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Supporting Information

Tandem additions of 3,4-dihydroisoquinolines to γ-hydroxy -α,β-unsaturated ketones: a green and new access to oxazolo [2,3-a]tetrahydroisoquinolines

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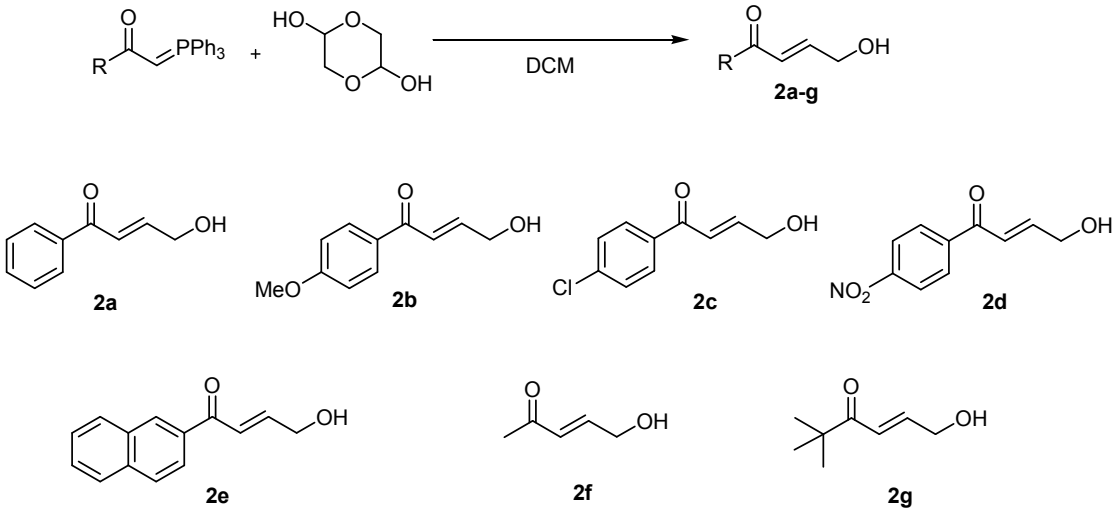
Content

General information

Reactions were carried out in round bottom flasks fitted with rubber septa under argon. Crude product solutions were dried on Na_2SO_4 and concentrated with a rotary evaporator below 40 ^oC at ~ 30 Torr. Silica gel column chromatography was performed employing 230 - 400 mesh silica gel. Proton nuclear magnetic resonance (^1H NMR) and carbon nuclear magnetic resonance (^{13}C NMR) spectra were obtained using Bruker Avance II (300 MHz) NMR spectrometer. Chemical shifts (δ scale) were expressed in parts per million downfield from tetramethylsilane (δ = 0.00). 1H NMR data were presented as follows: chemical shift, multiplicity (s = singlet, br = broad singlet, d = doublet, t = triplet, m = multiplet and/or multiple resonances), coupling constant in Hz (Hertz), integration. High-resolution mass spectra were determined on a Jasco JMS-HX 110 spectrometer. Reactions were monitored by thin layer chromatography (TLC) on Silicycle siliaplate^{TM}G TLC plates (F-254 indicator).

General procedures for the synthesis of γ-Hydroxyenones

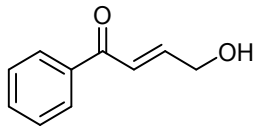
Scheme 1. Synthesis of γ-Hydroxyenones (2a-g)



To a solution of appropriate stabilizes ylide (1.5 mmol) in dry THF (30 mL) as added glycolaldehyde dimer (0.7 mmol), and the resulting solution was heated under reflux for 3 h. The

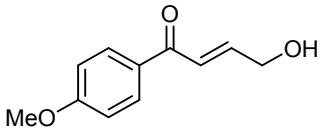
solution was cooled and concentrated under reduced pressure. The product was purified by chromatography(ethyl acetate: hexane = 1:1) to give the γ-Hydroxyenones (**2a-g**).

Characterization data of products



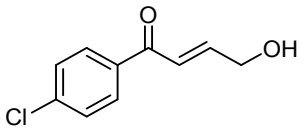
(*E*)-4-hydroxy-1-phenylbut-2-en-1-one (2a).

physical state: white solid; yield: 98% ; mp.:110-112 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ7.93 (d, 2H, *J* = 7.5 Hz), 7.53 (t, 1H, *J* = 7.2 Hz), 7.42 (t, 2H, *J* = 7.2 Hz), 7.08-7.29 (m, 2H), 4.44 (s, 2H), 3.64 (s, 1H); ^{13}C NMR (75 MHz $CDCl_3$) δ 190.9, 148.1, 137.1, 132.9, 128.4, 123.2, 61.7.



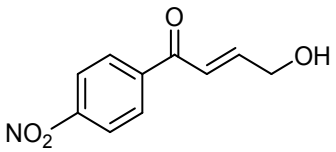
(*E*)-1-(4-methoxyphenyl)-4-hydroxybut-2-en-1-one (2b).

physical state: white solid; yield: 91% ; mp: 90-92 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (dt, *J* = 9, 2.7 Hz, 2H), 7.26-7.20 (m, 1H), 7.11 (dt, *J* = 15.3, 3.6 Hz, 1H), 6.95 (dt, *J* = 9, 3 Hz, 2H), 4.48-4.46 (m, 2H), 3.88 (s, 3H); ^{13}C NMR (75 MHz $CDCl_3$) δ 188.9, 163.7, 146.4, 131.2, 130.7, 123.7, 114.0, 62.6, 55.7.



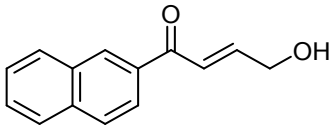
(*E*)-1-(4-Chlorophenyl)-4-hydroxybut-2-ene-1-one (2c).

physical state: yellow solid; yield: 91% ; mp: 39-40 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.89 Hz, 2H), 7.43 (d, *J* = 8.7 Hz, 2H), 7.22-7.10 (m, 2H), 4.47 (s, 2H), 2.55 (brs, 1H); ^{13}C NMR (75 MHz $CDCl_3$) δ189.3, 147.9, 139.5, 135.9, 130.1, 129.0, 123.2, 62.3.



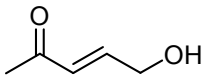
(*E*)-1-(4-nitrophenyl)-4-hydroxybut-2-ene-1-one (2d).

physical state: yellow solid; yield: 64% ; mp: 95-96 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.7 Hz, 2H), 8.11 (d, *J* = 8.7 Hz, 2H), 7.23-7.22 (m, 2H), 4.53 (s, 2H), 1.84 (brs, 1H); ^{13}C NMR (75 MHz $CDCl_3$) δ 188.9, 150.2, 149.4, 142.5, 129.6, 123.9, 123.1, 62.3; HRMS: Calcd. for $C_{11}H_{12}O_3$: 207.0532. Found: 207.0523.



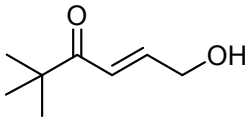
(*E*)-4-Hydroxy-10-(naphthalene-2-yl)but-2-ene-1-one (2e).

physical state: yellow solid; yield: 96% ; mp: 35-36 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49 (s, 1H), 8.05 (dd, *J* = 8.7, 1.5 Hz, 1H), 7.96-7.85 (m, 3H), 7.62-7.51 (m, 2H), 7.40 (dt, *J* = 15.3, 1.8 Hz, 1H), 7.26-7.17 (m, 1H), 4.52 (s, 2H), 2.24 (brs, 1H); ^{13}C NMR (75 MHz $CDCl_3$) δ 190.7, 147.9, 135.4, 134.6, 132.3, 130.4, 29.5, 128.5, 127.7, 126.7, 124.2, 123.5, 62.2.



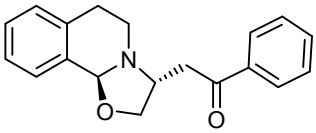
(*E*)-1-methl-4-hydroxybut-2-ene-1-one (2f).

physical state: colorless oil; yield: 84%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.88 (dt, *J* = 15.9, 3.9 Hz, 1H), 6.35 (dt, *J* = 15.9, 2.1 Hz, 1H), 4.38 (s, 2H), 2.28 (s, 3H); ^{13}C NMR (75 MHz $CDCl_3$) δ 198.6, 145.9, 129.1, 61.9, 27.5..



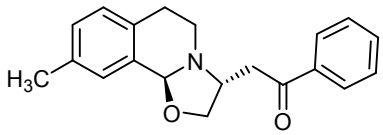
(*E*)-1-t-butyl -4-hydroxybut-2-ene-1-one (2g).

physical state: colorless oil; yield: 67%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (dt, *J* = 15.3, 3.9 Hz, 1H), 6.80 (dt, *J* = 15.3, 1.8 Hz, 1H), 4.40-4.37 (m, 2H), 1.83 (brs, 1H), 1.17 (s, 9H); ^{13}C NMR (75 MHz $CDCl_3$) δ 204.3, 145.1, 122.5, 62.4, 43.2, 26.2.



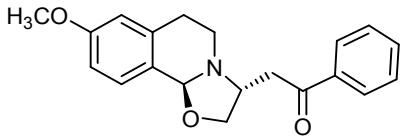
3-(2-phenyl-2-oxo-ethyl)-oxazolo[2,3-a]tetrahydroisoquinoline (3a).

Recrystallized from ethyl acetate/hexane, yield: 93% (15:1 mixture of two diastereomers); physical state: white solid; mp 124-125 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ□7.97 (d, *J* = 7.5 Hz, 2H), 7.58-7.37 (m, 4H), 7.25-7.12 (m, 3H), 5.29 (s, 1H), 4.37 (t, *J* = 7.8 Hz, 1H), 3.93-3.85 (m, 1H), 3.58-3.45 (m, 2H), 3.16 (dd, *J* = 17.7, 7.8 Hz, 1H), 3.03-2.85 (m, 3H), 2.71 (d, *J* = 12 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6, 136.9, 135.5, 133.3, 131.8, 128.9, 128.7, 128.3, 128.1, 126.3, 89, 69.3, 62.2, 46.9, 43.6, 29.8; HRMS: Calcd. for $C_{19}H_{19}NO_2$: 293.1416. Found: 293.1413.



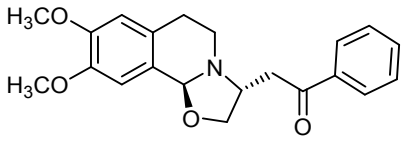
9-methyl-3-(2-phenyl-2-oxo-ethyl)-oxazolo[2,3-a]tetrahydroisoquinoline (3b).

Recrystallized from ethyl acetate/hexane, yield: 95% (14:1 mixture of two diastereomers); physical state: white solid; mp 122-124 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.5 Hz, 2H), 7.60-7.44 (m, 3H), 7.21-7.05 (m, 3H), 5.27 (s, 1H), 4.37 (t, *J* = 7.5 Hz, 1H), 3.93-3.85 (m, 1H), 3.59-3.46 (m, 2H), 3.17 (dd, *J* = 17.7, 7.8 Hz, 1H), 2.98-2.90 (m, 3H), 2.71-2.66 (m, 1H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.7, 136.9, 135.9, 133.4, 132.4, 131.6, 129.3, 128.7, 128.3, 128.1, 128.0, 89.2, 69.4, 62.3, 47.2, 43.6, 29.4, 21.1; HRMS: Calcd. for $C_{20}H_{21}NO_2$: 307.1572. Found: 307.1573.



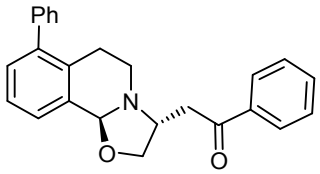
8-methoxy-3-(2-phenyl-2-oxo-ethyl)-oxazolo[2,3-a]tetrahydroisoquinoline (3c).

Recrystallized from ethyl acetate/hexane, yield: 95% (19:1 mixture of two diastereomers); physical state: white solid; mp 106-108 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.5 Hz, 2H), 7.58 (t, *J* = 7.5, Hz, 1H), 7.48 (t, *J* = 7.2 Hz, 2H), 7.06 (d, *J* = 8.4, Hz, 1H), 6.92 (d, *J* = 2.7, Hz, 1H), 6.83 (dd, *J* = 8.4, 2.7 Hz, 1H), 5.28 (s, 1H), 4.38 (t, *J* = 7.5 Hz, 1H), 3.95-3.86 (m, 7.2 Hz, 1H), 3.80 (s, 3H), 3.59-3.47 (m, 2H), 3.19 (dd, *J* = 17.7, 7.8 Hz, 1H), 2.99-2.88 (m, 3H), 2.71-2.64 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.7, 158.1, 136.9, 133.4, 132.8, 129.2, 128.7, 128.1, 127.6, 115.6, 112.7, 89.3, 69.4, 62.2, 55.4, 47.4, 43.6, 29.0; HRMS: Calcd. for $C_{20}H_{21}NO_3$: 323.1521. Found: 323.1526.



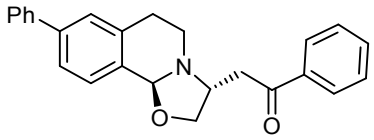
8,9-dimethoxy-3-(2-phenyl-2-oxo-ethyl)-oxazolo[2,3-a]tetrahydroisoquinoline (3d).

Recrystallized from ethyl acetate/hexane, yield: 95% (17:1 mixture of two diastereomers); physical state: white solid; mp: 126 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.8 Hz, 2H), 7.58 (t, *J* = 7.2, Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 6.88 (s, 1H), 6.62 (s, 1H), 5.24 (s, 1H), 4.39 (t, *J* = 8.1 Hz, 1H), 3.86 (d, *J* = 3.3 Hz, 6H), 3.59-3.45 (m, 2H), 3.18 (dd, *J* = 17.4, 7.8 Hz, 1H), 2.99-2.90 (m, 3H), 2.70-2.57 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.5, 148.9, 147.5, 136.7, 133.2, 128.6, 127.9, 123.6, 110.9, 110.4, 88.9, 69.2, 62.0, 55.8, 47.0, 43.5, 29.3; HRMS: Calcd. for $C_{21}H_{23}NO_4$: 353.1627. Found: 353.1624.



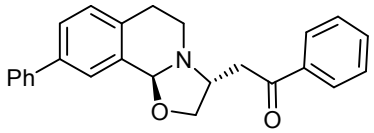
3-(2-phenyl-2-oxo-ethyl)-7-phenyl-oxazolo[2,3-a]tetrahydroisoquinoline (3e).

Recrystallized from ethyl acetate/hexane, yield: 90% (19:1 mixture of two diastereomers); physical state: white solid; mp 114-117 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.4 Hz, 2H), 7.60-7.22 (m, 11H), 5.39 (s, 1H), 4.38 (t, *J* = 7.5 Hz, 1H), 3.93-3.85 (m, 1H), 3.60-3.48 (m, 2H), 3.20 (dd, *J* = 17.4, 7.8 Hz, 1H), 2.97-2.74 (m, 3H), 2.57 (d, *J* = 15.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6, 141.2, 140.9, 136.9, 133.4, 133.2, 132.3, 129.7, 129.2, 128.7, 128.2, 128.1, 127.1, 126.3, 89.5, 69.3, 62.4, 47.2, 43.6, 28.8; HRMS: Calcd. for $C_{25}H_{23}NO_2$: 369.1729. Found: 369.1735.



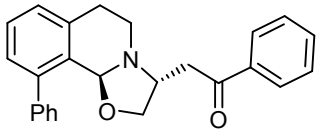
3-(2-phenyl-2-oxo-ethyl)-8-phenyl-oxazolo[2,3-a]tetrahydroisoquinoline (3f).

Recrystallized from ethyl acetate/hexane, yield: 93% (25:1 mixture of two diastereomers); physical state: white solid; mp 132-135 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, *J* = 7.5 Hz, 2H), 7.57-7.55 (m, 3H), 7.48-7.30 (m, 8H), 5.34 (s, 1H), 4.38 (t, *J* = 7.5 Hz, 1H), 3.96-3.87 (m, Hz, 1H), 3.59-3.48 (m, 2H), 3.17 (dd, *J* = 17.7, 7.8 Hz, 1H), 3.07-2.89 (m, 3H), 2.77 (d, *J* = 14.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6, 141.3, 140.8, 136.9, 135.9, 133.3, 130.9, 129.3, 128.8, 128.7, 128.1, 127.4, 127.2, 126.8, 125.3, 89.0, 69.4, 62.3, 47.0, 43.6, 30.0; .HRMS: Calcd. for $C_{25}H_{23}NO_2$: 369.1729. Found: 369.1732.



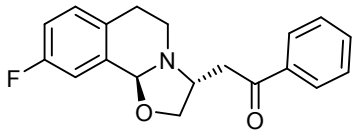
3-(2-phenyl-2-oxo-ethyl)-9-phenyl-oxazolo[2,3-a]tetrahydroisoquinoline (3g).

Recrystallized from ethyl acetate/hexane, yield: 97% (19:1 mixture of two diastereomers); physical state: white solid; mp 134-137 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.2 Hz, 2H), 7.63-7.55 (m, 4H), 7.49-7.39 (m, 4H), 7.34-7.29 (m, 1H), 7.24-7.20 (m, 1H), 5.36 (s, 1H), 4.40 (t, *J* = 7.8 Hz, 1H), 3.97-3.88 (m, 1H), 3.60-3.49 (m, 2H), 3.19 (dd, *J* = 17.7, 7.8 Hz, 1H), 3.07-2.89 (m, 3H), 2.76 (d, *J* = 11.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.7, 140.8, 139.5, 136.9, 134.7, 133.4, 132.3, 128.8, 128.6, 128.1, 127.6, 127.3, 127.2, 127.1, 89.2, 69.5, 62.3, 47.1, 43.7, 29.6; HRMS: Calcd. for $C_{25}H_{23}NO_2$: 369.1729. Found: 369.1721.



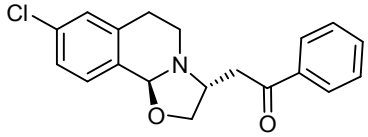
3-(2-phenyl-2-oxo-ethyl)-10-phenyl-oxazolo[2,3-a]tetrahydroisoquinoline (3h).

Recrystallized from ethyl acetate/hexane, yield: 91% (19:1 mixture of two diastereomers); physical state: white solid; mp 120-123 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.2 Hz, 2H), 7.55-7.24 (m, 10H), 7.16-7.09 (m, 2H), 4.96 (s, 1H), 4.30 (t, *J* = 8.1 Hz, 1H), 3.93-3.74 (m, 1H), 3.41 (dd, *J* = 17.7, 6.0 Hz, 1H), 3.13 (dd, *J* = 8.7, 5.1 Hz, 1H), 3.09-2.75 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.5, 143.5, 140.7, 136.7, 135.9, 133.3, 129.7, 128.6, 128.3, 128.0, 127.7, 127.5, 127.0, 86.9, 69.0, 61.8, 47.0, 43.7, 30.1; HRMS: Calcd. for $C_{25}H_{23}NO_2$: 369.1729. Found: 369.1723.



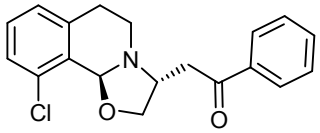
9-fluoro-3-(2-phenyl-2-oxo-ethyl)-oxazolo[2,3-a]tetrahydroisoquinoline (3i).

Recrystallized from ethyl acetate/hexane, yield: 87% (19:1 mixture of two diastereomers); physical state: white solid; mp 110-112 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.5 Hz, 2H), 7.59-7.43 (m, 3H), 7.11-7.06 (m, 2H), 6.94 (td, *J* = 8.7, 2.7 Hz, 1H), 5.23 (s, 1H), 4.35 (t, *J* = 7.8 Hz, 1H), 3.94-3.85 (m, 1H), 3.56-3.45 (m, 2H), 3.15 (dd, *J* = 17.7, 7.8 Hz, 1H), 3.00-2.87 (m, 3H), 2.72-2.65 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.4, 161.2 (d, *J* = 242.6 Hz), 136.8, 133.7 (d, *J* = 7.5 Hz), 133.3, 131.1, 129.6 (d, *J* = 7.5 Hz), 128.7, 128.0, 115.5 (d, *J* = 89.1 Hz), 115.2 (d, *J* = 90.6 Hz), 88.6, 69.3, 62.0, 46.9, 43.4, 29.0; HRMS: Calcd. for $C_{19}H_{18}FNO_2$: 311.1322. Found: 311.1325.



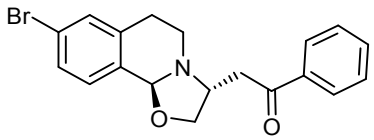
8-chloro-3-(2-phenyl-2-oxo-ethyl)-oxazolo[2,3-a]tetrahydroisoquinoline (3j).

Recrystallized from ethyl acetate/hexane, yield: 91% (14:1 mixture of two diastereomers); physical state: white solid; mp 113-115 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.2 Hz, 2H), 7.61-7.45 (m, 3H), 7.32 (d, *J* = 8.1, Hz, 1H), 7.23-7.14 (m, 2H), 5.24 (s, 1H), 4.37 (t, *J* = 7.8 Hz, 1H), 3.94-3.86 (m, 1H), 3.57-3.45 (m, 2H), 3.17 (dd, *J* = 17.7, 7.8 Hz, 1H), 3.00-2.83 (m, 3H), 2.73-2.67 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.4, 137.4, 136.7, 133.9, 133.3, 130.3, 130.2, 128.6, 128.0, 127.9, 126.6, 88.4, 69.3, 62.0, 46.4, 43.4, 29.6; HRMS: Calcd. for $C_{19}H_{18}ClNO_2$: 327.1026. Found: 327.1034.



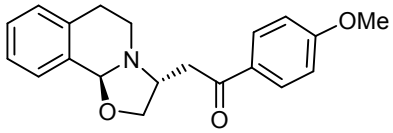
10-chloro-3-(2-phenyl-2-oxo-ethyl)-oxazolo[2,3-a]tetrahydroisoquinoline (3k).

Recrystallized from ethyl acetate/hexane, yield: 80% (14:1 mixture of two diastereomers); physical state: white solid; mp 110-112 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.5 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.25 (d, *J* = 7.5 Hz, 1H), 7.18 (d, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 7.2 Hz, 1H), 5.35 (s, 1H), 4.38 (t, *J* = 7.8 Hz, 1H), 3.97-3.88 (m, 1H), 3.59-3.51 (m, 2H), 3.19 (dd, *J* = 17.7, 7.5 Hz, 1H), 3.05-2.90 (m, 3H), 2.78-2.72 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.4, 138.2, 136.8, 134.9, 133.3, 129.4, 129.3, 128.7, 128.0, 127.6, 126.8, 86.6, 69.0, 61.7, 46.5, 43.5, 30.1; HRMS: Calcd. for $C_{19}H_{18}ClNO_2$: 327.1026. Found: 327.1029.



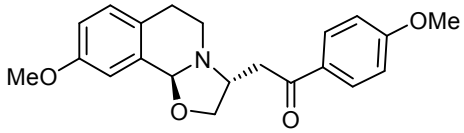
8-bromo-3-(2-phenyl-2-oxo-ethyl)-oxazolo[2,3-a]tetrahydroisoquinoline (3l).

Recrystallized from ethyl acetate/hexane, yield: 93% (14:1 mixture of two diastereomers); physical state: white solid; mp 102-105 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.5 Hz, 2H), 7.55-7.60 (m, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.38-7.31 (m, 2H), 7.27-7.24 (m, 1H), 5.22 (s, 1H), 4.36 (t, *J* = 7.8 Hz, 1H), 3.94-3.85 (m, 1H), 3.57-3.45 (m, 2H), 3.16 (dd, *J* = 17.7, 7.8 Hz, 1H), 3.00-2.85 (m, 3H), 2.73-2.65 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.5, 137.9, 136.8, 133.4, 131.0, 130.5, 129.6, 128.7, 128.1, 122.3, 88.6, 69.4, 62.2, 46.5, 43.6, 29.7; HRMS: Calcd. for $C_{19}H_{18}BrNO_2$: 371.0521. Found: 371.0519.



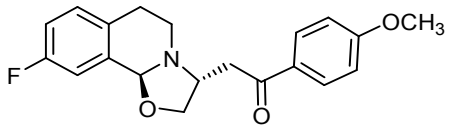
3-[2-(4-methoxy-phenyl)-2-oxo-ethyl]-oxazolo[2,3-a]tetrahydroisoquinoline (4a).

Recrystallized from ethyl acetate/hexane, yield: 90% (9:1 mixture of two diastereomers); physical state: white solid; mp 70-71 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.7 Hz, 2H), 7.41-7.38 (m, 1H), 7.26-7.23 (m, 2H), 7.16-7.13 (m, 1H), 6.94 (d, *J* = 8.7 Hz, 2H), 5.30 (s, 1H), 4.37 (t, *J* = 8.1 Hz, 1H), 3.93-3.85 (m, 4H), 3.54-3.46 (m, 2H), 3.14 (dd, *J* = 17.4, 8.1 Hz, 1H), 2.99-2.90 (m, 3H), 2.74-2.70 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.3, 163.8, 135.6, 132.0, 130.5, 130.2, 129.0, 128.4, 128.2, 126.4, 113.9, 89.2, 69.5, 62.5, 55.6, 47.1, 43.3, 29.9; HRMS: Calcd. for $C_{20}H_{21}NO_3$: 323.1521. Found: 323.1524.



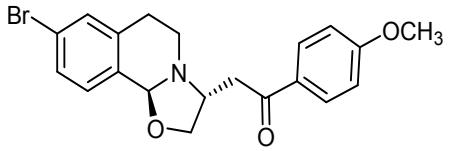
3-[2-(4-methoxy-phenyl)-2-oxo-ethyl]-9-methoxy-oxazolo[2,3-a]tetrahydroisoquinoline (4b).

Recrystallized from ethyl acetate/hexane, yield: 92% (17:1 mixture of two diastereomers); physical state: white solid; mp 81-82 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 9 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.94 (d, *J* = 9 Hz, 3H), 6.82 (dd, *J* = 8.4, 2.4 Hz, 1H), 5.27 (s, 1H), 4.36 (t, *J* = 7.8 Hz, 1H), 3.93-3.85 (m, 4H), 3.79 (s, 3H), 3.53-3.45 (m, 2H), 3.13 (dd, *J* = 17.4, 7.2 Hz, 1H), 2.98-2.87 (m, 3H), 2.70-2.63 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.2, 163.7, 158.1, 132.8, 130.4, 130.0, 129.1, 127.6, 115.5, 113.8, 112.7 89.2, 69.4, 62.3, 55.5, 55.4, 47.3; HRMS: Calcd. for $C_{21}H_{23}NO_4$: 353.1627. Found: 353.1636.



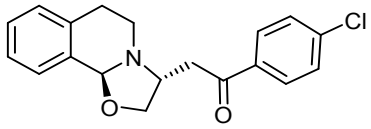
9-fluoro3-[2-(4-methoxy-phenyl)-2-oxo-ethyl]-oxazolo[2,3-a]tetrahydroisoquinoline (4c).

Recrystallized from ethyl acetate/hexane, yield: 95% (18:1 mixture of two diastereomers); physical state: white solid; mp 68-69 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.7 Hz, 2H), 7.12-7.08 (m, 2H), 6.98-6.93 (m, 3H), 5.29 (s, 1H), 4.36 (t, *J* = 8.1 Hz, 1H), 3.93-3.85 (m, 4H), 3.52-3.44 (m, 2H), 3.12 (dd, *J* = 17.4, 8.1 Hz, 1H), 3.00-2.86 (m, 3H), 2.74-2.67 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.0, 163.7, 161.3 (d, *J* = 242.9 Hz), 133.8 (d, *J* = 7.4 Hz), 131.2, 130.4, 130.0, 129.6 (d, *J* = 7.6 Hz), 115.6 (t, *J* = 87.9 Hz), 115.3 (d, *J* = 92.7 Hz), 113.8, 88.6, 69.5, 62.2, 55.5, 47.0, 43.1, 29.1; HRMS: Calcd. for $C_{20}H_{20}FNO_3$: 341.1427. Found: 341.1422.



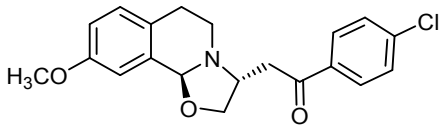
8-bromo-3-[2-(4-methoxy-phenyl)-2-oxo-ethyl]-oxazolo[2,3-a]tetrahydroisoquinoline (4d).

Recrystallized from ethyl acetate/hexane, yield: 88% (25:1 mixture of two diastereomers); physical state: white solid; mp 92-93 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.7 Hz, 2H), 7.38-7.25 (m, 4H), 6.94 (d, *J* = 8.7 Hz, 2H), 5.23 (s, 1H), 4.35 (t, *J* = 8.1 Hz, 1H), 3.93-3.85 (m, 4H), 3.52-3.44 (m, 2H), 3.11 (dd, *J* = 17.4, 7.8 Hz, 1H), 2.99-2.82 (m, 3H), 2.70-2.65 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.0, 163.7, 137.9, 131.0, 130.6, 130.4, 130.0, 129.6, 122.3, 113.9, 88.6, 69.5, 62.3, 55.6, 46.5, 43.2, 29.7; HRMS: Calcd. for $C_{20}H_{20}BrNO_3$: 401.0627. Found: 401.0633.



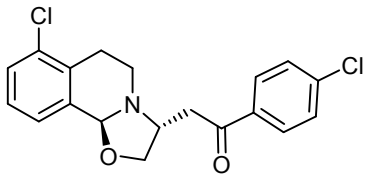
3-[2-(4-Chloro-phenyl)-2-oxo-ethyl]-oxazolo[2,3-a]tetrahydroisoquinoline (4e).

Recrystallized from ethyl acetate/hexane, yield: 90% (13:1 mixture of two diastereomers); physical state: white solid; mp 83-84 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.7 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.26-7.24 (m, 3H), 7.16-7.13 (m, 1H), 5.29 (s, 1H), 4.37 (t, *J* = 8.1 Hz, 1H), 3.93-3.84 (m, 1H), 3.55-3.46 (m, 2H), 3.13 (dd, *J* = 17.4, 7.5 Hz, 1H), 2.99-2.91 (m, 3H), 2.78-2.70 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.6, 139.9, 135.6, 135.4, 131.9, 130.2, 129.7, 129.1, 129.0, 128.5, 128.2, 126.5, 89.2, 69.4, 62.3, 47.1, 43.7, 29.9; HRMS: Calcd. for $C_{19}H_{18}ClNO_2$: 327.1026. Found: 327.1035.



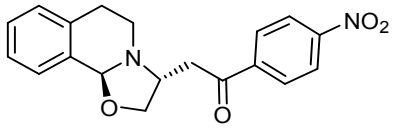
3-[2-(4-Chloro-phenyl)-2-oxo-ethyl]-9-methoxy-oxazolo[2,3-a]tetrahydroisoquinoline (4f).

Recrystallized from ethyl acetate/hexane, yield: 92% (13:1 mixture of two diastereomers); physical state: white solid; mp 113-114 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.92 (d, *J* = 2.4 Hz, 1H), 6.82 (dd, *J* = 8.4, 2.7 Hz, 1H), 5.26 (s, 1H), 4.36 (t, *J* = 7.8 Hz, 1H), 3.92-3.83 (m, 1H), 3.79 (s, 3H), 3.54-3.45 (m, 2H), 3.12 (dd, *J* = 17.4, 7.8 Hz, 1H), 2.97-2.86 (m, 3H), 2.70-2.63 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.5, 158.2, 139.9, 135.3, 132.8, 129.6, 129.2, 129.1, 127.6, 115.6, 112.9, 89.3, 69.4, 62.3, 55.5, 47.4, 43.7, 29.0; HRMS: Calcd. for $C_{20}H_{20}ClNO_3$: 357.1132. Found: .357.1125.



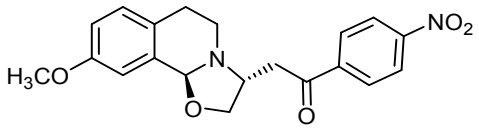
3-[2-(4-Chloro-phenyl)-2-oxo-ethyl]-7-chloro-oxazolo[2,3-a]tetrahydroisoquinoline (4g).

Recrystallized from ethyl acetate/hexane, yield: 90% (13:1 mixture of two diastereomers); physical state: white solid; mp 102 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.36-7.30 (m, 2H), 7.22-7.17 (m, 1H), 5.25 (s, 1H), 4.37 (t, *J* = 7.8 Hz, 1H), 3.89 (m, 1H), 3.54-3.45 (m, 2H), 3.12 (dd, *J* = 17.4, 7.5 Hz, 1H), 3.05-2.75 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ197.3, 139.9, 135.2, 133.8, 133.6, 129.5, 129.1, 127.5, 127.3, 88.7, 69.3, 62.0, 46.4, 43.5, 27.7; HRMS: Calcd. for $C_{19}H_{17}Cl_2NO_3$: 361.0636. Found: .361.0645.



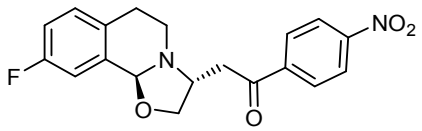
3-[2-(4-nitro-phenyl)-2-oxo-ethyl]-oxazolo[2,3-a]tetrahydroisoquinoline (4h).

Recrystallized from ethyl acetate/hexane, yield: 88% (25:1 mixture of two diastereomers); physical state: yellow solid; mp 94-95 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.7 Hz, 2H), 8.14 (d, *J* = 9.0, Hz, 2H), 7.41-7.38 (m, 1H), 7.27-7.24 (m, 2H), 7.16-7.13 (m, 1H), 5.29 (s, 1H), 4.38 (t, *J* = 8.1 Hz, 1H), 3.93-3.88 (m, 1H), 3.59 (dd, *J* = 17.7, 6.9 Hz, 1H), 3.52-3.48 (m, 1H), 3.17 (dd, *J* = 17.7, 6.9 Hz, 1H), 2.99-2.90 (m, 3H), 2.77-2.70 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.2, 150.4, 141.3, 135.4, 131.6, 129.2, 128.9, 128.5, 128.1, 126.4, 124.0, 89.1, 69.1, 62.1, 47.0, 44.1, 29.8; ESI-MS: Calcd. for $C_{19}H_{19}N_2O_4$: 339.1339. Found: 339.1342.



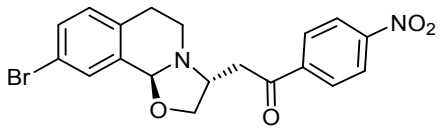
9-methoxy-3-[2-(4-nitro-phenyl)-2-oxo-ethyl]-oxazolo[2,3-a]tetrahydroisoquinoline (4i).

Recrystallized from ethyl acetate/hexane, yield: 92% (25:1 mixture of two diastereomers); physical state: yellow solid; mp 118-119 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.7 Hz, 2H), 8.13 (d, *J* = 8.7, Hz, 2H), 7.06 (d, *J* = 8.4, Hz, 1H), 6.92 (d, *J* = 2.4, Hz, 1H), 6.83 (dd, *J* = 8.4, 2.7, Hz, 1H), 5.26 (s, 1H), 4.38 (t, *J* = 7.8 Hz, 1H), 3.94-3.86 (m, 1H), 3.80 (s, 3H), 3.62-3.47 (m, 2H), 3.70 (dd, *J* = 17.4, 6.9 Hz, 1H), 2.98-2.86 (m, 1H), 2.98-2.86 (m, 3H), 2.71-2.63 (m, 1H);^{13}C NMR (50 MHz, $CDCl_3$) δ 197.2, 158.1, 150.4, 141.3, 132.5, 129.2, 127.5, 124.0, 115.5, 112.8, 89.2, 69.1, 62.1, 55.4, 47.4, 44.1, 29.0; ESI-MS: Calcd. for $C_{20}H_{21}N_2O_5$: 369.1445. Found: 369.1433.



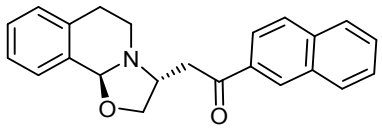
9-fluoro-3-[2-(4-nitro-phenyl)-2-oxo-ethyl]-oxazolo[2,3-a]tetrahydroisoquinoline (4j).

Recrystallized from ethyl acetate/hexane, yield: 90% (22:1 mixture of two diastereomers); physical state: yellow solid; mp 88-89 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.7 Hz, 2H), 8.13 (d, *J* = 8.7, Hz, 2H), 7.11-7.07 (m, 2H), 6.92 (td, *J* = 8.4, 2.7, Hz, 1H), 5.24 (s, 1H), 4.37 (t, *J* = 7.8 Hz, 1H), 3.95-3.87 (m, 1H), 3.61-3.47 (m, 2H), 3.17 (dd, *J* = 17.7, 6.9 Hz, 1H), 3.00-2.87 (m, 3H), 2.75-2.86 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 197.1, 161.34 (d, *J* = 243 Hz), 150.4, 141.2, 133.4 (d, *J* = 7.2 Hz), 131.1, 129.7 (d, *J* = 7.8 Hz), 129.1, 123.9, 115.7 (d, *J* = 21.8 Hz), 115.3 (d, *J* = 21.8 Hz), 88.2, 69.1, 61.9, 47.0, 44.0, 29.1; ESI-MS: Calcd. for $C_{19}H_{18}FN_2O_4$: 357.1245. Found: 357.1234.



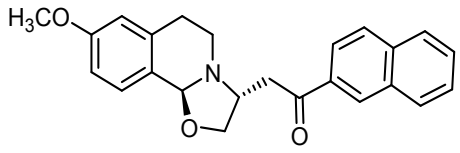
9-bromo-3-[2-(4-nitro-phenyl)-2-oxo-ethyl]-oxazolo[2,3-a]tetrahydroisoquinoline (4k).

Recrystallized from ethyl acetate/hexane, yield: 89% (25:1 mixture of two diastereomers); physical state: yellow solid; mp 120-121 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.7 Hz, 2H), 8.13 (d, *J* = 8.7, Hz, 2H), 7.54 (s, 1H), 7.37 (d, *J* = 8.1, Hz, 1H), 7.03 (d, *J* = 8.1, Hz, 1H), 5.22 (s, 1H), 4.37 (t, *J* = 7.8 Hz, 1H), 3.92-3.86 (m, 1H), 3.61-3.47 (m, 2H), 3.16 (dd, *J* = 17.7, 6.9 Hz, 1H), 3.01-2.81 (m, 3H), 2.73-2.66 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.0, 150.5, 159.6, 141.2, 134.5, 133.8, 131.7, 131.5, 129.8, 129.2, 124.0, 119.9, 88.4, 69.2, 61.9, 46.8, 44.0, 29.3; ESI-MS: Calcd. for $C_{19}H_{18}BrN_2O_4$: 417.0444. Found: 417.0462.



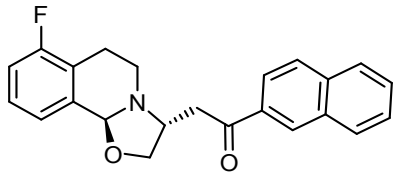
3-[2-(naphthalene-2-yl)-2-oxo-ethyl]-oxazolo[2,3-a]tetrahydroisoquinoline (4l).

Recrystallized from ethyl acetate/hexane, yield: 93% (15:1 mixture of two diastereomers); physical state: white solid; mp 100-101 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.04 (d, *J* = 8.7 Hz, 1H), 7.97-7.87 (m, 3H), 7.63-7.53 (m, 2H), 7.42-7.40 (m, 1H), 7.26-7.24 (m, 2H), 7.16-7.13(m, 1H), 5.35 (s, 1H), 4.42 (t, *J* = 8.1 Hz, 1H), 4.00-3.92 (m, 1H), 3.70 (dd, *J* = 17.7, 6.3 Hz, 1H), 3.54 (dd, *J* = 8.4, 4.8 Hz, 1H), 3.33 (dd, *J* = 17.4, 7.8 Hz, 1H), 3.03-2.92 (m, 3H), 2.78-2.71 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6, 135.7, 135.5, 134.2, 132.5, 131.9, 130.0, 129.7, 128.9, 128.7, 128.6, 128.4, 128.1, 127.9, 126.9, 126.4, 123.7, 89.1, 69.5, 62.4, 47.0, 43.7, 29.9; HRMS: Calcd. for $C_{23}H_{21}NO_2$: 343.1572. Found: 343.1570.



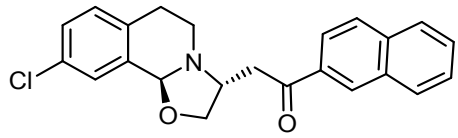
8-methoxy-3-[2-(naphthalene-2-yl)-2-oxo-ethyl]-oxazolo[2,3-a]tetrahydroisoquinoline (4m).

Recrystallized from ethyl acetate/hexane, yield: 90% (21:1 mixture of two diastereomers); physical state: white solid; mp 100-101 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.06 (d, *J* = 8.7 Hz, 1H), 7.99-7.89 (m, 3H), 7.66-7.55 (m, 2H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.96 (d, *J* = 2.4 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 5.35 (s, 1H), 4.43 (t, *J* = 7.8 Hz, 1H), 3.98 (m, 1H), 3.82 (s, 3H), 3.71 (dd, *J* = 17.4, 6 Hz, 1H), 3.56 (dd, *J* = 8.4, 4.8 Hz, 1H), 3.35 (dd, *J* = 17.4, 7.8 Hz, 1H), 3.03-2.89 (m, 3H), 2.74-2.67 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ; HRMS: Calcd. for $C_{24}H_{23}NO_3$: 373.1678. Found: 373.1669.



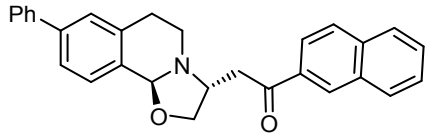
7-fluoro-3-[2-(naphthalene-2-yl)-2-oxo-ethyl]-oxazolo[2,3-a]tetrahydroisoquinoline (4n).

Recrystallized from ethyl acetate/hexane, yield: 92% (14:1 mixture of two diastereomers); physical state: white solid; mp 118 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.04 (d, *J* = 8.7 Hz, 1H), 7.97-7.89 (m, 3H), 7.64-7.53 (m, 2H), 7.22-7.21 (m, 2H), 7.02-6.96 (m, 1H), 5.33 (s, 1H), 4.42 (t, *J* = 8.1 Hz, 1H), 4.02-3.93 (m, 1H), 3.69 (dd, *J* = 17.7, 6.3 Hz, 1H), 3.55 (dd, *J* = 8.4, 4.8 Hz, 1H), 3.32 (dd, *J* = 17.7, 7.8 Hz, 1H), 3.07-3.03 (m, 1H), 2.97-2.69 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.4, 160.4 (d, *J* = 243.7 Hz), 135.8, 134.2, 132.5, 130.0, 129.7, 128.7 (d, *J* = 4.5Hz), 127.9, 127.5(d, *J* = 7.6 Hz), 127.0, 124.5, 123.7, 123.4, 123.2, 114.7 (d, *J* = 21.2 Hz), 88.4, 69.5, 62.2, 46.1, 43.7, 22.9; HRMS: Calcd. for $C_{24}H_{25}FNO_3$: 361.1478. Found: 361.1485.



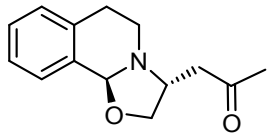
9-chloro-3-[2-(naphthalene-2-yl)-2-oxo-ethyl]-oxazolo[2,3-a]tetrahydroisoquinoline (4o).

Recrystallized from ethyl acetate/hexane, yield: 93% (16:1 mixture of two diastereomers); physical state: white solid; mp 95-96 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.97-7.86 (m, 3H), 7.63-7.53 (m, 2H), 7.40 (s, 1H), 7.25-7.20 (m, 1H), 7.07 (d, *J* = 7.8 Hz, 1H), 5.28 (s, 1H), 4.40 (t, *J* = 7.8 Hz, 1H), 3.97-3.64 (m, 1H), 3.67 (dd, *J* = 17.7, 6.3 Hz, 1H), 3.56-3.51 (m, 1H), 3.29 (dd, *J* = 17.4, 7.5 Hz, 1H), 3.02-2.89 (m, 3H), 2.72-2.67 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.4, 135.7, 134.1, 134.0, 133.7, 132.5, 131.9, 129.9, 129.5, 128.8, 128.7, 128.6, 128.5, 127.8, 126.9, 123.6, 88.5, 69.4, 62.2, 46.8, 43.6, 29.3; HRMS: Calcd. for $C_{23}H_{20}ClNO_2$: 377.1183. Found: 377.1184.



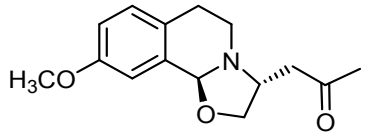
3-[2-(naphthalene-2-yl)-2-oxo-ethyl]-8-phenyl-oxazolo[2,3-a]tetrahydroisoquinoline (4p).

Recrystallized from ethyl acetate/hexane, yield: 92% (17:1 mixture of two diastereomers); physical state: white solid; mp 95-96 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.06 (dd, *J* = 8.7, 1.5 Hz, 1H), 7.98-7.87 (m, 3H), 7.64-7.54 (m, 4H), 7.48-7.34 (m, 6H), 5.40 (s, 1H), 4.43 (t, *J* = 7.5 Hz, 1H), 4.01-3.96 (m, 1H), 3.71 (dd, *J* = 17.4, 6.3 Hz, 1H), 3.57 (dd, *J* = 8.4, 4.8 Hz, 1H), 3.34 (dd, *J* = 17.4, 7.8 Hz, 1H), 3.06-2.96 (m, 3H), 2.82-2.78 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6, 141.3, 140.9, 136.0, 135.8, 134.3, 132.6, 131.0, 130.0, 129.7, 129.3, 128.8, 128.7, 129.7, 127.5, 127.2, 127.0, 126.8, 125.4, 123.8, 89.1, 69.5, 62.4, 47.1, 43.8, 30.1.



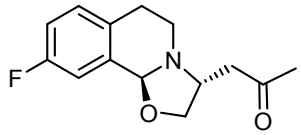
3-(2-methyl-2-oxo-ethyl)-oxazolo[2,3-a]tetrahydroisoquinoline (4q).

Physical state: yellow oil, yield: 92% (12:1 mixture of two diastereomers); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.35 (m, 1H), 7.24-7.21 (m, 2H), 7.14 (m, 1H), 5.20 (s, 1H), 4.23 (t, *J* = 8.1 Hz, 1H), 3.73-3.64 (m, 1H), 3.36 (dd, *J* = 8.4, 4.8 Hz, 1H), 2.97-2.86 (m, 4H), 2.73-2.55 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.3, 135.3, 131.6, 128.8, 128.3, 128.0, 126.2, 88.9, 68.7, 61.8, 48.1, 46.8, 30.7, 29.6; HRMS: Calcd. for $C_{14}H_{17}NO_2$: 231.1259. Found: 231.1257.



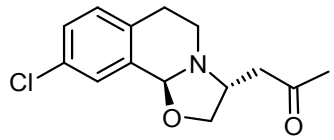
9-methoxy-3-(2-methyl-2-oxo-ethyl)-oxazolo[2,3-a]tetrahydroisoquinoline (4r).

Physical state: yellow oil, yield: 95% (7:1 mixture of two diastereomers); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.05 (d, *J* = 8.7 Hz, 1H), 6.90 (d, *J* = 2.7 Hz, 1H), 6.82 (dd, *J* = 8.7, 2.7 Hz, 1H), 5.19 (s, 1H), 4.24 (t, *J* = 7.9 Hz, 1H), 3.79 (s, 3H), 3.74-3.65 (m, 1), 3.37 (dd, *J* = 8.4, 4.8 Hz, 1H), 2.98-2.82 (m, 4H), 2.66-2.57 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.1, 157.9, 132.5, 128.9, 127.3, 115.2, 112.6, 88.9, 68.6, 61.7, 55.2, 47.9, 47.0, 30.6, 28.7; HRMS: Calcd. for $C_{15}H_{19}NO_3$: 261.1365. Found: 261.1358.



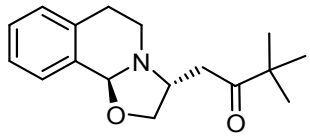
9-fluoro-3-(2-methyl-2-oxo-ethyl)-oxazolo[2,3-a]tetrahydroisoquinoline (4s).

Physical state: yellow oil, yield: 90% (25:1 mixture of two diastereomers); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12-7.06 (m, 2H), 6.99-6.92 (m, 1H), 5.16 (s, 1H), 4.24 (t, *J* = 7.8 Hz, 1H), 3.73-3.69 (m, 1H), 3.37 (dd, *J* = 8.4, 4.8 Hz, 1H), 2.97-2.81 (m, 4H), 2.72-2.57 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.0, 161.0 (d, *J* = 242.6 Hz), 133.5 (d, *J* = 7.2 Hz), 131.0, 129.4 (d, *J* = 7.5 Hz), 115.3 (d, *J* = 88.5 Hz), 115.0 (d, *J* = 89.7 Hz), 88.3, 68.6, 61.5, 47.8, 46.7, 30.5, 28.8; HRMS: Calcd. for $C_{14}H_{16}FNO_2$: 249.1165. Found: 249.1162.



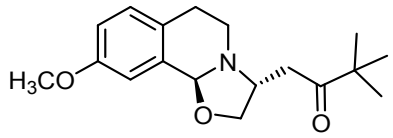
9- chloro-3-(2-methyl-2-oxo-ethyl)-oxazolo[2,3-a]tetrahydroisoquinoline (4t).

Physical state: yellow oil, yield: 91% (14:1 mixture of two diastereomers); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12-7.06 (m, 2H), 6.98-6.92 (m, 1H), 5.16 (s, 1H), 4.23 (t, *J* = 7.8 Hz, 1H), 3.75-3.66 (m, 1H), 3.37 (dd, *J* = 8.4, 4.8 Hz, 1H), 2.97-2.80 (m, 4H), 2.71-2.62 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.1, 133.9, 133.5, 131.8, 129.4, 128.7, 128.4, 88.3, 68.8, 61.7, 48.0, 46.6, 30.7, 29.2; HRMS: Calcd. for $C_{14}H_{16}ClNO_2$: 265.0870. Found: 265.0865.



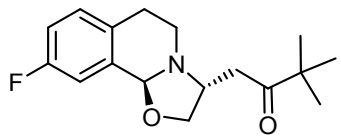
3-[2-(*t*-butyl)-2-oxo-ethyl]-2-oxo-ethyl-oxazolo[2,3-a]tetrahydroisoquinoline (4u).

Physical state: yellow oil, yield: 96% (25:1 mixture of two diastereomers); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.36 (m, 1H), 7.27-7.22 (m, 2H), 7.14-7.11 (m, 1H), 5.22 (s, 1H), 4.27 (t, *J* = 7.8 Hz, 1H), 3.76-3.68 (m, 1H), 3.33 (dd, *J* = 8.1, 4.8 Hz, 1H), 3.05 (dd, *J* = 7.7, 6.3 Hz, 1H), 2.97-2.84 (m, 3H), 2.72-2.63 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.7, 135.4, 131.8, 128.8, 128.3, 128.0, 126.3, 88.9, 69.2, 62.2, 46.9, 44.1, 41.5, 29.8, 26.3; HRMS: Calcd. for $C_{17}H_{23}NO_2$: 2731729. Found: 273.1722.



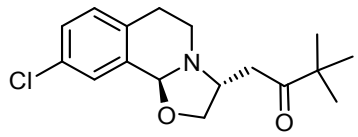
3-[2-(*t*-butyl)-2-oxo-ethyl]-9-methoxy-2-oxo-ethyl-oxazolo[2,3-a]tetrahydroisoquinoline (4v).

Physical state: yellow oil, yield: 96% (25:1 mixture of two diastereomers); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.03 (d, *J* = 8.4 Hz, 1H), 6.9 (d, *J* = 6.9 Hz, 1H), 6.81 (dd, *J* = 8.1, 2.4 Hz, 1H), 5.19 (s, 1H), 4.26 (t, *J* = 8.1 Hz, 1H), 3.78-3.67 (m, 4H), 3.33 (dd, *J* = 8.4, 4.8 Hz, 1H), 3.04 (dd, *J* = 17.4, 6.0 Hz, 1H), 2.90-2.80 (m, 3H), 2.72-2.61 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.7, 158.1, 132.8, 129.1, 127.6, 115.5, 112.7, 89.1, 69.2, 62.2, 55.3, 47.3, 44.1, 41.6, 29.0; HRMS: Calcd. for $C_{18}H_{25}NO_3$: 303.1834. Found: 303.1831.



9-fluoro-3-[2-(*t*-butyl)-2-oxo-ethyl]-2-oxo-ethyl-oxazolo[2,3-a]tetrahydroisoquinoline (4w).

Physical state: yellow oil, yield: 91% (25:1 mixture of two diastereomers); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12-7.06 (m, 2H), 6.94 (td, *J* = 8.4, 2.4 Hz, 1H), 5.17 (s, 1H), 4.26 (t, *J* = 8.1 Hz, 1H), 3.77-3.68 (m, 1H), 3.33 (dd, *J* = 8.4, 4.8 Hz, 1H), 3.03 (dd, *J* = 17.4, 6.3 Hz, 1H), 2.92-2.80 (m, 3H), 2.71-2.63 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.7, 161.3 (d, *J* = 242.5 Hz), 133.9 (d, *J* = 7.2 Hz), 131.3, 129.7 (d, *J* = 7.5 Hz), 115.6 (d, *J* = 87.3 Hz), 115.3 (d, *J* = 88.5 Hz), 88.7, 69.3, 62.2, 47.0, 44.2, 41.6, 29.2, 26.4; HRMS: Calcd. for $C_{17}H_{22}FNO_2$: 291.1635. Found: 291.1631.



9- chloro-3-[2-(*t*-butyl)-2-oxo-ethyl]-2-oxo-ethyl-oxazolo[2,3-a]tetrahydroisoquinoline (4x).

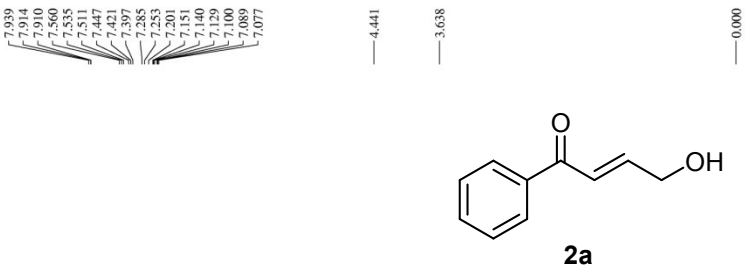
Physical state: yellow oil, yield: 92% (25:1 mixture of two diastereomers); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (s, 1H), 7.20 (d, *J* = 8.1 Hz, 1H), 7.06 (d, *J* = 8.1 Hz, 1H), 5.16 (s, 1H), 4.26 (t, *J* = 7.8 Hz, 1H), 3.76-3.67 (m, 1H), 3.33 (dd, *J* = 8.4, 4.8 Hz, 1H), 3.03 (dd, *J* = 17.7, 6.3 Hz, 1H), 2.93-2.80 (m, 3H), 2.70-2.62 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.7, 134.1, 133.8, 131.9, 129.5, 128.8, 128.5, 88.5, 69.3, 62.2, 46.8, 44.2, 41.6, 29.4, 26.4; HRMS: Calcd. for $C_{17}H_{22}ClNO_2$: 307.1339. Found: 307.1337.

Reference

[1] T. Inokuma, K. Takasu, T. Sakaeda, and Y. Takemoto, *Org. Lett.,* **2006**, *11*, 2425-2428.

[2] B. W. Greatrex, M. C. Kimber, D. K. Taylor, E. R. T. Tiekink., *J. Org. Chem*. **2003**, *68*, 4239-4246.

NMR Spectra of Product



2a

Figure S1: ^{1}H NMR spectra of compound **2a**.

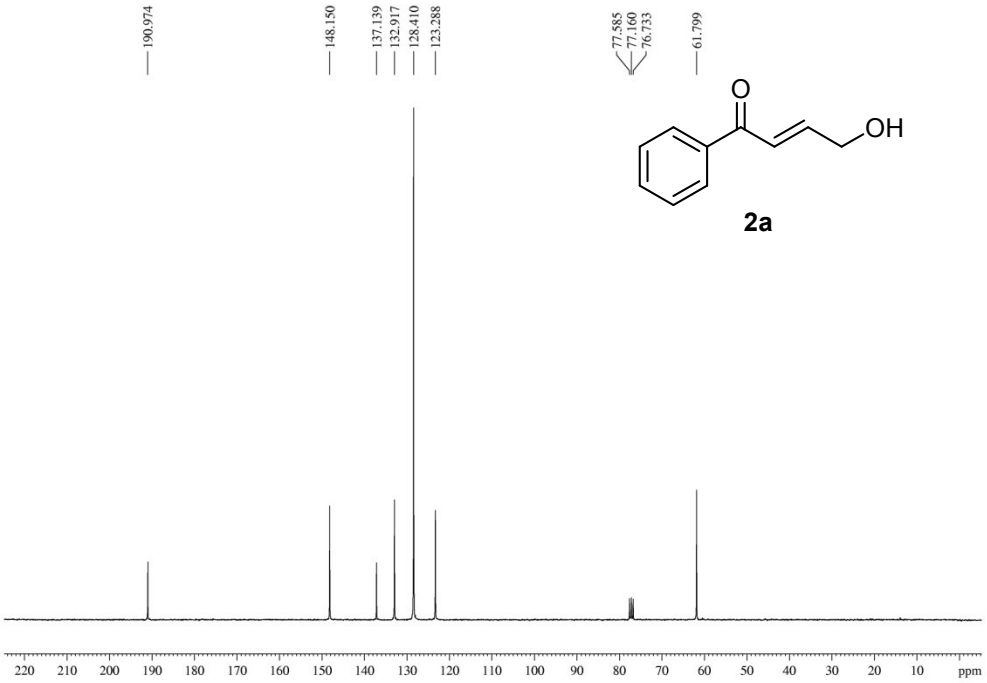


Figure S2: ^{13}C NMR spectra of compound **2a**.

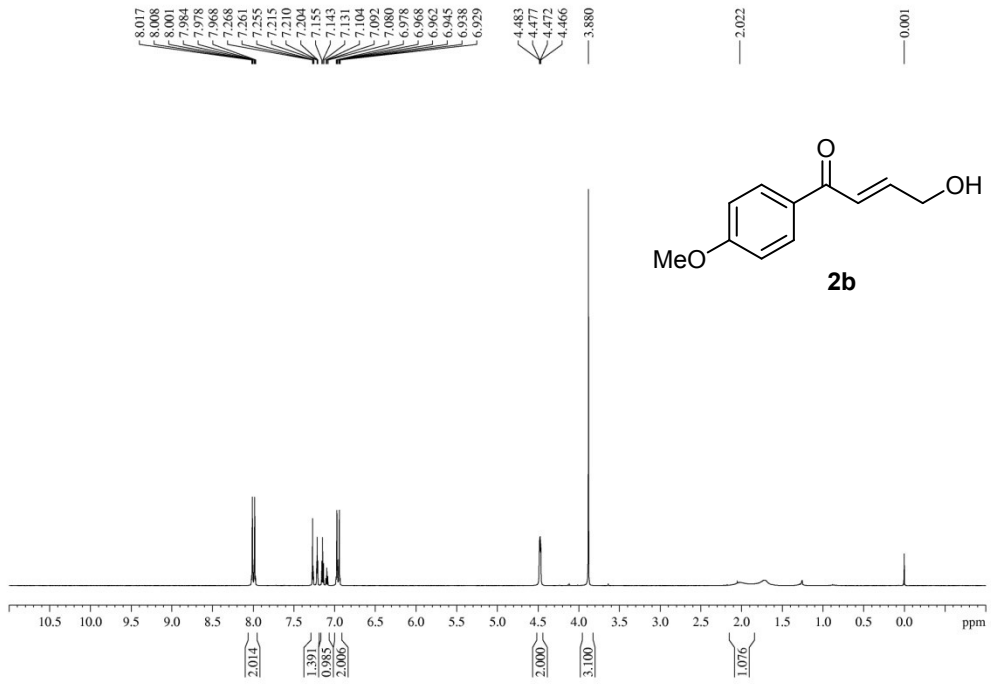


Figure S3: ^{1}H NMR spectra of compound **2b**.

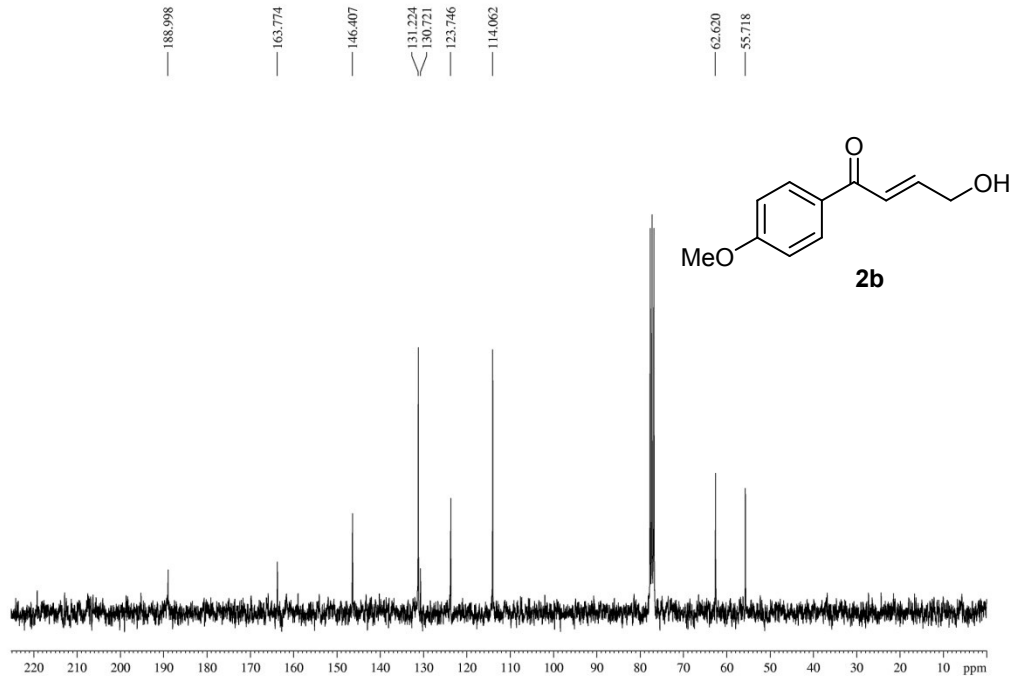


Figure S4: ^{13}C NMR spectra of compound **2b**.

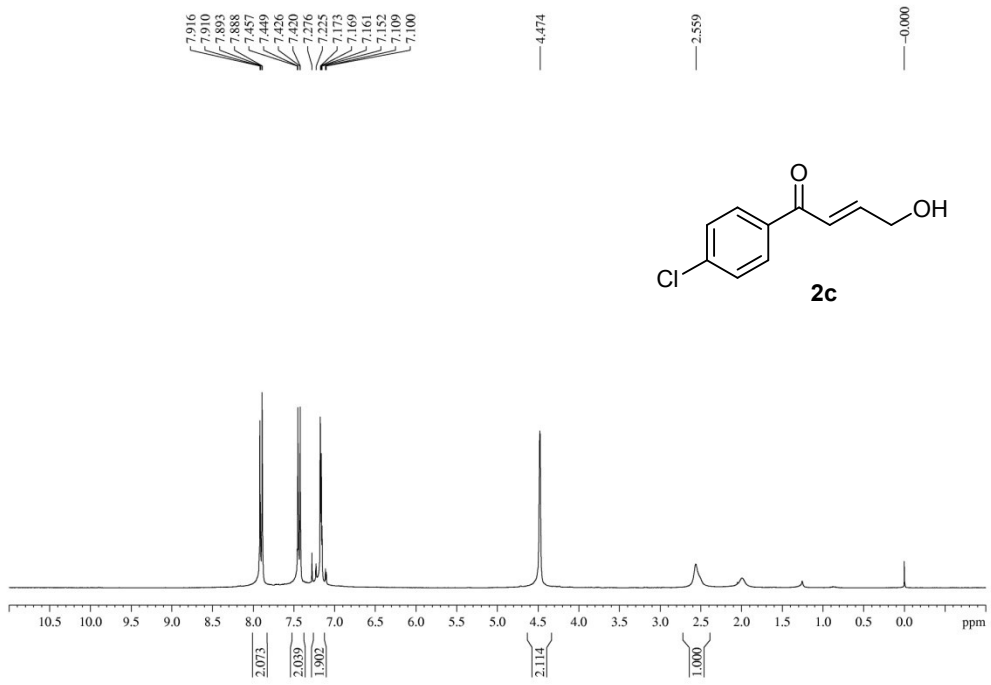


Figure S5: ^{1}H NMR spectra of compound **2c**.

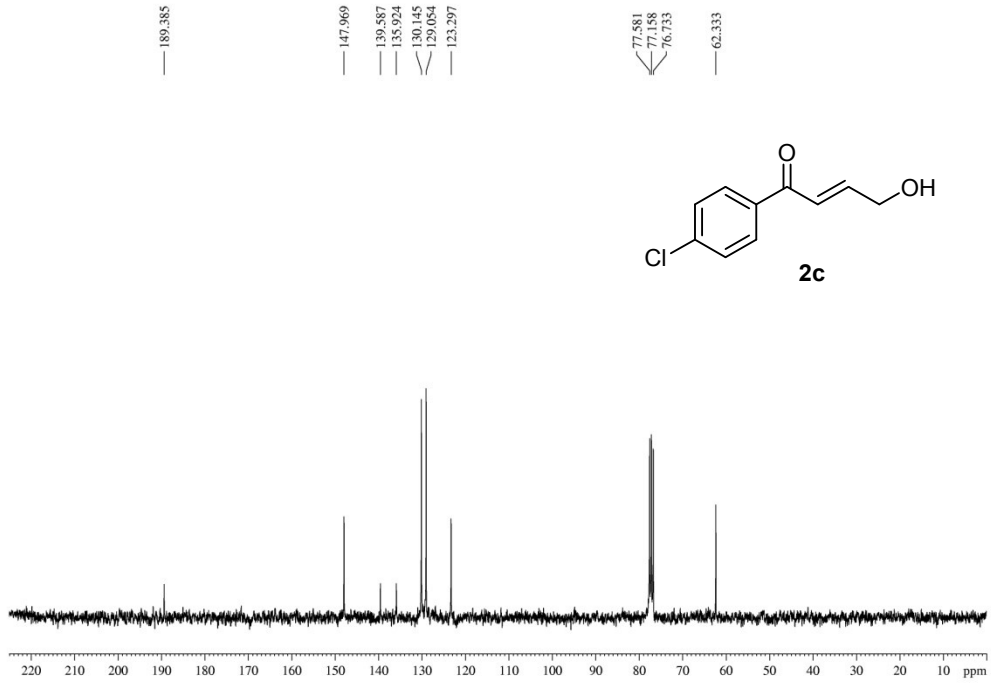


Figure S6: ^{13}C NMR spectra of compound **2c**.

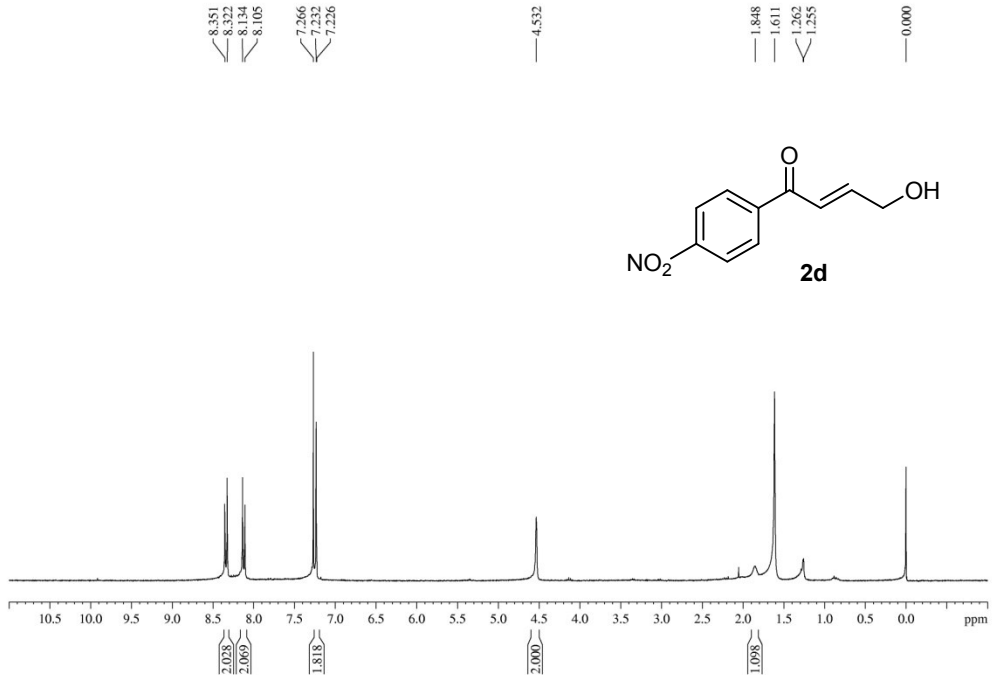


Figure S7: ^{1}H NMR spectra of compound **2d**.

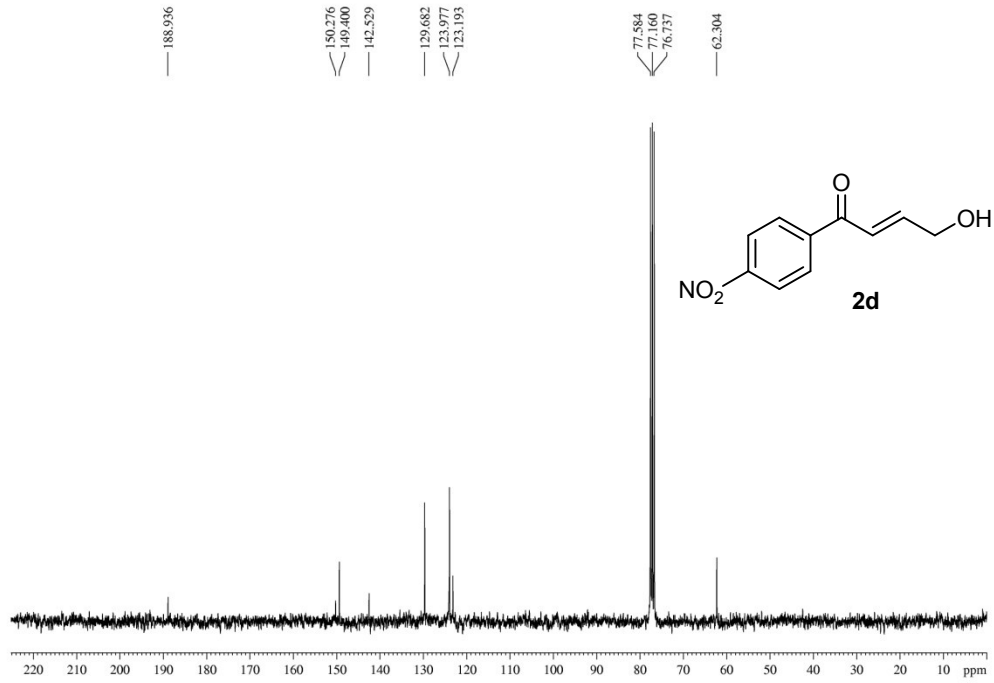


Figure S8: ^{13}C NMR spectra of compound **2d**.

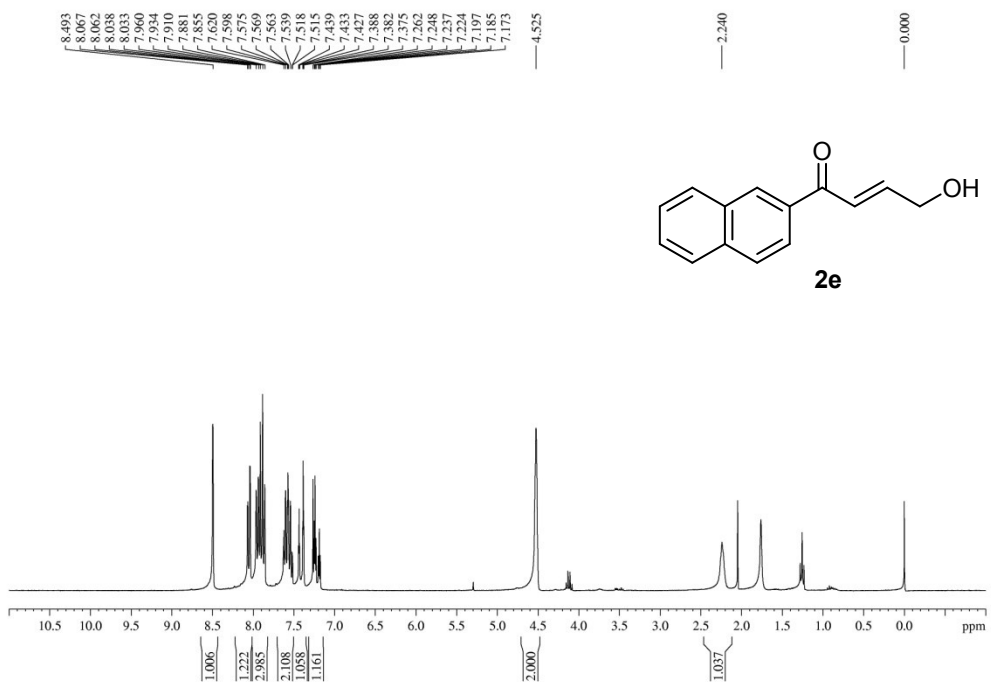


Figure S9: ^{1}H NMR spectra of compound **2e**.

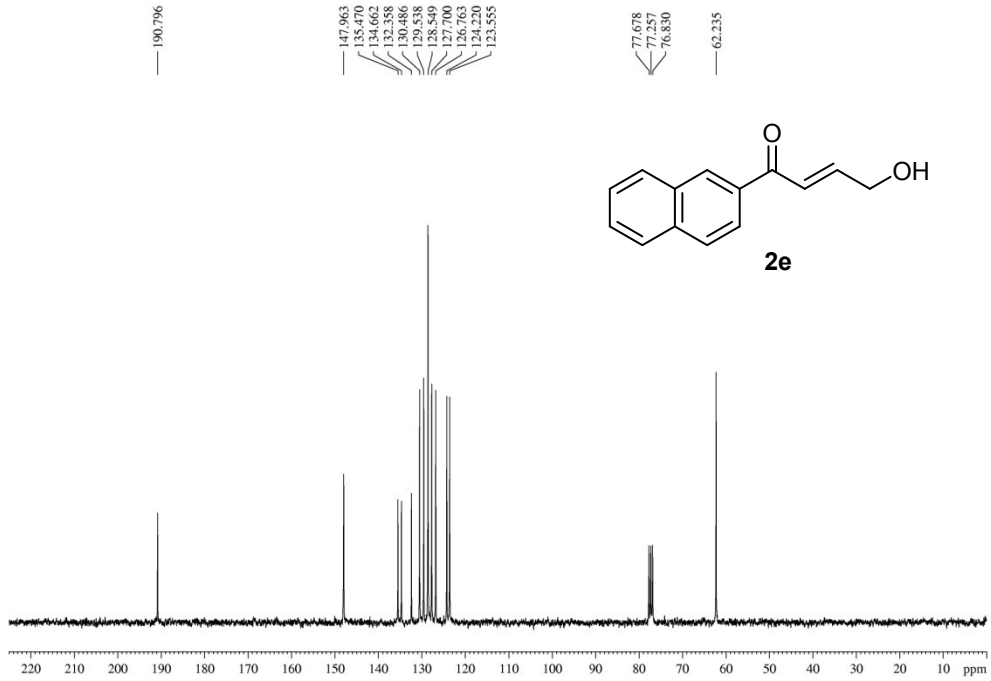


Figure S10: ^{13}C NMR spectra of compound **2e**.

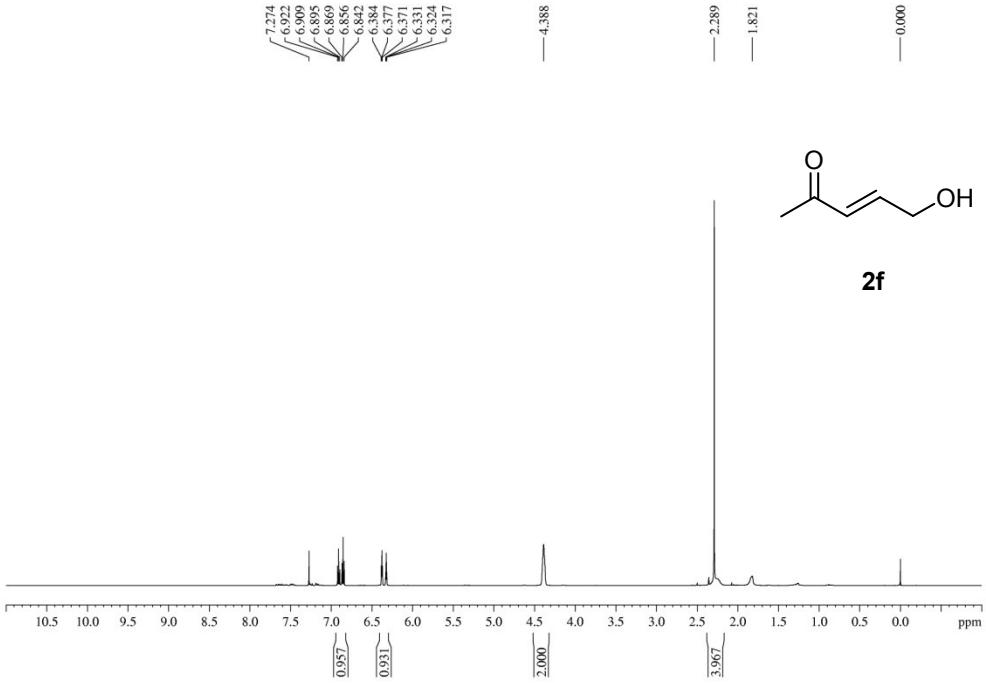


Figure S11: ^{1}H NMR spectra of compound **2f**.

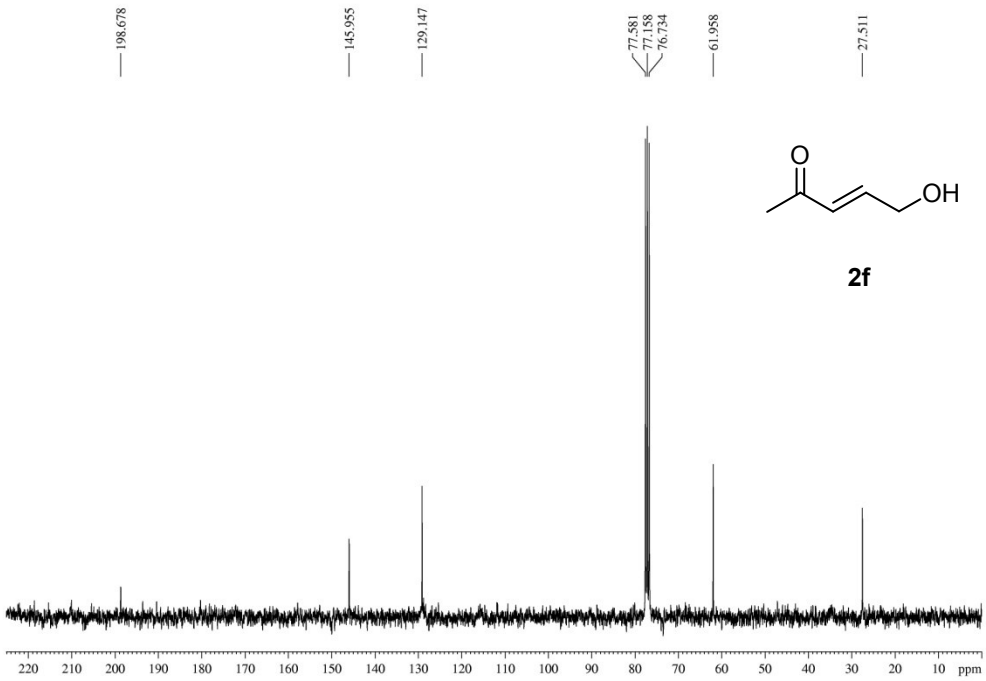


Figure S12: ^{13}C NMR spectra of compound **2f**.

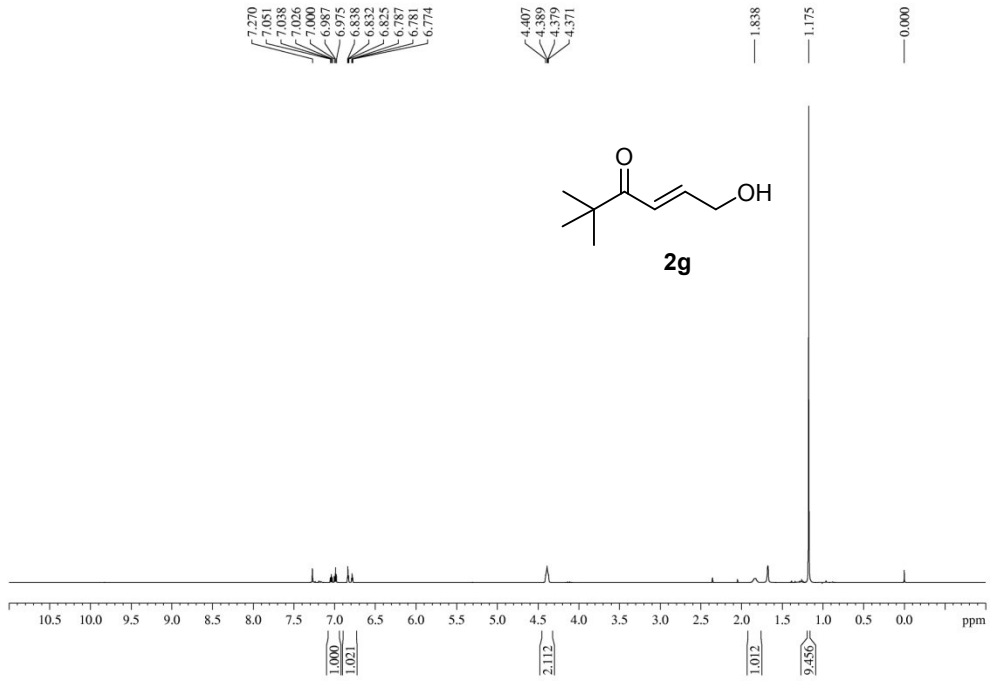


Figure S13: ^{1}H NMR spectra of compound **2g**.

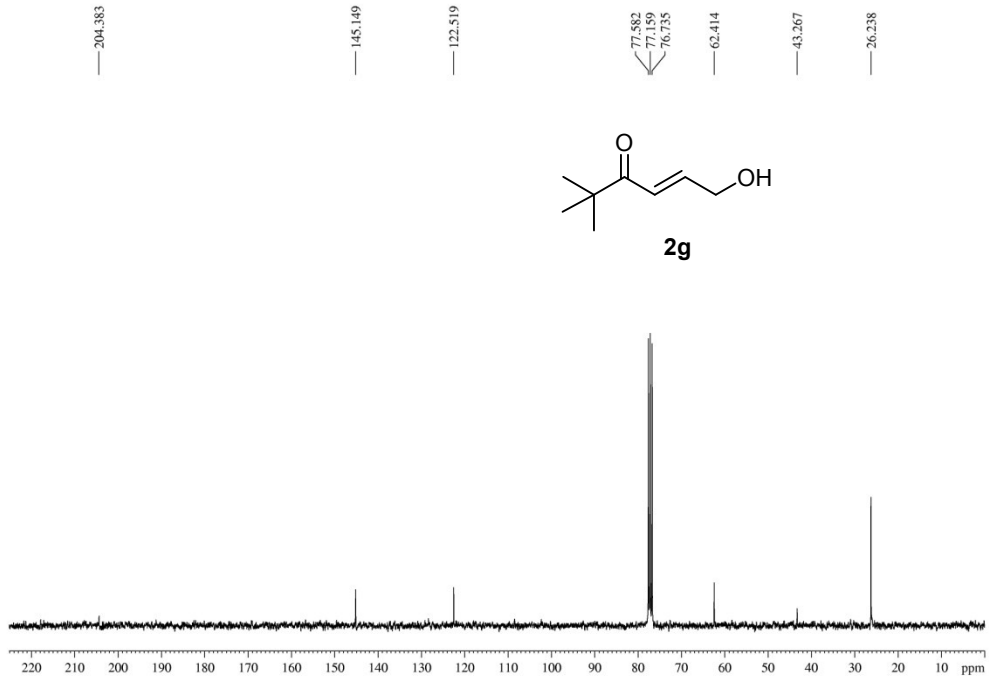


Figure S14: ^{13}C NMR spectra of compound **2g**.

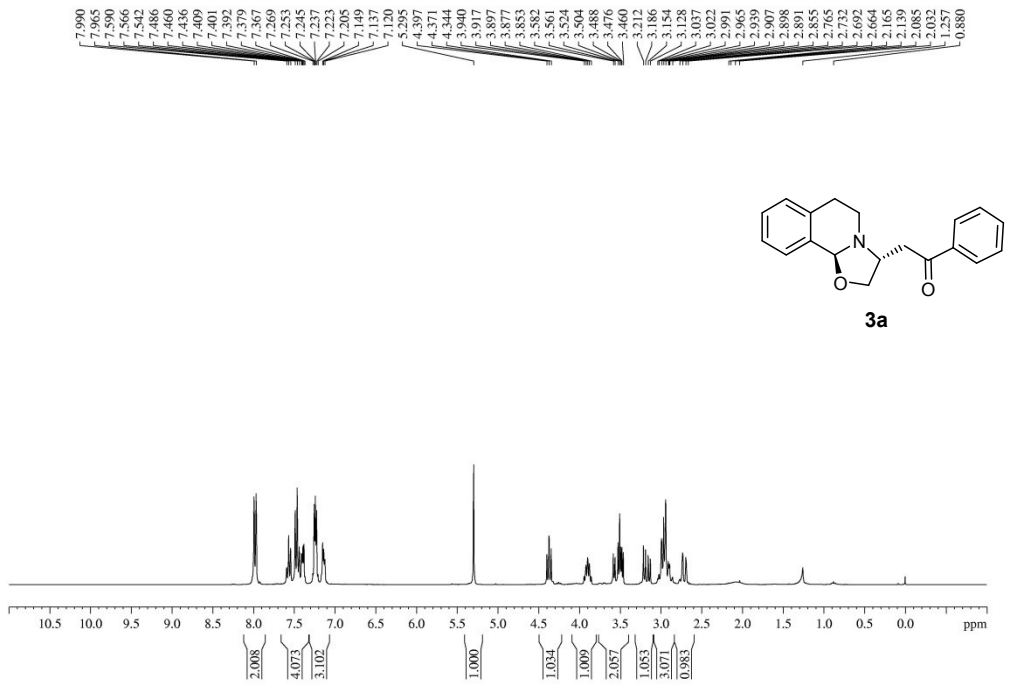


Figure S15: ^{1}H NMR spectra of compound **3a**.

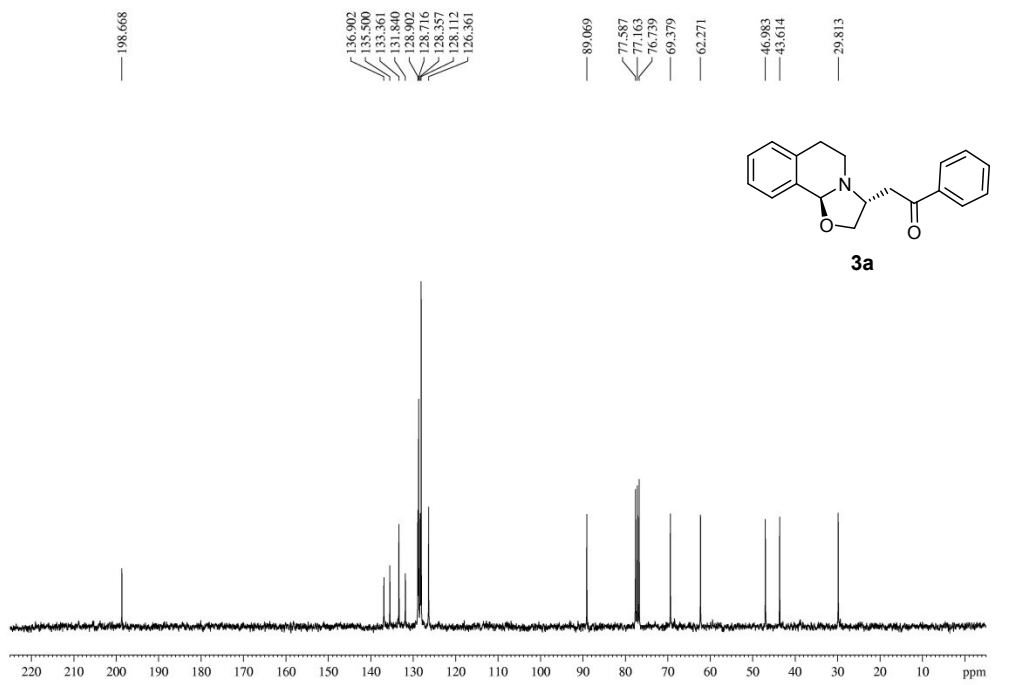


Figure S16: ^{13}C NMR spectra of compound **3a**.

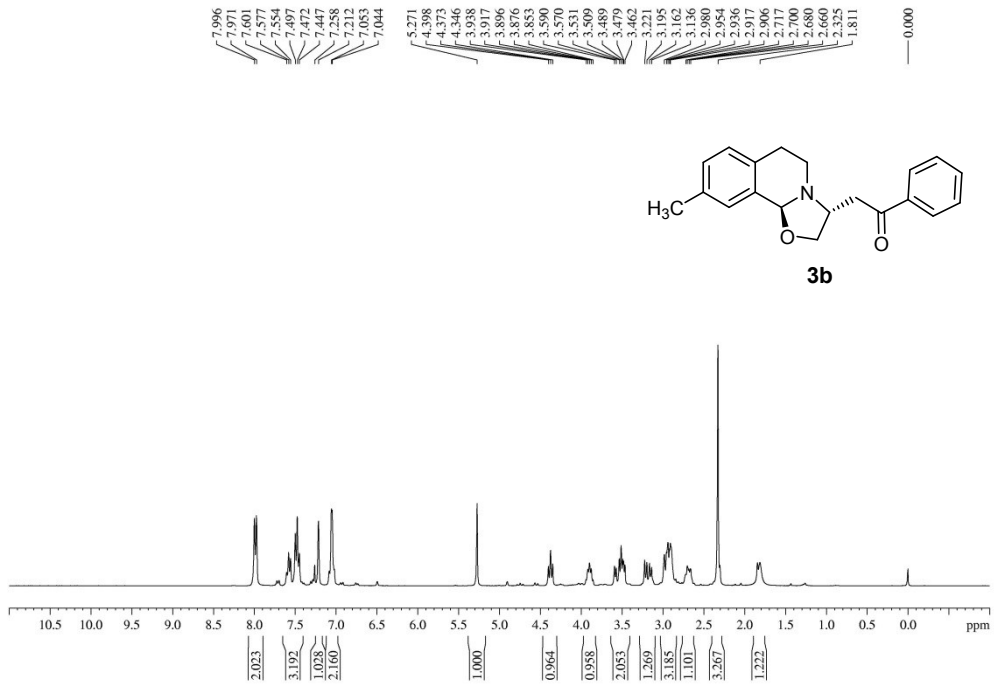


Figure S17: [1]H NMR spectra of compound **3b**.

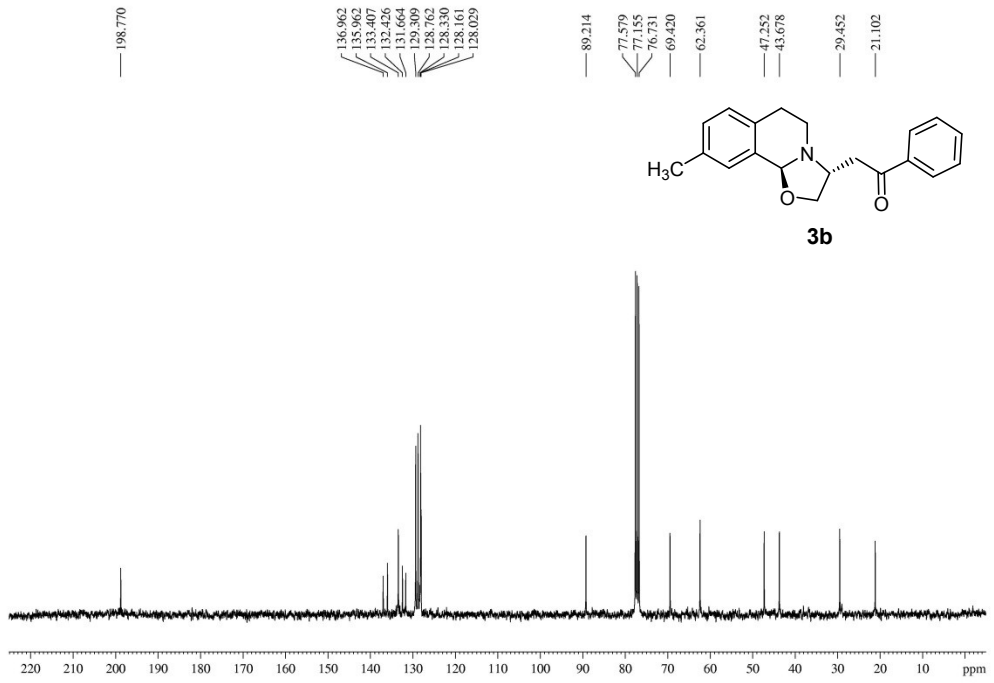


Figure S18: [13]C NMR spectra of compound **3b**.

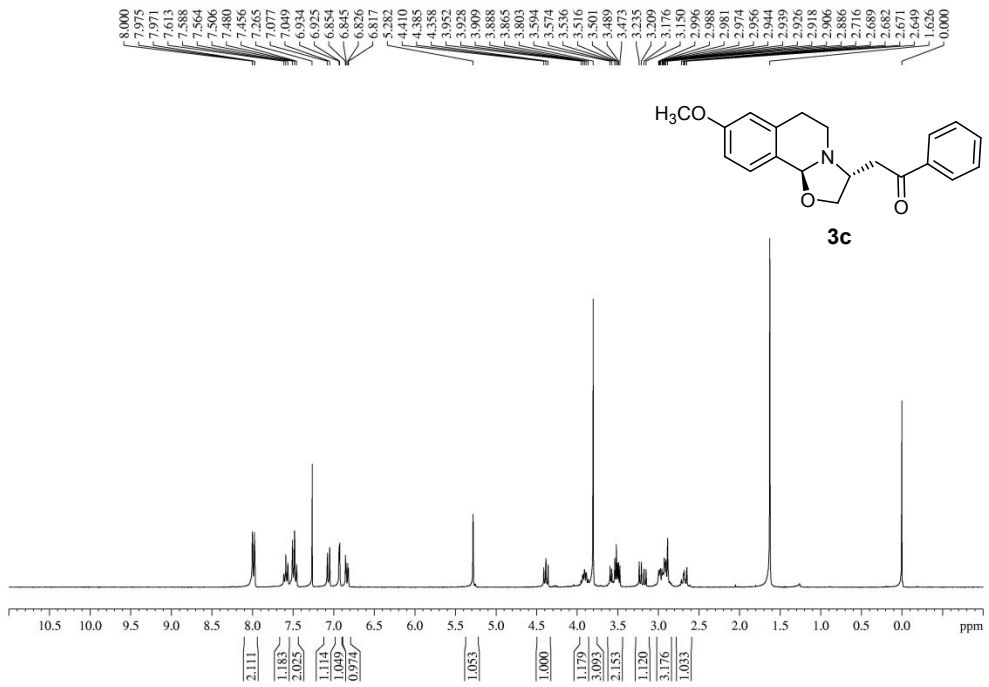


Figure S19: ^{1}H NMR spectra of compound **3c**.

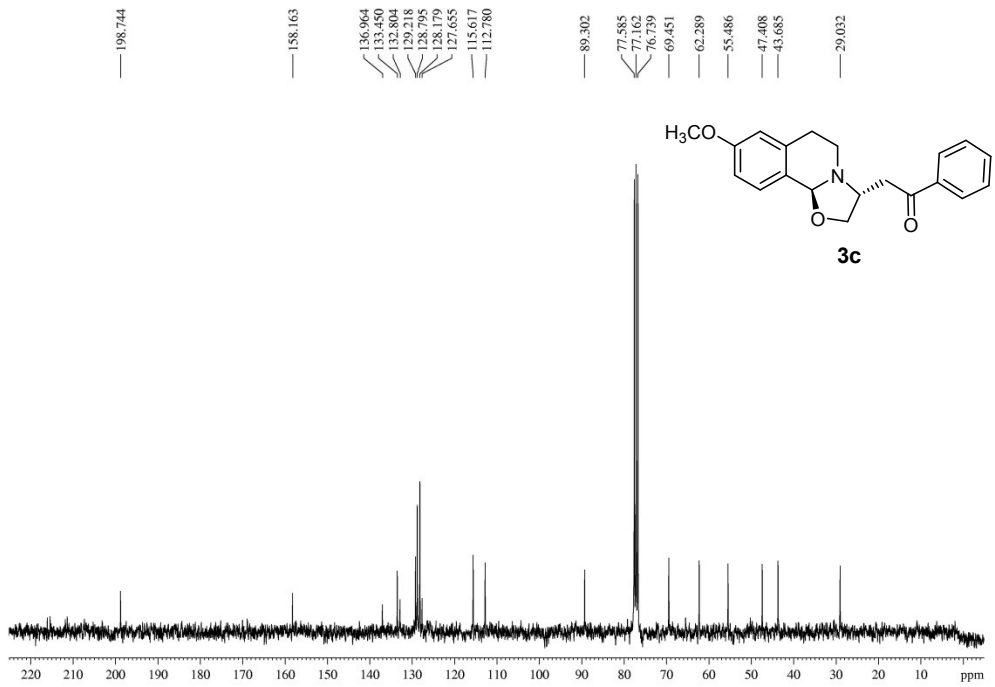


Figure S20: ^{13}C NMR spectra of compound **3c**.

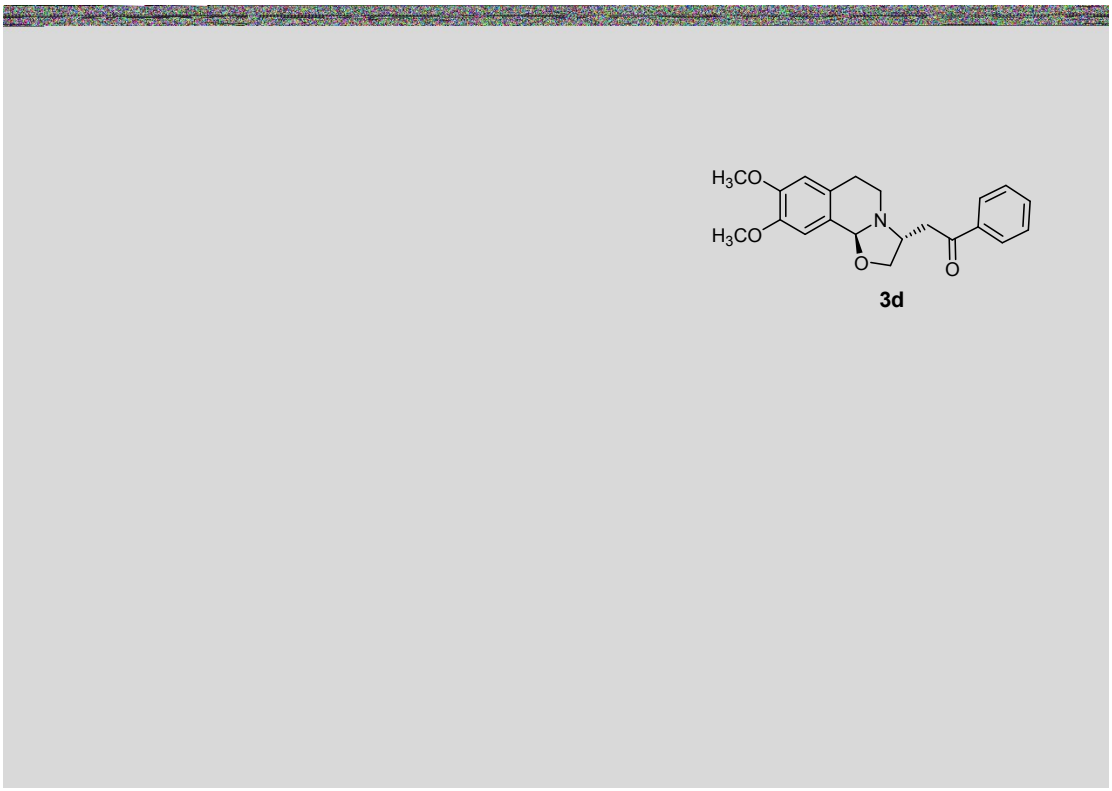


Figure S21: ^{1}H NMR spectra of compound **3d**.

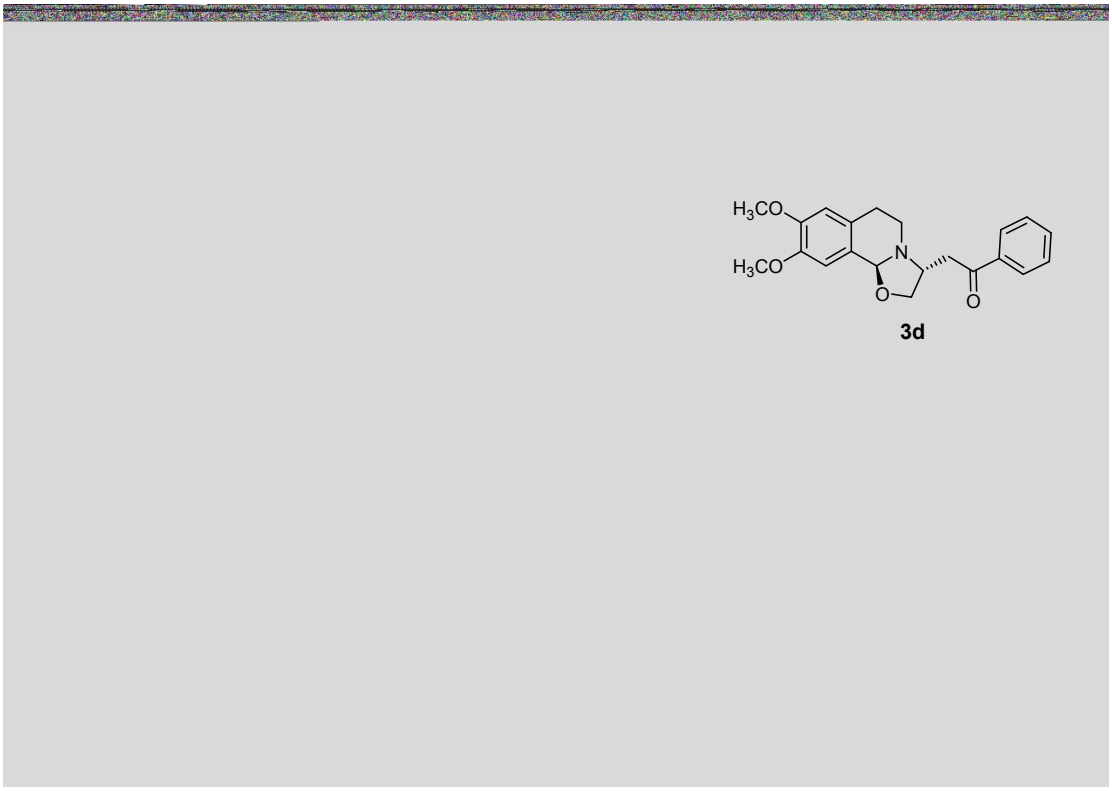


Figure S22: ^{13}C NMR spectra of compound **3d**.

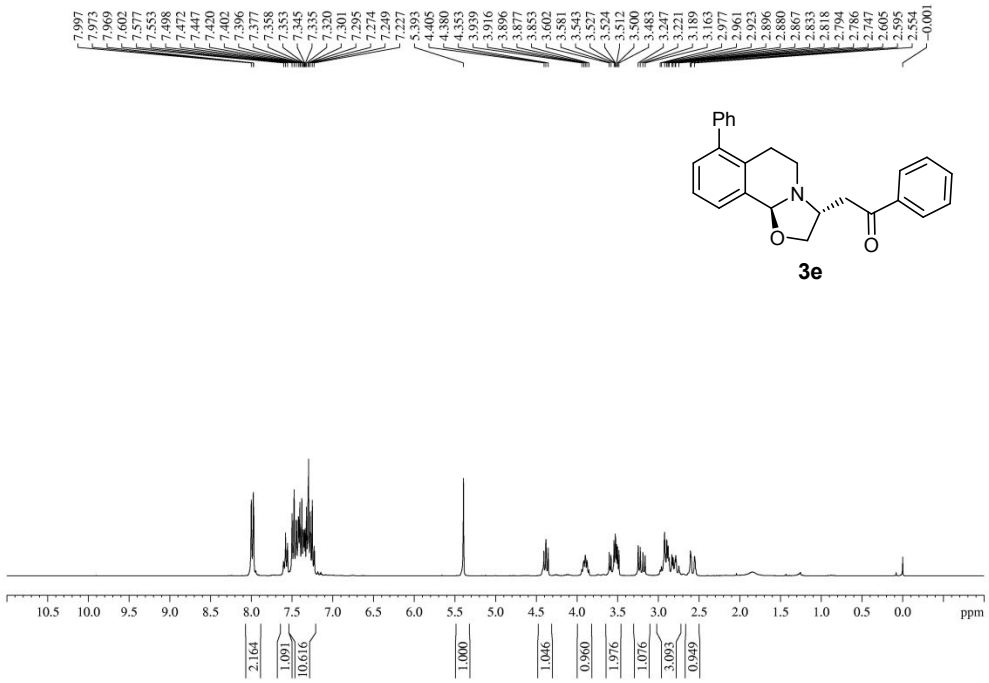


Figure S23: ^{1}H NMR spectra of compound **3e**.

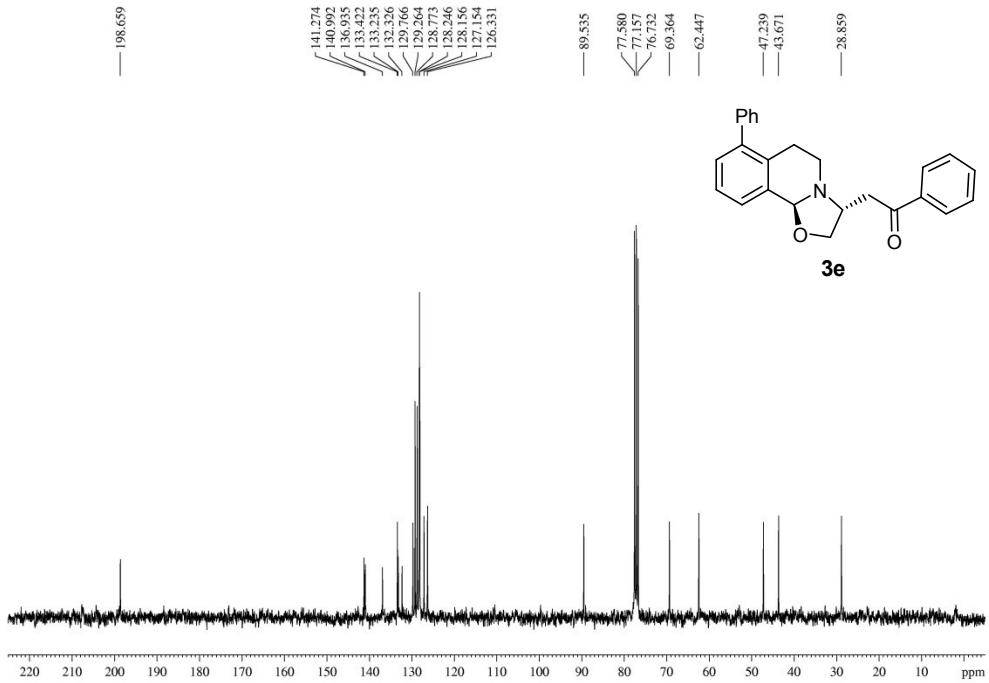


Figure S24: ^{13}C NMR spectra of compound **3e**.

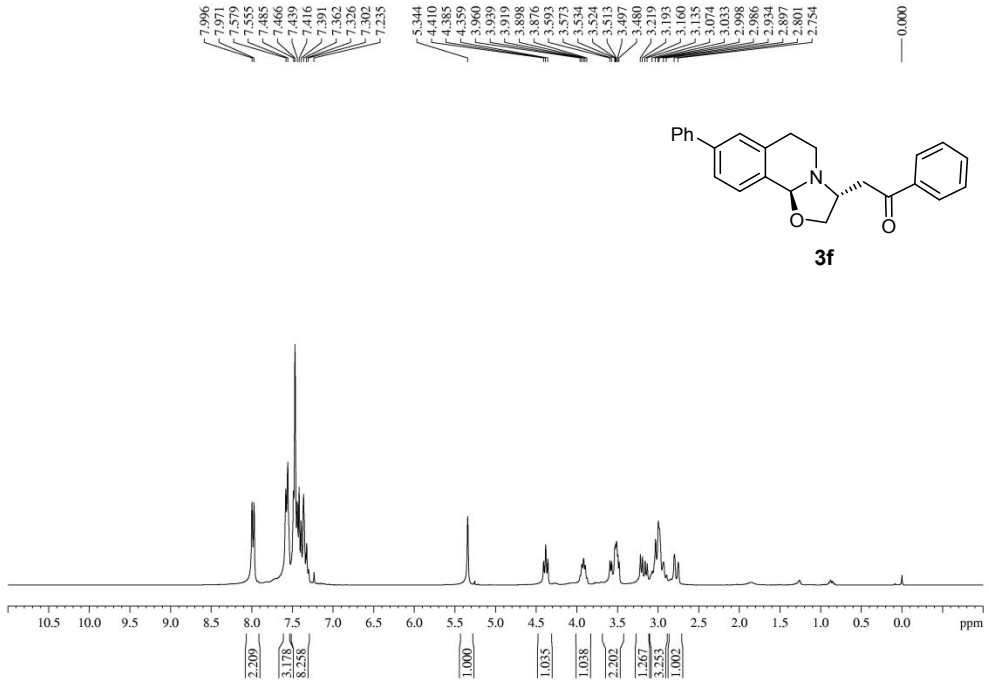


Figure S25: [1]H NMR spectra of compound **3f.**

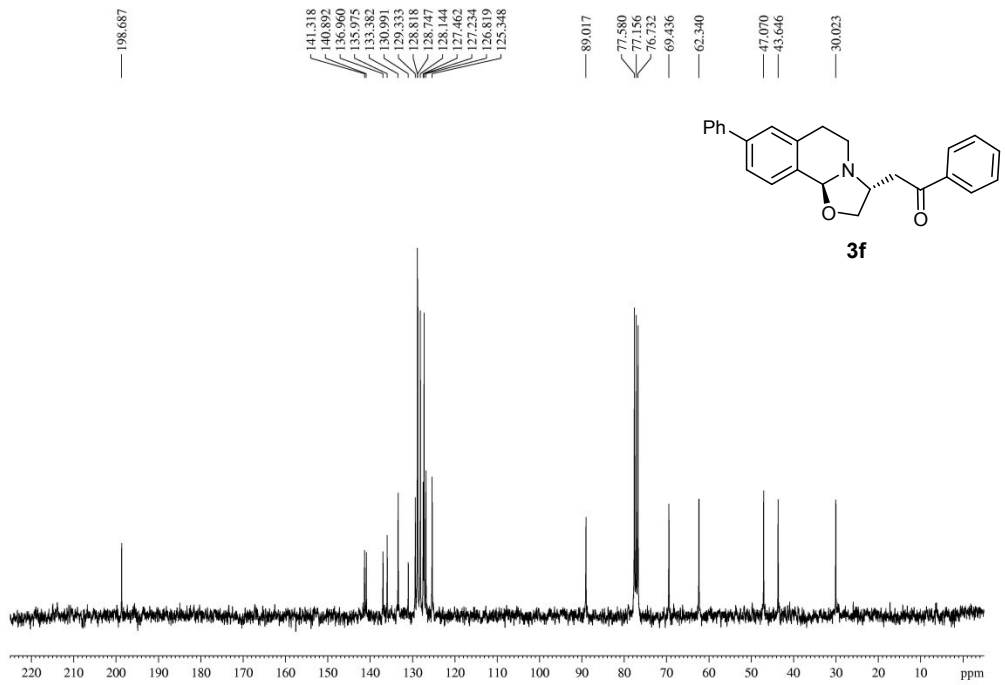


Figure S26: [13]C NMR spectra of compound **3f**.

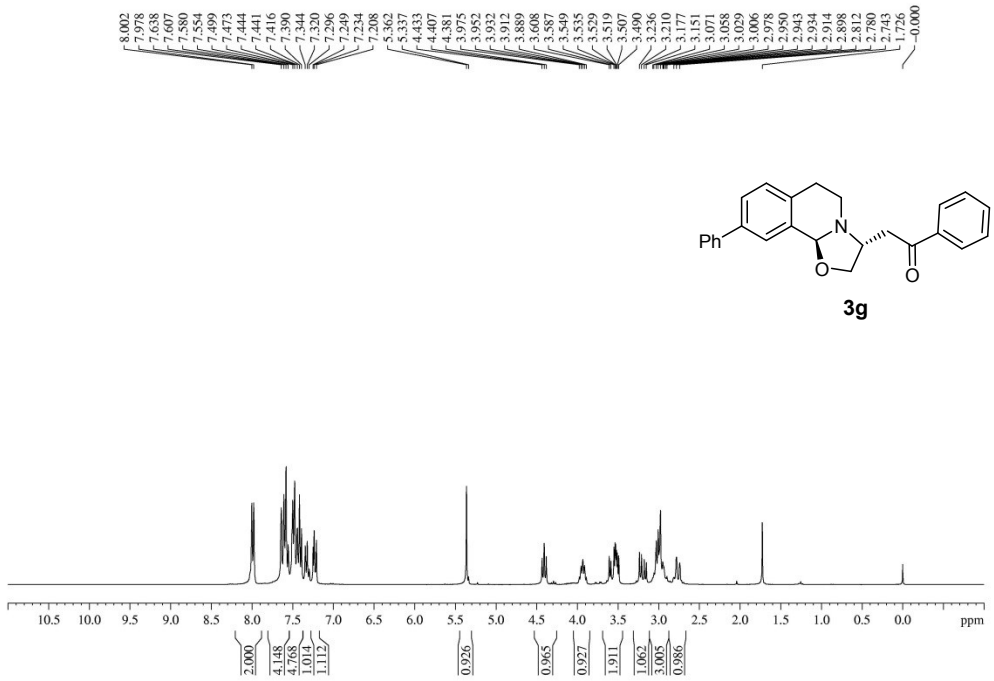


Figure S27: ^{1}H NMR spectra of compound **3g.**

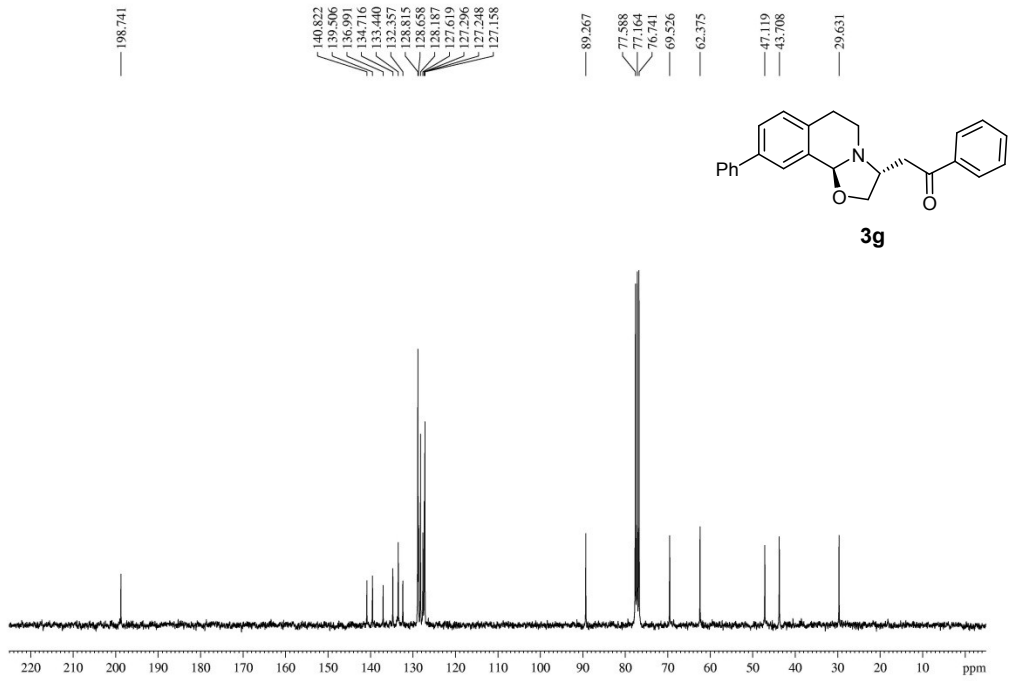


Figure S28: ^{13}C NMR spectra of compound **3g**.

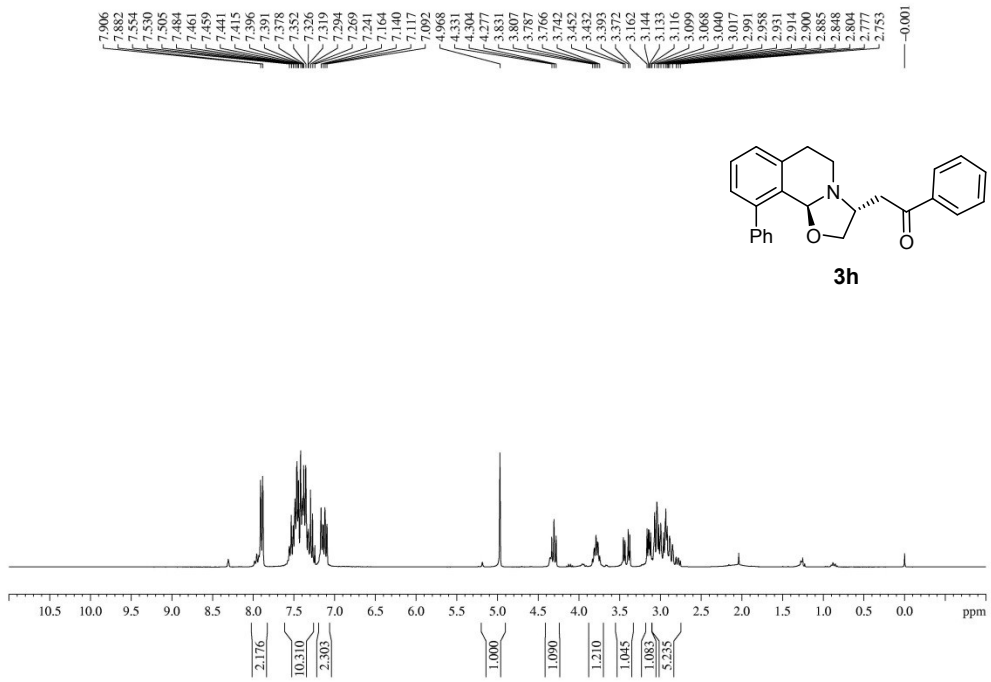


Figure S29: ^{1}H NMR spectra of compound **3h.**

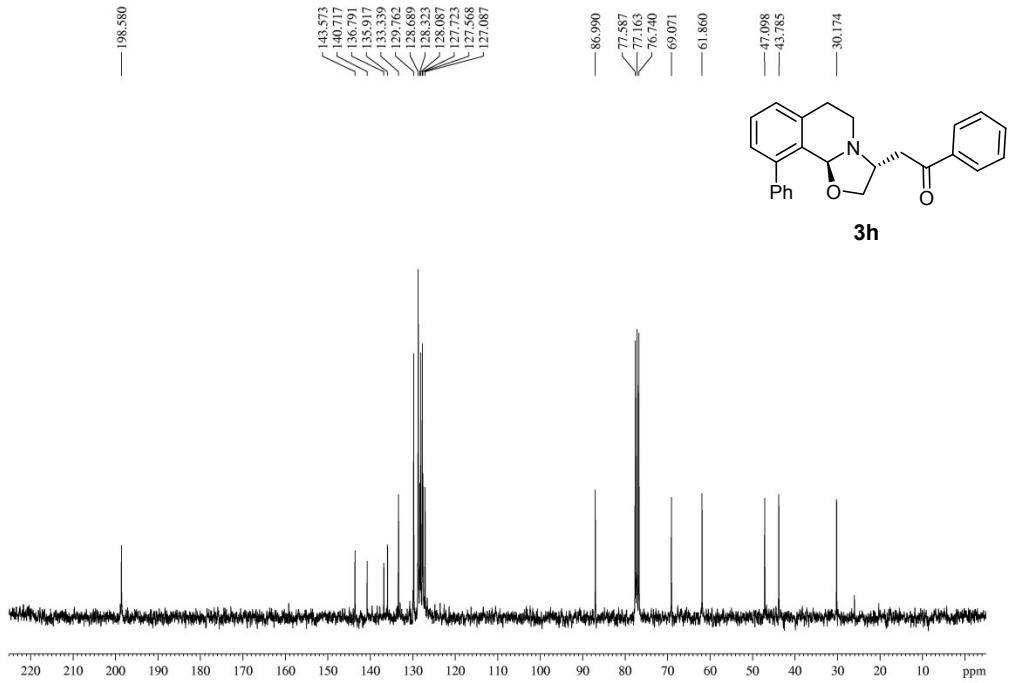


Figure S30: ^{13}C NMR spectra of compound **3h**.

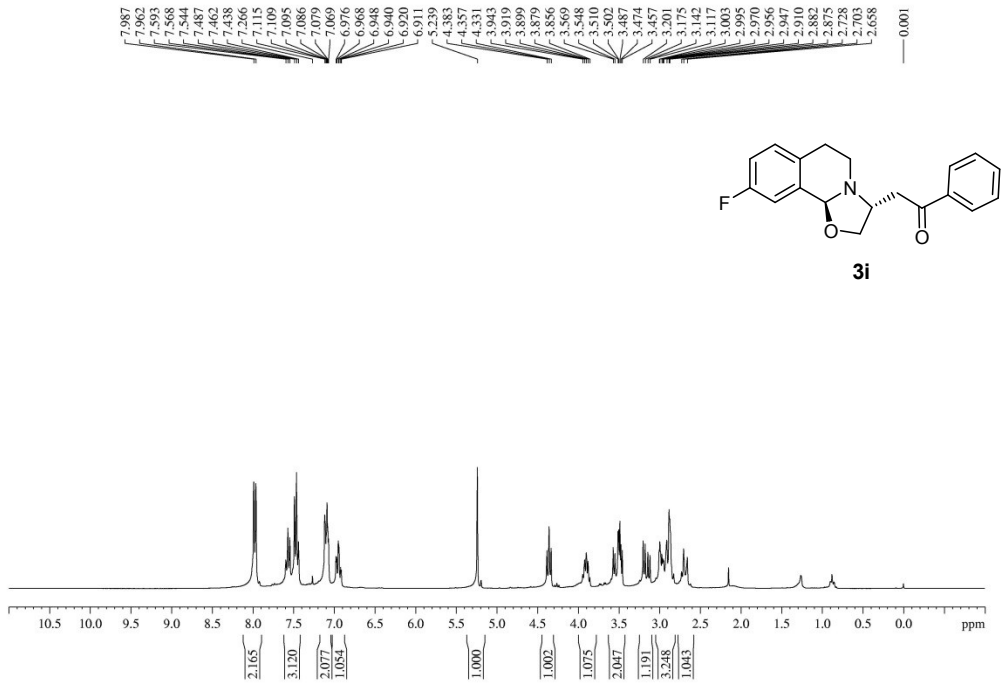


Figure S31: ^{1}H NMR spectra of compound **3i.**

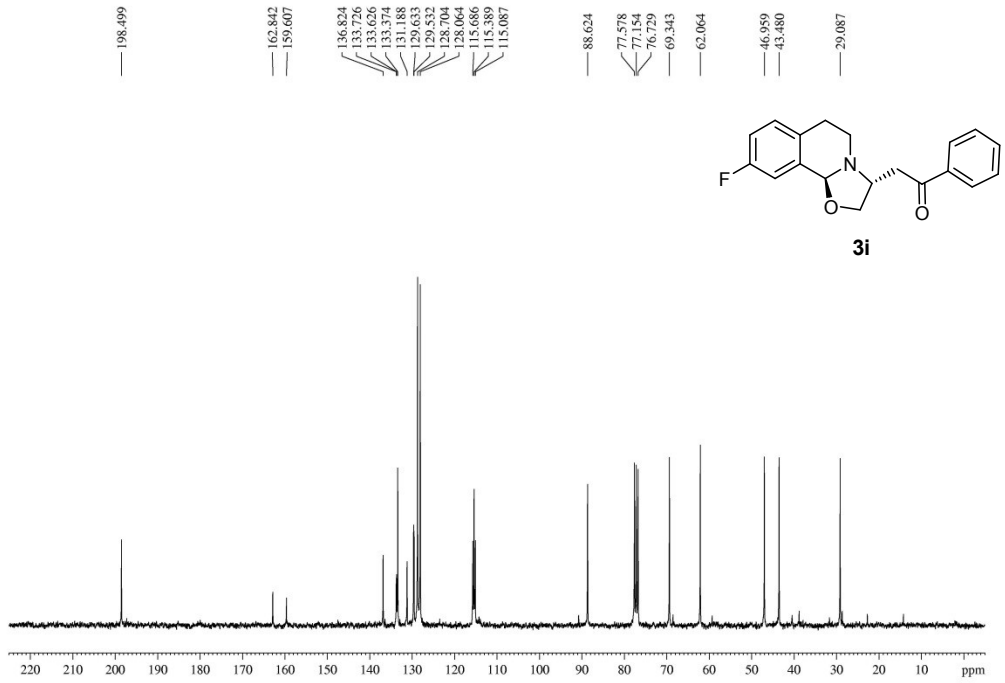


Figure S32: ^{13}C NMR spectra of compound **3i**.

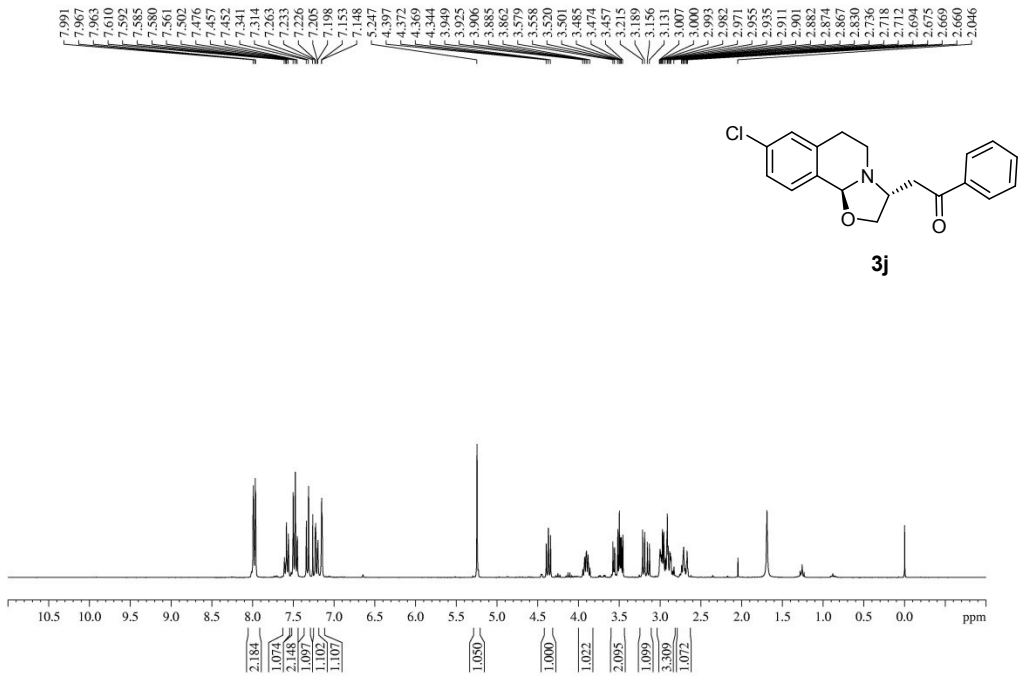


Figure S33: ^{1}H NMR spectra of compound **3j**.

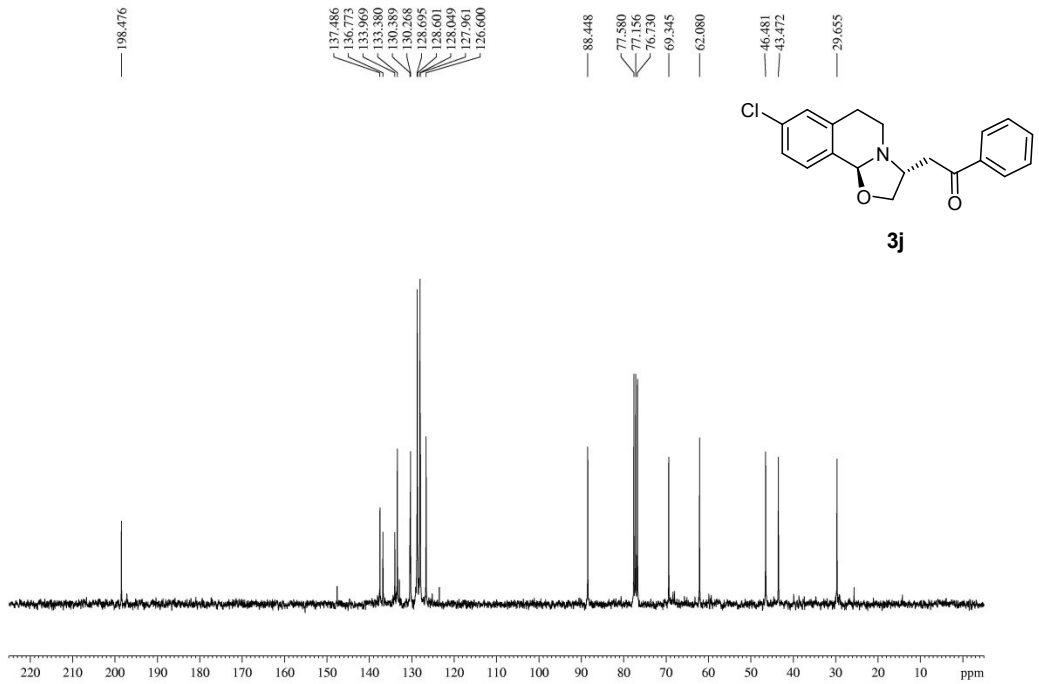


Figure S34: ^{13}C NMR spectra of compound **3j**.

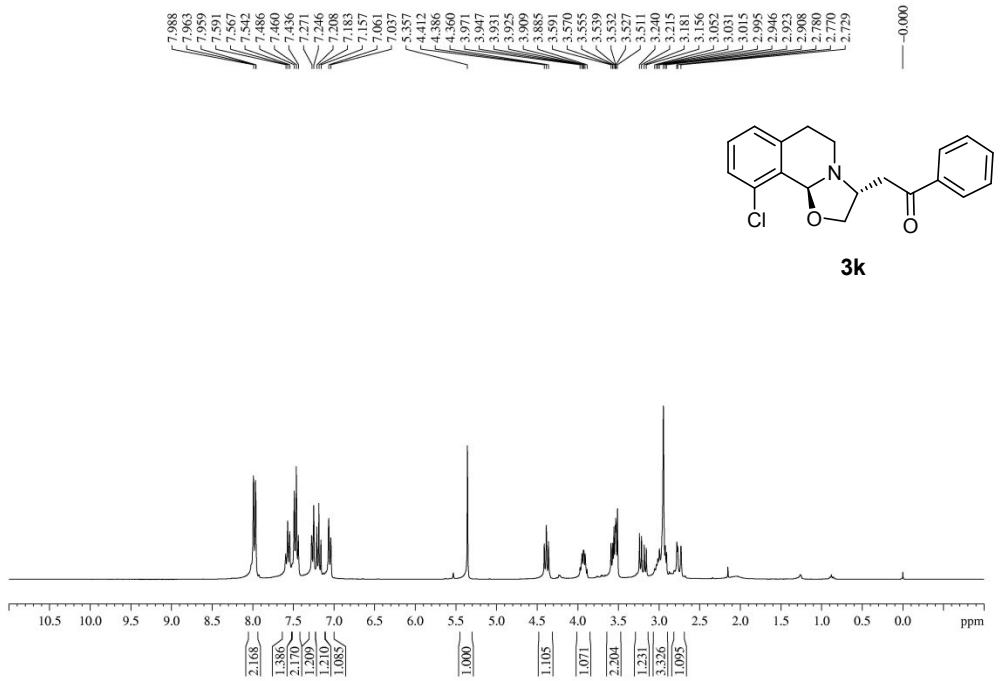


Figure S35: ^{1}H NMR spectra of compound **3k**.

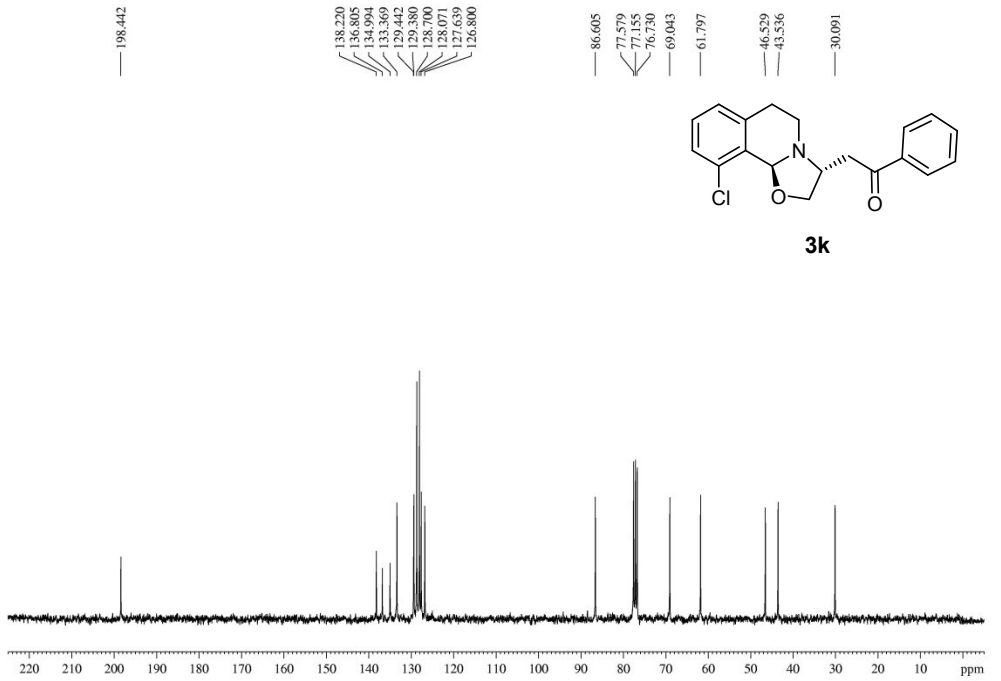


Figure S36: ^{13}C NMR spectra of compound **3k**.

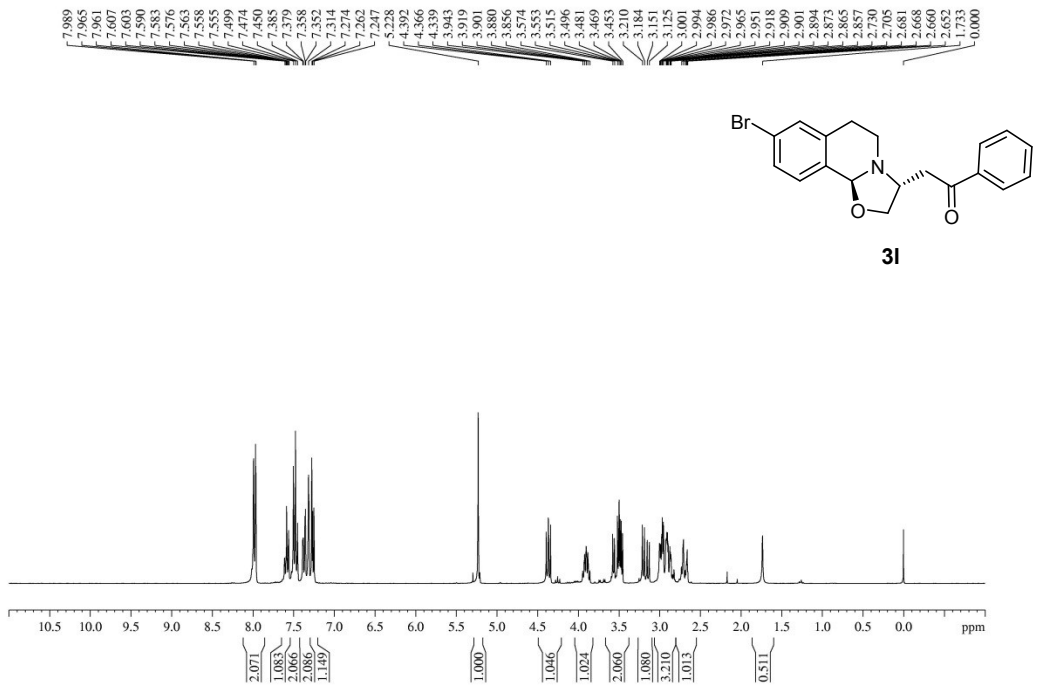


Figure S37: ^{1}H NMR spectra of compound **3l**

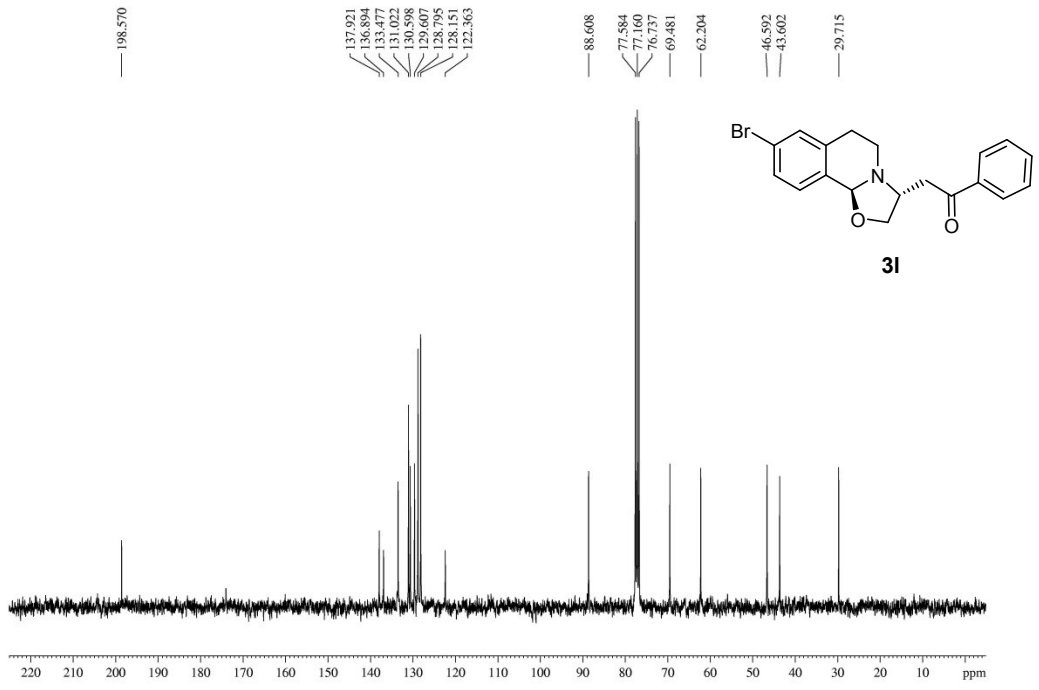


Figure S38: ^{13}C NMR spectra of compound **3l**.

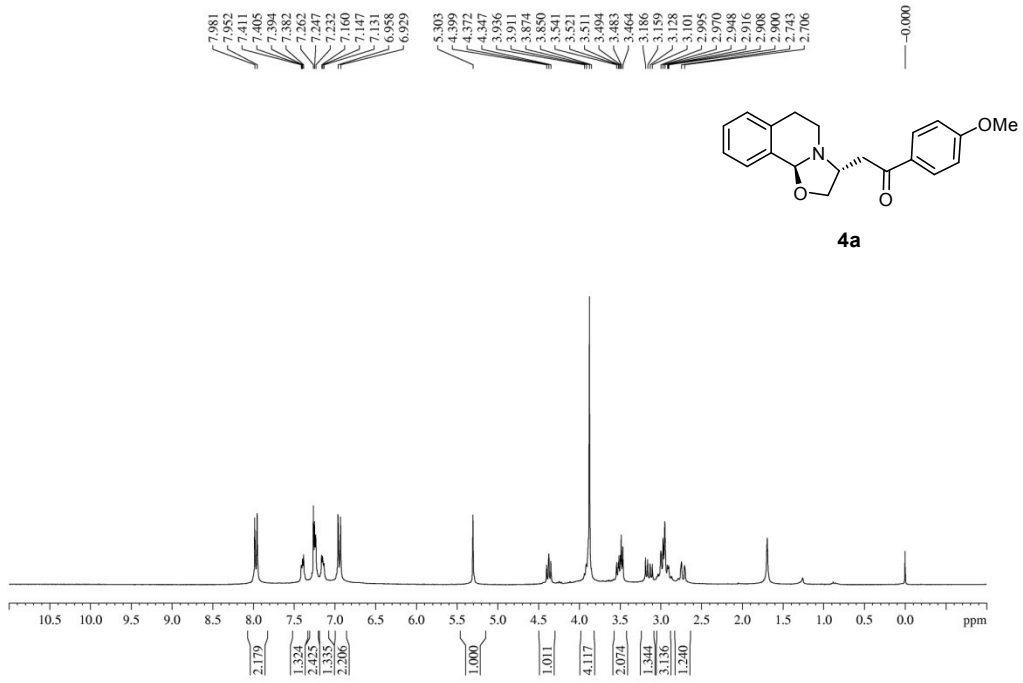


Figure S39: ^{1}H NMR spectra of compound **4a.**

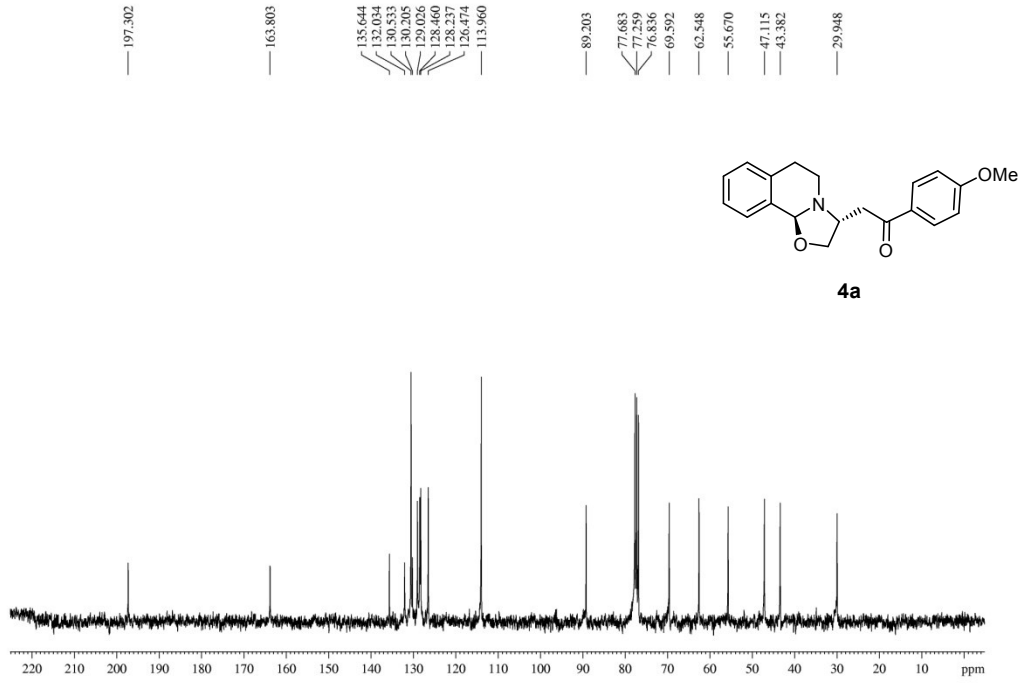


Figure S40: ^{13}C NMR spectra of compound **4a**.

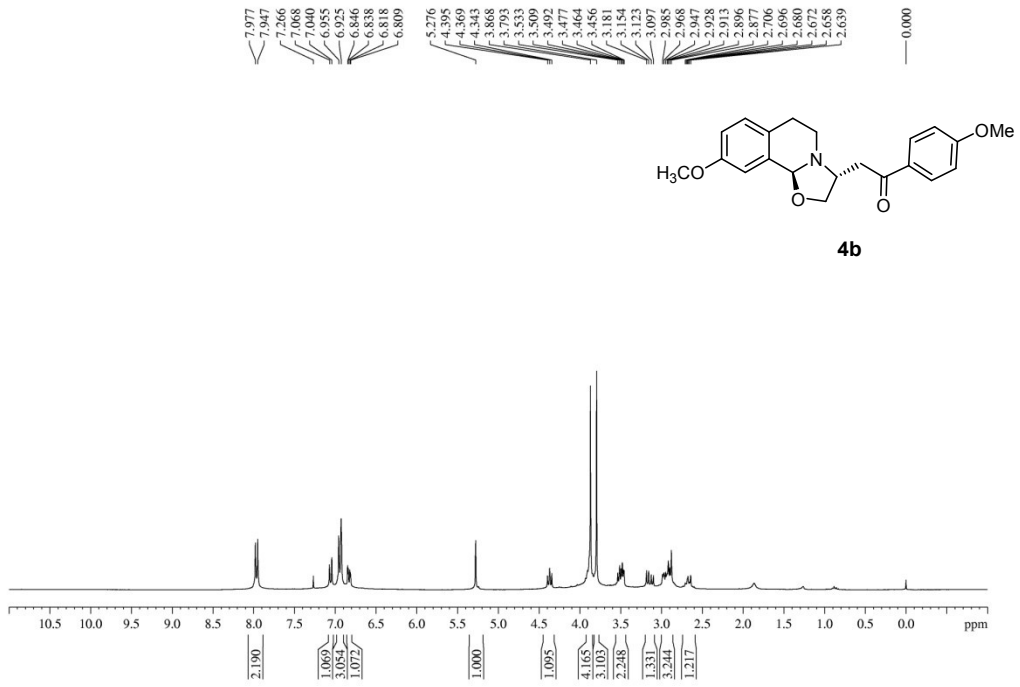


Figure S41: ^{1}H NMR spectra of compound **4b**

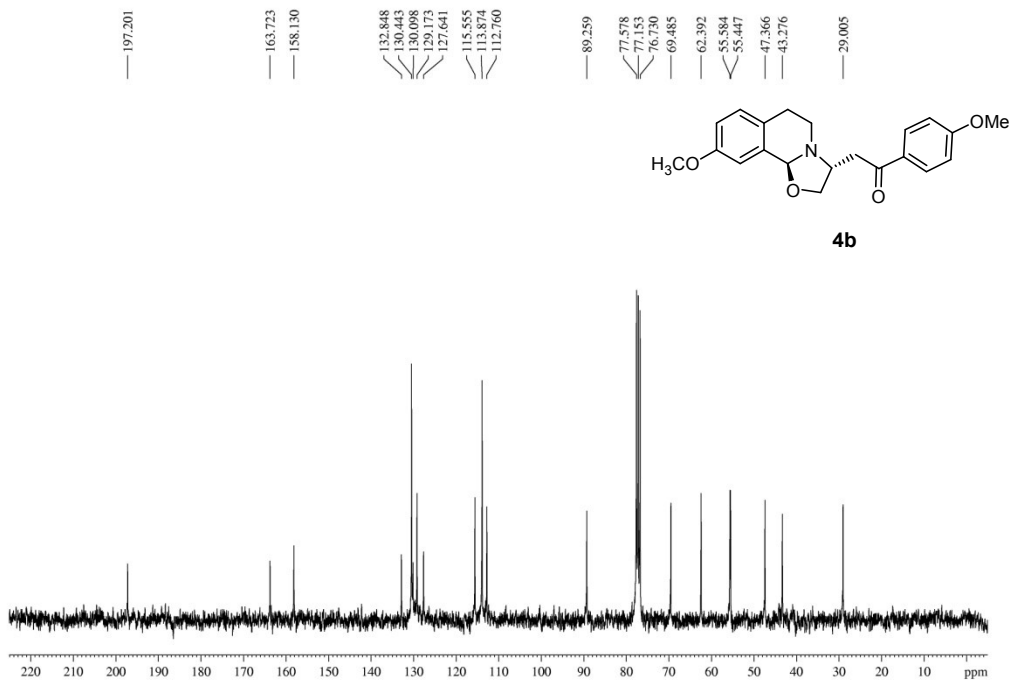


Figure S42: ^{13}C NMR spectra of compound **4b**.

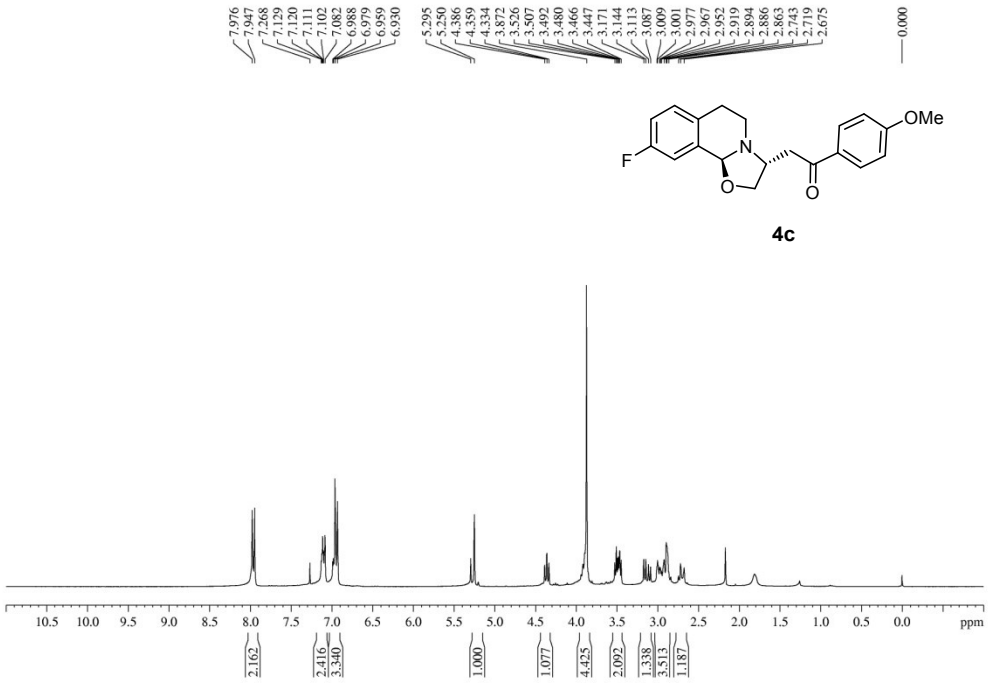


Figure S43: [1]H NMR spectra of compound **4c**

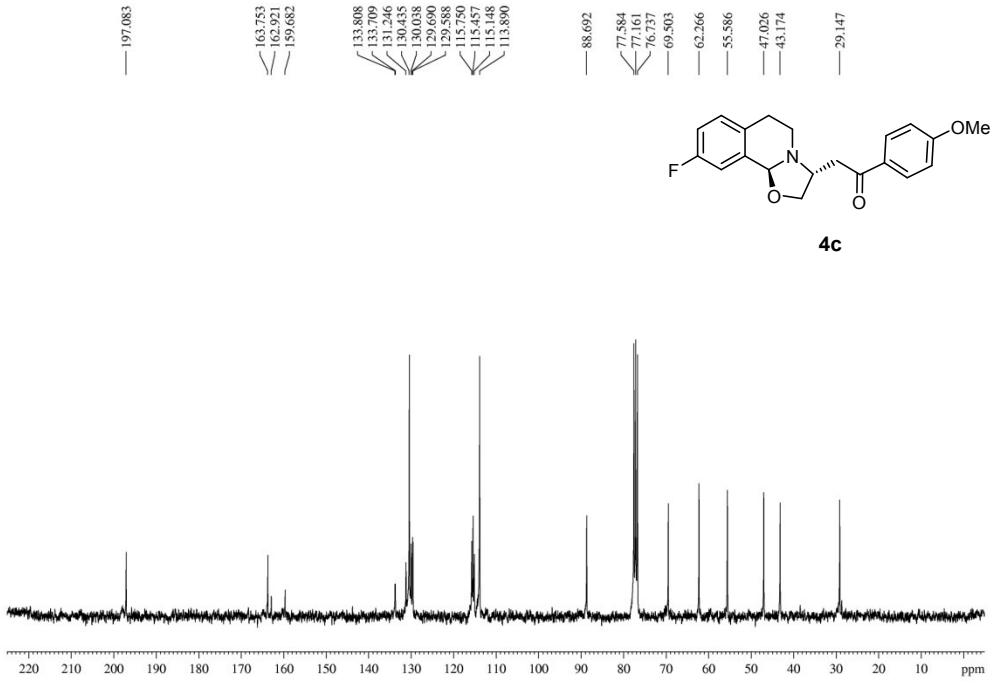


Figure S44: [13]C NMR spectra of compound **4c**.

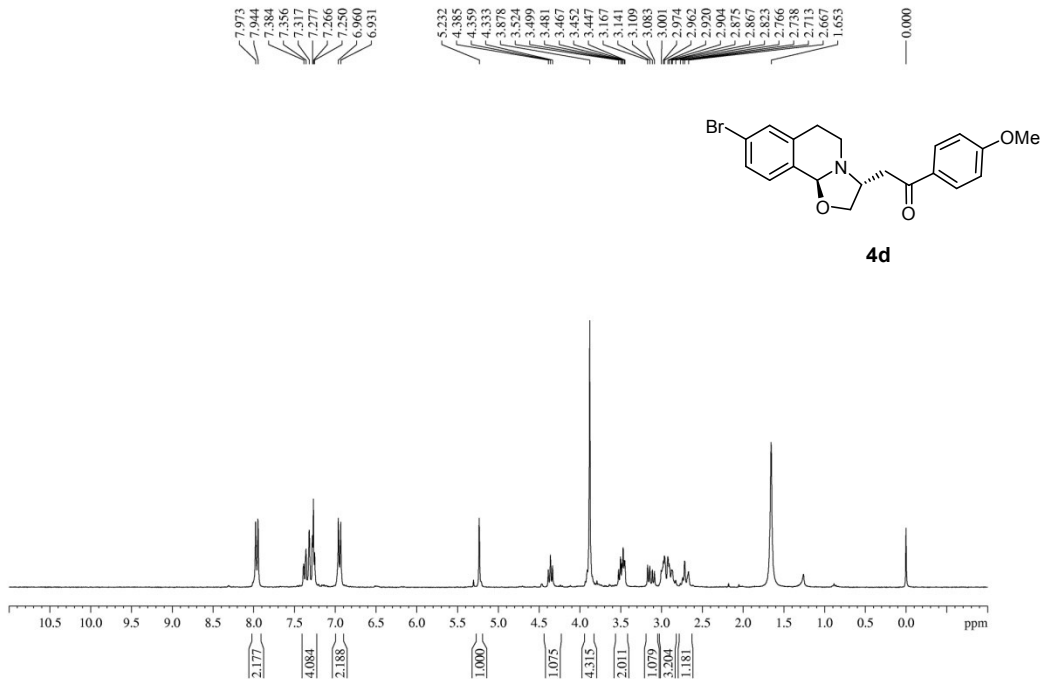


Figure S45: ^{1}H NMR spectra of compound **4d**

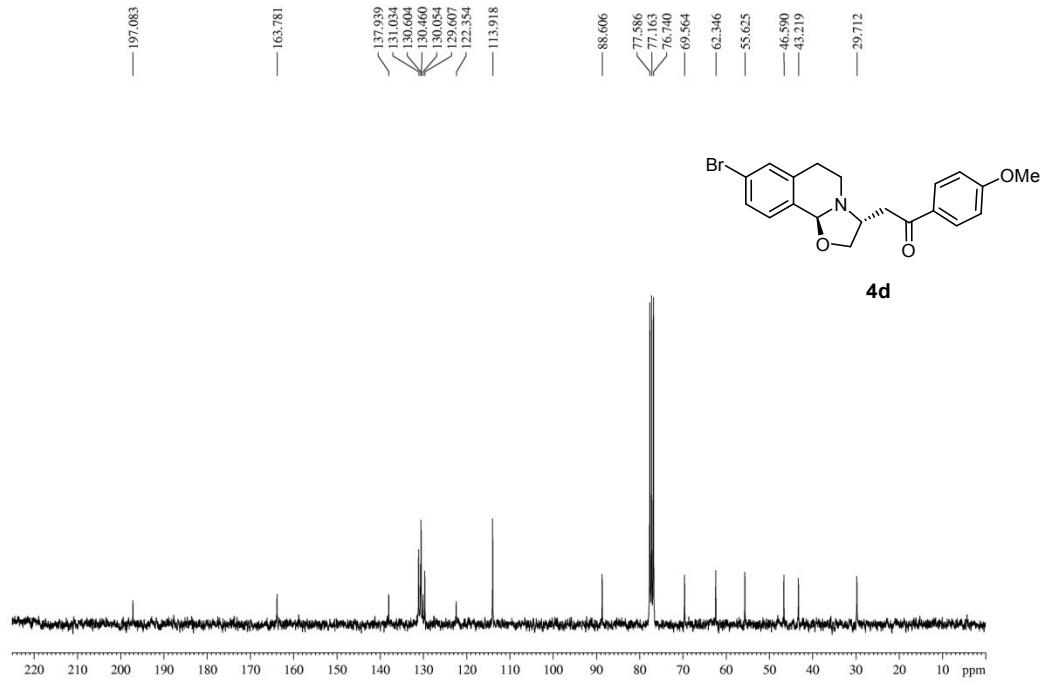


Figure S46: ^{13}C NMR spectra of compound **4d**.

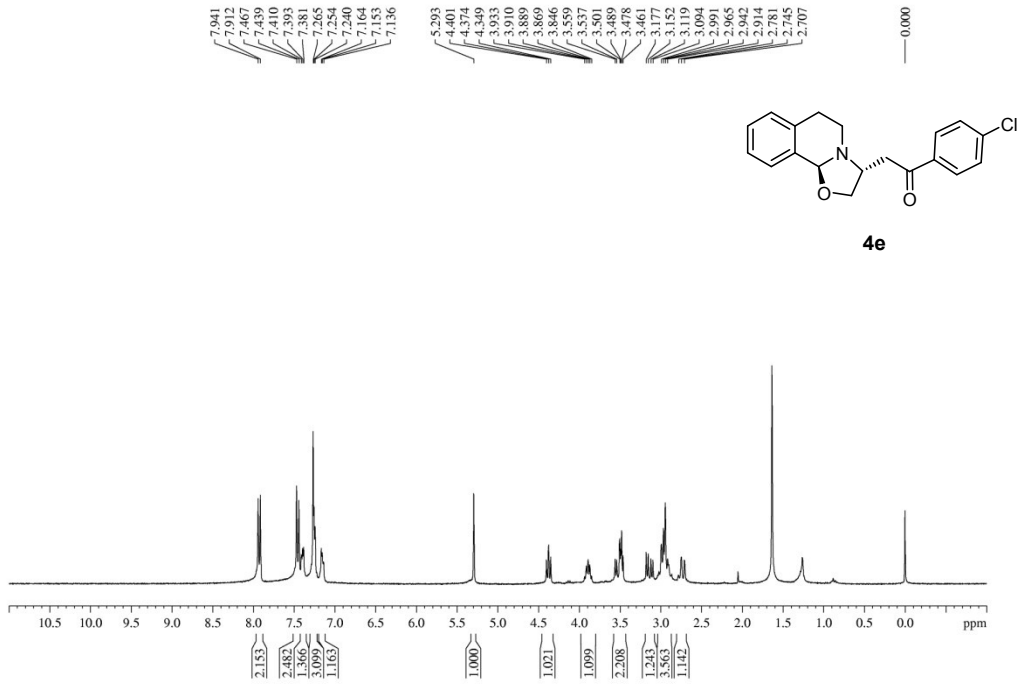


Figure S47: ^{1}H NMR spectra of compound **4e**

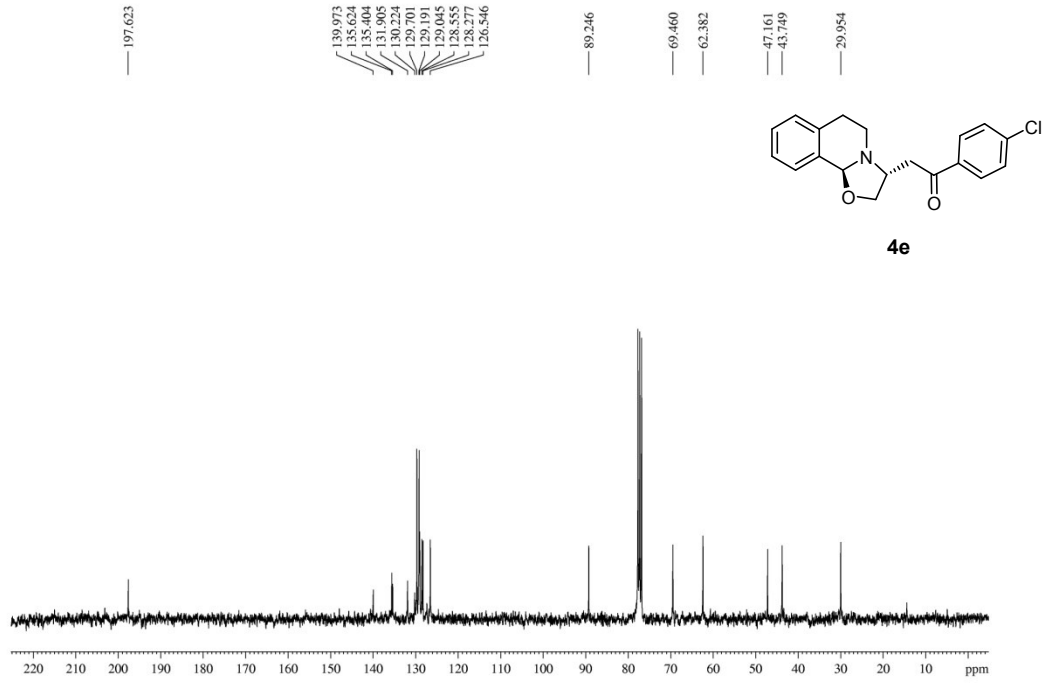


Figure S48: ^{13}C NMR spectra of compound **4e**.

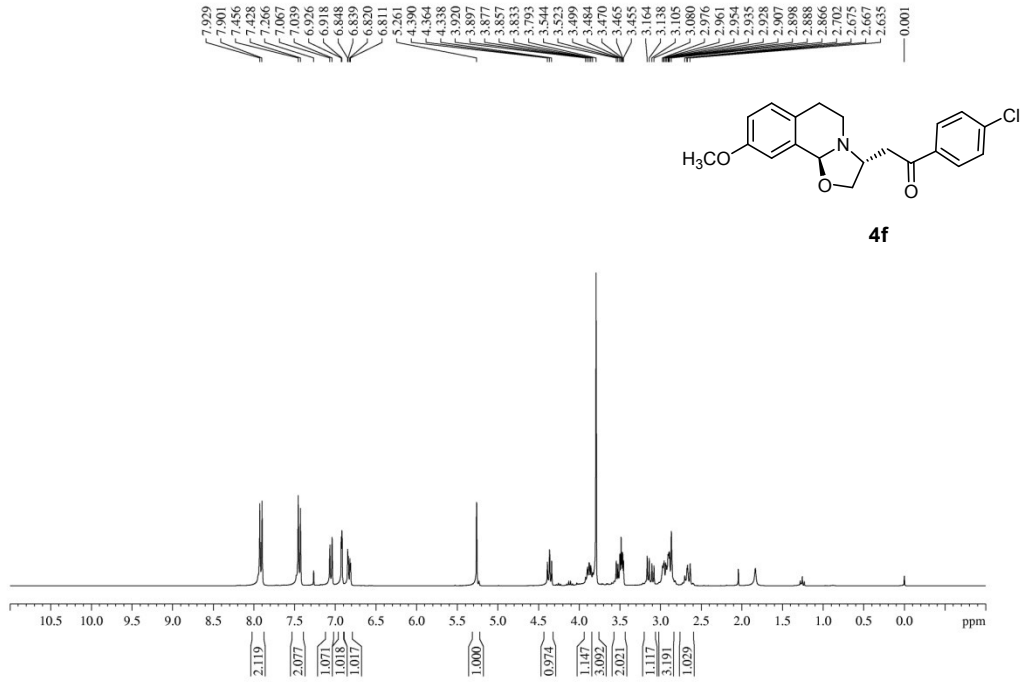


Figure S49: ^{1}H NMR spectra of compound **4f**

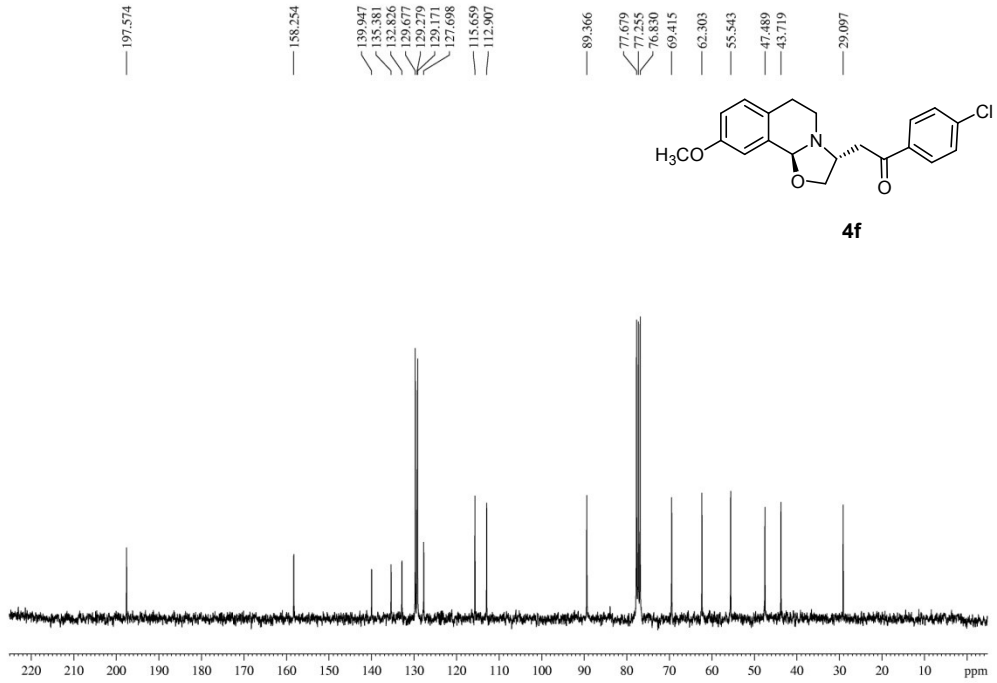


Figure S50: ^{13}C NMR spectra of compound **4f**.

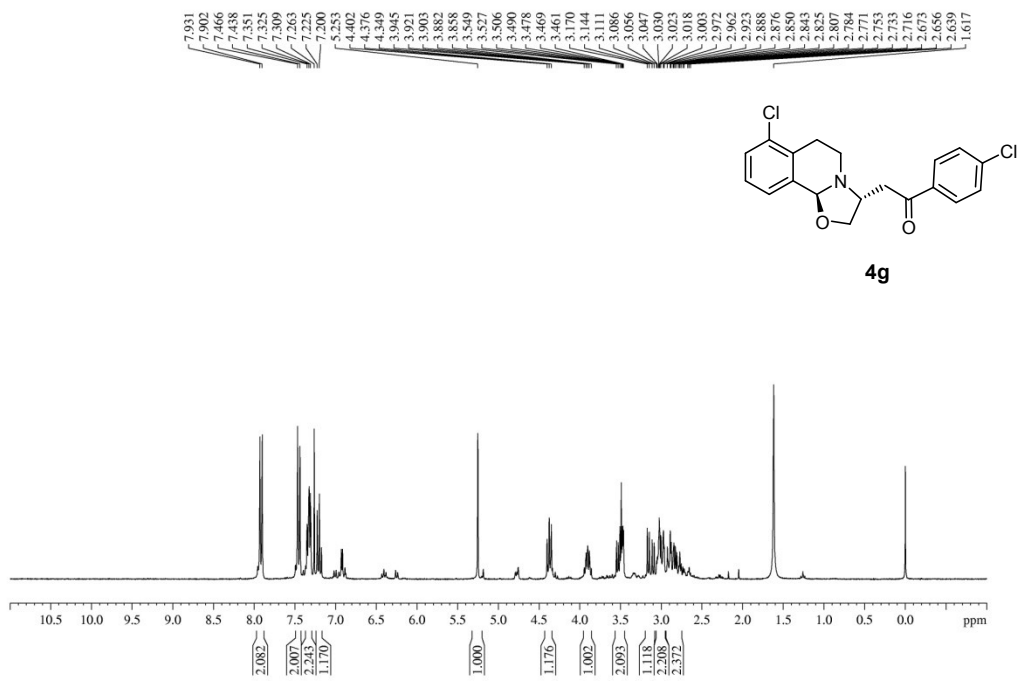


Figure S51: ^{1}H NMR spectra of compound **4g**.

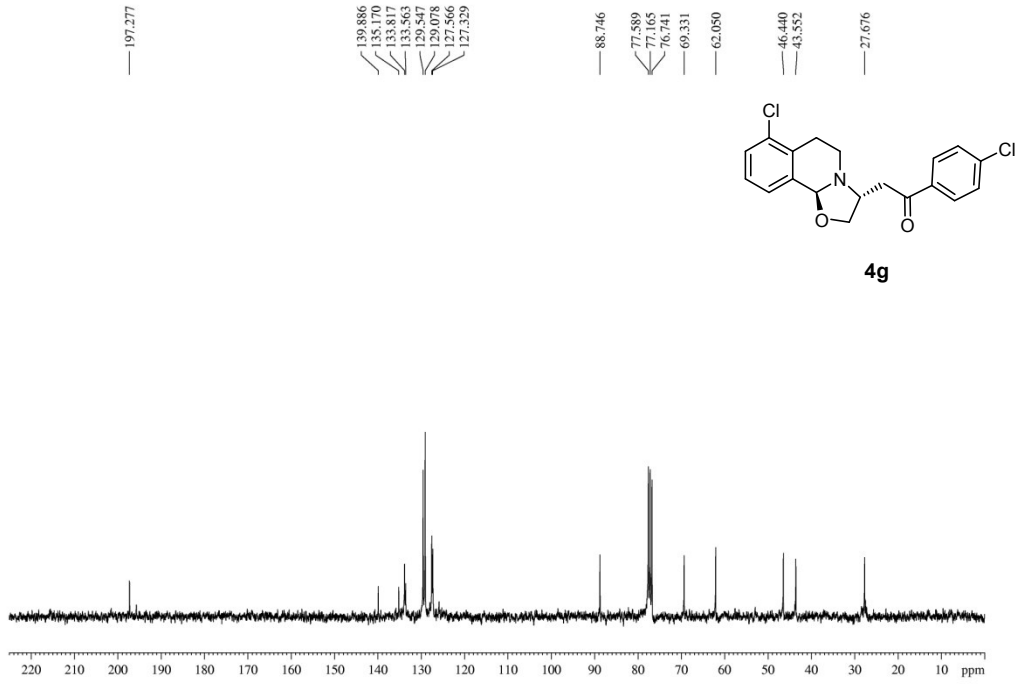


Figure S52: ^{13}C NMR spectra of compound **4g**.

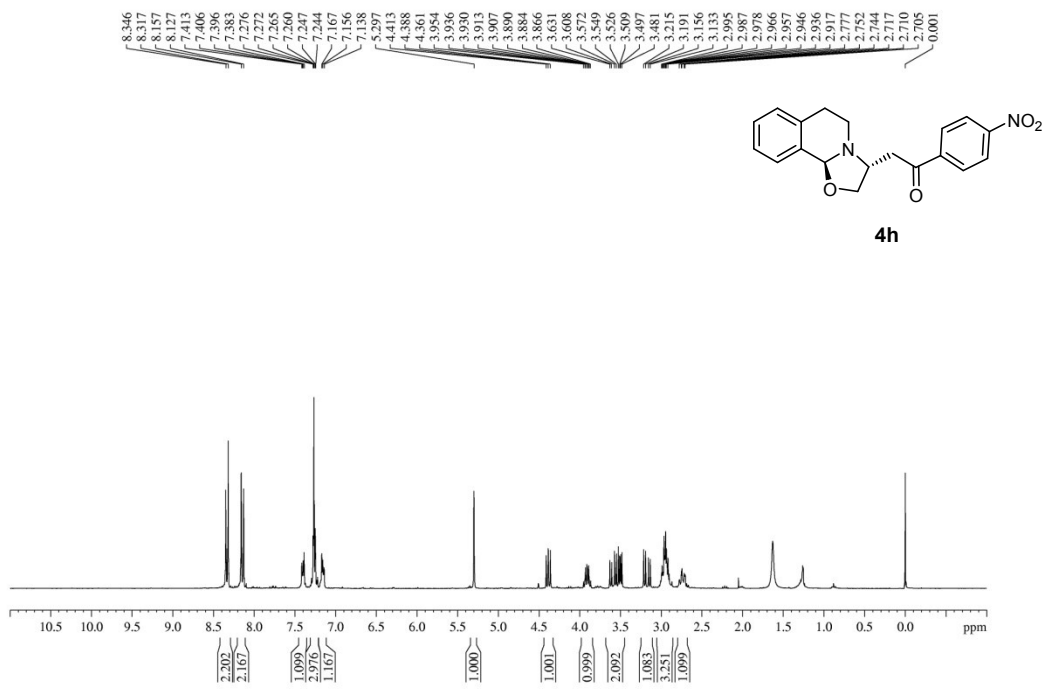


Figure S53: ^{1}H NMR spectra of compound **4h**.

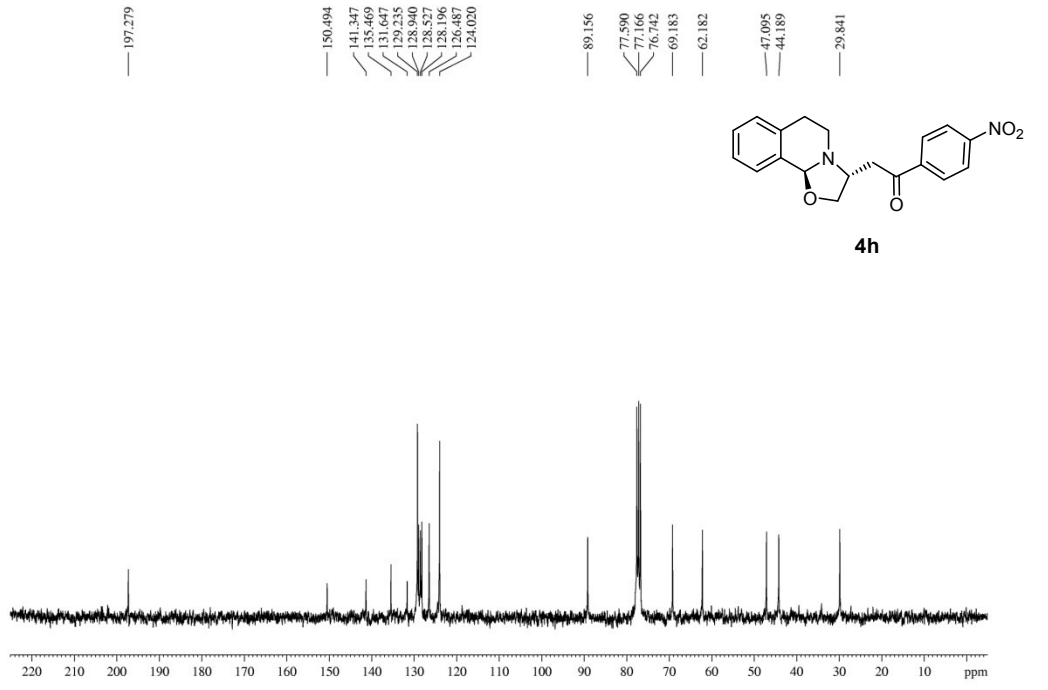


Figure S54: ^{13}C NMR spectra of compound **4h**.

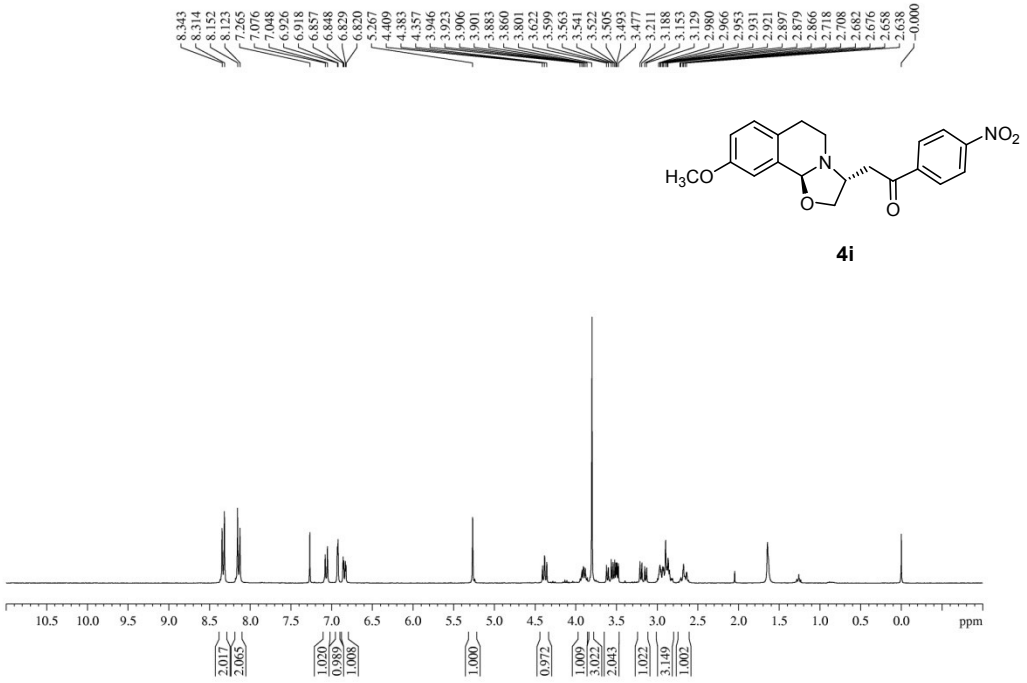


Figure S55: ^{1}H NMR spectra of compound **4i**.

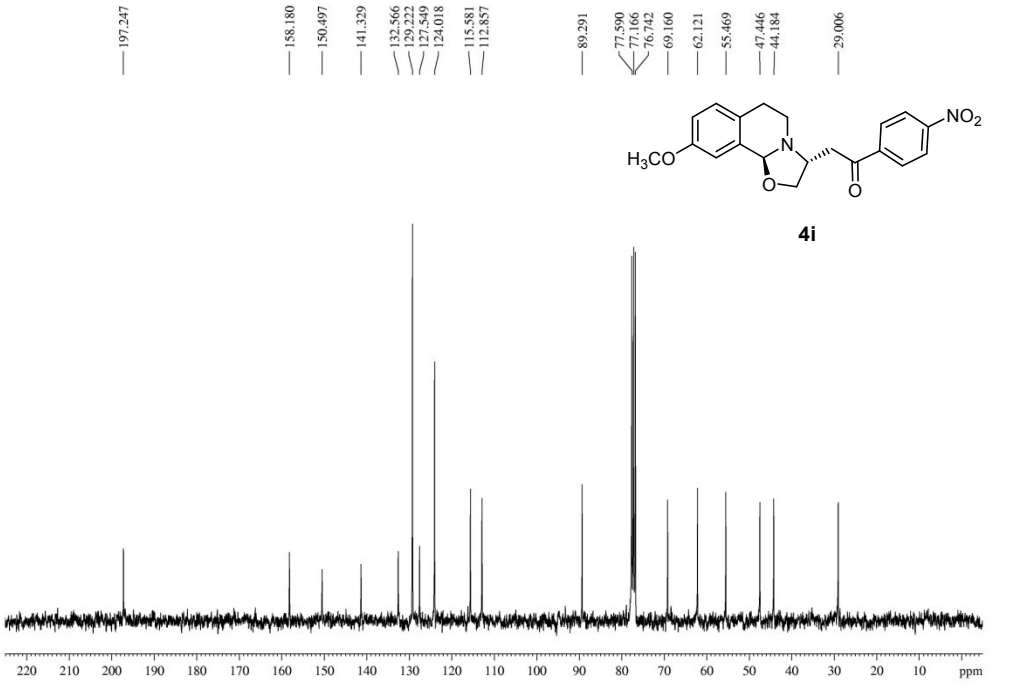


Figure S56: ^{13}C NMR spectra of compound **4i**.

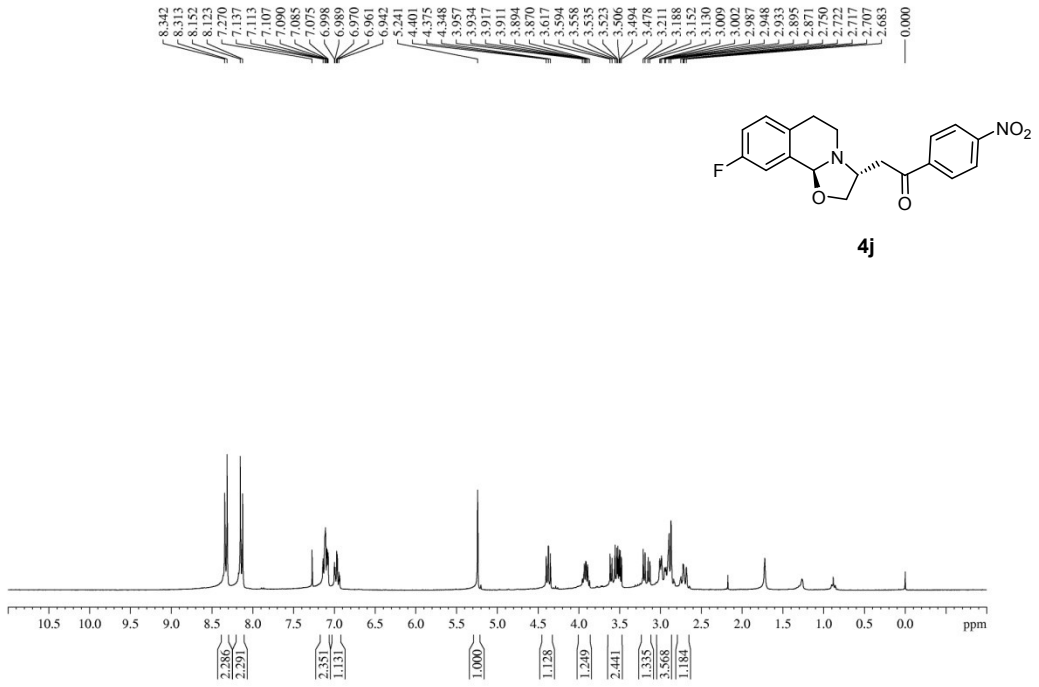


Figure S57: ^{1}H NMR spectra of compound **4j**.

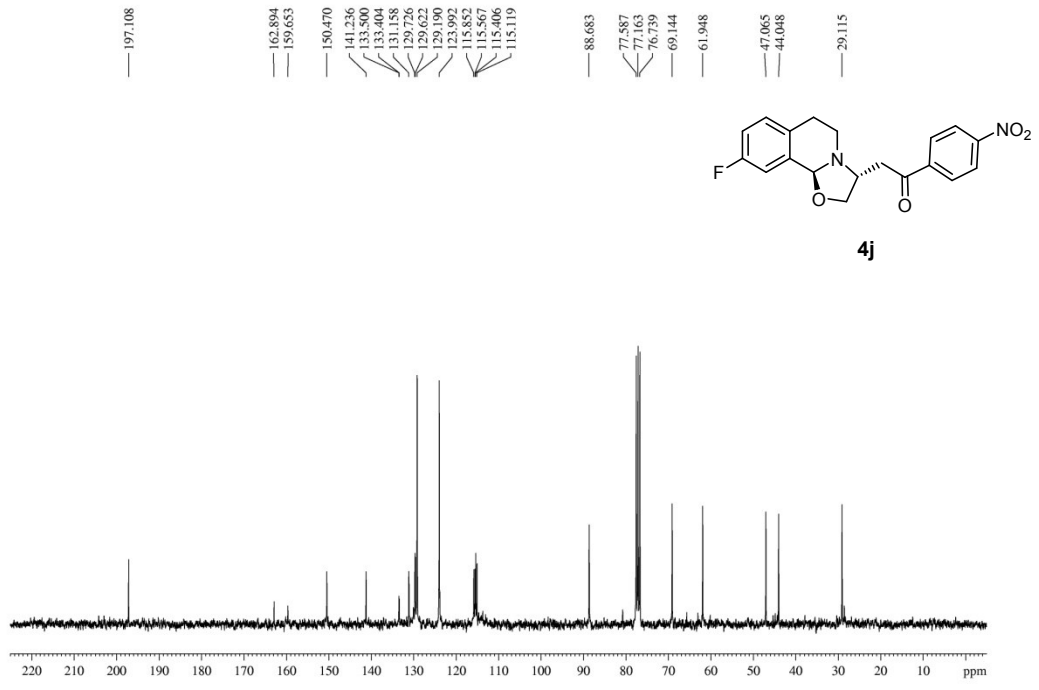


Figure S58: ^{13}C NMR spectra of compound **4j**.

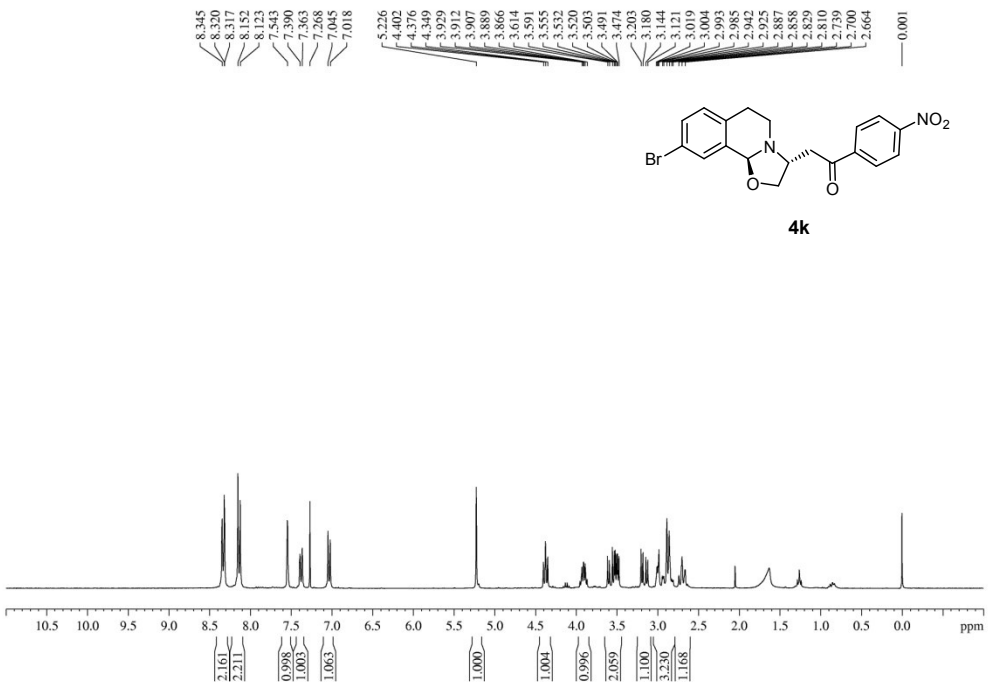


Figure S59: ^{1}H NMR spectra of compound **4k**.

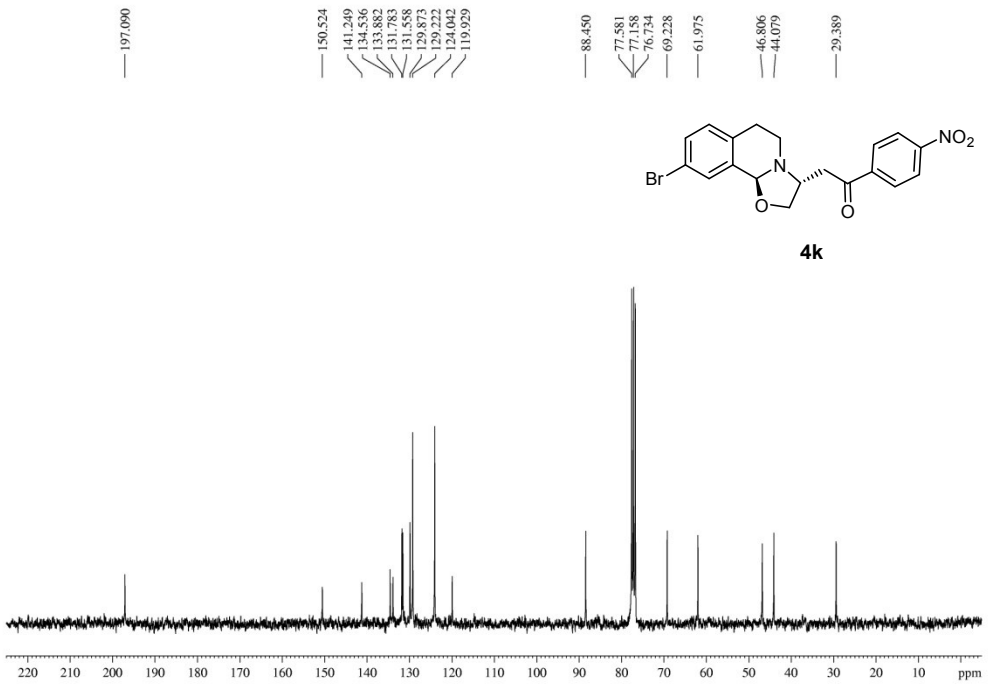


Figure S60: ^{13}C NMR spectra of compound **4k**.

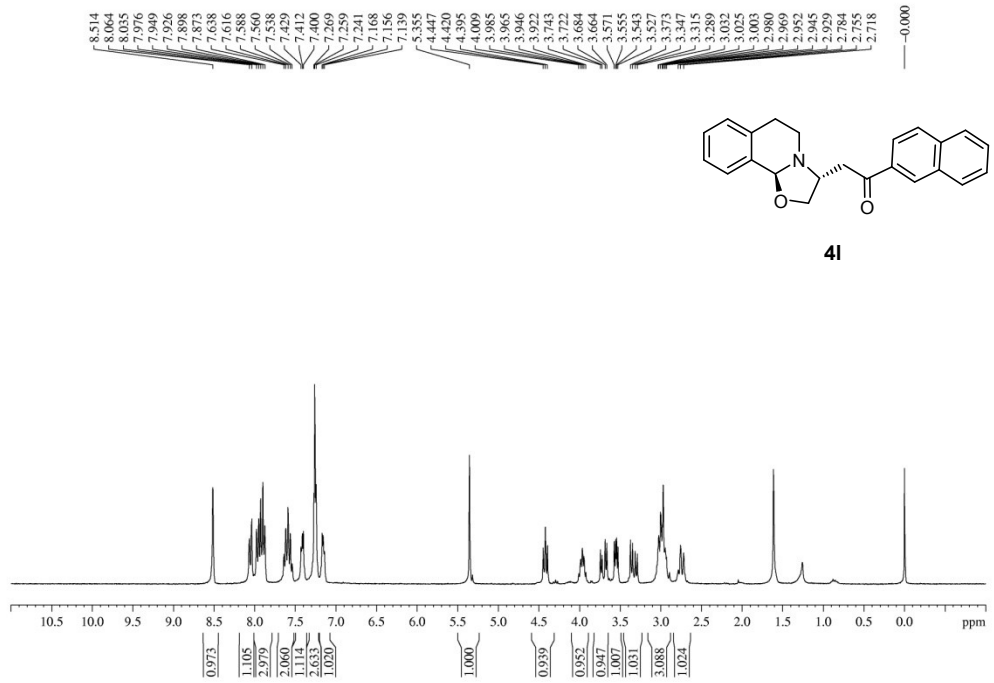


Figure S61: ^{1}H NMR spectra of compound **4l**.

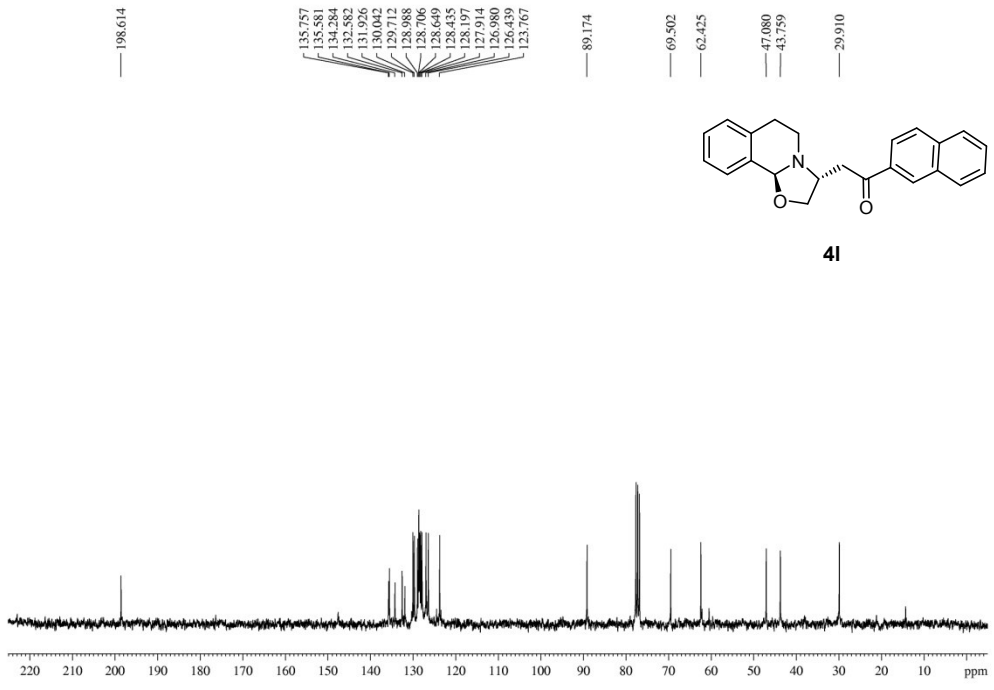


Figure S62: ^{13}C NMR spectra of compound **4l**.

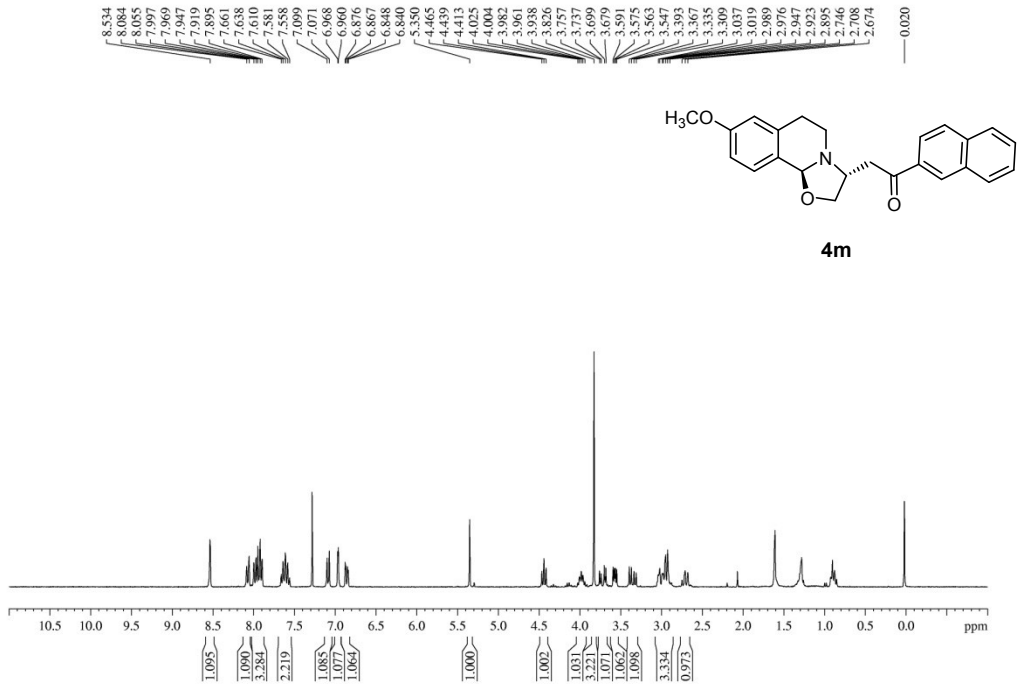


Figure S63: [1]H NMR spectra of compound **4m**.

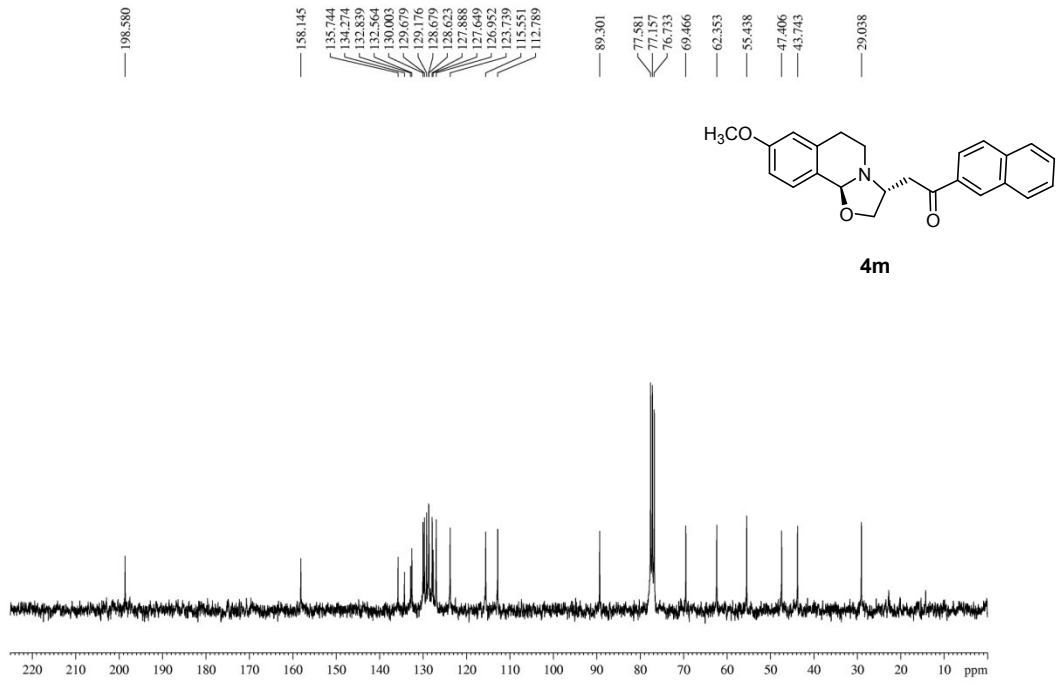


Figure S64: [13]C NMR spectra of compound **4m**.

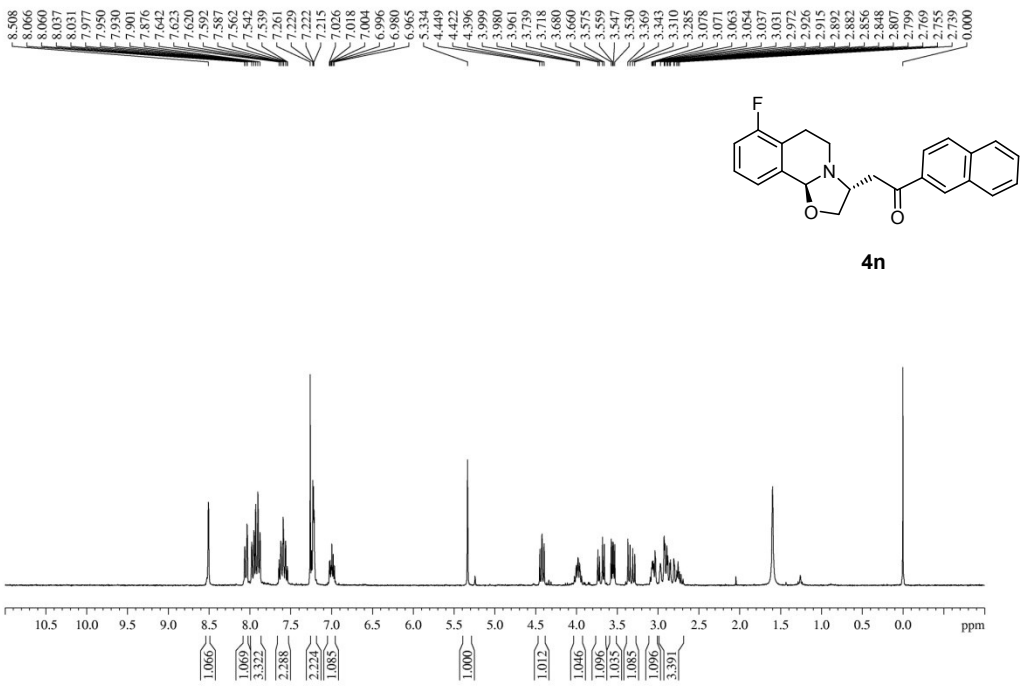


Figure S65: ^{1}H NMR spectra of compound **4n**.

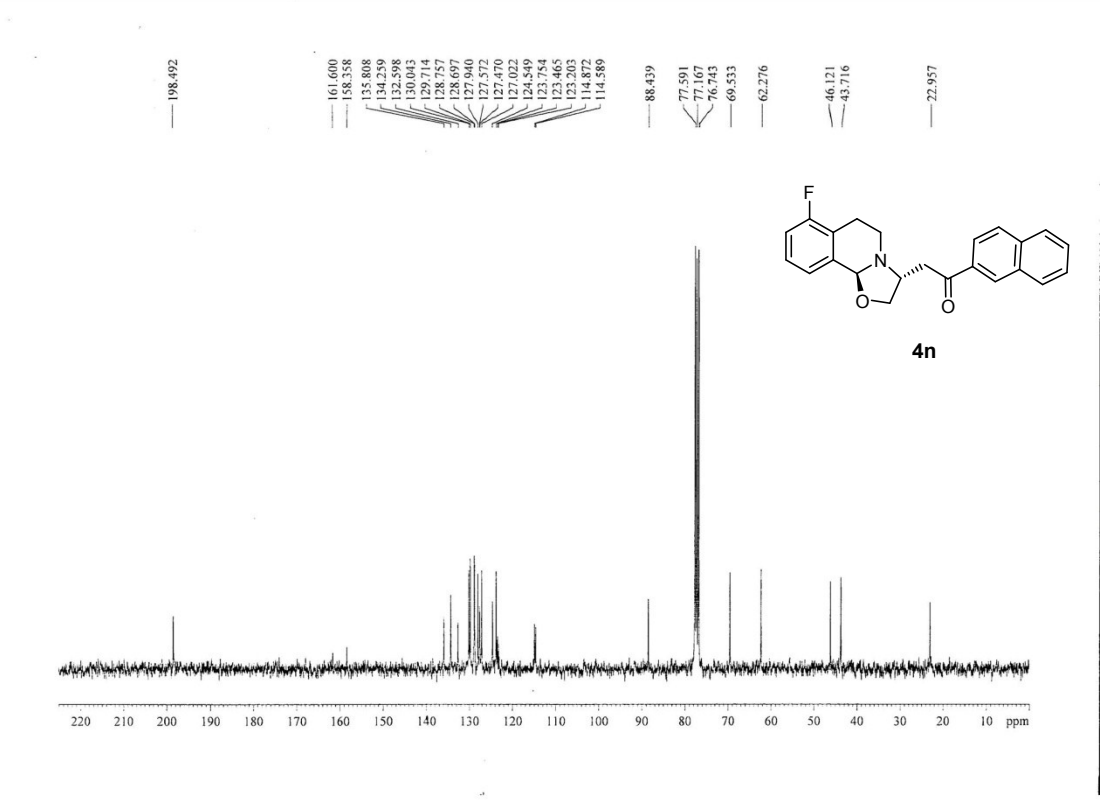


Figure S66: ^{13}C NMR spectra of compound **4n**.

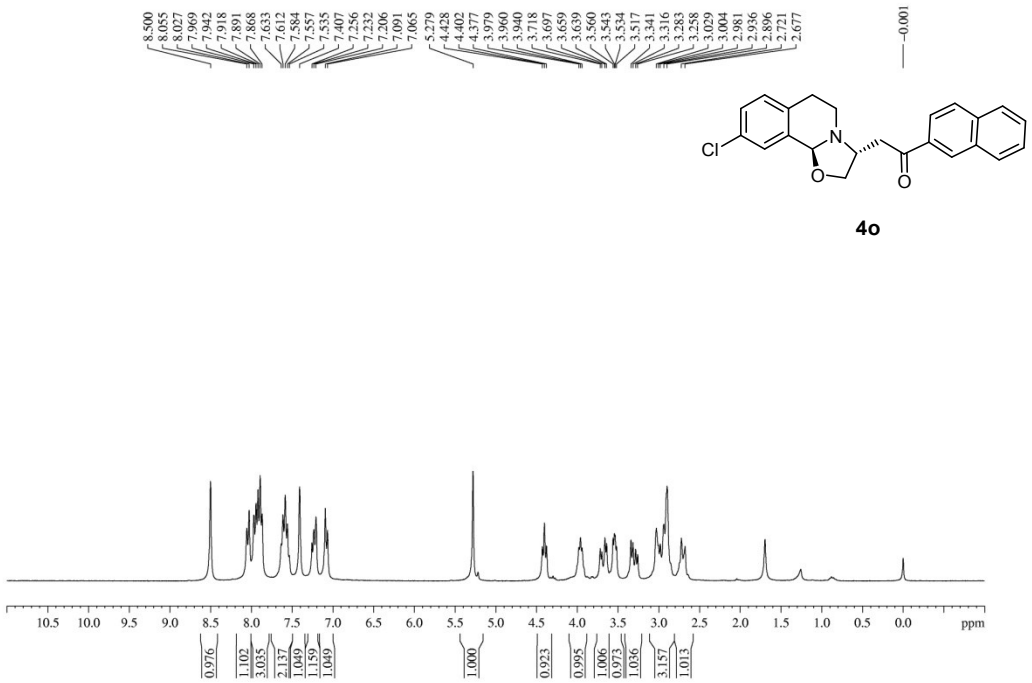


Figure S67: ^{1}H NMR spectra of compound **4o**.

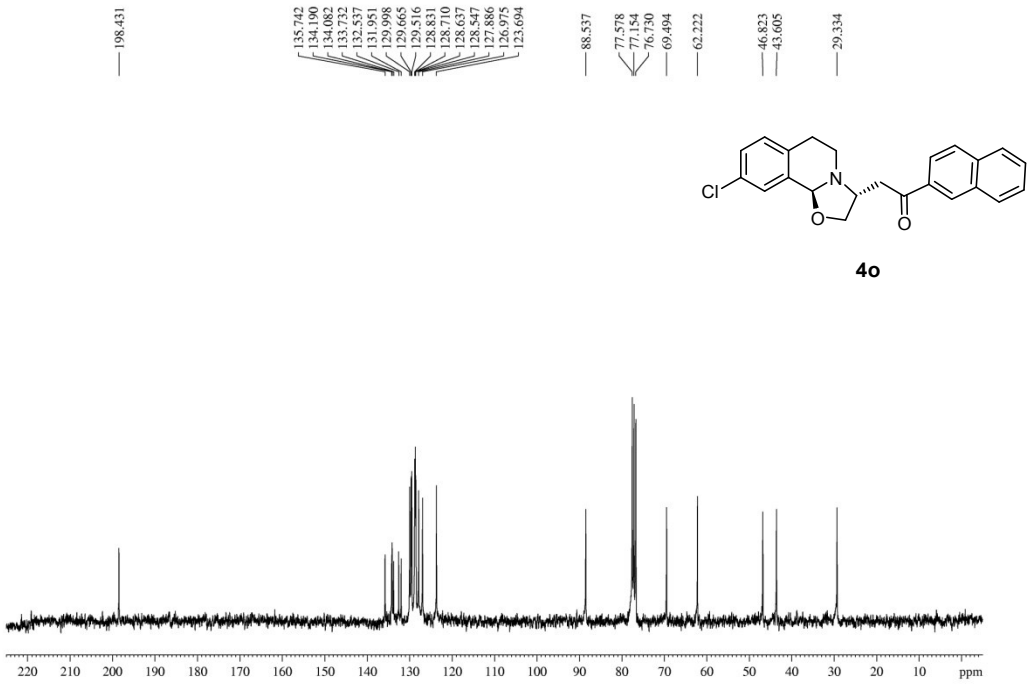


Figure S68: ^{13}C NMR spectra of compound **4o**.

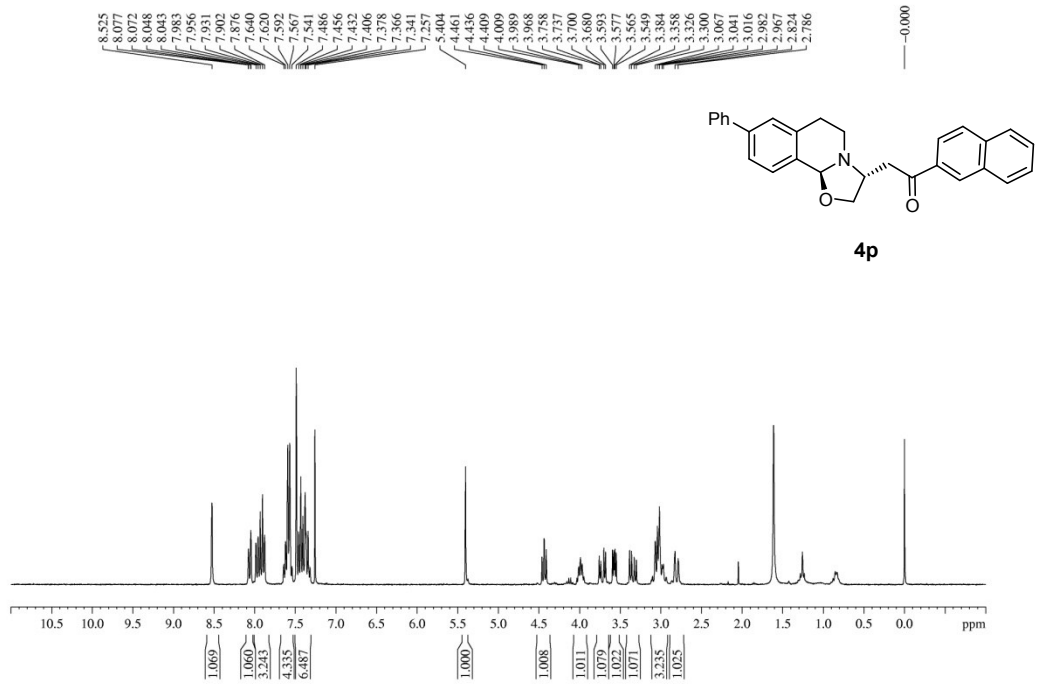


Figure S69: ^{1}H NMR spectra of compound **4p**.

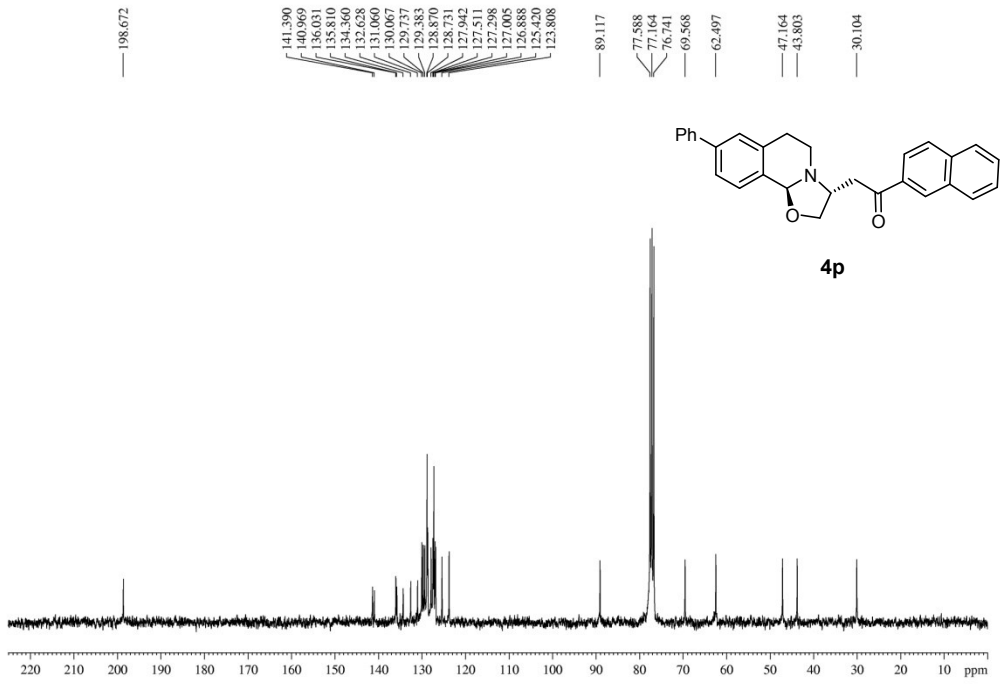


Figure S70: ^{13}C NMR spectra of compound **4p**.

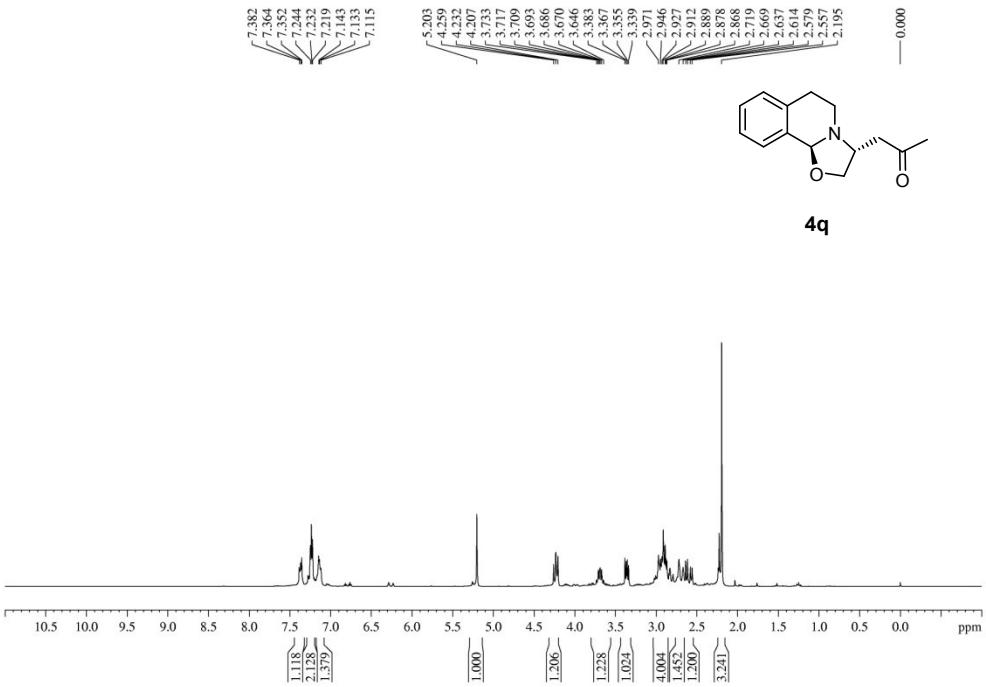


Figure S71: ^{13}C NMR spectra of compound **4q**.

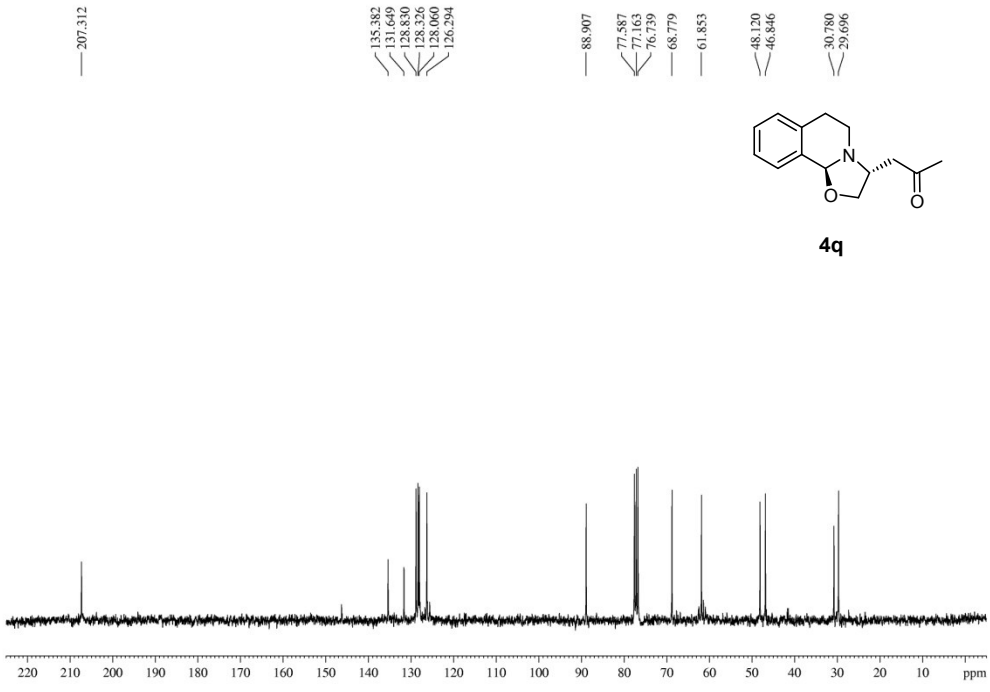


Figure S72: ^{13}C NMR spectra of compound **4q**.

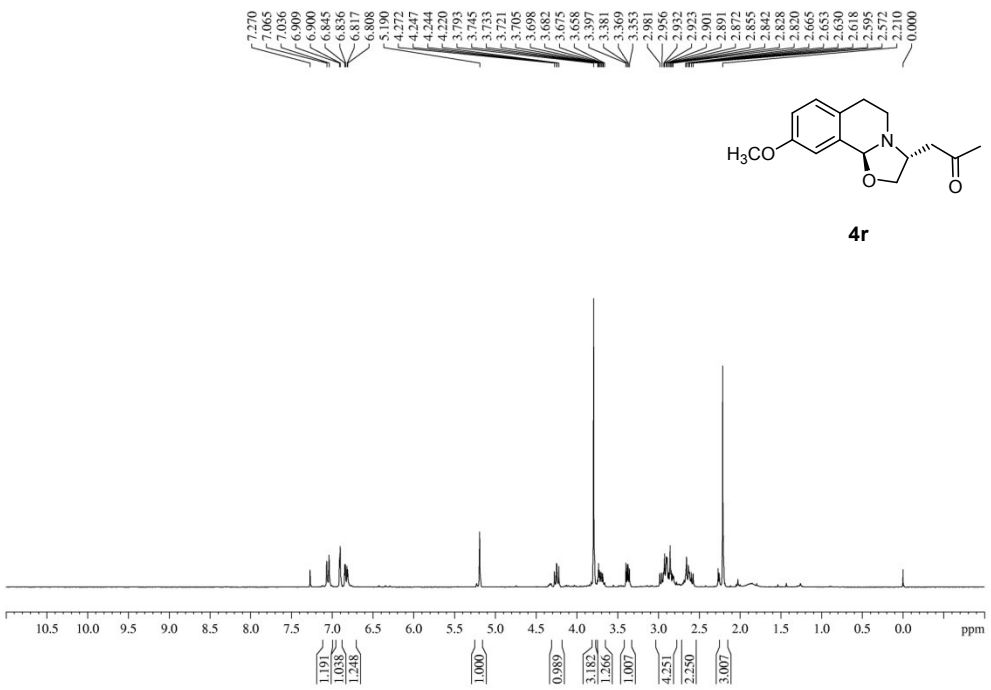


Figure S73: ^{1}H NMR spectra of compound **4r**.

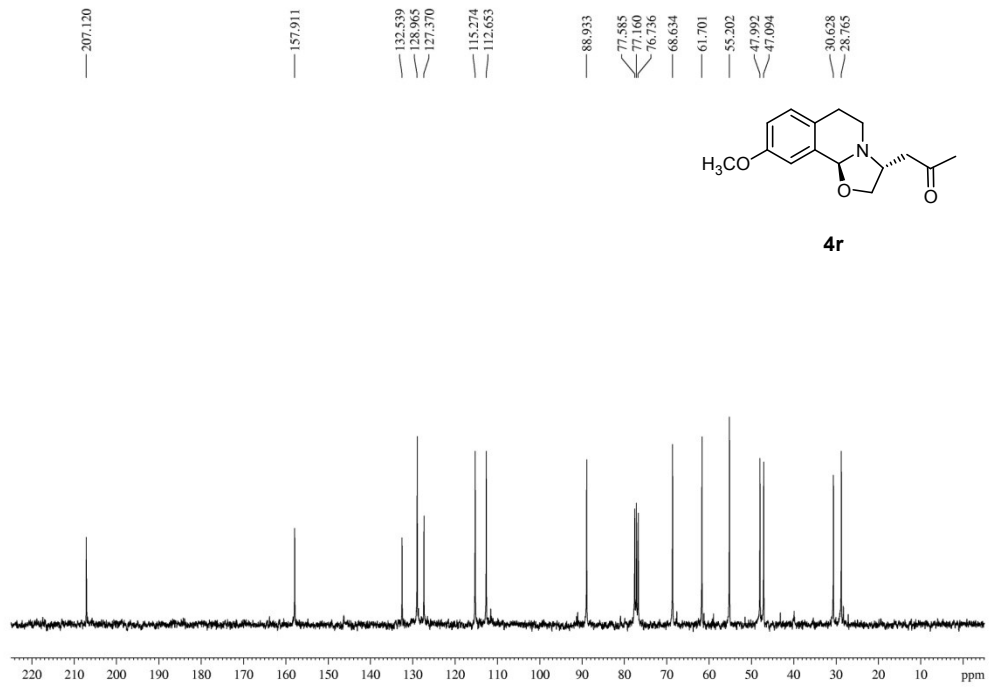


Figure S74: ^{13}C NMR spectra of compound **4r**.

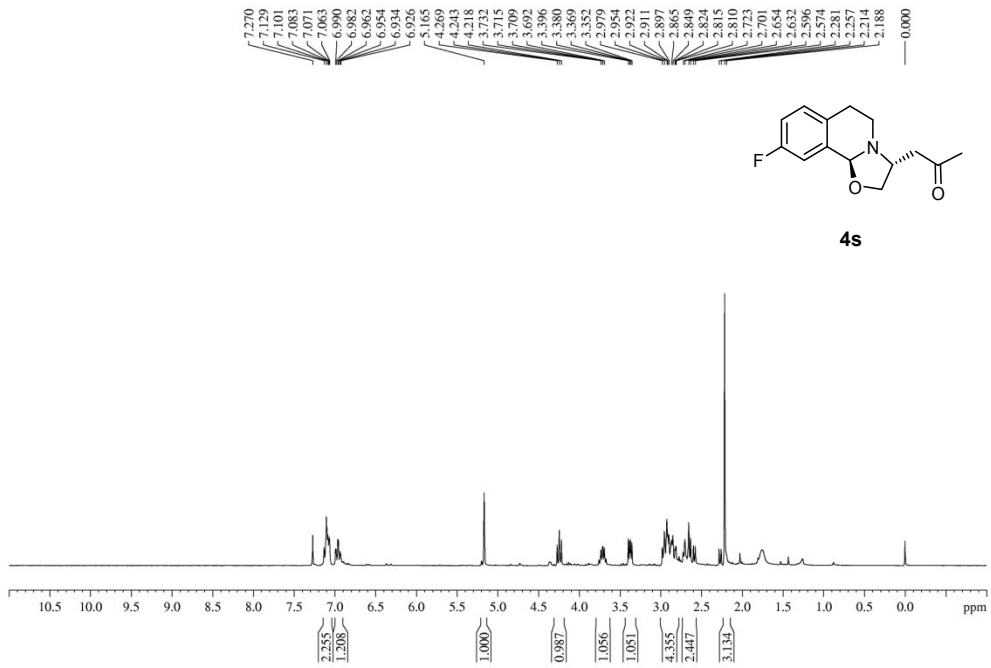


Figure S75: ^{1}H NMR spectra of compound **4s**.

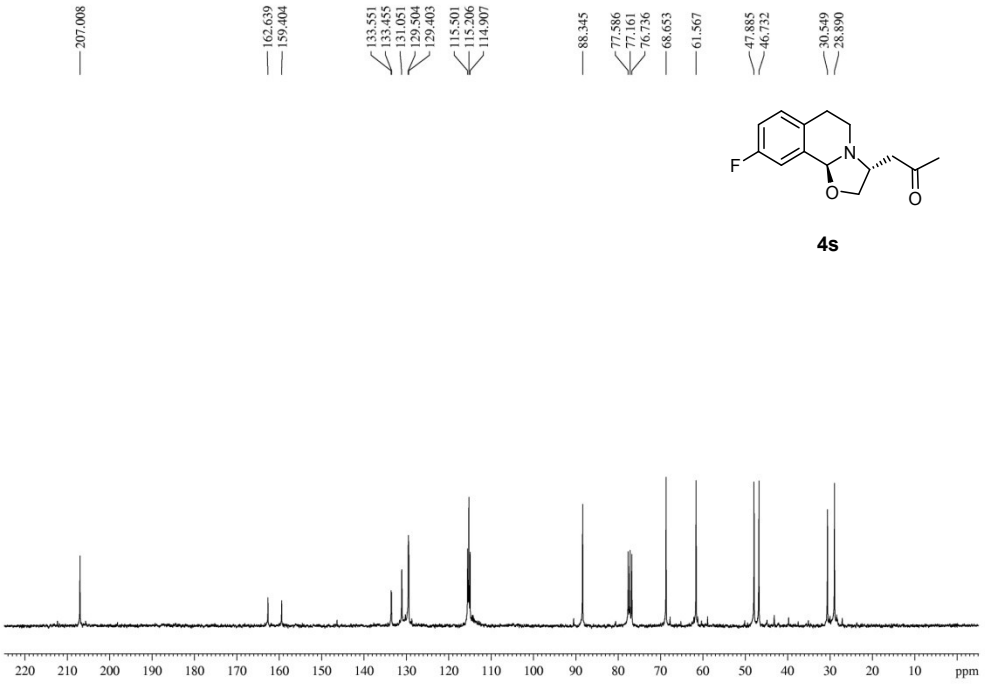


Figure S76: ^{13}C NMR spectra of compound **4s**.

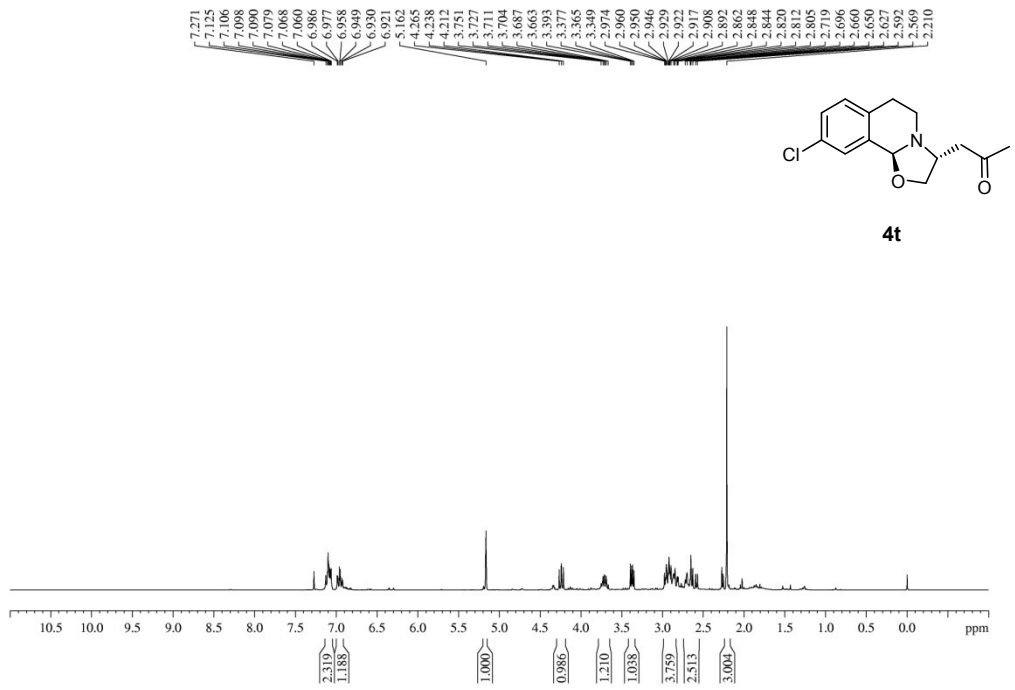


Figure S77: ^{1}H NMR spectra of compound **4t**.

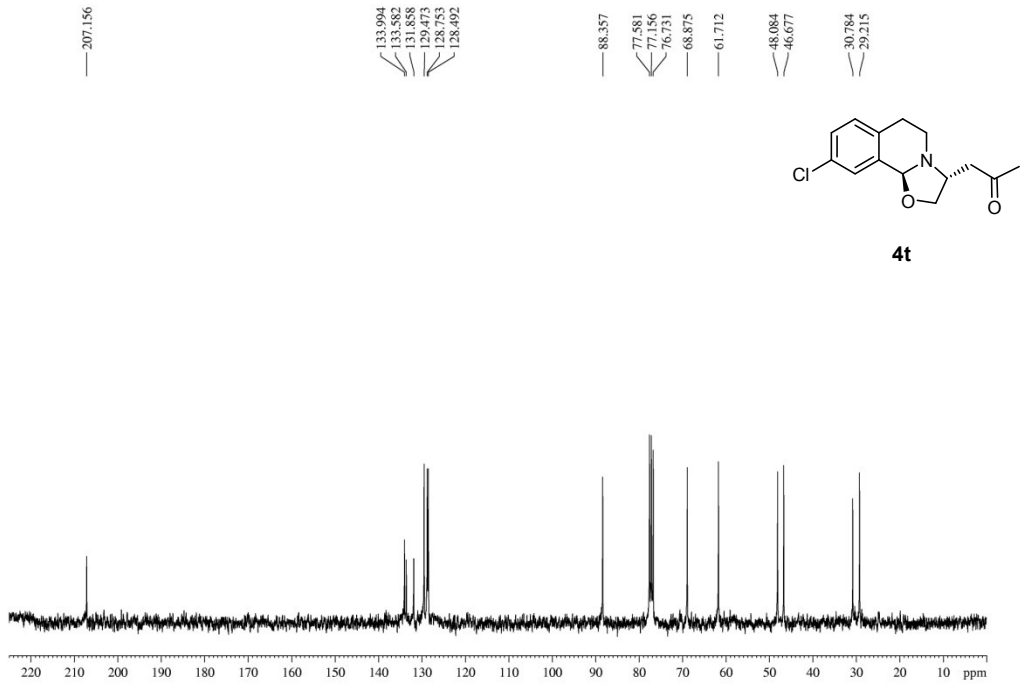


Figure S78: ^{13}C NMR spectra of compound **4t**.

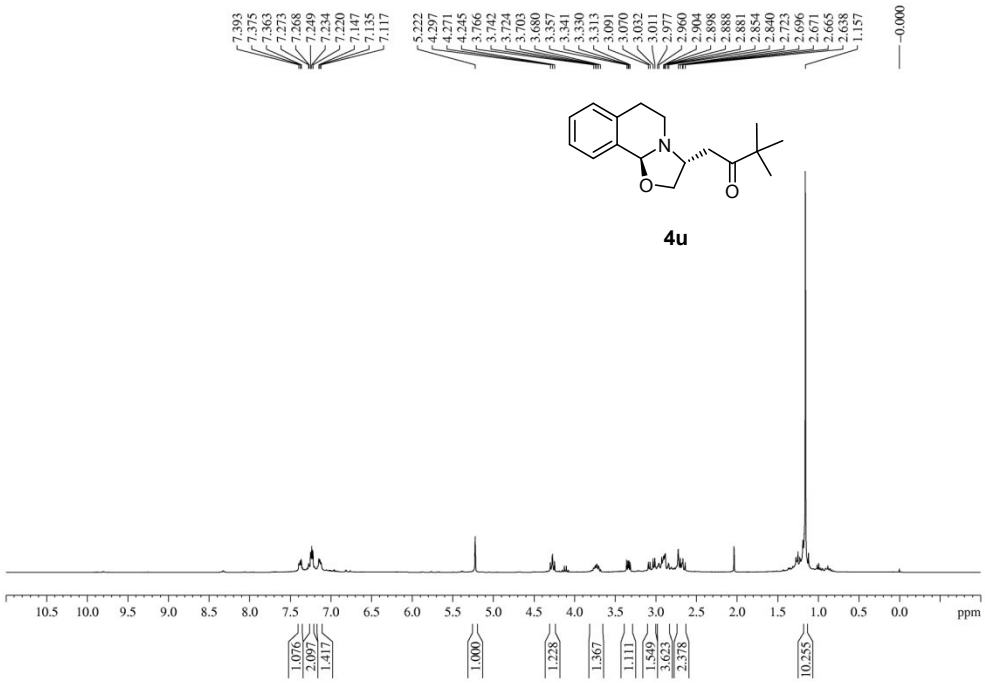


Figure S79: ^{1}H NMR spectra of compound **4u**.

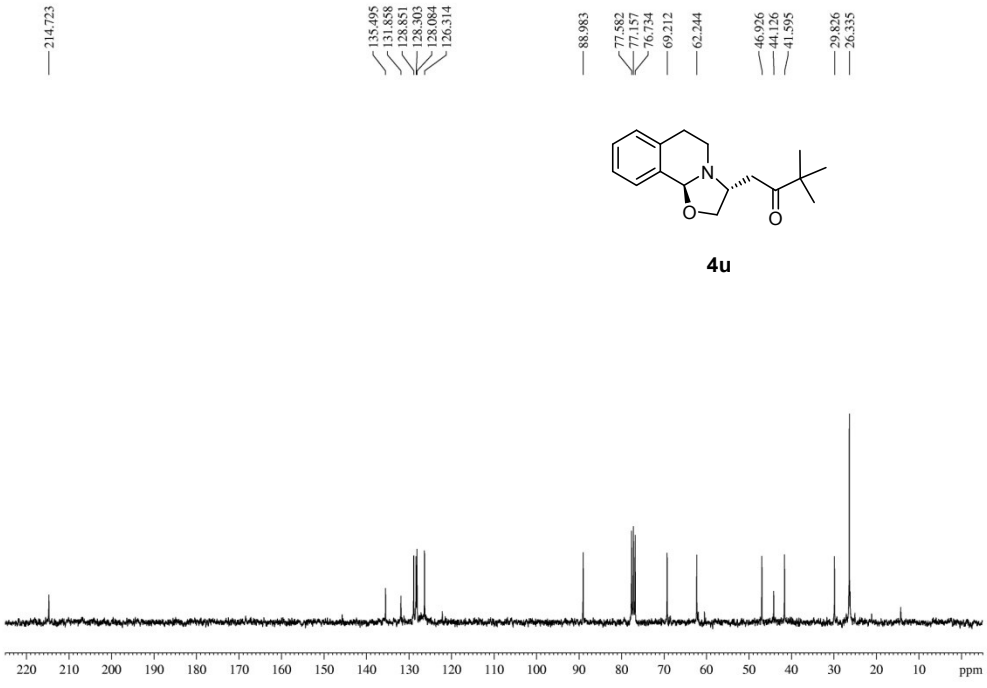


Figure S80: ^{13}C NMR spectra of compound **4u**.

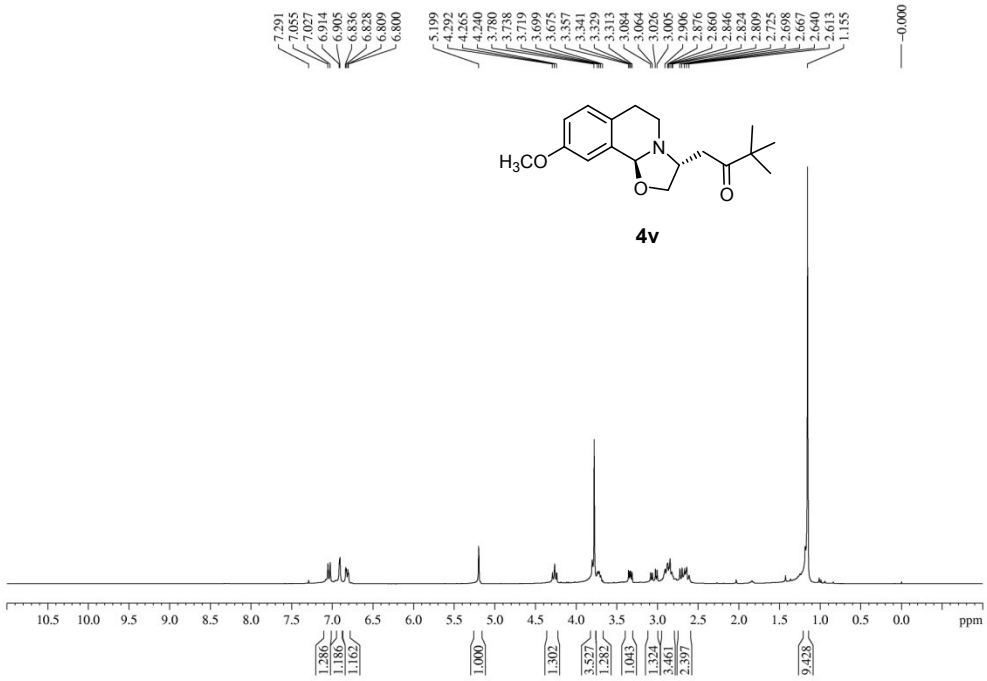


Figure S81: ^{1}H NMR spectra of compound **4v**.

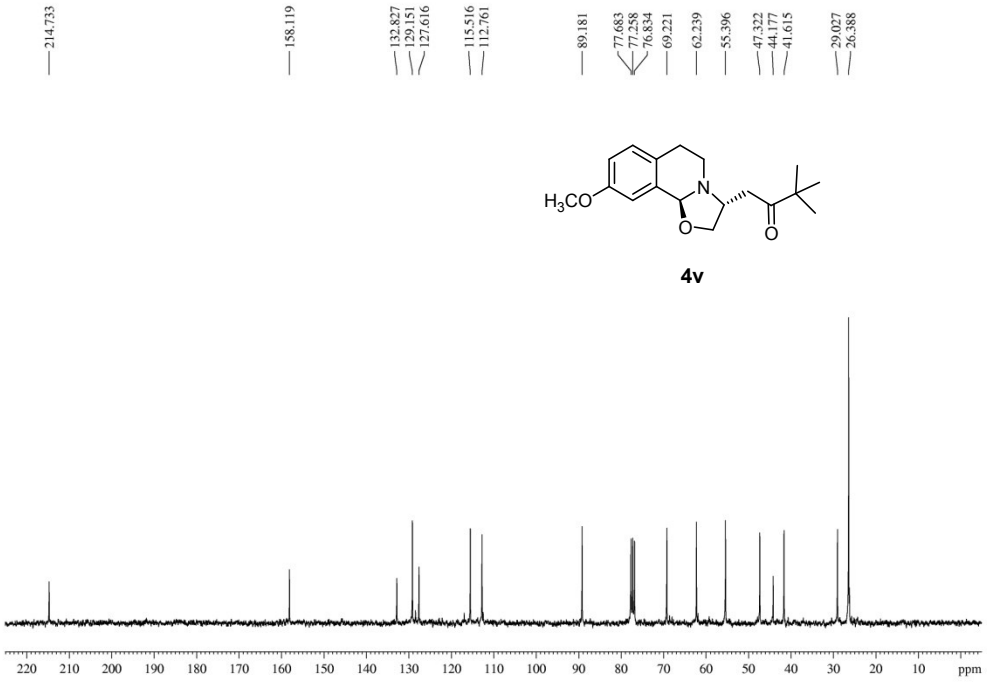


Figure S82: ^{13}C NMR spectra of compound **4v**.

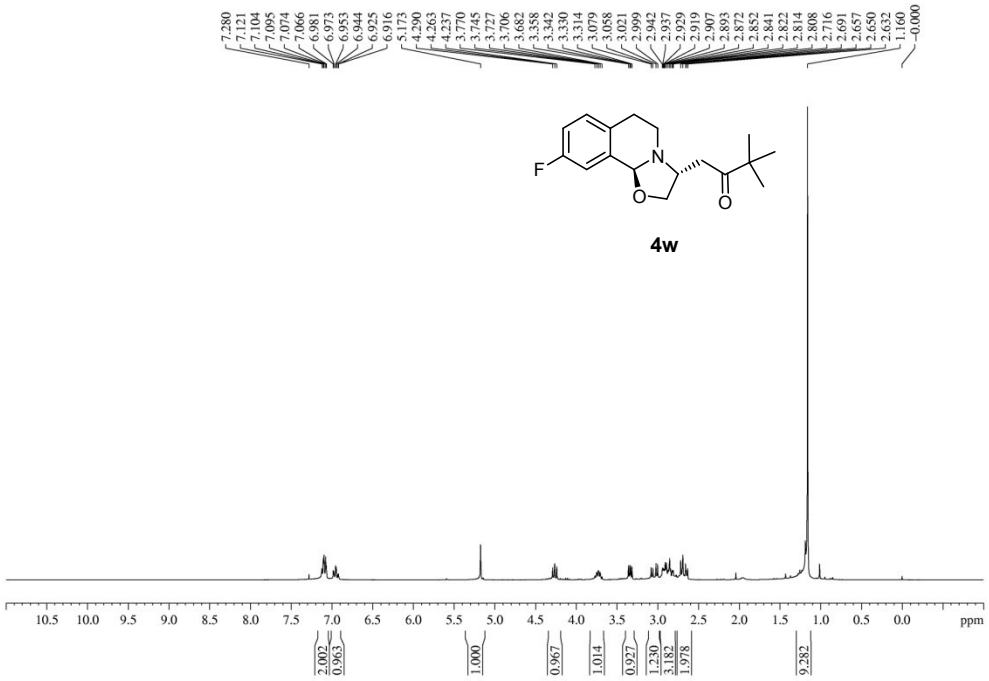


Figure S83: ^{1}H NMR spectra of compound **4w**.

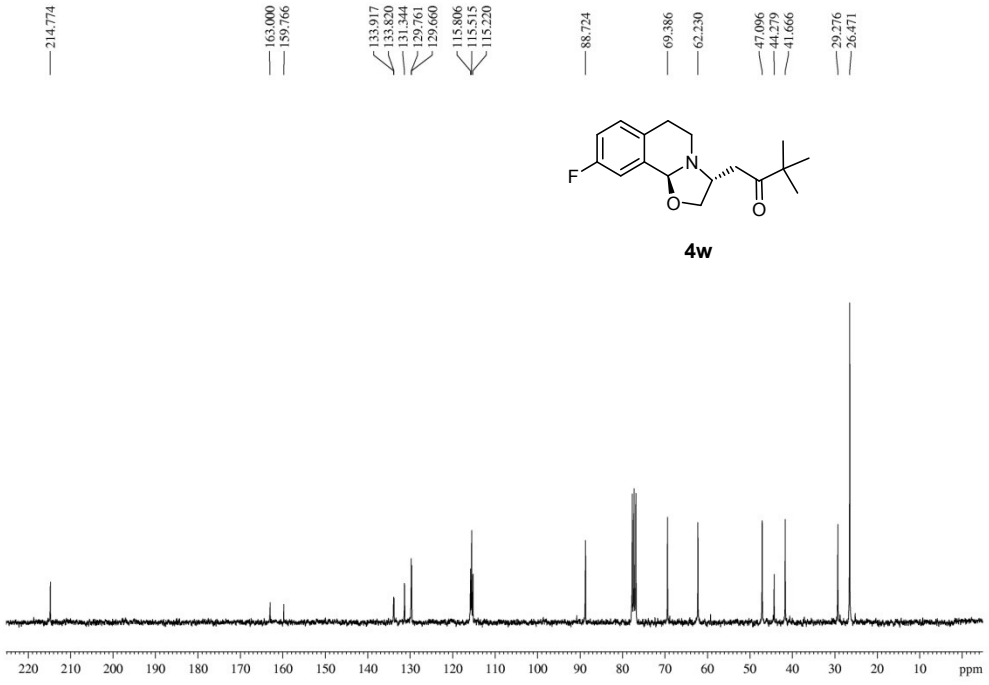


Figure S84: ^{13}C NMR spectra of compound **4w**.

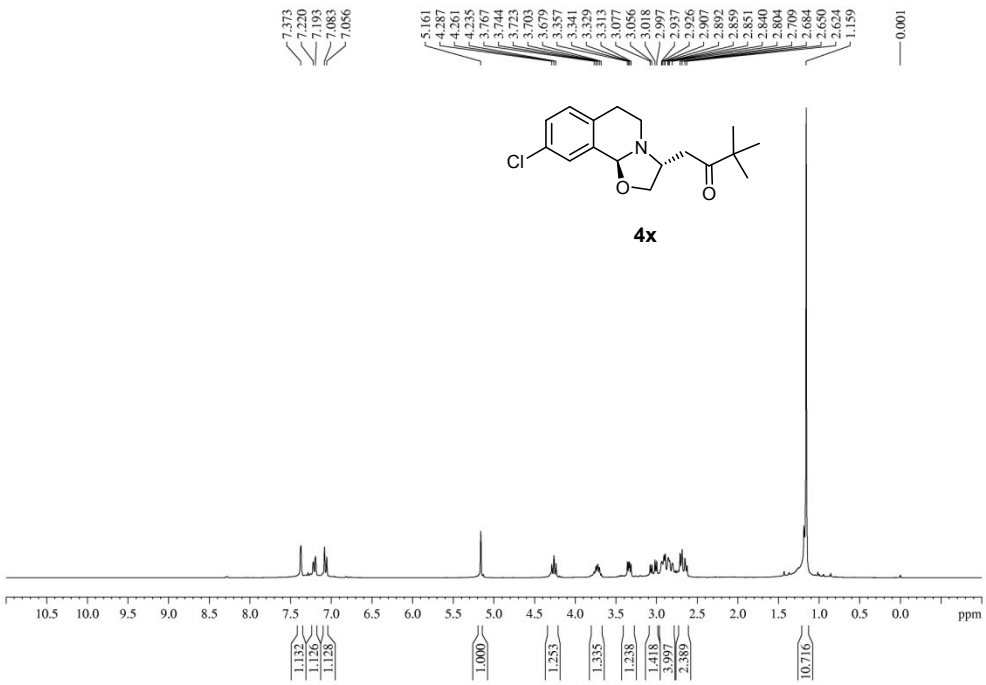


Figure S85: ^{1}H NMR spectra of compound **4x**.

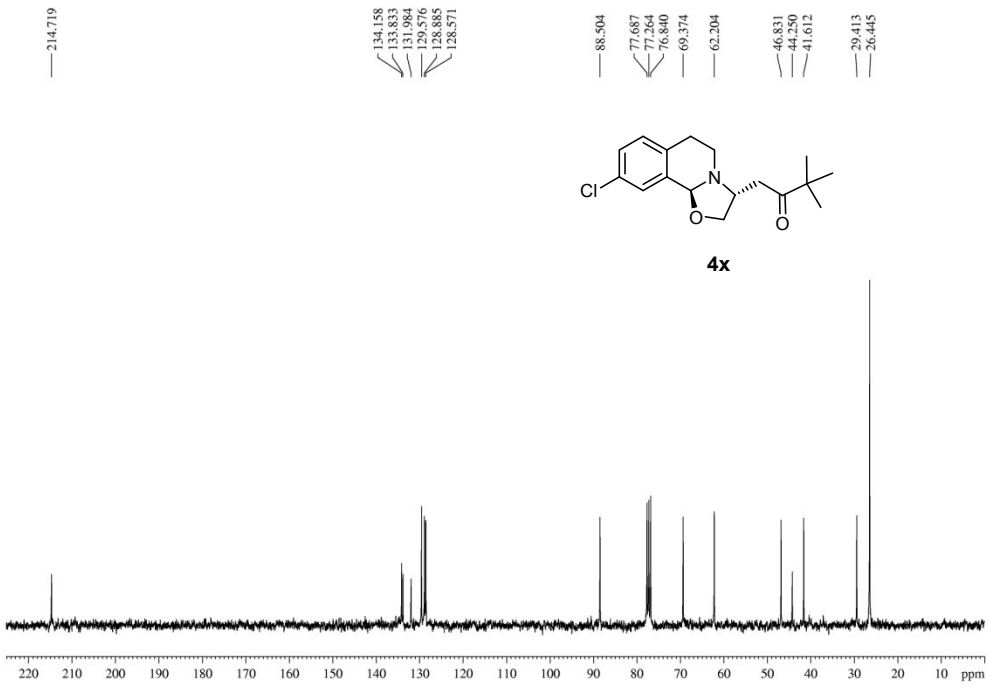


Figure S86: ^{13}C NMR spectra of compound **4x**.

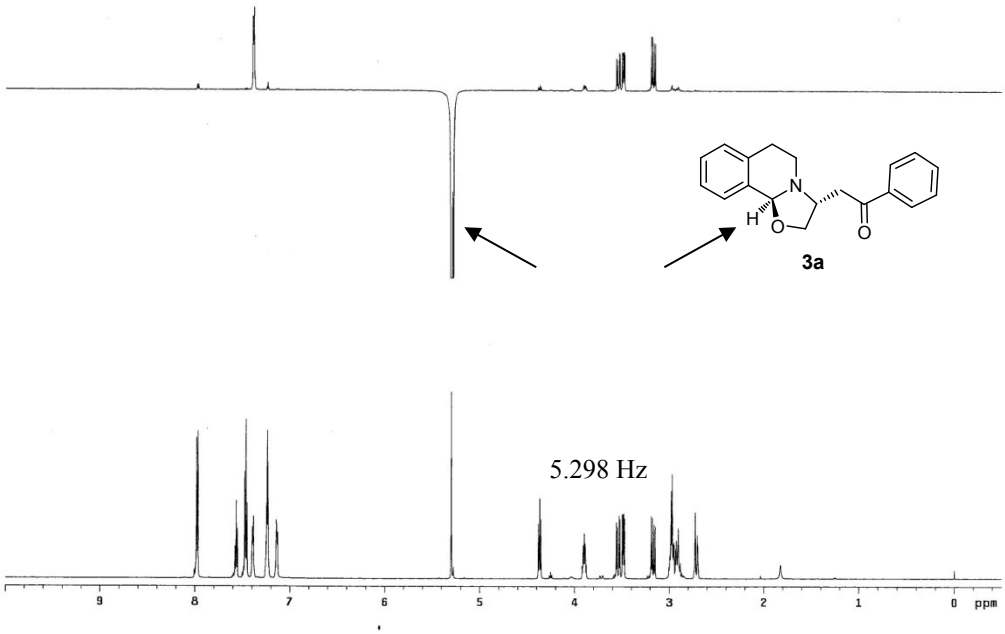


Figure S87. Selective 1D NOESY spectrum of **3a**.

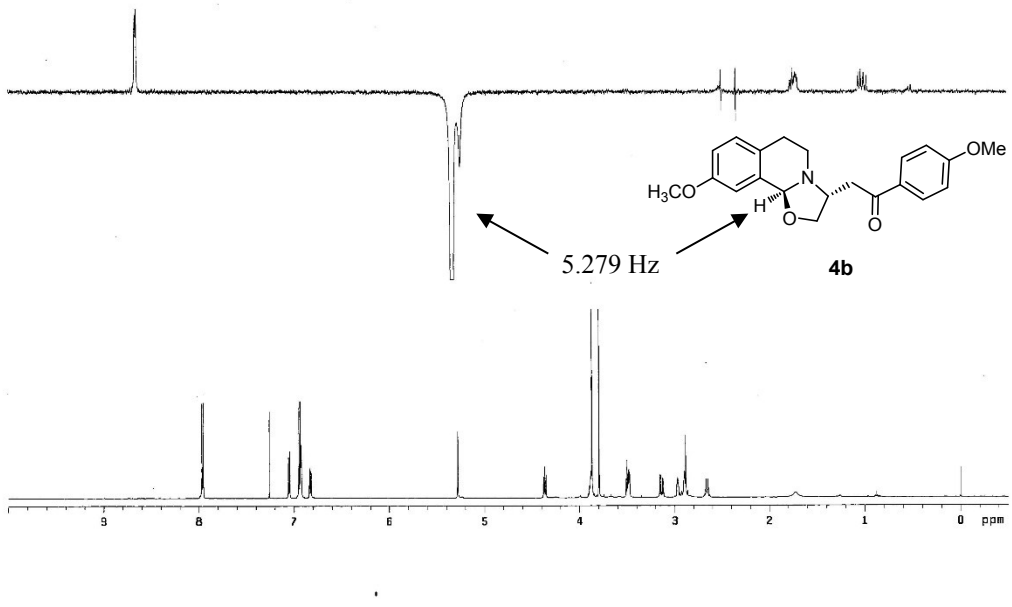


Figure S88. Selective 1D NOESY spectrum of **4b**.

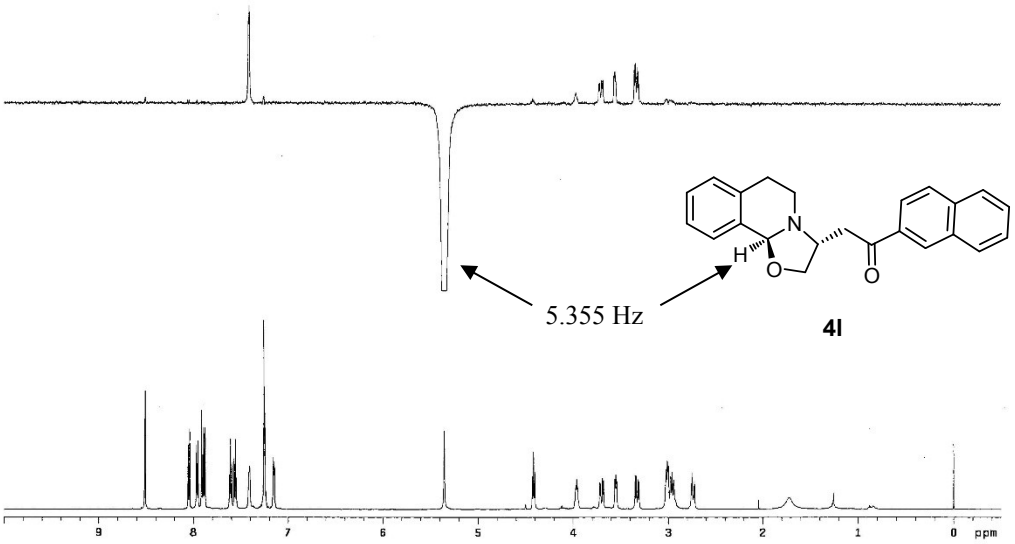


Figure S89. Selective 1D NOESY spectrum of **4l**.

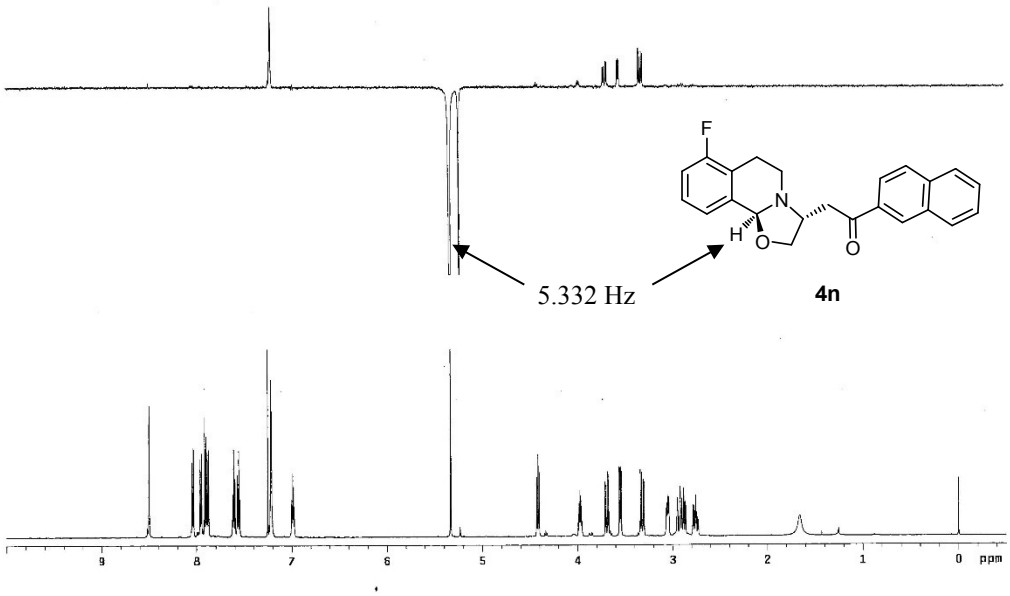


Figure S90. Selective 1D NOESY spectrum of **4n**.

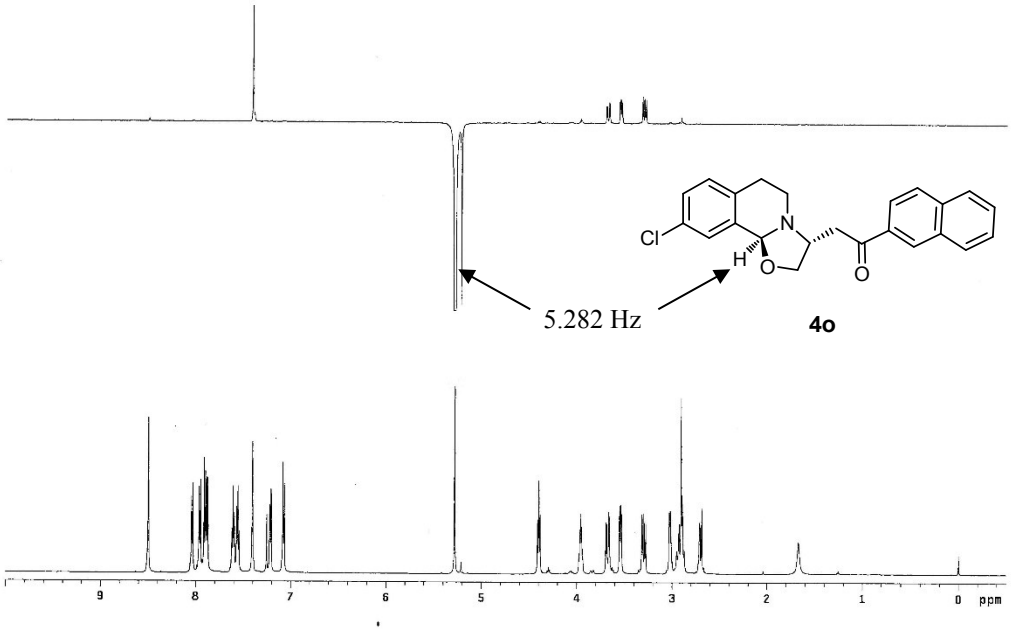


Figure S91. Selective 1D NOESY spectrum of **4o**.

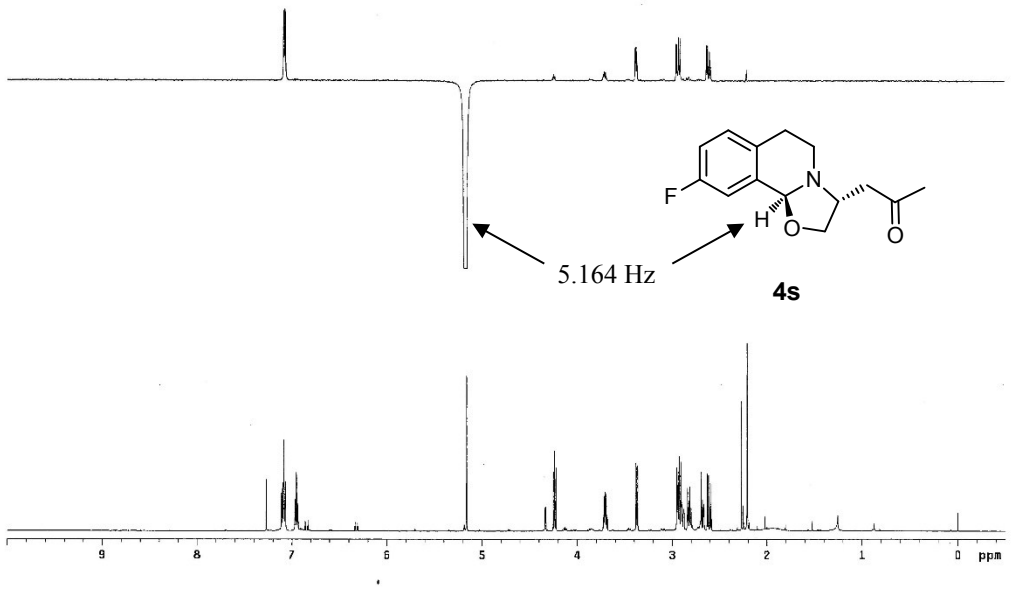


Figure S92. Selective 1D NOESY spectrum of **4s**.

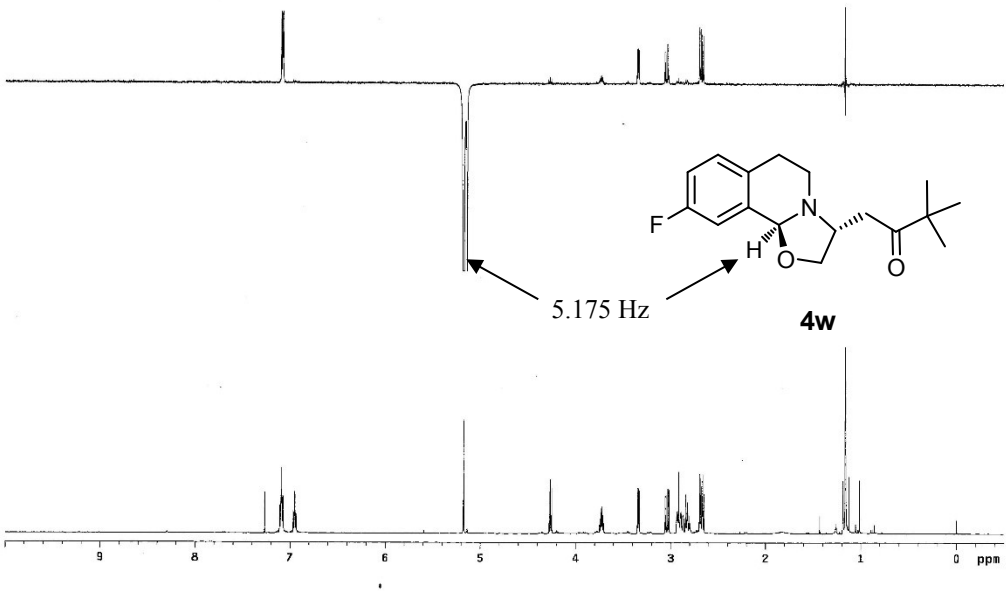


Figure S93. Selective 1D NOESY spectrum of **4w**.

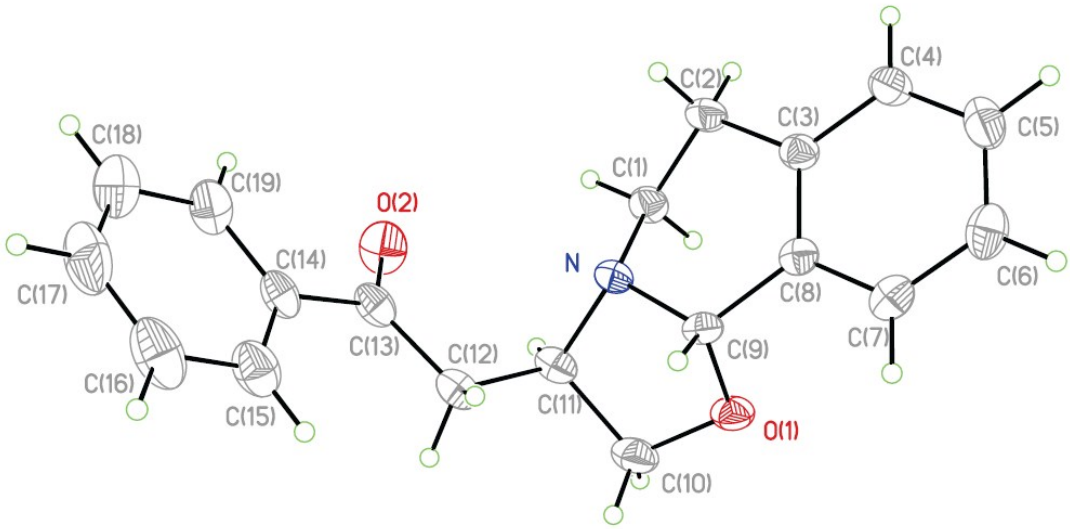


Figure S94. X-ray Crystallographic Data of compound **3a.**

Table 1. Crystal data and structure refinement for **3a**.

Identification code	**3a**	
Empirical formula	C19 H19 N O2	
Formula weight	293.35	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	?	
Space group	?	
Unit cell dimensions	a = 8.0476(5) Å	α= 90°.
	b = 8.1366(5) Å	β= 94.493(2)°.
	c = 23.2624(14) Å	γ = 90°.
Volume	1518.54(16) $Å^3$	
Z	4	
Density (calculated)	1.283 Mg/m^3	
Absorption coefficient	0.083 mm^{-1}	
F(000)	624	
Crystal size	0.52 x 0.47 x 0.44 mm^3	
Theta range for data collection	3.06 to 26.39°.	
Index ranges	-10<=h<=10, -10<=k<=10, -29<=l<=29	
Reflections collected	38076	
Independent reflections	3106 [R(int) = 0.0286]	
Completeness to theta = 26.39°	99.8 %	
Max. and min. transmission	0.9644 and 0.9581	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3106 / 0 / 199	
Goodness-of-fit on F^2	1.044	
Final R indices [I>2sigma(I)]	R1 = 0.0420, wR2 = 0.1093	
R indices (all data)	R1 = 0.0496, wR2 = 0.1178	
Largest diff. peak and hole	0.214 and -0.287 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **3a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	10301(1)	7651(1)	2488(1)	28(1)
O(2)	8110(2)	7033(1)	396(1)	40(1)
N	8189(1)	7388(1)	1756(1)	22(1)
C(1)	7471(2)	9053(2)	1709(1)	26(1)
C(2)	5852(2)	9063(2)	1999(1)	30(1)
C(3)	6119(2)	8485(2)	2614(1)	24(1)
C(4)	5036(2)	8932(2)	3029(1)	31(1)
C(5)	5326(2)	8426(2)	3596(1)	35(1)
C(6)	6703(2)	7458(2)	3760(1)	34(1)
C(7)	7761(2)	6977(2)	3351(1)	28(1)
C(8)	7485(2)	7489(1)	2779(1)	22(1)
C(9)	8667(1)	6937(2)	2350(1)	22(1)
C(10)	11153(2)	7306(2)	1985(1)	33(1)
C(11)	9778(2)	7243(2)	1476(1)	27(1)
C(12)	9779(2)	5648(2)	1136(1)	30(1)
C(13)	8602(2)	5718(2)	595(1)	28(1)
C(14)	8037(2)	4154(2)	305(1)	28(1)
C(15)	8648(2)	2617(2)	478(1)	39(1)
C(16)	8036(3)	1208(2)	199(1)	51(1)
C(17)	6800(2)	1328(2)	-246(1)	54(1)
C(18)	6189(3)	2842(2)	-427(1)	52(1)
C(19)	6814(2)	4246(2)	-153(1)	39(1)

Table 3. Bond lengths [Å] and angles [°] for **3a**.

O(1)-C(10)	1.4305(17)
O(1)-C(9)	1.4506(14)
O(2)-C(13)	1.2190(17)
N-C(9)	1.4520(16)
N-C(1)	1.4736(15)
N-C(11)	1.4841(15)
C(1)-C(2)	1.5135(18)
C(1)-H(1A)	0.9900
C(1)-H(1B)	0.9900
C(2)-C(3)	1.5057(18)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(4)	1.3987(18)
C(3)-C(8)	1.3951(17)
C(4)-C(5)	1.383(2)
C(4)-H(4A)	0.9500
C(5)-C(6)	1.389(2)
C(5)-H(5A)	0.9500
C(6)-C(7)	1.381(2)
C(6)-H(6A)	0.9500
C(7)-C(8)	1.3958(18)
C(7)-H(7A)	0.9500
C(8)-C(9)	1.5016(17)
C(9)-H(9A)	1.0000
C(10)-C(11)	1.5557(19)
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(11)-C(12)	1.5202(18)
C(11)-H(11A)	1.0000
C(12)-C(13)	1.515(2)
C(12)-H(12A)	0.9900
C(12)-H(12B)	0.9900
C(13)-C(14)	1.4951(19)
C(14)-C(15)	1.391(2)
C(14)-C(19)	1.394(2)
C(15)-C(16)	1.389(2)

C(15)-H(15A)	0.9500
C(16)-C(17)	1.382(3)
C(16)-H(16A)	0.9500
C(17)-C(18)	1.380(3)
C(17)-H(17A)	0.9500
C(18)-C(19)	1.384(2)
C(18)-H(18A)	0.9500
C(19)-H(19A)	0.9500

C(10)-O(1)-C(9)	102.91(9)
C(9)-N-C(1)	112.09(10)
C(9)-N-C(11)	102.91(9)
C(1)-N-C(11)	112.80(10)
N-C(1)-C(2)	108.56(10)
N-C(1)-H(1A)	110.0
C(2)-C(1)-H(1A)	110.0
N-C(1)-H(1B)	110.0
C(2)-C(1)-H(1B)	110.0
H(1A)-C(1)-H(1B)	108.4
C(3)-C(2)-C(1)	110.99(10)
C(3)-C(2)-H(2A)	109.4
C(1)-C(2)-H(2A)	109.4
C(3)-C(2)-H(2B)	109.4
C(1)-C(2)-H(2B)	109.4
H(2A)-C(2)-H(2B)	108.0
C(4)-C(3)-C(8)	118.74(12)
C(4)-C(3)-C(2)	121.65(11)
C(8)-C(3)-C(2)	119.61(11)
C(5)-C(4)-C(3)	120.87(13)
C(5)-C(4)-H(4A)	119.6
C(3)-C(4)-H(4A)	119.6
C(4)-C(5)-C(6)	120.12(13)
C(4)-C(5)-H(5A)	119.9
C(6)-C(5)-H(5A)	119.9
C(7)-C(6)-C(5)	119.59(13)
C(7)-C(6)-H(6A)	120.2
C(5)-C(6)-H(6A)	120.2
C(6)-C(7)-C(8)	120.69(13)

C(6)-C(7)-H(7A)	119.7
C(8)-C(7)-H(7A)	119.7
C(7)-C(8)-C(3)	119.97(12)
C(7)-C(8)-C(9)	118.90(11)
C(3)-C(8)-C(9)	121.12(11)
O(1)-C(9)-N	106.17(10)
O(1)-C(9)-C(8)	110.05(10)
N-C(9)-C(8)	115.05(10)
O(1)-C(9)-H(9A)	108.5
N-C(9)-H(9A)	108.5
C(8)-C(9)-H(9A)	108.5
O(1)-C(10)-C(11)	105.75(10)
O(1)-C(10)-H(10A)	110.6
C(11)-C(10)-H(10A)	110.6
O(1)-C(10)-H(10B)	110.6
C(11)-C(10)-H(10B)	110.6
H(10A)-C(10)-H(10B)	108.7
N-C(11)-C(12)	109.39(10)
N-C(11)-C(10)	104.48(10)
C(12)-C(11)-C(10)	113.30(11)
N-C(11)-H(11A)	109.8
C(12)-C(11)-H(11A)	109.8
C(10)-C(11)-H(11A)	109.8
C(13)-C(12)-C(11)	112.00(11)
C(13)-C(12)-H(12A)	109.2
C(11)-C(12)-H(12A)	109.2
C(13)-C(12)-H(12B)	109.2
C(11)-C(12)-H(12B)	109.2
H(12A)-C(12)-H(12B)	107.9
O(2)-C(13)-C(14)	119.83(13)
O(2)-C(13)-C(12)	120.77(12)
C(14)-C(13)-C(12)	119.40(11)
C(15)-C(14)-C(19)	118.79(13)
C(15)-C(14)-C(13)	123.12(13)
C(19)-C(14)-C(13)	118.08(12)
C(14)-C(15)-C(16)	120.14(16)
C(14)-C(15)-H(15A)	119.9
C(16)-C(15)-H(15A)	119.9

C(17)-C(16)-C(15)	119.99(16)
C(17)-C(16)-H(16A)	120.0
C(15)-C(16)-H(16A)	120.0
C(18)-C(17)-C(16)	120.68(16)
C(18)-C(17)-H(17A)	119.7
C(16)-C(17)-H(17A)	119.7
C(17)-C(18)-C(19)	119.22(17)
C(17)-C(18)-H(18A)	120.4
C(19)-C(18)-H(18A)	120.4
C(18)-C(19)-C(14)	121.16(15)
C(18)-C(19)-H(19A)	119.4
C(14)-C(19)-H(19A)	119.4

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 5c. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	18(1)	29(1)	36(1)	-5(1)	-2(1)	-1(1)
O(2)	56(1)	24(1)	40(1)	5(1)	1(1)	2(1)
N	20(1)	20(1)	26(1)	0(1)	3(1)	3(1)
C(1)	29(1)	23(1)	27(1)	4(1)	2(1)	7(1)
C(2)	25(1)	34(1)	30(1)	2(1)	1(1)	12(1)
C(3)	21(1)	23(1)	28(1)	-2(1)	1(1)	-1(1)
C(4)	24(1)	35(1)	34(1)	-5(1)	4(1)	2(1)
C(5)	36(1)	40(1)	32(1)	-8(1)	11(1)	-7(1)
C(6)	44(1)	31(1)	26(1)	1(1)	2(1)	-9(1)
C(7)	31(1)	22(1)	29(1)	1(1)	-4(1)	-4(1)
C(8)	21(1)	17(1)	26(1)	-2(1)	0(1)	-3(1)
C(9)	17(1)	18(1)	29(1)	-1(1)	-2(1)	0(1)
C(10)	20(1)	34(1)	44(1)	-4(1)	5(1)	2(1)
C(11)	22(1)	24(1)	34(1)	0(1)	8(1)	2(1)
C(12)	29(1)	27(1)	36(1)	-2(1)	8(1)	6(1)
C(13)	32(1)	25(1)	29(1)	2(1)	13(1)	2(1)
C(14)	34(1)	25(1)	27(1)	0(1)	15(1)	0(1)
C(15)	52(1)	28(1)	39(1)	0(1)	10(1)	7(1)
C(16)	76(1)	24(1)	55(1)	-2(1)	21(1)	4(1)
C(17)	67(1)	37(1)	58(1)	-20(1)	18(1)	-12(1)
C(18)	60(1)	48(1)	48(1)	-16(1)	1(1)	-2(1)
C(19)	51(1)	34(1)	32(1)	-3(1)	6(1)	4(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{-3}) for 5c.

	x	y	z	U(eq)
H(1A)	7261	9363	1298	31
H(1B)	8258	9858	1898	31
H(2A)	5388	10191	1991	35
H(2B)	5035	8336	1784	35
H(4A)	4089	9591	2920	37
H(5A)	4581	8742	3873	42
H(6A)	6916	7128	4150	40
H(7A)	8687	6290	3461	33
H(9A)	8770	5714	2372	26
H(10A)	11745	6242	2025	39
H(10B)	11974	8181	1920	39
H(11A)	9906	8198	1213	32
H(12A)	10923	5423	1027	36
H(12B)	9446	4733	1382	36
H(15A)	9486	2532	788	47
H(16A)	8466	161	314	61
H(17A)	6367	359	-430	64
H(18A)	5348	2920	-736	63
H(19A)	6403	5290	-279	47

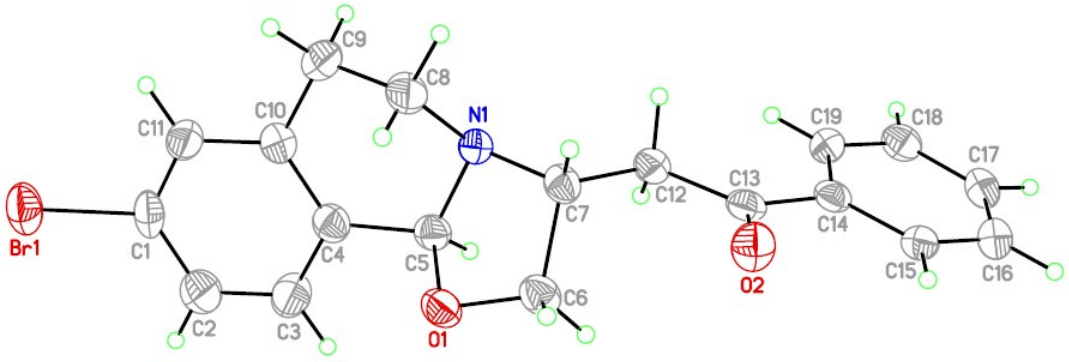


Figure S95. X-ray Crystallographic Data of compound **3l.**

Table 6. Crystal data and structure refinement for **3l**.

Identification code	ic17273	
Empirical formula	C19 H18 Br N O2	
Formula weight	372.25	
Temperature	200(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 10.9980(5) Å	α= 90°.
	b = 7.5779(3) Å	β= 90°.
	c = 38.7212(13) Å	γ = 90°.
Volume	3227.1(2) $Å^3$	
Z	8	
Density (calculated)	1.532 Mg/m^3	
Absorption coefficient	3.545 mm^{-1}	
F(000)	1520	
Crystal size	0.20 x 0.15 x 0.10 mm^3	
Theta range for data collection	4.62 to 67.99°.	
Index ranges	-8<=h<=13, -9<=k<=8, -46<=l<=42	
Reflections collected	6271	
Independent reflections	2903 [R(int) = 0.0402]	
Completeness to theta = 67.99°	99.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.77316	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2903 / 0 / 208	
Goodness-of-fit on F^2	0.934	

Final R indices [I>2sigma(I)]	R1 = 0.0473, wR2 = 0.1262
R indices (all data)	R1 = 0.0718, wR2 = 0.1514
Largest diff. peak and hole	0.570 and -0.375 e.Å^{-3}

Table 7. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **3l**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	8533(1)	1435(1)	7296(1)	47(1)
O(1)	11746(2)	-1855(4)	8626(1)	33(1)
O(2)	12339(2)	-4706(4)	9600(1)	38(1)
N(1)	9893(3)	-2840(5)	8833(1)	29(1)
C(1)	9102(4)	637(6)	7734(1)	35(1)
C(2)	10007(4)	1564(7)	7901(1)	44(1)
C(3)	10420(4)	930(6)	8214(1)	41(1)
C(4)	9971(3)	-626(5)	8353(1)	31(1)
C(5)	10508(3)	-1320(5)	8685(1)	28(1)
C(6)	12042(3)	-2832(6)	8933(1)	32(1)
C(7)	10826(3)	-3609(5)	9063(1)	28(1)
C(8)	9514(5)	-4087(6)	8562(1)	46(1)
C(9)	8591(5)	-3242(7)	8329(1)	57(2)
C(10)	9057(4)	-1530(6)	8183(1)	37(1)
C(11)	8624(4)	-880(7)	7868(1)	37(1)
C(12)	10549(3)	-3151(5)	9440(1)	28(1)
C(13)	11477(3)	-3820(5)	9692(1)	29(1)
C(14)	11323(3)	-3339(5)	10067(1)	26(1)
C(15)	12247(3)	-3736(5)	10300(1)	30(1)
C(16)	12156(4)	-3235(6)	10643(1)	36(1)
C(17)	11125(4)	-2349(5)	10756(1)	33(1)
C(18)	10188(4)	-1994(5)	10532(1)	32(1)
C(19)	10288(3)	-2471(5)	10187(1)	30(1)

Table 8. Bond lengths [Å] and angles [°] for **3l**.

Br(1)-C(1)	1.906(4)
O(1)-C(5)	1.438(5)
O(1)-C(6)	1.437(5)
O(2)-C(13)	1.214(5)
N(1)-C(5)	1.454(5)
N(1)-C(8)	1.470(5)
N(1)-C(7)	1.480(5)
C(1)-C(11)	1.367(7)
C(1)-C(2)	1.381(6)
C(2)-C(3)	1.378(6)
C(3)-C(4)	1.388(6)
C(4)-C(10)	1.385(6)
C(4)-C(5)	1.507(5)
C(6)-C(7)	1.546(5)
C(7)-C(12)	1.530(5)
C(8)-C(9)	1.502(7)
C(9)-C(10)	1.506(6)
C(10)-C(11)	1.397(6)
C(12)-C(13)	1.500(5)
C(13)-C(14)	1.505(6)
C(14)-C(15)	1.392(5)
C(14)-C(19)	1.395(5)
C(15)-C(16)	1.383(6)
C(16)-C(17)	1.388(6)
C(17)-C(18)	1.374(6)
C(18)-C(19)	1.390(6)
C(5)-O(1)-C(6)	103.3(3)
C(5)-N(1)-C(8)	111.1(3)
C(5)-N(1)-C(7)	103.1(3)
C(8)-N(1)-C(7)	111.9(3)
C(11)-C(1)-C(2)	121.8(4)
C(11)-C(1)-Br(1)	118.6(3)
C(2)-C(1)-Br(1)	119.5(4)
C(3)-C(2)-C(1)	118.2(4)
C(2)-C(3)-C(4)	121.4(4)

C(3)-C(4)-C(10)	119.5(4)
C(3)-C(4)-C(5)	119.3(4)
C(10)-C(4)-C(5)	121.2(4)
O(1)-C(5)-N(1)	106.2(3)
O(1)-C(5)-C(4)	109.6(3)
N(1)-C(5)-C(4)	115.4(3)
O(1)-C(6)-C(7)	105.7(3)
N(1)-C(7)-C(12)	110.4(3)
N(1)-C(7)-C(6)	104.7(3)
C(12)-C(7)-C(6)	113.4(3)
N(1)-C(8)-C(9)	110.2(4)
C(10)-C(9)-C(8)	111.4(4)
C(11)-C(10)-C(4)	119.3(4)
C(11)-C(10)-C(9)	121.1(4)
C(4)-C(10)-C(9)	119.5(4)
C(1)-C(11)-C(10)	119.8(4)
C(13)-C(12)-C(7)	114.1(3)
O(2)-C(13)-C(12)	121.9(4)
O(2)-C(13)-C(14)	120.2(4)
C(12)-C(13)-C(14)	117.9(3)
C(15)-C(14)-C(19)	118.8(4)
C(15)-C(14)-C(13)	119.4(3)
C(19)-C(14)-C(13)	121.8(3)
C(14)-C(15)-C(16)	120.7(4)
C(17)-C(16)-C(15)	119.6(4)
C(18)-C(17)-C(16)	120.5(4)
C(17)-C(18)-C(19)	119.8(4)
C(18)-C(19)-C(14)	120.5(4)

Symmetry transformations used to generate equivalent atoms:

Table 9. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **3l**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	49(1)	63(1)	29(1)	7(1)	-2(1)	12(1)
O(1)	30(1)	38(2)	31(1)	5(1)	6(1)	-1(1)
O(2)	35(2)	43(2)	35(2)	-1(1)	1(1)	10(1)
N(1)	30(2)	36(2)	23(2)	0(1)	-1(1)	-8(2)
C(1)	35(2)	50(3)	20(2)	2(2)	0(2)	16(2)
C(2)	48(3)	42(3)	41(2)	7(2)	-2(2)	-4(2)
C(3)	47(2)	37(2)	38(2)	2(2)	-10(2)	-4(2)
C(4)	31(2)	33(2)	28(2)	-2(2)	4(2)	1(2)
C(5)	29(2)	30(2)	26(2)	-4(2)	4(2)	-3(2)
C(6)	29(2)	35(2)	33(2)	5(2)	5(2)	4(2)
C(7)	33(2)	27(2)	24(2)	-1(2)	3(2)	-1(2)
C(8)	65(3)	37(3)	36(2)	8(2)	-9(2)	-28(2)
C(9)	60(3)	69(4)	41(3)	15(3)	-19(2)	-35(3)
C(10)	36(2)	46(3)	27(2)	1(2)	2(2)	-6(2)
C(11)	31(2)	52(3)	28(2)	-5(2)	-1(2)	-3(2)
C(12)	28(2)	32(2)	26(2)	0(2)	3(2)	-2(2)
C(13)	28(2)	28(2)	31(2)	3(2)	3(2)	-9(2)
C(14)	27(2)	22(2)	31(2)	5(2)	2(2)	-5(2)
C(15)	24(2)	33(2)	31(2)	5(2)	1(2)	-2(2)
C(16)	36(2)	42(2)	29(2)	8(2)	-3(2)	-2(2)
C(17)	40(2)	30(2)	28(2)	4(2)	2(2)	-1(2)
C(18)	32(2)	30(2)	34(2)	1(2)	7(2)	2(2)
C(19)	26(2)	33(2)	29(2)	3(2)	-1(2)	-1(2)