.02-0.99 1.06 2.26 2.05 4.10 4.05 4.0 fl (ppm) 7.00 6.95 6.90 6.72 f1 (ppm) 3.48 8.44 fl (ppm) 7.76 7.72 7.68 7.40 fl (ppm) 7.30 7.2 fl (ppm) 2 6.68 f1 (ppm) 5.96 5.92 fl (ppm) 7.35 7.25 7.20 7.15 7.05 5.92 23.644 3.614 3.614 3.616 3.505 3.595 3.576 3.576 3.557 3.1133.0833.0833.0603.0303.0192.9992.9992.9652.9652.9462.9312.926- 3.964 ÇO₂Et Ph Me λ^μγγγγ E ŮĤ -10.1 Ρ'n ö 3.07 3.95 3.90 fl (ppm) 3.85 3.65 3.60 3.55 3.10 3.05 3.00 2.95 f1 (ppm) fl (ppm) 8, ¹H NMR, 300 MHz, CDCl₃ 1.064 3.064 0.994 H00.1 1.01 3.06 3.06 3.02 3.02 3.97 1.02 1.02 4 H66.0 3.07 3.02H 3.044 9.0 7.5 4.0 3.0 1.0 8.5 8.0 7.0 6.5 6.0 5.5 5.0 4.5 f1 (ppm) 3.5 2.5 2.0 1.5 0.5 0.0 196.628 - 169.998 - 166.670 $\underbrace{ \left\{ \begin{array}{c} 77.583 \\ 77.160 \\ 76.736 \end{array} \right. } \\$ - 21.155 \sim 59.650 - 54.014 \sim 48.079 \sim 39.600 - 32.987 — 14.244 - 96.669 ~ 130.476 ~ 130.432 129.019 128.942 - 126.846 - 129.274 128.657 128.158 127.722 -127.103126.649 1 Λ 130.5 130.0 129.5 129.0 128.5 128.0 127.5 127.0 126.5 fl (ppm) ÇO₂Et Ph Me ∥Ĥ| O Ph 0 ¹³C NMR, 75 MHz, CDCl₃ R 0 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 fl (ppm)

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

S56

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).

