

[4+3] annulation of diazoenals and 3-substituted 2-oxindoles: rapid access to indolo-oxazepines and a 5-HT₄ receptor antagonist core

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1. General Methods:

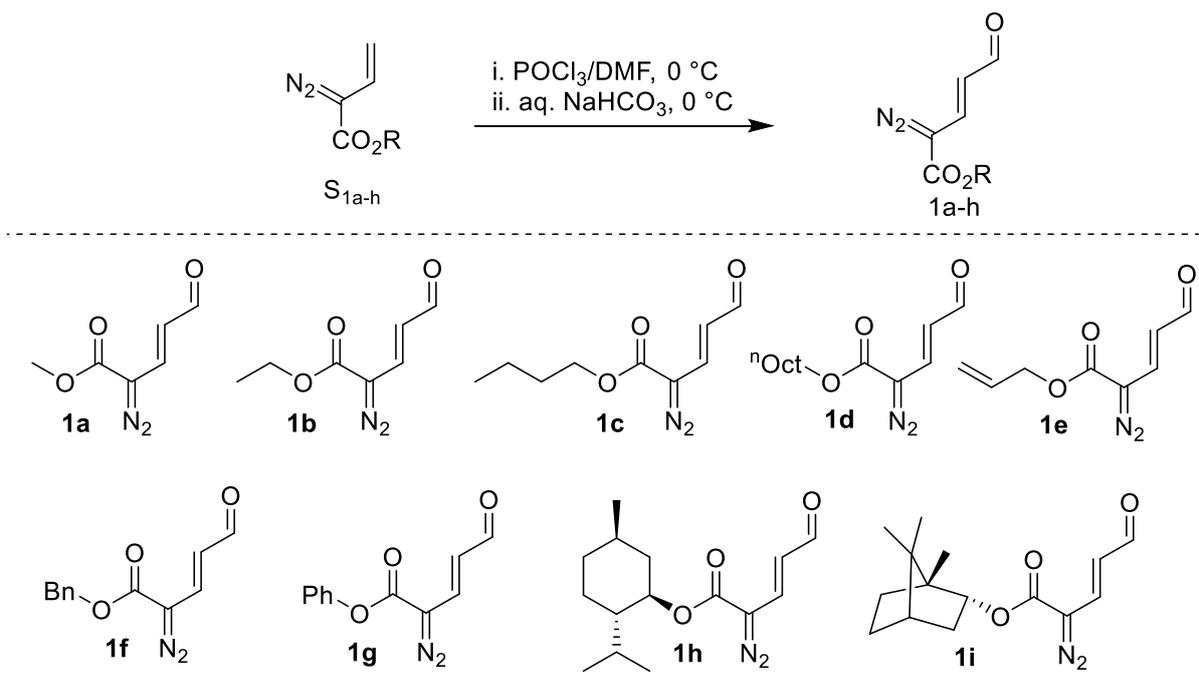
All the reactions were performed in oven-dried glassware. Solvents were dried using standard methods. Unless otherwise stated, all the commercial reagents were used as received. Reactions that require heating were carried out using an oil bath. The progress of the reaction was monitored by thin-layer chromatography (Merck Silica gel 60 F-254, 0.25 nm, precoated plates on alumina). Column chromatographic purifications were performed on Merck silica gel (100-200 mesh). Melting points were recorded on a digital melting point apparatus and were uncorrected.

Spectroscopic characterizations were carried out at the Central Instrumentation Facility (CIF), Indian Institute of Science Education and Research (IISER) Bhopal. ¹H-NMR spectra were recorded on Bruker Avance III FT-NMR spectrometers at 400 MHz and 500 MHz, ¹³C-NMR spectra were recorded at 101 MHz, 126 MHz. ¹H-NMR chemical shifts are reported in ppm relative to the TMS ($\delta=0$) or CDCl₃ signal ($\delta=7.26$) and are abbreviated as follows: s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), m (multiplet). ¹³C-NMR chemical shifts are reported in ppm relative to the residual CDCl₃ signal ($\delta=77.16$). Single-crystal X-ray diffraction data were collected using a Bruker SMART APEX II CCD diffractometer with graphite monochromated Mo K α ($\lambda = 0.71073 \text{ \AA}$) radiation at low temperatures. HRMS data were obtained on a Bruker micro TOF-QII or Agilent 5975C high-resolution mass spectrometers.

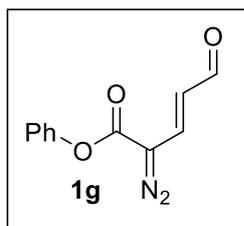
2. Preparation of starting materials:

(a) Preparation of diazoenals

Diazoenals **1a-h** were prepared according to our reported procedures.¹⁻⁴



Scheme S1. Preparation of diazoenals

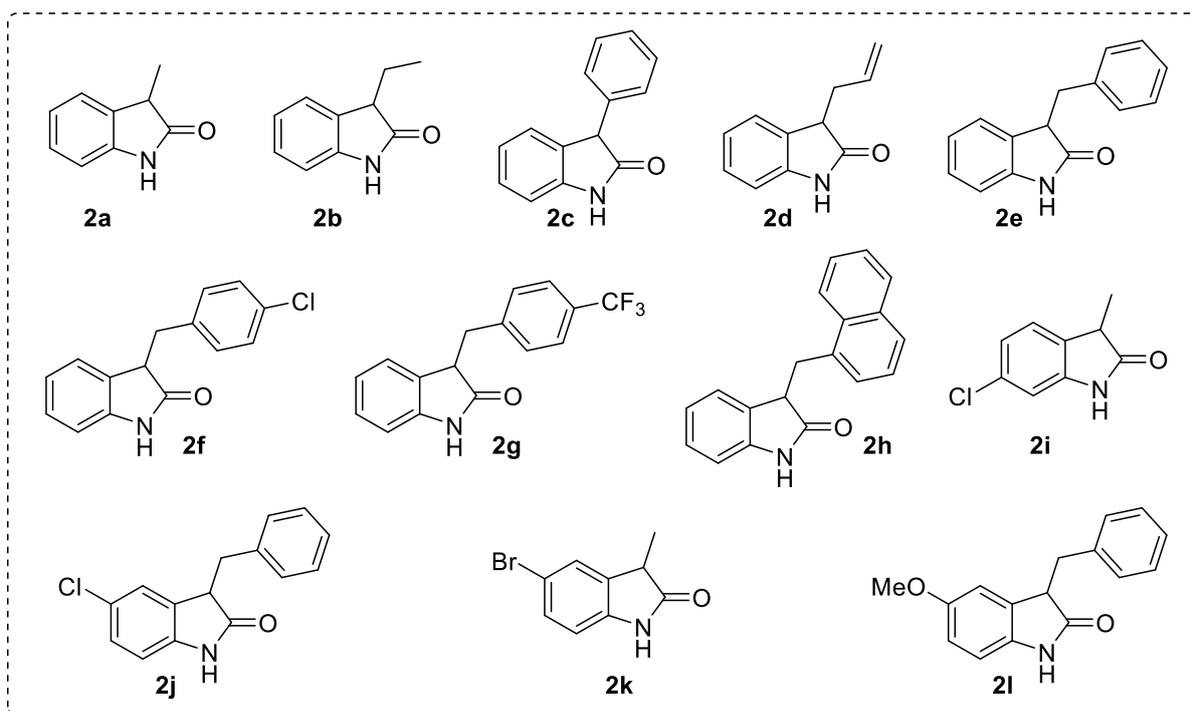


Phenyl (E)-2-diazo-5-oxopent-3-enoate (1g):

Links: [DETAILS](#) [NMR](#)

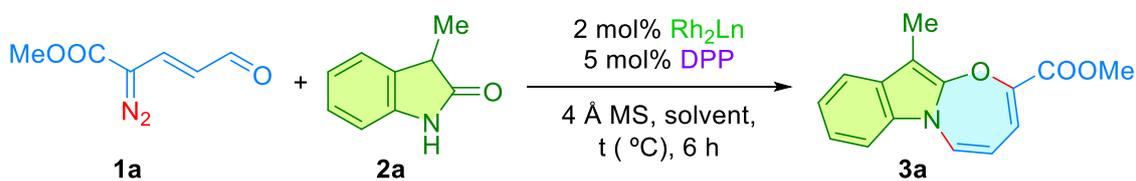
Prepared by general literature procedure and obtained as yellow liquid; $R_f = 0.5$ (EtOAc/Hexane: 20:80); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 9.60 (d, $J = 7.6$ Hz, 1H), 7.44 (t, $J = 7.9$ Hz, 2H), 7.32 (d, $J = 7.8$ Hz, 1H), 7.30 – 7.26 (m, 1H), 7.18 (d, $J = 8.1$ Hz, 2H), 6.09 (dd, $J = 15.8, 7.6$ Hz, 1H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 190.74, 160.98, 150.01, 138.55, 129.80, 126.66, 122.79, 121.45. **HRMS** (ESI) m/z calc. for $\text{C}_{11}\text{H}_9\text{N}_2\text{O}_3$ ($\text{M}+\text{H}$) $^+$ 217.0608 found 217.0610

(b) Preparation of 3-substituted 2-oxindoles: The 3-methyl 2-oxindole **2a** was received from a commercial source; the other 3-substituted 2-oxindoles **2b-2l** were prepared according to the literature procedures.⁶⁻⁷



Scheme S2: 3-substituted 2-oxindoles.

3. Table S1: Optimization of the [4+3] annulation reaction



Entry	Rh ₂ L _n	Solvent	t (°C)	Yield (%)
1	Rh ₂ (oct) ₄	Dichloroethane	80	69
2	Rh ₂ (OAc) ₄	Dichloroethane	80	59
3	Rh ₂ (esp) ₂	Dichloroethane	80	57
4	Rh ₂ (S-DOSP) ₄	Dichloroethane	80	43
5	Rh ₂ (TFA) ₄	Dichloroethane	80	34
6	Rh ₂ (oct) ₄	Dichloroethane	60	41
7	Rh ₂ (oct) ₄	Chloroform	60	58
8	Rh ₂ (oct) ₄	Dichloromethane	40	20

9	Rh ₂ (oct) ₄	Toluene	80	51
10 ^a	Rh ₂ (oct) ₄	Dichloroethane	80	<10

^awithout molecular sieves

General procedure for optimization:

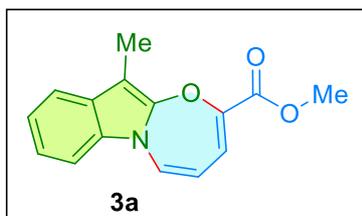
An oven-dried 10 mL round-bottom flask equipped with a magnetic stir bar under a nitrogen atmosphere was charged with the specified rhodium catalyst (2 mol%), Diphenyl phosphate (5 mol%; except entry 10), 3-methyl indolin-2-one (**2a**, 0.20 mmol), 4 Å MS (60 mg), and 2 mL of dry solvent. To the gently stirring contents at the specified temperature was added a solution of ester diazoenal (**1a**, 0.50 mmol) in 2 mL dry solvent *via* syringe pump over a period of 2 h. The reaction was further continued for another 4 h (monitored by TLC). The solvent was then removed under reduced pressure, and the crude product was purified by silica gel column chromatography (eluent: EtOAc/Hexane, 5:95) to yield the 1,3-oxazepine product **3a**.

4. Substrate scope of the [4+3] annulation reaction

General procedure A: Synthesis of 1,3-oxazepine (**3a-3z**):

An oven-dried 10 mL round-bottom flask equipped with a magnetic stir bar under a nitrogen atmosphere was charged with Rh₂(oct)₄ (2 mol%), Diphenyl phosphate (5 mol%), 3-substituted indolin-2-one (**2**, 0.20 mmol), 4 Å MS (60 mg), and 2 mL of dry DCE. To the gently stirring contents at 80 °C temperature was added a solution of ester diazoenal (**1**, 0.50 mmol) in 2 mL dry DCE *via* syringe pump over a period of 2 h. The reaction was further continued for another 4 h. The solvent was then removed under reduced pressure, and the crude product was purified by silica gel column chromatography (eluent: EtOAc/Hexane, 5:95) to yield the 1,3-oxazepine product **3**.

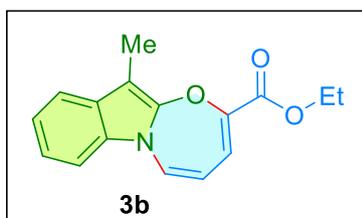
Analytical Data:



Methyl 11-methyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3a**):**

Links: [DETAILS](#) [NMR](#)

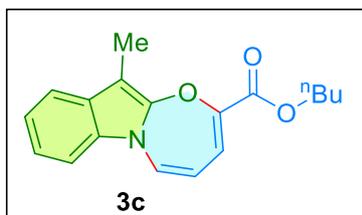
Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 69% (35 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.43 (d, $J = 7.5$ Hz, 1H), 7.24 – 7.11 (m, 4H), 6.72 (d, $J = 6.8$ Hz, 1H), 5.42 (dd, $J = 8.7, 7.1$ Hz, 1H), 3.86 (s, 3H), 2.26 (s, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 162.3, 147.5, 143.7, 130.7, 129.6, 127.7, 122.6, 121.4, 121.0, 119.0, 108.2, 104.0, 98.3, 52.2, 6.6. **HRMS** (ESI) m/z calc. for $\text{C}_{15}\text{H}_{14}\text{NO}_3$ ($\text{M}+\text{H}$) $^+$ 256.0968 found 256.0967.



Ethyl 11-methyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3b):

Links: [DETAILS](#) [NMR](#)

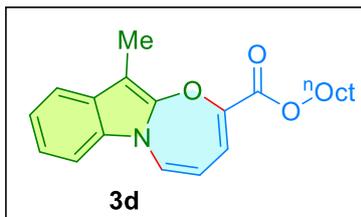
Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 64% (34.5 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.43 (d, $J = 7.5$ Hz, 1H), 7.23 – 7.12 (m, 4H), 6.73 (d, $J = 6.9$ Hz, 1H), 5.42 (dd, $J = 8.9, 6.9$ Hz, 1H), 4.32 (q, $J = 7.1$ Hz, 2H), 2.28 (s, 3H), 1.39 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 162.1, 147.9, 144.4, 130.9, 129.9, 127.9, 122.8, 121.7, 121.1, 119.3, 108.5, 104.4, 98.4, 61.6, 14.4, 6.9; **HRMS** (ESI) m/z calc. for $\text{C}_{16}\text{H}_{15}\text{NNaO}_3$ ($\text{M}+\text{Na}$) $^+$ 292.0944, found 292.0950.



Butyl 11-methyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3c):

Links: [DETAILS](#) [NMR](#)

Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 65% (38.5 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.43 (q, $J = 7.5$ Hz, 1H), 7.23 – 7.11 (m, 4H), 6.72 (d, $J = 6.9$ Hz, 1H), 5.42 (dd, $J = 9.0, 6.9$ Hz, 1H), 4.26 (t, $J = 6.6$ Hz, 2H), 2.27 (s, 3H), 1.73 (q, $J = 14.2$ Hz, 2H), 1.46 (h, $J = 7.4$ Hz, 2H), 0.97 (t, $J = 7.4$ Hz, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 162.2, 147.9, 144.3, 131.0, 129.9, 127.8, 122.8, 121.6, 121.0, 119.2, 108.5, 104.4, 98.4, 65.4, 30.8, 19.3, 13.8, 6.9. **HRMS** (ESI) m/z calc. for $\text{C}_{18}\text{H}_{20}\text{NO}_3$ ($\text{M}+\text{H}$) $^+$ 298.1438 found 298.1433.

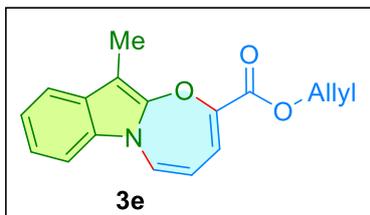


Octyl 11-methyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate

(3d):

Links: [DETAILS](#) [NMR](#)

Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 60% (42.5 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (400 MHz,) δ 7.43 (d, $J = 7.5$ Hz, 1H), 7.25 – 7.11 (m, 4H), 6.72 (d, $J = 6.8$ Hz, 1H), 5.43 (dd, $J = 9.0, 6.9$ Hz, 1H), 4.24 (t, $J = 6.7$ Hz, 2H), 2.26 (s, 3H), 1.79 – 1.68 (m, 2H), 1.48 – 1.36 (m, 2H), 1.36 – 1.22 (m, 8H), 0.92 – 0.84 (m, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 162.2, 147.9, 144.3, 131.0, 129.9, 127.8, 122.8, 121.6, 121.0, 119.3, 108.5, 104.4, 98.4, 65.8, 31.9, 29.37, 29.33, 28.8, 26.1, 22.7, 14.2, 6.9. **HRMS** (ESI) m/z calc. for $\text{C}_{22}\text{H}_{28}\text{NO}_3$ (M+H) $^+$ 354.2064 found 354.2059.

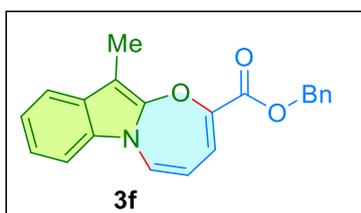


Allyl 11-methyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate

(3e):

Links: [DETAILS](#) [NMR](#)

Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 63% (35.5 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.42 (d, $J = 7.6$ Hz, 1H), 7.25 – 7.11 (m, 4H), 6.75 (d, $J = 6.9$ Hz, 1H), 6.00 (ddt, $J = 16.4, 10.9, 5.7$ Hz, 1H), 5.47 – 5.35 (m, 2H), 5.29 (d, $J = 10.4$ Hz, 1H), 4.75 (d, $J = 5.2$ Hz, 2H), 2.26 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 162.1, 148.1, 144.3, 132.2, 131.3, 130.2, 128.3, 123.2, 122.0, 121.8, 119.6, 119.2, 108.8, 104.6, 98.9, 66.4, 7.3. **HRMS** (ESI) m/z calc. for $\text{C}_{17}\text{H}_{16}\text{NO}_3$ (M+H) $^+$ 282.1125 found 282.1117.

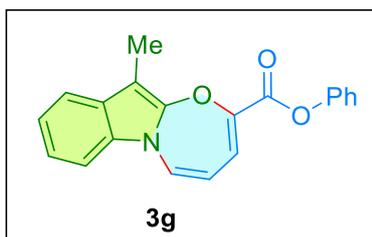


Benzyl 11-methyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3f):

Links: [DETAILS](#) [NMR](#)

Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 66% (44.7 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.46 – 7.31 (m, 6H), 7.23 – 7.10 (m, 4H), 6.76 (d, $J = 6.9$ Hz, 1H), 5.41 (dd, $J = 9.0, 6.9$ Hz, 1H), 5.29 (s, 2H), 2.19 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 161.9, 147.8, 144.0, 135.7, 131.0, 129.9, 128.7, 128.56,

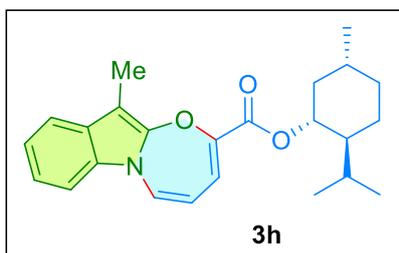
128.53, 128.0, 122.9, 121.7, 121.6, 119.3, 108.5, 104.2, 98.6, 67.3, 6.9. **HRMS** (ESI) m/z calc. for $C_{21}H_{18}NO_3$ ($M+H$)⁺ 332.1281, found 332.1283.



Phenyl 11-methyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3g):

Links: [DETAILS](#) [NMR](#)

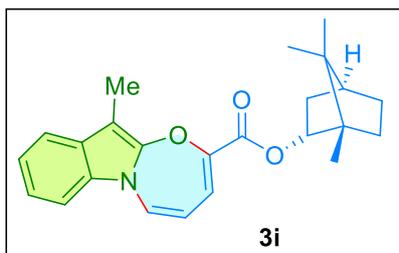
Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 61% (41 mg); R_f = 0.6 (EtOAc/Hexane: 10:90); **¹H NMR** (400 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 1H), 7.47 – 7.41 (m, 2H), 7.33 – 7.27 (m, 2H), 7.27 – 7.18 (m, 5H), 6.97 (d, J = 6.9 Hz, 1H), 5.52 (dd, J = 8.9, 7.1 Hz, 1H), 2.31 (s, 3H). **¹³C NMR** (101 MHz, $CDCl_3$) δ 160.60, 150.76, 147.80, 143.33, 131.07, 130.00, 129.68, 128.59, 126.18, 123.07, 123.06, 121.90, 121.62, 119.44, 108.56, 104.15, 99.04, 6.99. **HRMS** (ESI) m/z calc. for $C_{20}H_{15}NNaO_3$ ($M+Na$)⁺ 340.0944 found 340.0963.



(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl 11-methyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3h):

Links: [DETAILS](#) [NMR](#)

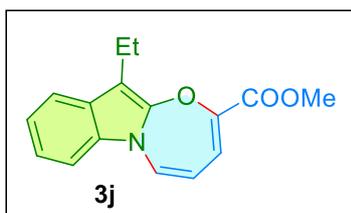
Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 56% (42.5 mg); R_f = 0.6 (EtOAc/Hexane: 10:90); **¹H NMR** (400 MHz, $CDCl_3$) δ 7.43 (d, J = 7.5 Hz, 1H), 7.23 – 7.09 (m, 4H), 6.71 (d, J = 6.8 Hz, 1H), 5.43 (dd, J = 9.0, 6.8 Hz, 1H), 4.84 (td, J = 10.9, 4.4 Hz, 1H), 2.26 (s, 3H), 2.16 – 2.02 (m, 1H), 2.02 – 1.88 (m, 1H), 1.77 – 1.65 (m, 2H), 1.55 – 1.47 (m, 2H), 1.18 – 0.94 (m, 3H), 0.93 (d, J = 2.3 Hz, 3H), 0.91 (d, J = 2.7 Hz, 3H), 0.78 (d, J = 7.0 Hz, 3H). **¹³C NMR** (101 MHz, $CDCl_3$) δ 161.7, 148.0, 144.6, 130.9, 129.9, 127.8, 122.8, 121.6, 120.9, 119.2, 108.5, 104.5, 98.3, 75.6, 47.3, 41.0, 34.3, 31.5, 26.3, 23.5, 22.1, 20.9, 16.4, 6.9. **HRMS** (ESI) m/z calc. for $C_{24}H_{30}NO_3$ ($M+H$)⁺ 380.2220 found 380.2214.



(1S,2R,4S)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl 11-methyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3i):

Links: [DETAILS](#) [NMR](#)

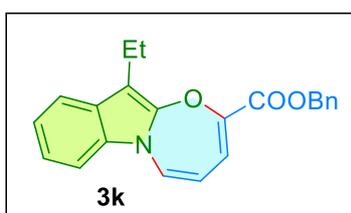
Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 53% (40 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.42 (d, $J = 7.6$ Hz, 1H), 7.24 – 7.17 (m, 2H), 7.19 – 7.12 (m, 2H), 6.71 (d, $J = 7.0$ Hz, 1H), 5.42 (dd, $J = 8.9, 7.0$ Hz, 1H), 5.09 – 5.02 (m, 1H), 2.49 – 2.39 (m, 1H), 2.28 (s, 3H), 2.10 (ddd, $J = 13.4, 9.4, 4.4$ Hz, 1H), 1.80 (tq, $J = 12.1, 4.1$ Hz, 1H), 1.73 (t, $J = 4.5$ Hz, 1H), 1.44 – 1.34 (m, 1H), 1.34 – 1.27 (m, 1H), 1.11 (dd, $J = 13.9, 3.5$ Hz, 1H), 0.95 (s, 3H), 0.91 (s, 3H), 0.90 (s, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 162.4, 147.9, 144.5, 131.1, 129.8, 127.7, 122.6, 121.7, 120.6, 119.2, 108.5, 104.3, 98.6, 81.5, 49.2, 48.1, 45.0, 36.8, 28.2, 27.4, 19.8, 19.0, 13.7, 7.1. **HRMS** (ESI) m/z calc. for $\text{C}_{24}\text{H}_{28}\text{NO}_3$ ($\text{M}+\text{H}$) $^+$ 378.2064 found 378.2059.



Methyl 11-ethyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3j):

Links: [DETAILS](#) [NMR](#)

Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 61% (33.7 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.49 (d, $J = 7.6$ Hz, 1H), 7.23 – 7.12 (m, 4H), 6.73 (d, $J = 6.8$ Hz, 1H), 5.43 (dd, $J = 9.0, 6.9$ Hz, 1H), 3.86 (s, 3H), 2.79 (qd, $J = 7.5, 1.2$ Hz, 2H), 1.28 (td, $J = 7.6, 1.3$ Hz, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 162.5, 147.4, 144.1, 131.1, 129.0, 128.0, 122.7, 121.6, 121.5, 119.5, 108.6, 104.7, 104.4, 52.5, 15.8, 14.4. **HRMS** (ESI) m/z calc. for $\text{C}_{16}\text{H}_{15}\text{NNaO}_3$ ($\text{M}+\text{Na}$) $^+$ 292.0944, found 292.0943.

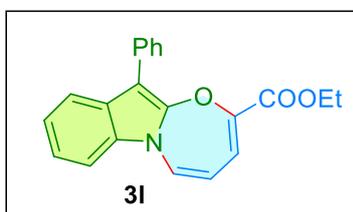


Benzyl 11-ethyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3k):

Links: [DETAILS](#) [NMR](#)

Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 63% (44.5 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.47 (d, $J = 7.6$ Hz, 1H), 7.45 – 7.33 (m, 5H), 7.22 – 7.18 (m, 2H), 7.17 – 7.12 (m, 2H), 6.77 (d, $J = 6.9$ Hz, 1H), 5.42

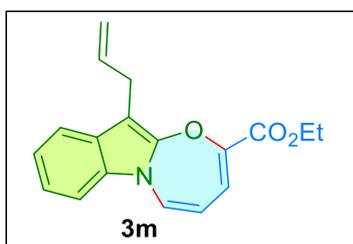
(dd, $J = 9.0, 6.9$ Hz, 1H), 5.29 (s, 2H), 2.72 (qd, $J = 7.5, 1.9$ Hz, 2H), 1.19 (td, $J = 7.6, 2.0$ Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 161.9, 147.4, 144.0, 135.6, 131.1, 129.0, 128.7, 128.55, 128.54, 128.1, 122.7, 121.6, 119.5, 108.6, 104.8, 104.4, 67.3, 15.8, 14.4. HRMS (ESI) m/z calc. for $\text{C}_{22}\text{H}_{20}\text{NO}_3$ ($\text{M}+\text{H}$) $^+$ 346.1438, found 346.1420.



Ethyl 11-phenyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3l):

Links: [DETAILS](#) [NMR](#)

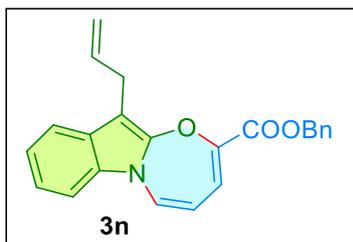
Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 58% (38.5 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); ^1H NMR (400 MHz, CDCl_3) δ 7.77 (d, $J = 6.8$ Hz, 2H), 7.72 (d, $J = 7.8$ Hz, 1H), 7.46 (t, $J = 7.7$ Hz, 2H), 7.31 (t, $J = 7.4$ Hz, 1H), 7.27 – 7.15 (m, 4H), 6.76 (d, $J = 6.9$ Hz, 1H), 5.52 (dd, $J = 9.0, 6.9$ Hz, 1H), 4.16 (q, $J = 7.1$ Hz, 2H), 1.14 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 162.2, 147.8, 145.3, 132.0, 131.7, 129.9, 128.6, 128.2, 127.0, 123.6, 122.7, 121.5, 120.6, 109.1, 106.2, 104.5, 61.9, 14.4. HRMS (ESI) m/z calc. for $\text{C}_{21}\text{H}_{17}\text{NNaO}_3$ ($\text{M}+\text{Na}$) $^+$ 354.1101, found 354.1113.



Ethyl 11-allyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3m):

Links: [DETAILS](#) [NMR](#)

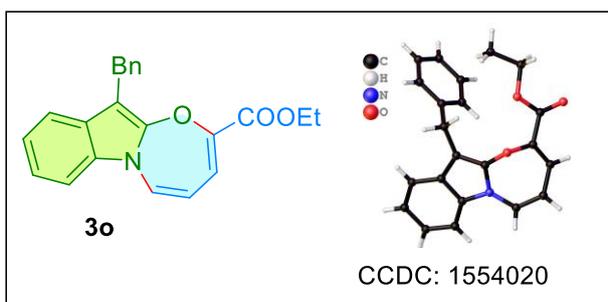
Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 62% (37 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); ^1H NMR (500 MHz, CDCl_3) δ 7.47 (dt, $J = 7.7, 1.0$ Hz, 1H), 7.21 – 7.19 (m, 3H), 7.14 (dt, $J = 8.1, 4.2$ Hz, 1H), 6.74 (d, $J = 6.8$ Hz, 1H), 6.04 – 5.96 (m, 1H), 5.47 (dd, $J = 9.0, 6.8$ Hz, 1H), 5.15 (dq, $J = 17.1, 1.8$ Hz, 1H), 5.05 (dq, $J = 10.0, 1.6$ Hz, 1H), 4.31 (q, $J = 7.1$ Hz, 2H), 3.55 (dt, $J = 6.3, 1.6$ Hz, 2H), 1.37 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 162.2, 148.2, 144.7, 136.4, 131.3, 129.2, 128.2, 123.0, 122.0, 121.6, 120.1, 115.7, 108.9, 105.2, 100.5, 61.9, 27.2, 14.6. HRMS (ESI) m/z calc. for $\text{C}_{18}\text{H}_{17}\text{NNaO}_3$ ($\text{M}+\text{Na}$) $^+$ 318.1101, found 318.1113.



Benzyl 11-allyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3n):

Links: [DETAILS](#) [NMR](#)

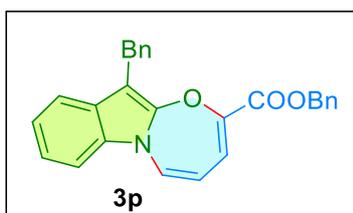
Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 65% (47 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (500 MHz,) δ 7.45 (dt, $J = 7.7, 1.0$ Hz, 1H), 7.43 – 7.40 (m, 2H), 7.39 – 7.32 (m, 3H), 7.22 – 7.18 (m, 3H), 7.13 (ddd, $J = 8.2, 4.6, 3.6$ Hz, 1H), 6.77 (d, $J = 6.9$ Hz, 1H), 5.99 – 5.81 (m, 1H), 5.45 (dd, $J = 9.0, 6.9$ Hz, 1H), 5.28 (s, 2H), 5.06 (dq, $J = 17.0, 1.7$ Hz, 1H), 4.99 (dq, $J = 9.9, 1.5$ Hz, 1H), 3.46 (dt, $J = 6.3, 1.6$ Hz, 2H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 161.8, 147.8, 144.1, 136.0, 135.6, 131.1, 129.0, 128.7, 128.5, 128.1, 122.8, 121.79, 121.77, 119.9, 115.4, 108.6, 104.8, 100.5, 67.4, 26.9. **HRMS** (ESI) m/z calc. for $\text{C}_{23}\text{H}_{19}\text{NNaO}_3$ ($\text{M}+\text{Na}$) $^+$ 380.1257, found 380.1269.



Ethyl 11-benzyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3o):

Links: [DETAILS](#) [NMR](#) [SCXRD](#)

Prepared by general procedure A and obtained as yellow solid; yield = 66%; (46 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); m.p. = 109-111 °C; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.35 (dd, $J = 7.7, 0.8$ Hz, 3H), 7.28 (t, $J = 7.6$ Hz, 2H), 7.24 – 7.18 (m, 4H), 7.12 – 7.09 (m, 1H), 6.81 (d, $J = 6.8$ Hz, 1H), 5.51 (dd, $J = 9.0, 6.8$ Hz, 1H), 4.30 (t, $J = 7.1$ Hz, 2H), 4.18 (s, 2H), 1.33 (t, $J = 7.1$ Hz, 3H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 162.1, 148.4, 144.6, 140.5, 131.2, 128.9, 128.6, 128.5, 127.9, 126.0, 122.9, 121.8, 121.4, 119.9, 108.6, 105.0, 101.6, 61.7, 28.6, 14.3. **HRMS** (ESI) m/z calc. for $\text{C}_{22}\text{H}_{20}\text{NO}_3$ ($\text{M}+\text{H}$) $^+$ 346.1438, found 346.1452.

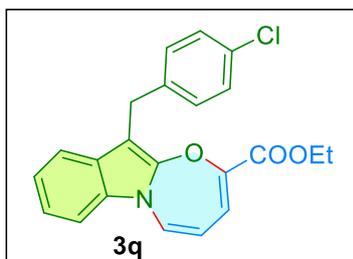


Benzyl 11-benzyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3p):

Links: [DETAILS](#) [NMR](#)

Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 70% (57.6 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.42 – 7.40 (m, 1H),

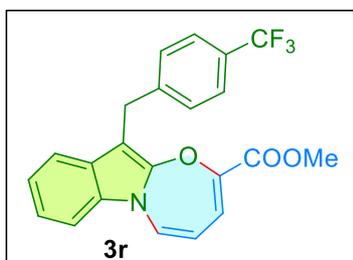
7.40 – 7.31 (m, 5H), 7.32 – 7.24 (m, 4H), 7.24 – 7.18 (m, 4H), 7.12 – 7.09 (m, 1H), 6.84 (d, $J = 6.9$ Hz, 1H), 5.49 (dd, $J = 9.0, 6.9$ Hz, 1H), 5.30 (s, 2H), 4.10 (s, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 162.0, 148.4, 144.4, 140.6, 135.7, 131.4, 129.1, 128.9, 128.87, 128.82, 128.7, 128.6, 128.3, 126.2, 123.1, 122.1, 122.0, 120.2, 108.8, 105.0, 102.0, 67.6, 28.81. HRMS (ESI) m/z calc. for $\text{C}_{27}\text{H}_{21}\text{NNaO}_3$ ($\text{M}+\text{Na}$) $^+$ 430.1414, found 430.1407.



Ethyl 11-(4-chlorobenzyl)-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3q):

Links: [DETAILS](#) [NMR](#)

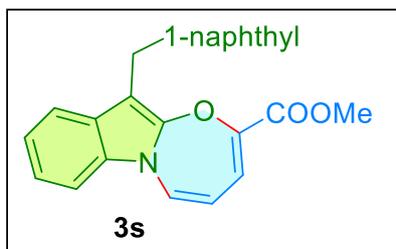
Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 67% (51.5 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); ^1H NMR (500 MHz, CDCl_3) δ 7.28 – 7.18 (m, 8H), 7.09 – 7.06 (m, 1H), 6.77 (d, $J = 6.8$ Hz, 1H), 5.50 (dd, $J = 9.0, 6.8$ Hz, 1H), 4.27 (q, $J = 7.1$ Hz, 2H), 4.10 (s, 2H), 1.29 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 161.9, 148.5, 144.5, 138.9, 131.8, 131.1, 129.9, 128.6, 128.5, 128.0, 123.0, 121.9, 121.5, 119.8, 108.7, 105.3, 101.0, 61.7, 28.0, 14.3. HRMS (ESI) m/z calc. for $\text{C}_{22}\text{H}_{18}\text{ClNNaO}_3$ ($\text{M}+\text{Na}$) $^+$ 402.0867, found 402.0868.



Methyl 11-(4-(trifluoromethyl)benzyl)-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3r):

Links: [DETAILS](#) [NMR](#)

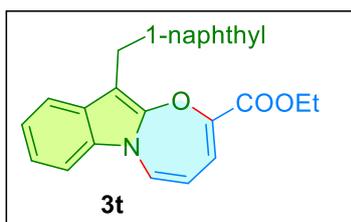
Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 64% (52.6 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); ^1H NMR (500 MHz, CDCl_3) δ 7.50 (d, $J = 8.2$ Hz, 2H), 7.42 (d, $J = 8.0$ Hz, 2H), 7.28 (d, $J = 7.9$ Hz, 1H), 7.24 – 7.18 (m, 3H), 7.13 – 7.05 (m, 1H), 6.77 (d, $J = 6.8$ Hz, 1H), 5.51 (dd, $J = 9.0, 6.8$ Hz, 1H), 4.18 (s, 2H), 3.80 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 162.1, 148.2, 144.4, 143.9, 130.8, 128.6, 128.3, 128.2, 128.0, 127.8, 125.18 (q, $J = 3.8$ Hz) 122.8, 121.8, 121.4, 119.3, 108.5, 105.0, 100.3, 52.3, 28.2. HRMS (ESI) m/z calc. for $\text{C}_{22}\text{H}_{17}\text{F}_3\text{NO}_3$ ($\text{M}+\text{H}$) $^+$ 400.1155, found 400.1151.



Methyl 11-(naphthalen-1-ylmethyl)-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3s):

Links: [DETAILS](#) [NMR](#)

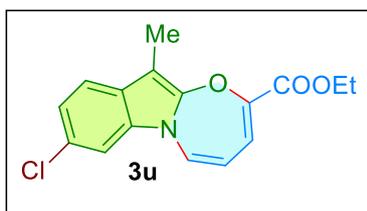
Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 53% (40.7 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.35 (d, $J = 8.3$ Hz, 1H), 7.85 (d, $J = 7.9$ Hz, 1H), 7.71 (d, $J = 7.4$ Hz, 1H), 7.54 (t, $J = 7.4$ Hz, 1H), 7.51 (t, $J = 7.6$ Hz, 1H), 7.36 – 7.31 (m, 2H), 7.25 (t, $J = 8.1$ Hz, 2H), 7.19 (d, $J = 7.6$ Hz, 1H), 7.17 – 7.13 (m, 1H), 7.01 (t, $J = 7.4$ Hz, 1H), 6.79 (d, $J = 6.8$ Hz, 1H), 5.50 (dd, $J = 9.0, 6.8$ Hz, 1H), 4.60 (s, 2H), 3.64 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 162.1, 147.9, 143.2, 135.5, 133.6, 131.9, 130.8, 128.9, 128.4, 127.8, 126.6, 125.8, 125.6, 125.3, 123.6, 122.5, 121.5, 121.3, 119.9, 108.3, 104.8, 100.4, 52.1, 25.7. **HRMS** (ESI) m/z calc. for $\text{C}_{25}\text{H}_{19}\text{NNaO}_3$ ($\text{M}+\text{Na}$) $^+$ 404.1257, found 404.1262.



Ethyl 11-(naphthalen-1-ylmethyl)-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3t):

Links: [DETAILS](#) [NMR](#)

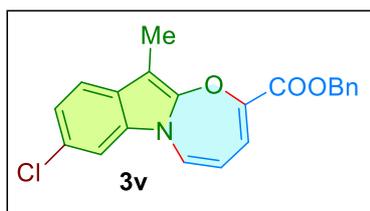
Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 50% (39.8 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 8.40 (d, $J = 8.4$ Hz, 1H), 7.89 (d, $J = 8.1$ Hz, 1H), 7.75 (d, $J = 7.5$ Hz, 1H), 7.59 – 7.55 (m, 1H), 7.52 (t, $J = 8.1$ Hz, 1H), 7.39 – 7.35 (m, 2H), 7.27 (d, $J = 6.1$ Hz, 1H), 7.24 (t, $J = 8.5$ Hz, 2H), 7.22 – 7.17 (m, 1H), 7.04 (t, $J = 7.5$ Hz, 1H), 6.84 (d, $J = 6.8$ Hz, 1H), 5.54 (dd, $J = 9.0, 6.8$ Hz, 1H), 4.65 (s, 2H), 4.20 (q, $J = 7.1$ Hz, 2H), 1.16 (t, $J = 7.2$ Hz, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 161.8, 148.1, 144.3, 135.5, 133.6, 132.0, 130.9, 128.9, 128.5, 127.7, 126.7, 125.8, 125.7, 125.36, 125.35, 123.7, 122.5, 121.5, 121.2, 120.0, 108.3, 104.9, 100.3, 61.4, 25.8, 13.8. **HRMS** (ESI) m/z calc. for $\text{C}_{26}\text{H}_{22}\text{NO}_3$ ($\text{M}+\text{H}$) $^+$ 396.1594, found 396.1585.



Ethyl 8-chloro-11-methyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3u):

Links: [DETAILS](#) [NMR](#)

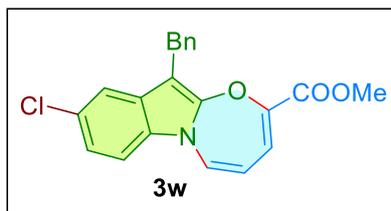
Prepared by general procedure A and obtained as faint yellow solid; m.p. = 131-133 °C; yield = 46% (27 mg); R_f = 0.6 (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.33 (d, J = 7.8 Hz, 1H), 7.19 (d, J = 1.8 Hz, 1H), 7.11 (dd, J = 8.3, 1.8 Hz, 1H), 7.09 (d, J = 9.0 Hz, 1H), 6.72 (d, J = 6.8 Hz, 1H), 5.47 (dd, J = 9.0, 6.8 Hz, 1H), 4.31 (q, J = 7.1 Hz, 2H), 2.24 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 161.7, 148.1, 144.4, 130.9, 128.3, 128.0, 127.2, 121.8, 120.7, 119.9, 108.7, 105.2, 98.0, 61.4, 14.1, 6.6. HRMS (ESI) m/z calc. for $\text{C}_{16}\text{H}_{15}\text{ClNO}_3$ ($\text{M}+\text{H}$) $^+$ 304.0735, found 304.0729.



Benzyl 8-chloro-11-methyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3v):

Links: [DETAILS](#) [NMR](#)

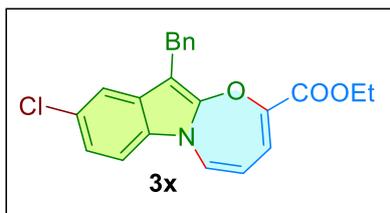
Prepared by general procedure A and obtained as faint yellow solid; m.p. = 117-119 °C; yield = 49% (34.5 mg); R_f = 0.6 (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.43 – 7.40 (m, 2H), 7.40 – 7.32 (m, 3H), 7.30 (d, J = 8.3 Hz, 1H), 7.18 (d, J = 1.8 Hz, 1H), 7.11 (dd, J = 8.3, 1.8 Hz, 1H), 7.08 (d, J = 9.0 Hz, 1H), 6.75 (d, J = 6.9 Hz, 1H), 5.45 (dd, J = 9.0, 6.9 Hz, 1H), 5.28 (s, 2H) 2.16 (s, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 161.5, 148.0, 144.0, 135.3, 131.0, 128.5, 128.4, 128.37, 128.32, 128.1, 127.4, 121.8, 121.1, 119.9, 108.7, 105.0, 98.3, 67.1, 6.6. HRMS (ESI) m/z calc. for $\text{C}_{21}\text{H}_{17}\text{ClNO}_3$ ($\text{M}+\text{H}$) $^+$ 366.0891, found 366.0868.



Methyl 11-benzyl-9-chloro-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3w):

Links: [DETAILS](#) [NMR](#)

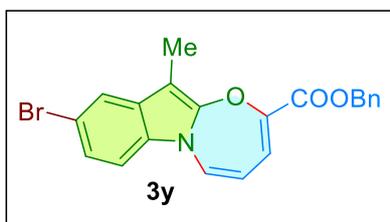
Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 52% (36 mg); R_f = 0.6 (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.33 – 7.26 (m, 5H), 7.22 – 7.18 (m, 1H), 7.18 – 7.15 (m, 2H), 7.13 (t, J = 7.0 Hz, 1H), 6.79 (d, J = 6.8 Hz, 1H), 5.54 (dd, J = 9.0, 6.8 Hz, 1H), 4.11 (s, 2H), 3.83 (s, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 162.0, 148.9, 144.1, 139.7, 129.7, 129.8, 128.35, 128.30, 127.6, 127.3, 126.0, 122.8, 121.2, 119.2, 109.5, 105.5, 101.1, 52.3, 28.2. HRMS (ESI) m/z calc. for $\text{C}_{21}\text{H}_{16}\text{ClNNaO}_3$ ($\text{M}+\text{Na}$) $^+$ 388.0711, found 388.0718.



Ethyl 11-benzyl-9-chloro-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3x):

Links: [DETAILS](#) [NMR](#)

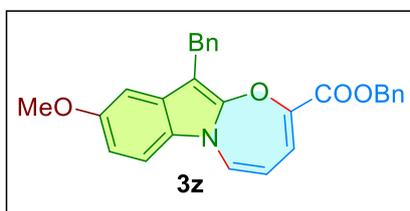
Prepared by general procedure A and obtained as faint yellow solid; yield = 56% (41.2 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.29 – 7.22 (m, 5H), 7.19 – 7.14 (m, 1H), 7.13 (s, 1H), 7.11 – 7.06 (m, 2H), 6.75 (d, $J = 6.8$ Hz, 1H), 5.51 (dd, $J = 9.0, 6.7$ Hz, 1H), 4.25 (q, $J = 7.1$ Hz, 2H), 4.08 (s, 2H), 1.27 (t, $J = 7.3$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 161.5, 148.9, 144.4, 139.7, 129.6, 129.1, 128.28, 128.24, 127.4, 127.2, 125.9, 122.7, 121.0, 119.2, 109.4, 105.6, 100.9, 61.5, 28.1, 13.9. **HRMS** (ESI) m/z calc. for $\text{C}_{22}\text{H}_{18}\text{ClNNaO}_3$ ($\text{M}+\text{Na}$) $^+$ 402.0867, found 402.0882



Benzyl 9-bromo-11-methyl-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3y):

Links: [DETAILS](#) [NMR](#)

Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 53% (43.5 mg); $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.52 (d, $J = 1.9$ Hz, 1H), 7.44 – 7.32 (m, 5H), 7.29 – 7.27 (m, 1H), 7.09 (d, $J = 9.0$ Hz, 1H), 7.03 (d, $J = 8.6$ Hz, 1H), 6.75 (d, $J = 6.8$ Hz, 1H), 5.45 (dd, $J = 9.0, 6.9$ Hz, 1H), 5.29 (s, 2H), 2.14 (s, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 161.9, 148.8, 144.4, 135.8, 131.8, 129.8, 129.0, 128.88, 128.83, 128.0, 125.8, 122.3, 121.8, 115.2, 110.3, 105.5, 98.4, 67.6, 7.0. **HRMS** (ESI) m/z calc. for $\text{C}_{21}\text{H}_{16}\text{BrNNaO}_3$ ($\text{M}+\text{Na}$) $^+$ 432.0206, found 432.0233.



Benzyl 11-benzyl-9-methoxy-[1,3]oxazepino[3,2-a]indole-2-carboxylate (3z):

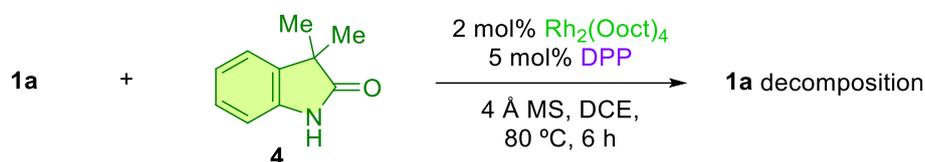
Links: [DETAILS](#) [NMR](#)

Prepared by general procedure A and obtained as faint yellow viscous liquid; yield = 59% (51 mg); m.p. = 80-82 °C; $R_f = 0.6$ (EtOAc/Hexane: 10:90); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.38 – 7.31 (m, 5H), 7.23 (d, $J = 4.6$ Hz, 4H), 7.18 – 7.14 (m, 1H), 7.12 (d, $J = 9.0$ Hz, 1H), 7.07 (d, $J = 8.7$ Hz, 1H), 6.80 – 6.75 (m, 3H), 5.42 (dd, $J = 9.0, 6.9$ Hz, 1H), 5.24 (s, 2H), 4.02 (s, 2H), 3.73 (s, 3H); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 161.9, 155.5, 148.5, 143.9, 140.3, 135.6, 129.7,

128.7, 128.6, 128.6, 128.5, 128.4, 128.4, 126.0, 125.9, 122.0, 111.2, 109.5, 104.4, 103.4, 101.7, 67.4, 55.6, 28.6. HRMS (ESI) m/z calc. for $C_{28}H_{23}NNaO_4$ ($M+Na$)⁺ 460.1519, found 460.1517.

5. Control Experiments:

a. Reaction with 3,3-disubstituted-2-oxindole:



Scheme S3: Reaction with 3,3-dimethyl-2-oxindole

To examine the necessity of the benzylic proton at the 2-position of the oxindole, diazoenal **1a** was reacted with 3,3-dimethyl-2-oxindole **4** under the optimized conditions. No annulation product was obtained, highlighting the importance of the C2-hydrogen in facilitating the aromatization and subsequent cyclization step.

An oven-dried 10 mL round-bottom flask equipped with a magnetic stir bar under a nitrogen atmosphere was charged with $Rh_2(oct)_4$ (2 mol%), Diphenyl phosphate (5 mol%), 3,3-dimethyl indolin-2-one (**4**, 0.20 mmol), 4 Å MS (60 mg), and 2 mL of dry DCE. To the gently stirring contents at 80 °C temperature was added a solution of ester diazoenal (**1a**, 0.50 mmol) in 2 mL dry DCE *via* syringe pump over a period of 2 h. The reaction was further continued for another 4 h. The oxindole remained unreacted and the diazoenal was decomposed.

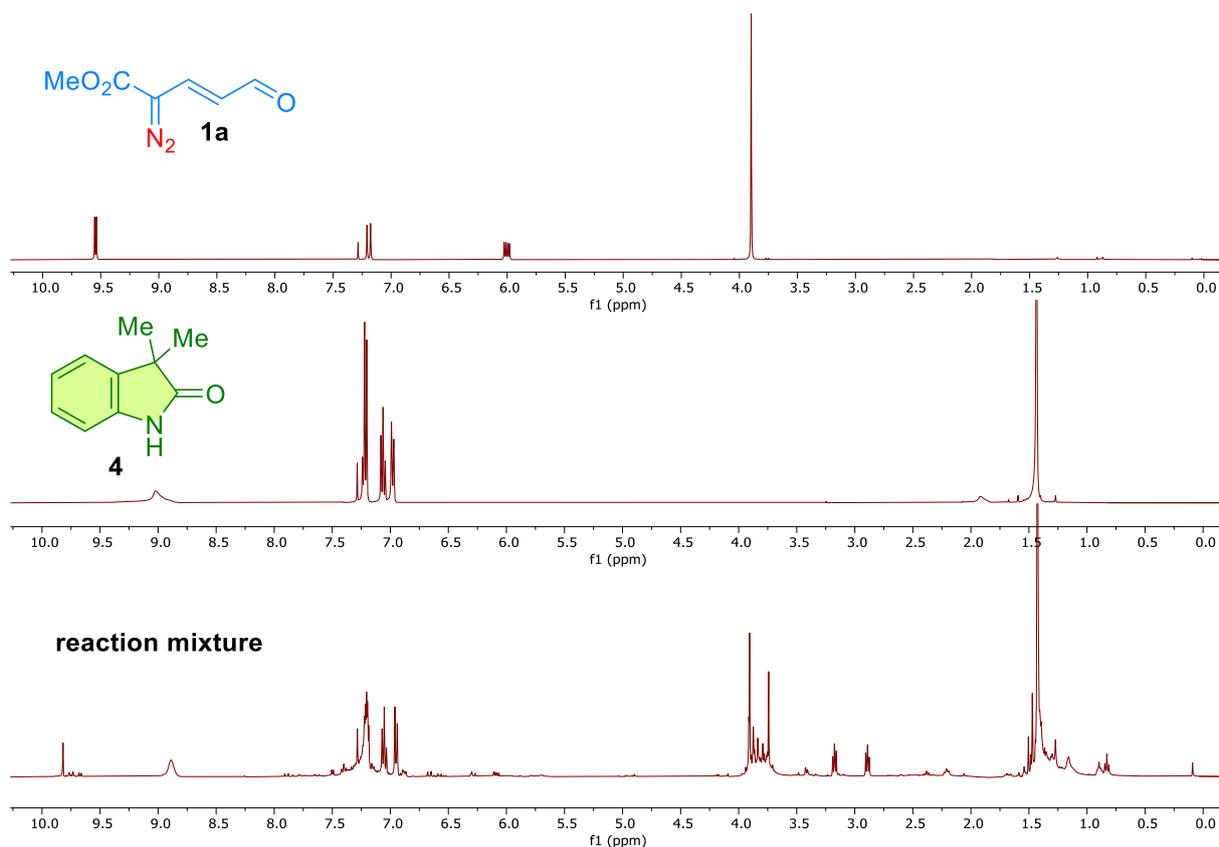
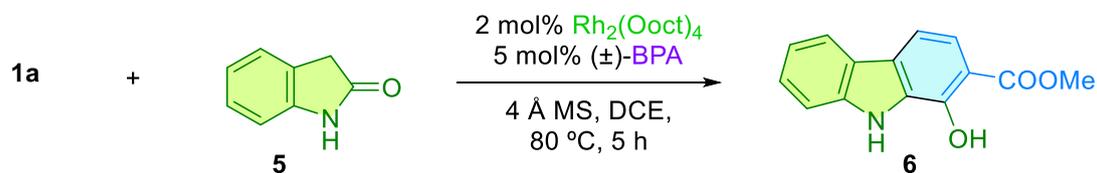


Figure 1: NMR studies of the reaction mixture with starting materials.

b. Reaction with 3-unsubstituted-2-oxindole:

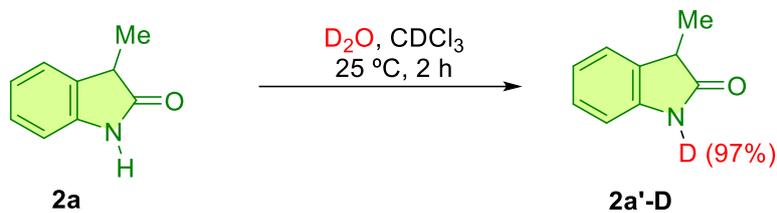


Scheme S4: Reaction with 2-oxindoles

In our previous report of carbazole synthesis,⁸ we demonstrated that simple oxindole **5**, when treated with diazoenal **1a** in the presence of Rh(II)/Brønsted acid co-catalyst, underwent [4+2] annulation to afford the corresponding carbazole derivative **6**. This study further suggests that one substituent is required at the 2-position for the [4+3] annulation.

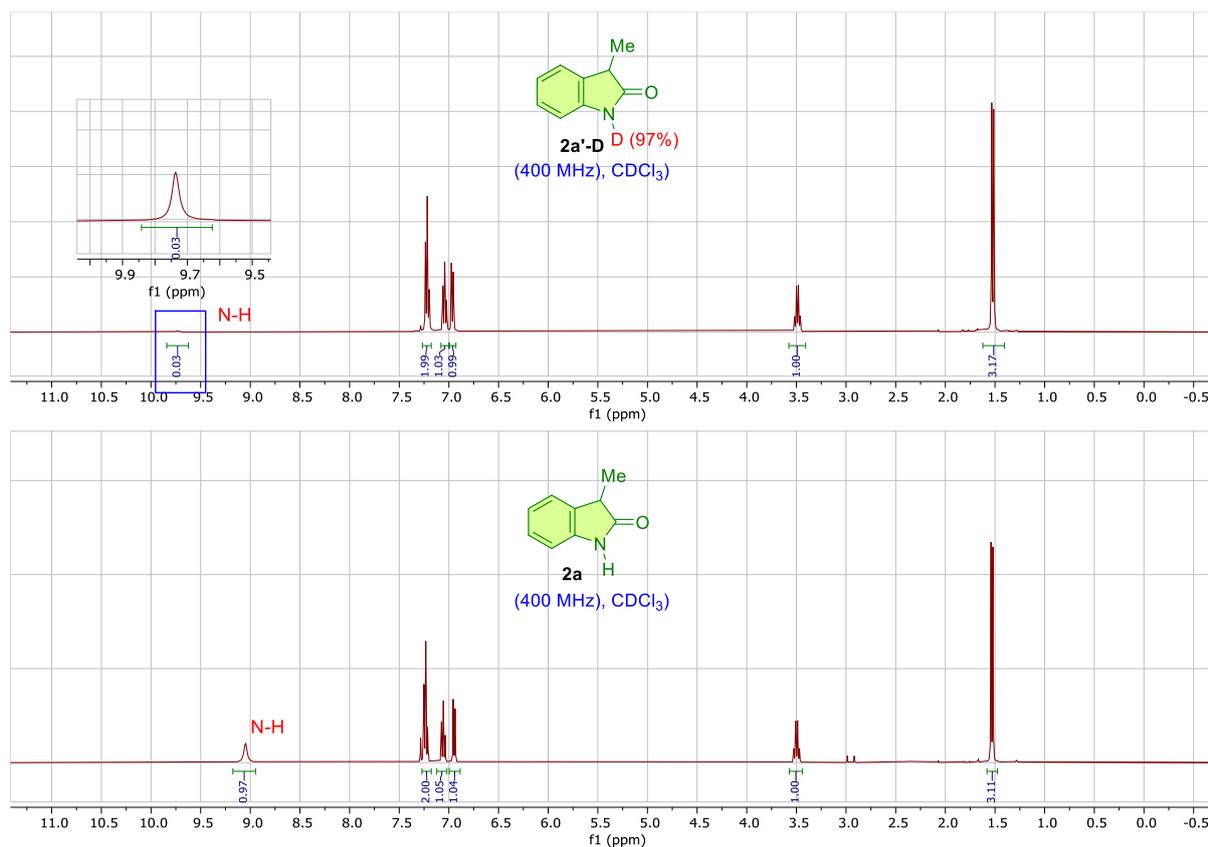
c. Deuterium labelling studies:

Preparation of 2a'-D:



Scheme S5: Preparation of **2a'-D**

An oven-dried 10 mL round-bottom flask equipped with a magnetic stir bar was charged with 3-methyl 2-oxindoles **2a** (50 mg), 0.1 mL of D_2O , and 1 mL of $CDCl_3$. The content was stirred for 2 h. The solvent was then removed under reduced pressure and dried under vacuum to get the N-deuterated 3-methyl 2-oxindole **2a'-D**. The deuterium content was determined by 1H -NMR spectrum.

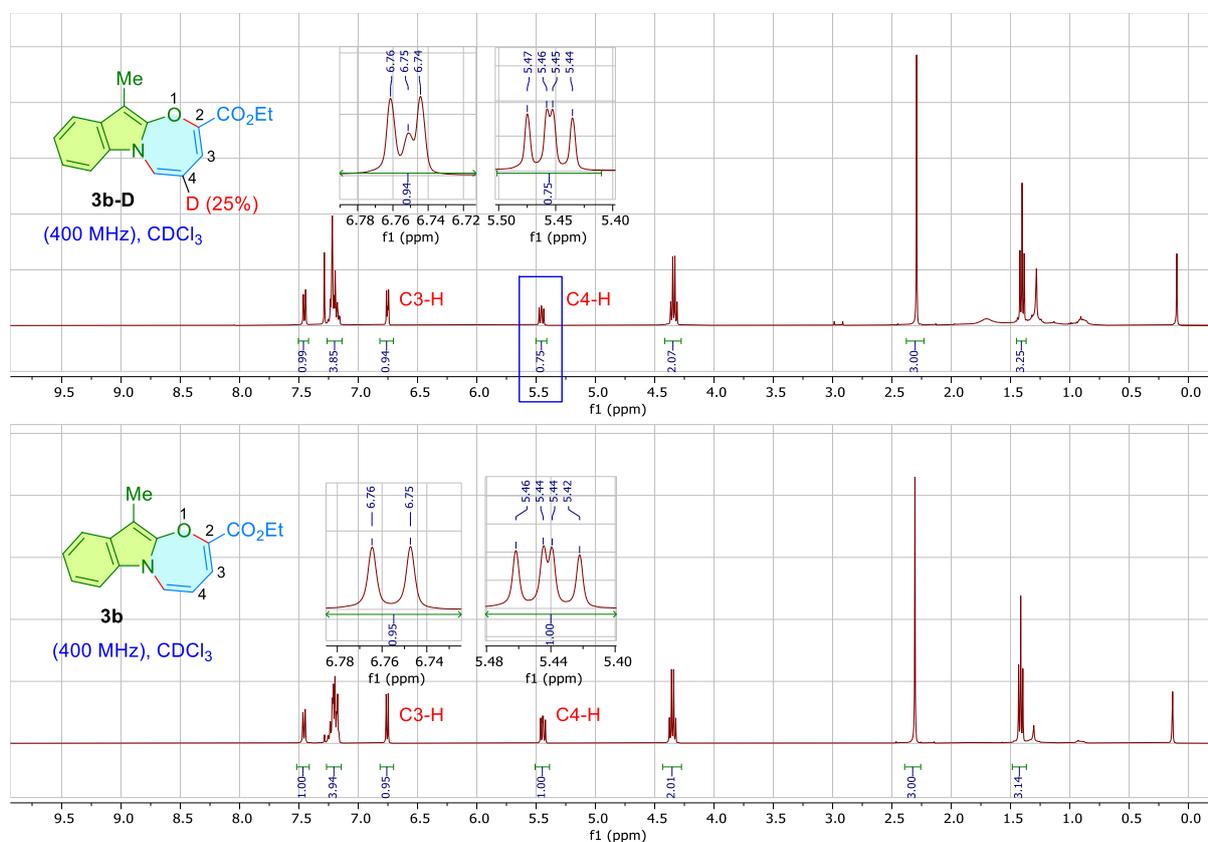


Reaction of 1b with 2a'-D:

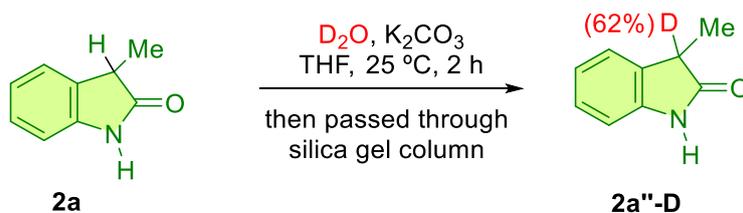


Scheme S6: Reaction of 1b with 2a'-D

The reaction was carried out by following **General Procedure A**. The ¹H-NMR spectrum of the product indolo-oxazepine **3b-D** revealed 25% D-incorporation at the C4-position.

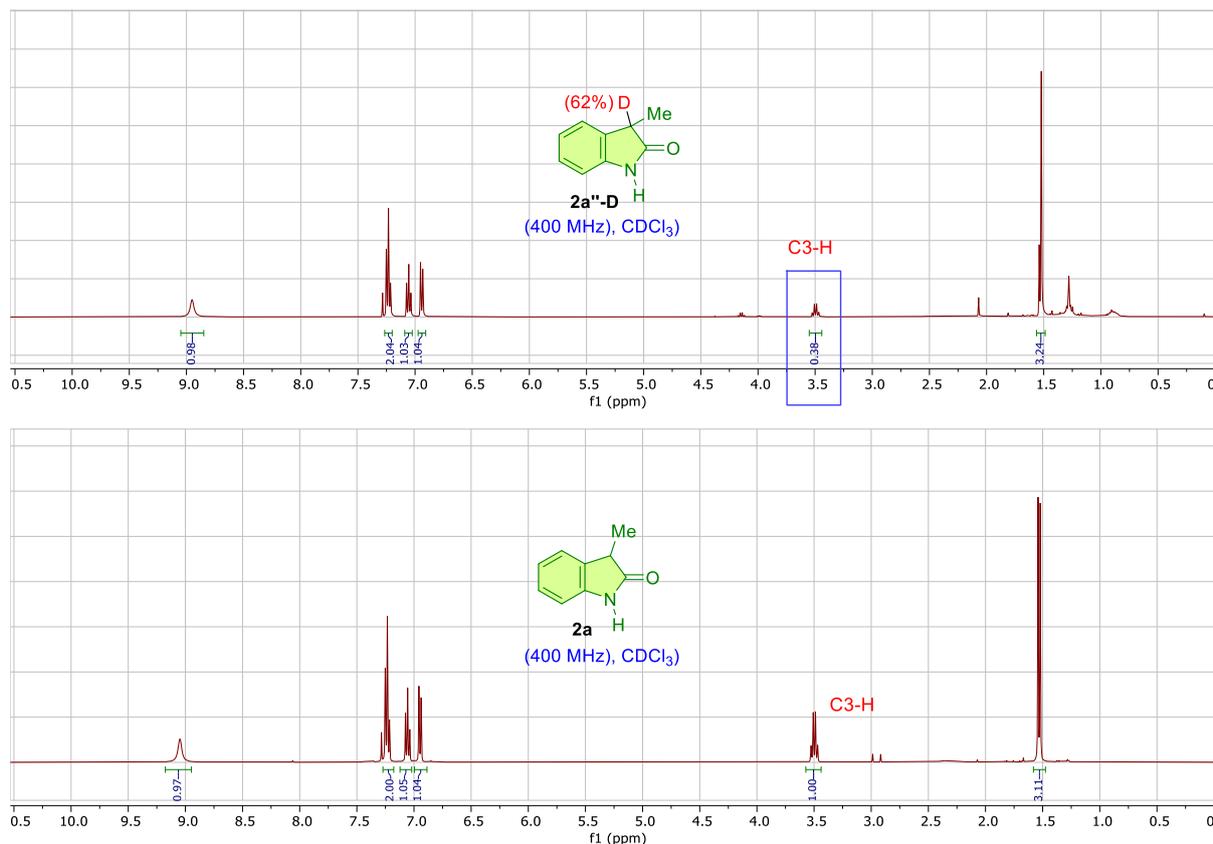


Preparation of 2a''-D:



Scheme S7: Preparation of 2a''-D

An oven-dried 10 mL round-bottom flask equipped with a magnetic stir bar was charged with 3-methyl 2-oxindoles **2a** (200 mg, 1 equiv.), K₂CO₃ (2 equiv.), 0.2 mL of D₂O and 0.5 mL of THF. The content was stirred for 2 h and quenched with NH₄Cl. The organic layer was extracted with ethyl acetate and dried over Mg₂SO₄. The solvent was then removed under reduced pressure, and the crude material was purified by silica gel column chromatography (eluent: EtOAc/Hexane, 5:95) to give **2a''-D**. The deuterium content was determined by ¹H-NMR spectrum.

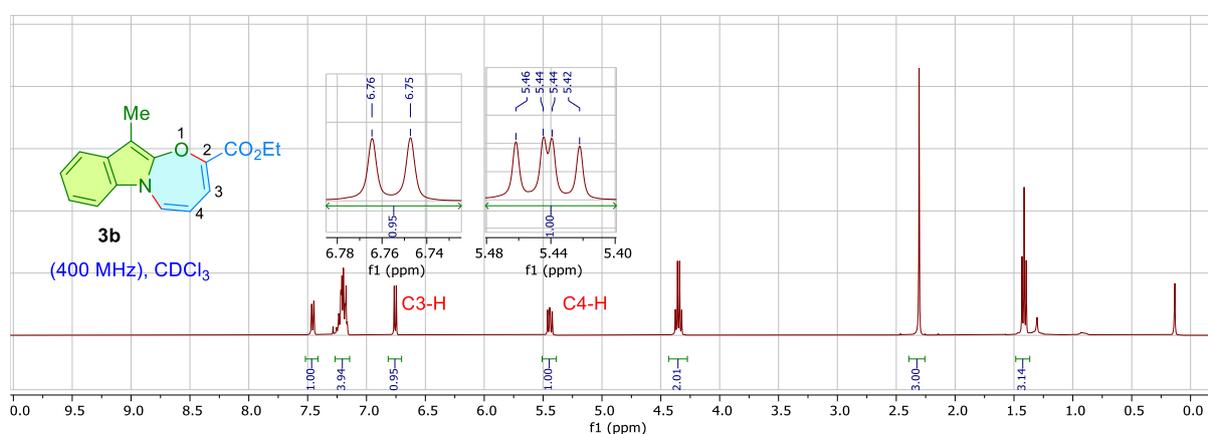
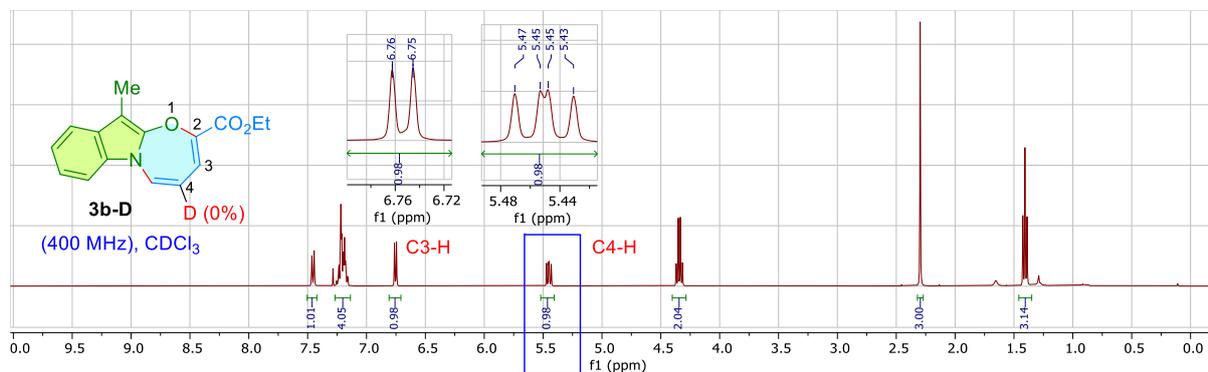


Reaction of 1b with 2a''-D:

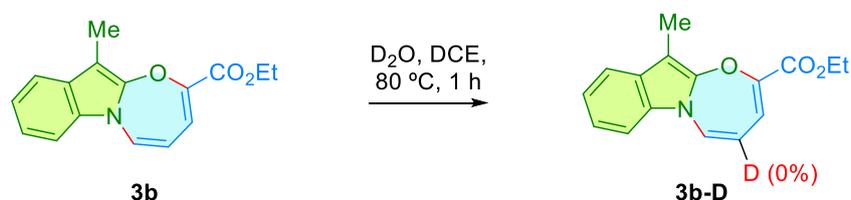


Scheme S8: Reaction of **1b** with **2a''-D**

The reaction was carried out by following **General Procedure A**. The $^1\text{H-NMR}$ spectrum of the product indolo-oxazepine **3b** revealed 0% D-incorporation.

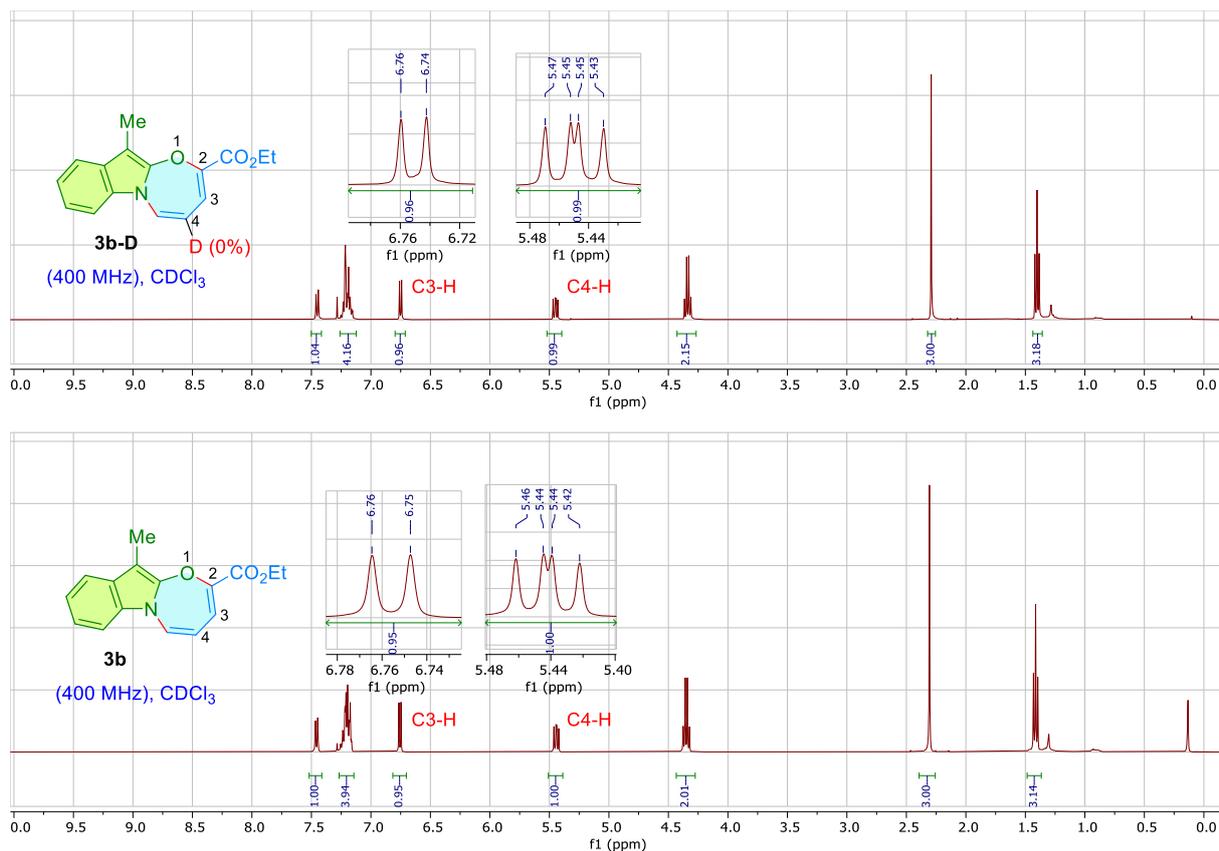


Reaction of **3b** with D_2O :



Scheme S9: Reaction of **3b** with D_2O

An oven-dried 10 mL round-bottom flask equipped with a magnetic stir bar and reflux condenser was charged with indolo-oxazepine **3b** (20 mg), 0.1 mL of D_2O , and 1 mL of DCE. The content was stirred for 2 h at 80 $^\circ\text{C}$. The organic layer was dried over Mg_2SO_4 , and solvent was removed under reduced pressure. The $^1\text{H-NMR}$ spectrum of the product revealed 0% D-incorporation.



6. Synthetic application:

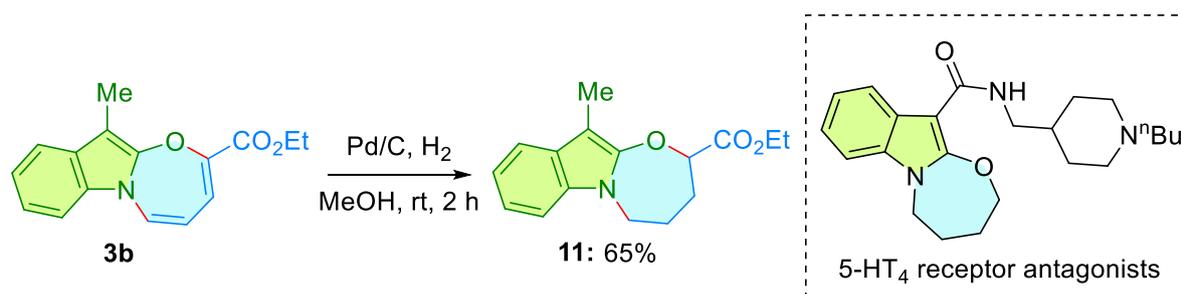
(a) Large-scale synthesis of **3b**:



Scheme S10: Large-scale synthesis of **3b**

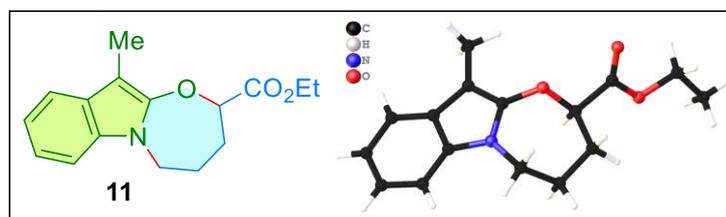
An oven-dried 100 mL round-bottom flask equipped with a magnetic stir bar under a nitrogen atmosphere was charged with Rh₂(oct)₄ (2 mol%), Diphenyl phosphate (5 mol%), 3-methyl indolin-2-one (**2**, 3.4 mmol), 4 Å MS (1 g), and 40 mL of dry DCE. To the gently stirring contents at 80 °C temperature was added a solution of ester diazoenal (**1b**) in 20 mL dry DCE *via* syringe pump over a period of 4 h. The reaction was further continued for another 4 h. The solvent was then removed under reduced pressure, and the crude product was purified by silica gel column chromatography (eluent: EtOAc/Hexane, 5:95) to yield the indolo-oxazepine product **3b**.

(b) One-step access to the 5-HT₄ receptor antagonist derivative:



Scheme S11: Transformation of **3b** to 5-HT₄ receptor antagonist core

An oven-dried 10 ml round-bottom flask was charged with the [1,3]oxazepino[3,2-a]indole **3b** (30 mg, 0.11 mmol), 3 ml of anhydrous methanol, and 10% Pd/C (5.5 mg). The reaction vessel was thoroughly flushed with argon, followed by hydrogen. The reaction mixture was stirred under a hydrogen atmosphere (hydrogen balloon) at room temperature. After 2 h, the reaction mixture was filtered through a celite pad, and the solvent was evaporated under reduced pressure. Purification of the crude material on a silica gel flash column chromatography using ethyl acetate/petroleum ether (20:80) as the eluent furnished the 2,3,4,5-tetrahydro-[1,3]oxazepino[3,2-a]indole **11**.



Ethyl 11-methyl-2,3,4,5-tetrahydro-[1,3]oxazepino[3,2-a]indole-2-carboxylate (11)

Links: [DETAILS](#) [NMR](#) [SCXRD](#)

Obtained as colourless solid; yield = 65% (20 mg); R_f = 0.4 (EtOAc/Hexane: 20:80); m.p. = 119-122 °C **¹H NMR** (400 MHz, CDCl₃) δ 7.47 (d, J = 7.7 Hz, 1H), 7.23 – 7.12 (m, 2H), 7.09 (t, J = 8.0 Hz, 1H), 4.41 – 4.31 (m, 2H), 4.33 – 4.28 (m, 1H), 4.25 (d, J = 11.0 Hz, 1H), 3.94 – 3.83 (m, 1H), 2.45 – 2.34 (m, 1H), 2.23 (s, 3H), 2.21 – 2.10 (m, 2H), 1.81 – 1.66 (m, 1H), 1.37 (t, J = 7.1 Hz, 3H). **¹³C NMR** (101 MHz, CDCl₃) δ 170.2, 148.8, 131.3, 127.2, 120.6, 119.1, 118.6, 108.3, 93.6, 82.6, 61.7, 43.0, 33.8, 27.4, 14.3, 7.0. **HRMS** (ESI) m/z calc. for C₁₆H₁₉NNaO₃ (M+Na)⁺ 296.1257, found 296.1261.

7. References:

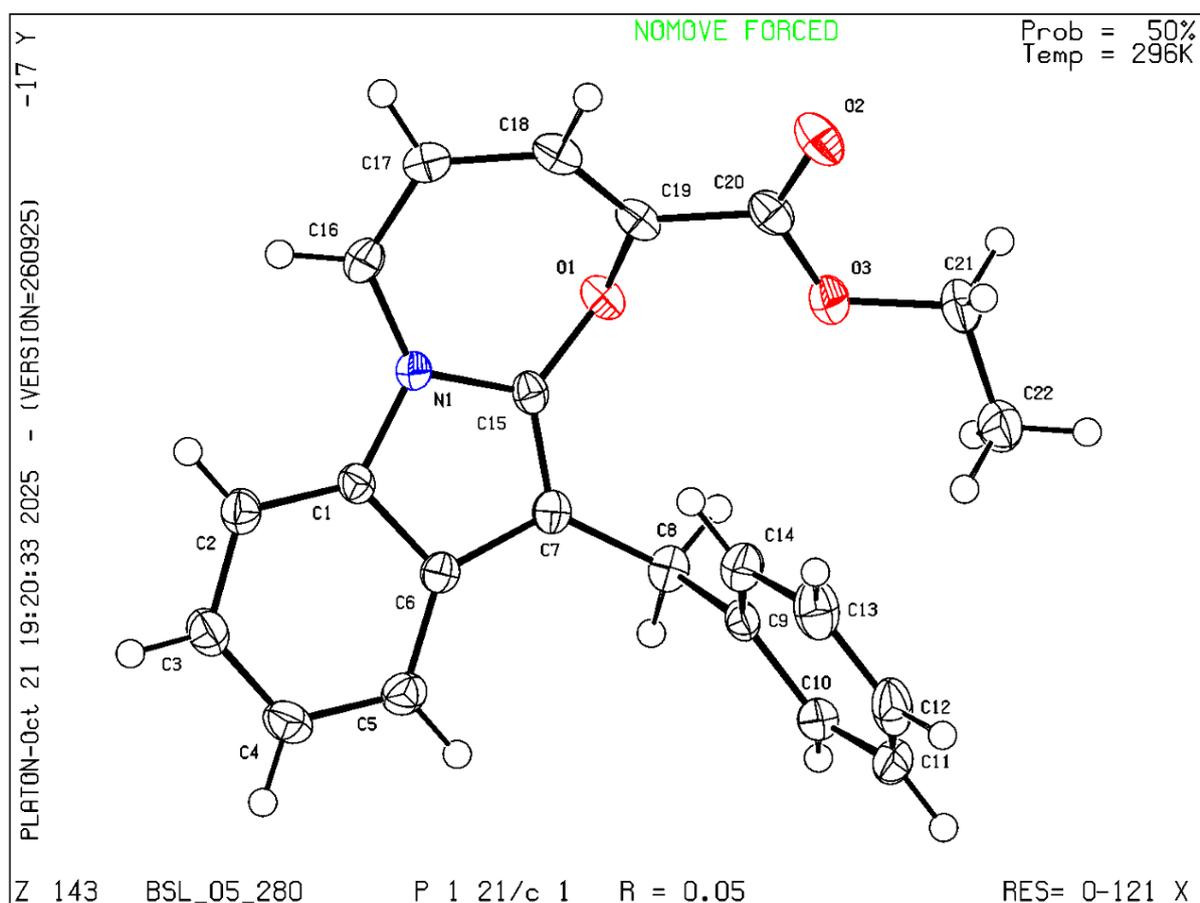
1. S. G. Dawande, V. Kanchupalli, J. Kalepu, H. Chennamsetti, B. S. Lad and S. Katukojvala, *Angew. Chem. Int. Ed.*, 2014, **53**, 4076-4080.
2. K. S. Rathore, M. Harode and S. Katukojvala, *Org. Biomol. Chem.*, 2014, **12**, 8641-8645.
3. P. K. Mandal and S. Katukojvala, *Chem. Eur. J.*, 2024, **30**, e202303862.
4. C. K. Kundu, Shubham and S. Katukojvala, *Org. Lett.*, **2025**, DOI: 10.1021/acs.orglett.5c04229.
5. B. M. Trost, Y. Zhang and T. Zhang, *J. Org. Chem.*, 2009, **74**, 5115-5117.
6. L. Cheng, L. Liu, D. Wang and Y.-J. Chen, *Org. Lett.*, 2009, **11**, 3874-3877.
7. B. M. Trost, J. Xie and J. D. Sieber, *J. Am. Chem. Soc.*, 2011, **133**, 20611-20622.
8. K. S. Rathore, B. S. Lad, H. Chennamsetti and S. Katukojvala, *Chem. Commun.*, 2016, **52**, 5812-5815.

8. Crystallographic data:

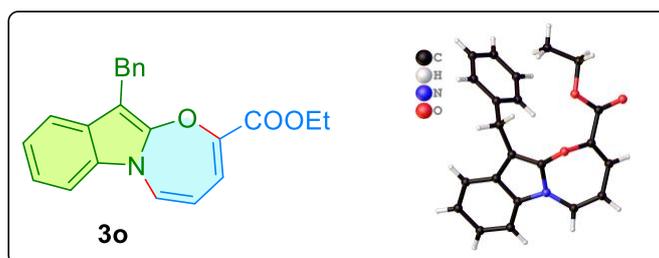
Table S2: Crystal data and structure refinement parameters for **3o**

Links: [DETAILS](#) [NMR](#) [SCXRD](#)

Method for sample preparation: Single crystals suitable for X-ray diffraction were obtained by slow evaporation of the solvent from a DCM/hexane (1:1) solution of **3o** at 4 °C. Crystal data collection and refinement parameters of **3o** are summarized in Table S2.



Thermal ellipsoid plot for **3o** (ellipsoid contour 50% probability)



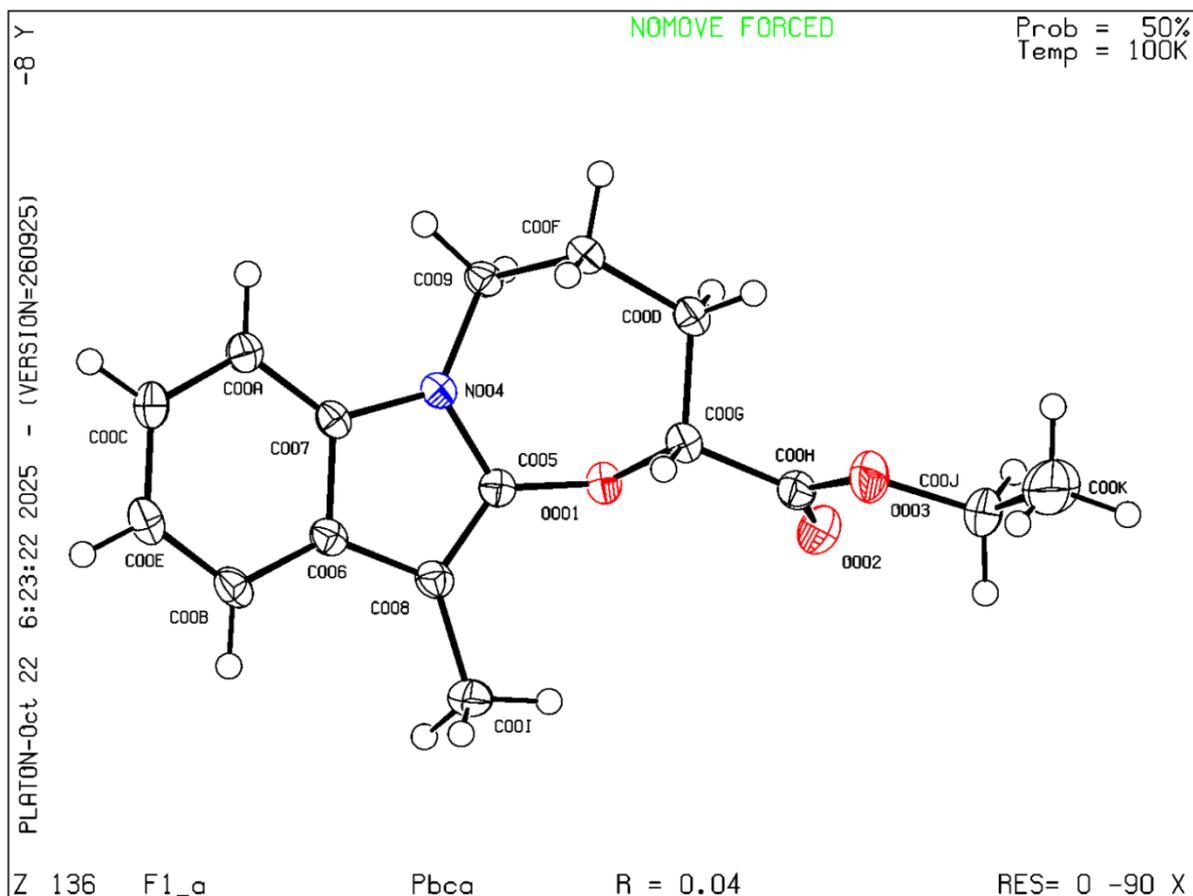
ORTEP diagram for **3o** (ellipsoid contour 50% probability)

CCDC	1554020
Empirical formula	C ₂₂ H ₁₉ NO ₃
Formula weight	345.38
Temperature/K	296.15
Crystal system	monoclinic
Space group	P2 ₁ /c
a/Å	15.0392(3)
b/Å	5.64820(10)
c/Å	20.2067(4)
α/°	90
β/°	93.4100(10)
γ/°	90
Volume/Å ³	1713.41(6)
Z	4
ρ _{calc} /cm ⁻³	1.339
μ/mm ⁻¹	0.089
F(000)	728.0
Crystal size/mm ³	0.12 × 0.1 × 0.08
Radiation	MoKα (λ = 0.71073)
2θ range for data collection/°	4.038 to 60.47
Index ranges	-21 ≤ h ≤ 21, -7 ≤ k ≤ 6, -28 ≤ l ≤ 27
Reflections collected	18181
Independent reflections	4996 [R _{int} = 0.0433, R _{sigma} = 0.0659]
Data/restraints/parameters	4996/0/237
Goodness-of-fit on F ²	1.103
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0544, wR ₂ = 0.1106
Final R indexes [all data]	R ₁ = 0.0847, wR ₂ = 0.1214
Largest diff. peak/hole / e Å ⁻³	0.29/-0.23

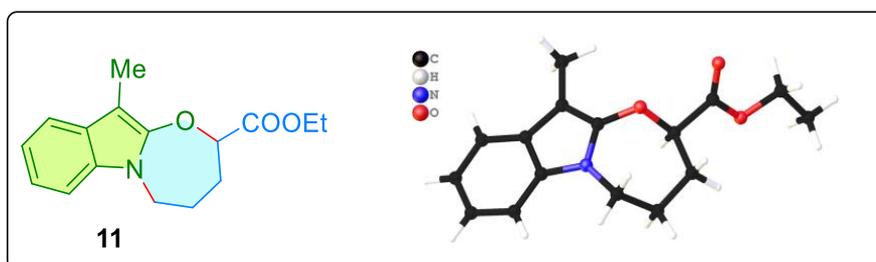
Table S2: Crystal data and structure refinement parameters for **11**

Links: [DETAILS](#) [NMR](#) [SCXRD](#)

Method for sample preparation: Single crystals suitable for X-ray diffraction were obtained by slow evaporation of the solvent from a DCM/hexane (1:1) solution of **11** at 25 °C. Crystal data collection and refinement parameters of **11** are summarized in Table S2.



Thermal ellipsoid plot for **11** (ellipsoid contour 50% probability)

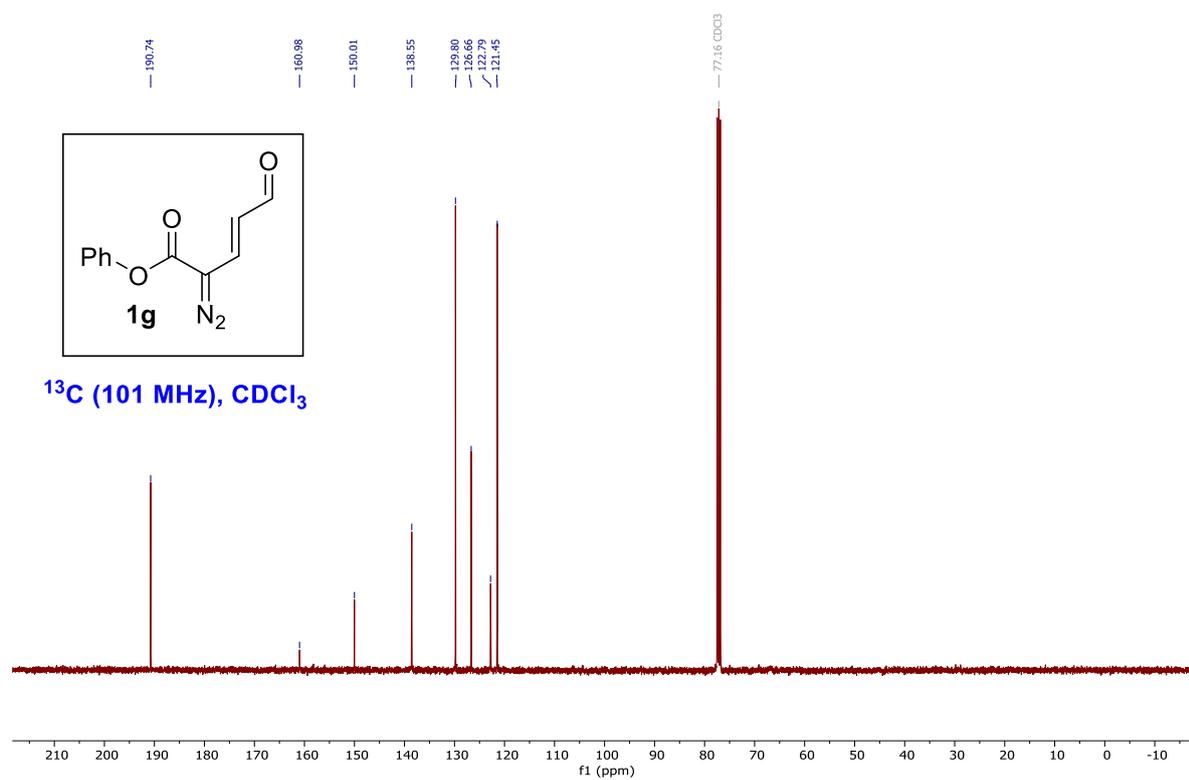
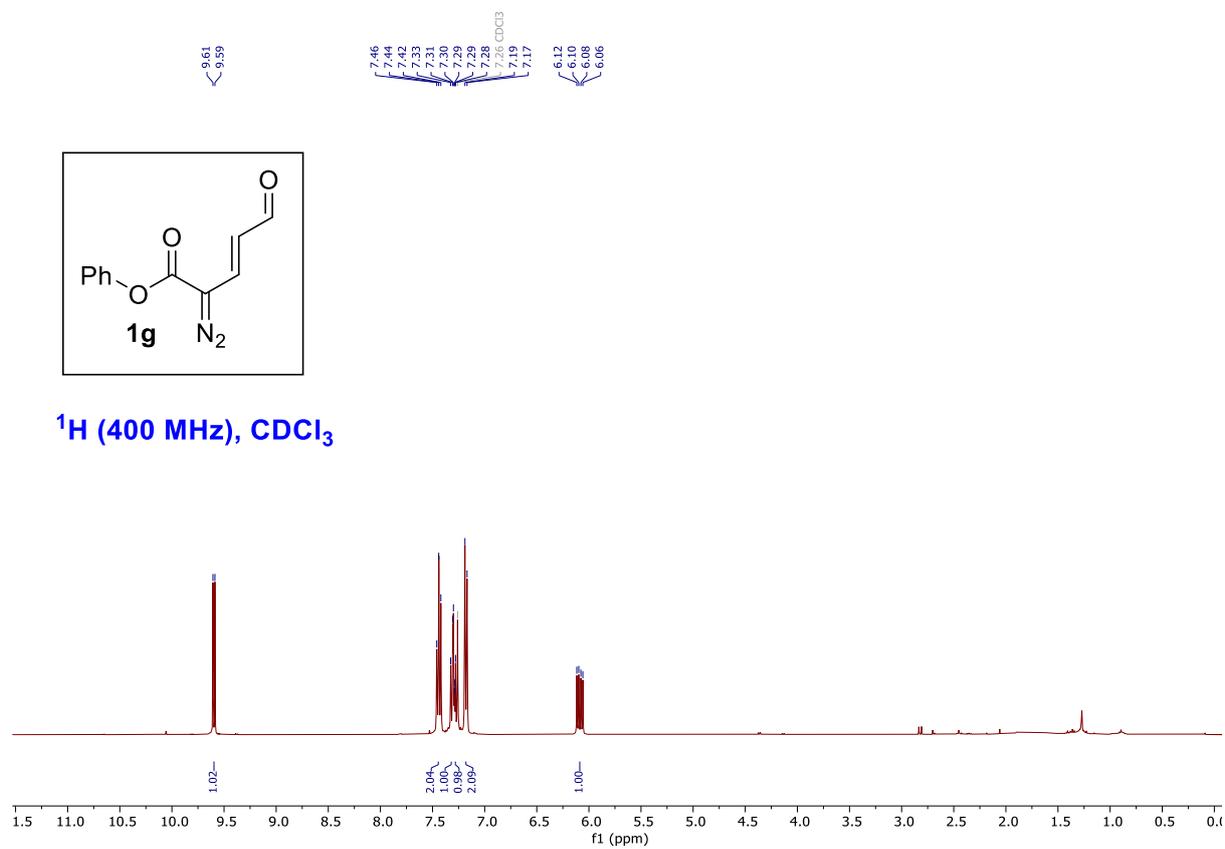


ORTEP diagram for **11** (ellipsoid contour 50% probability)

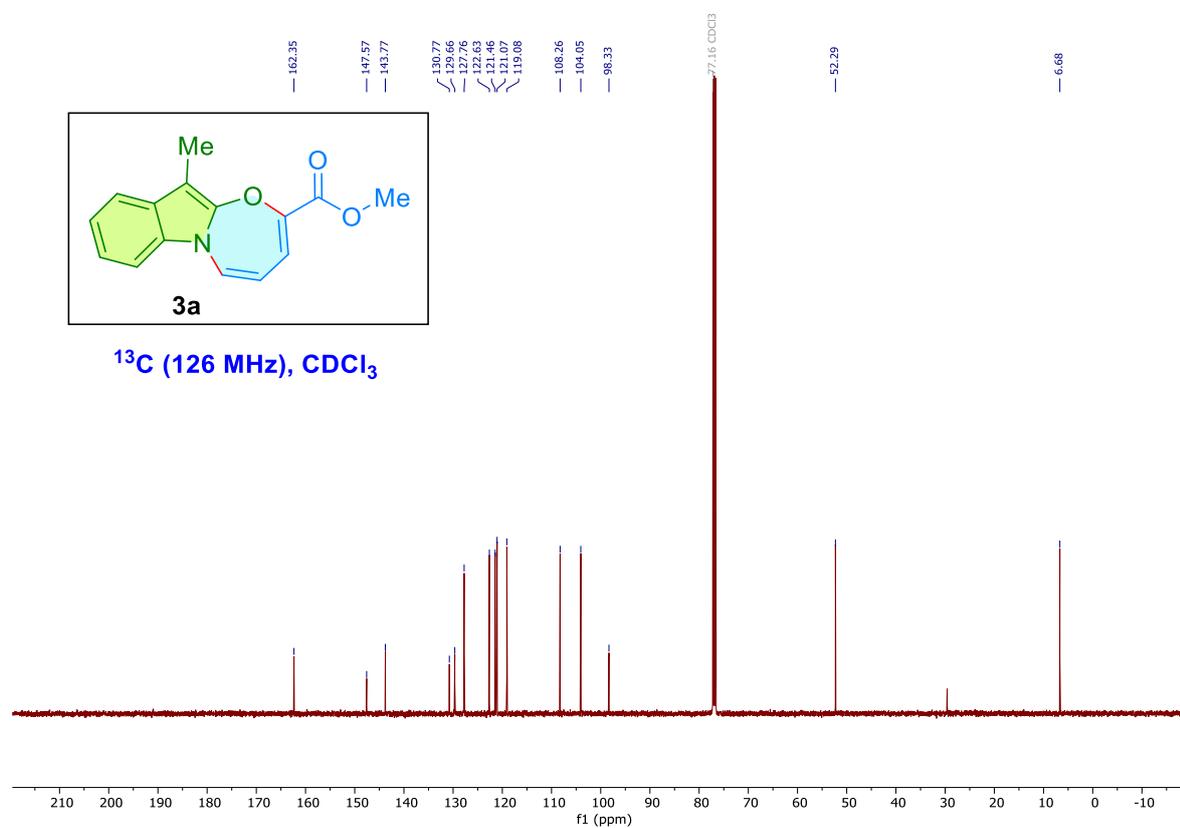
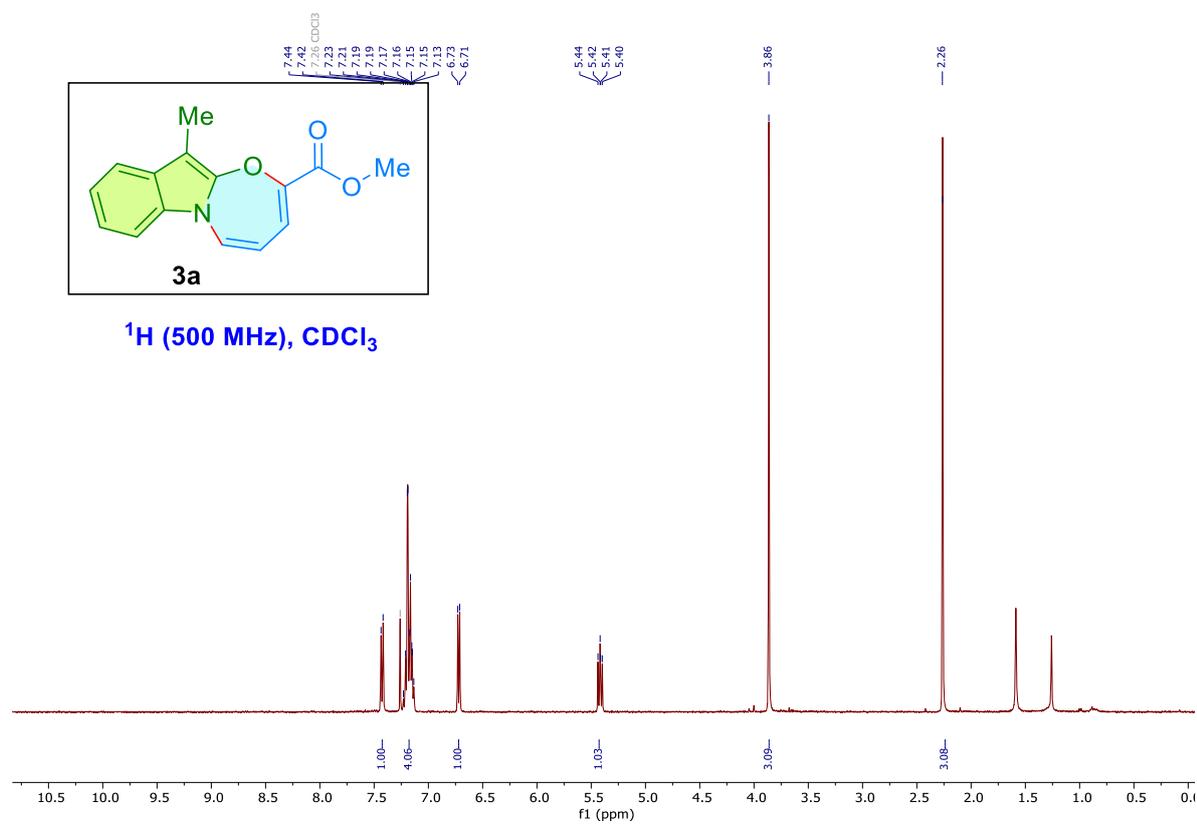
CCDC	2497118
Empirical formula	C ₁₆ H ₁₉ NO ₃
Formula weight	274.342
Temperature/K	100.00
Crystal system	orthorhombic
Space group	Pbca
a/Å	9.2002(4)
b/Å	8.2262(3)
c/Å	37.1993(15)
α/°	90
β/°	90
γ/°	90
Volume/Å ³	2815.3(2)
Z	8
ρ _{calc} /cm ³	1.294
μ/mm ⁻¹	0.089
F(000)	1176.8
Crystal size/mm ³	0.13 × 0.1 × 0.08
Radiation	Mo Kα (λ = 0.71073)
2θ range for data collection/°	7.42 to 55.9
Index ranges	-12 ≤ h ≤ 12, -10 ≤ k ≤ 10, -48 ≤ l ≤ 49
Reflections collected	64808
Independent reflections	3325 [R _{int} = 0.0487, R _{sigma} = 0.0173]
Data/restraints/parameters	3325/0/183
Goodness-of-fit on F ²	0.939
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0408, wR ₂ = 0.1075
Final R indexes [all data]	R ₁ = 0.0441, wR ₂ = 0.1108
Largest diff. peak/hole / e Å ⁻³	0.32/-0.28

9. NMR Spectra

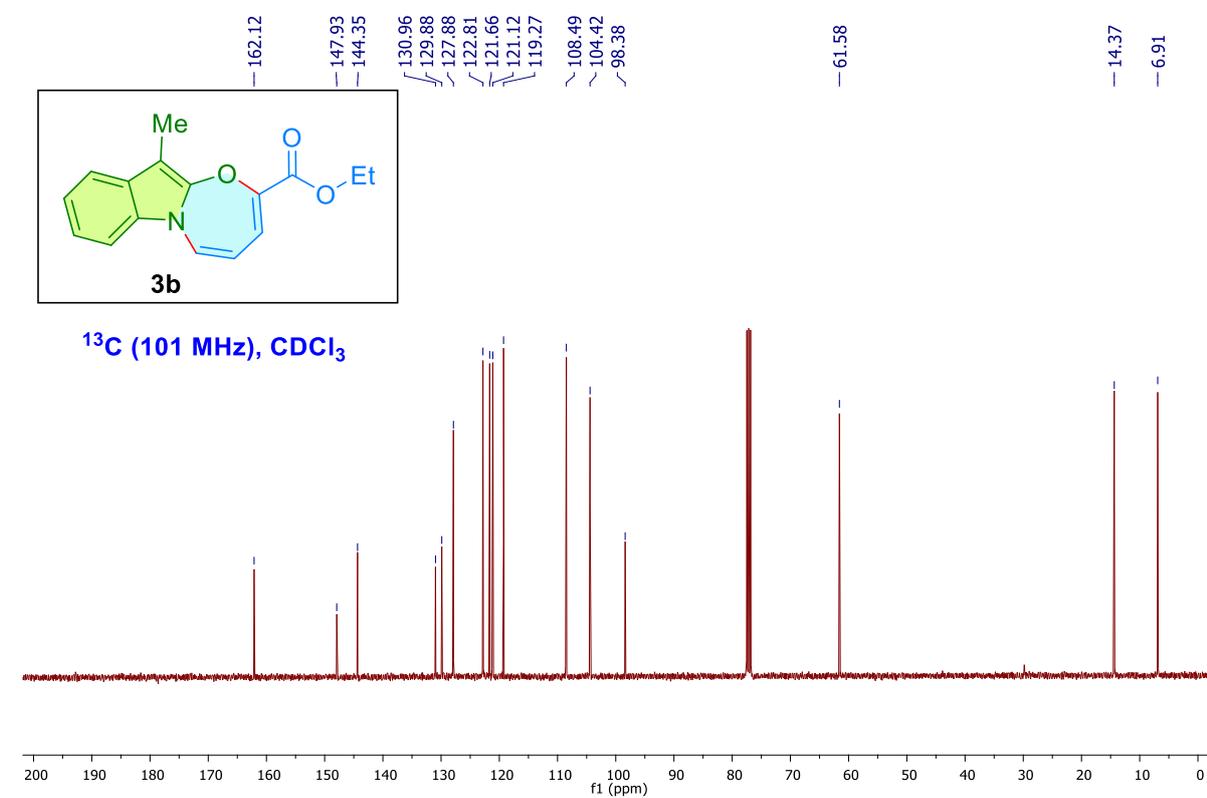
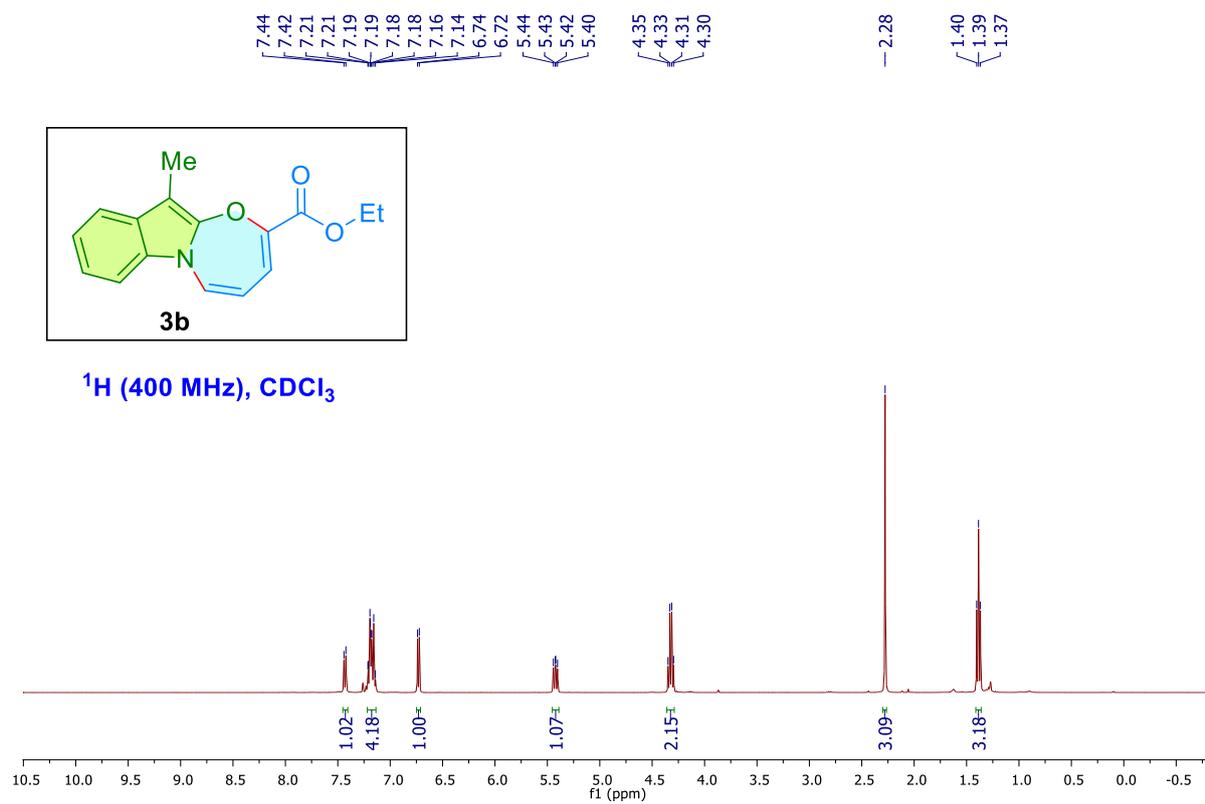
Links: [DETAILS](#) [NMR](#)



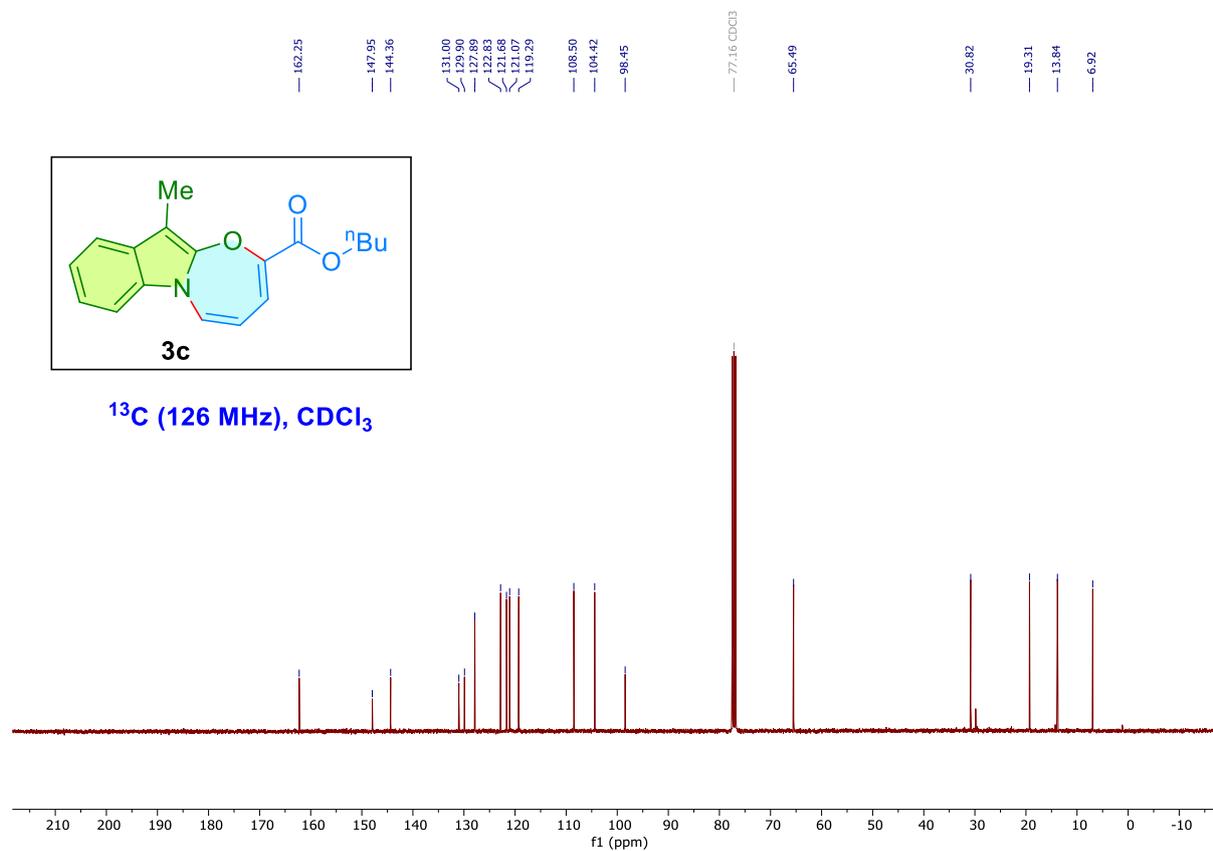
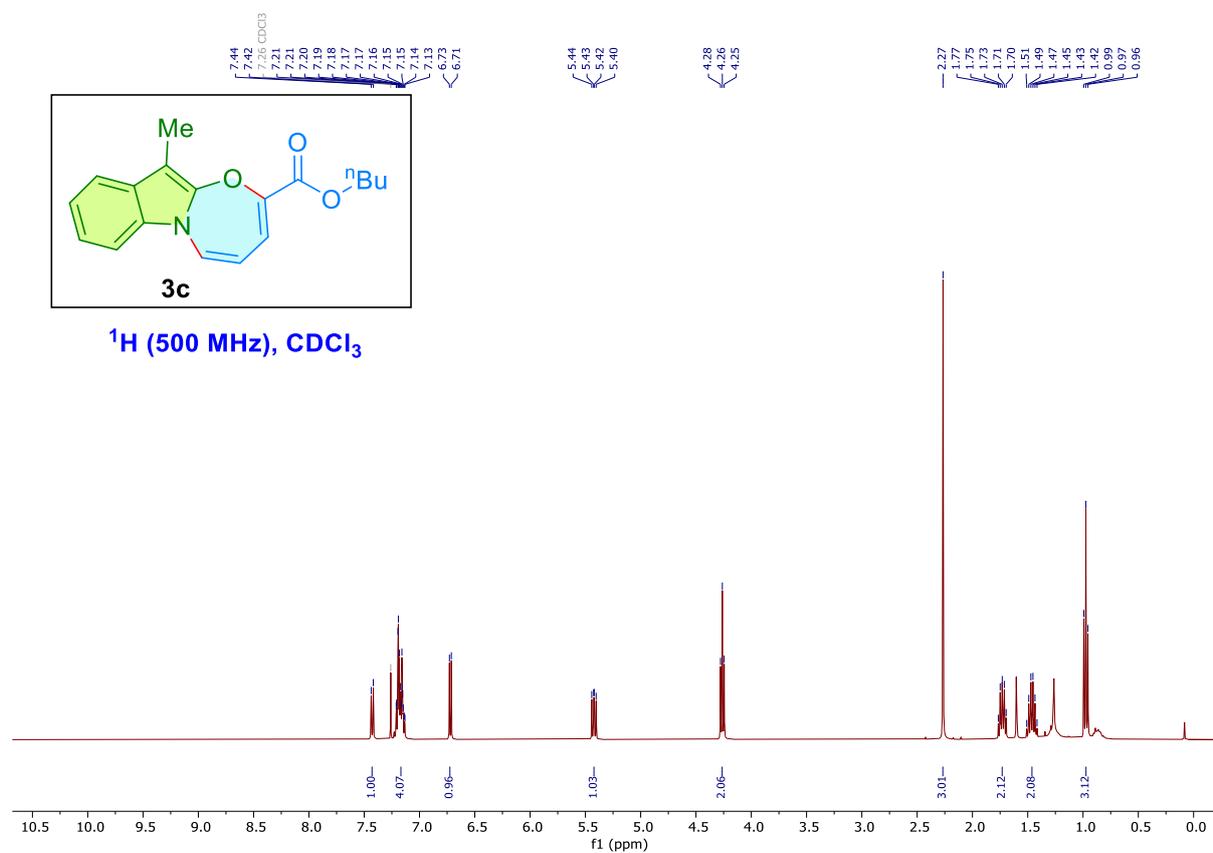
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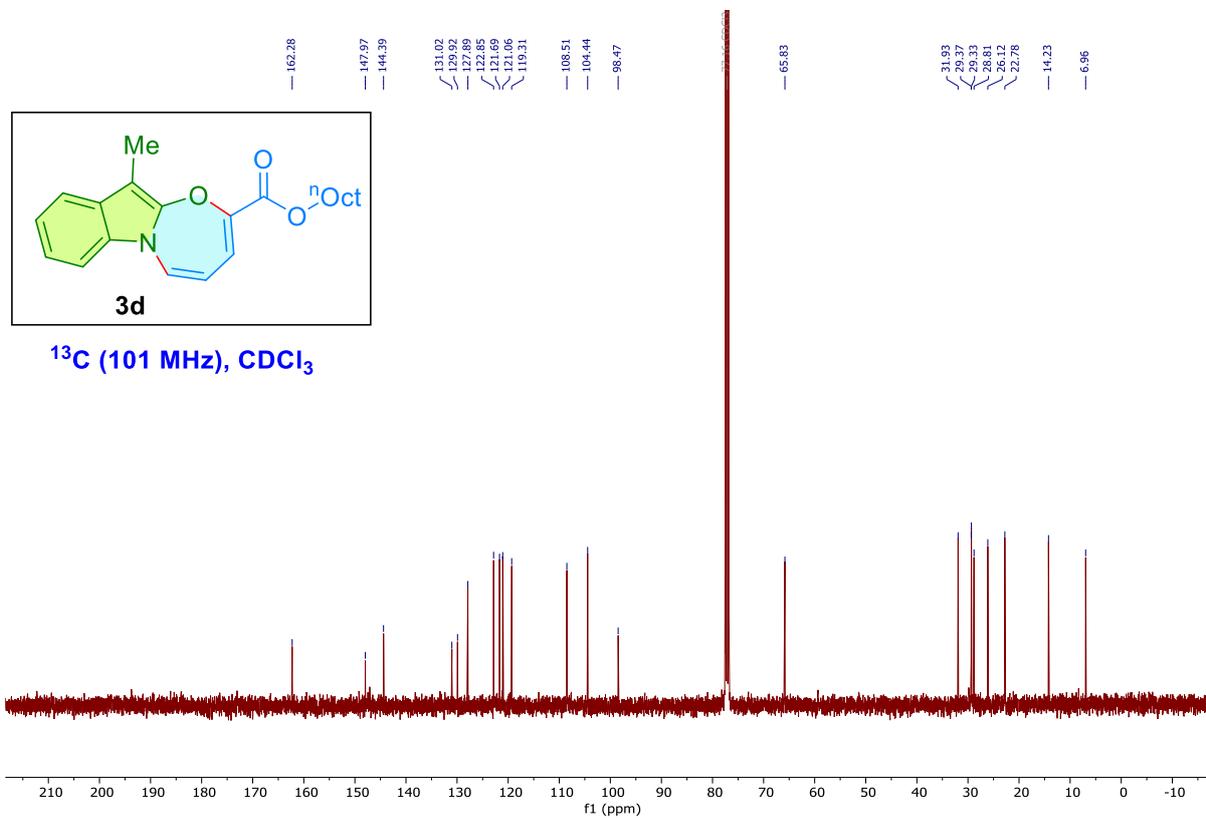
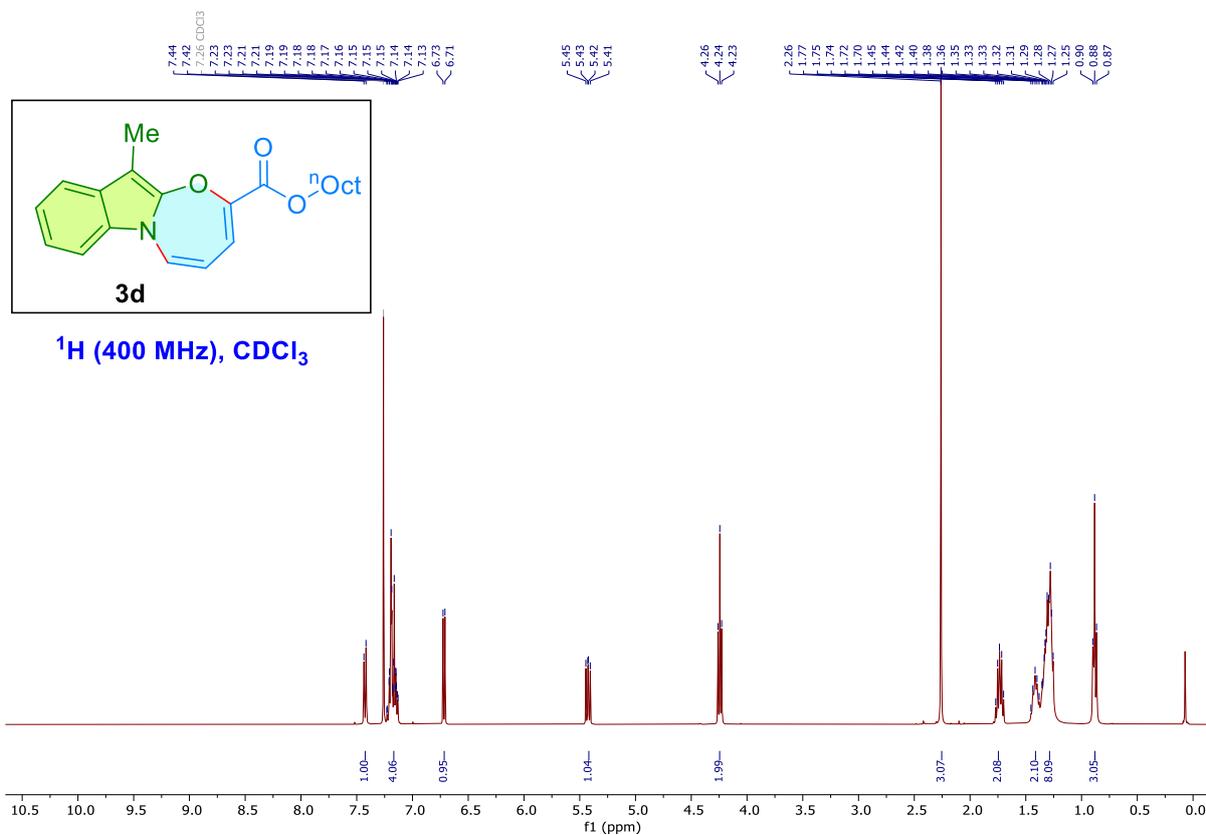
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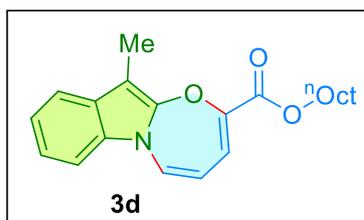


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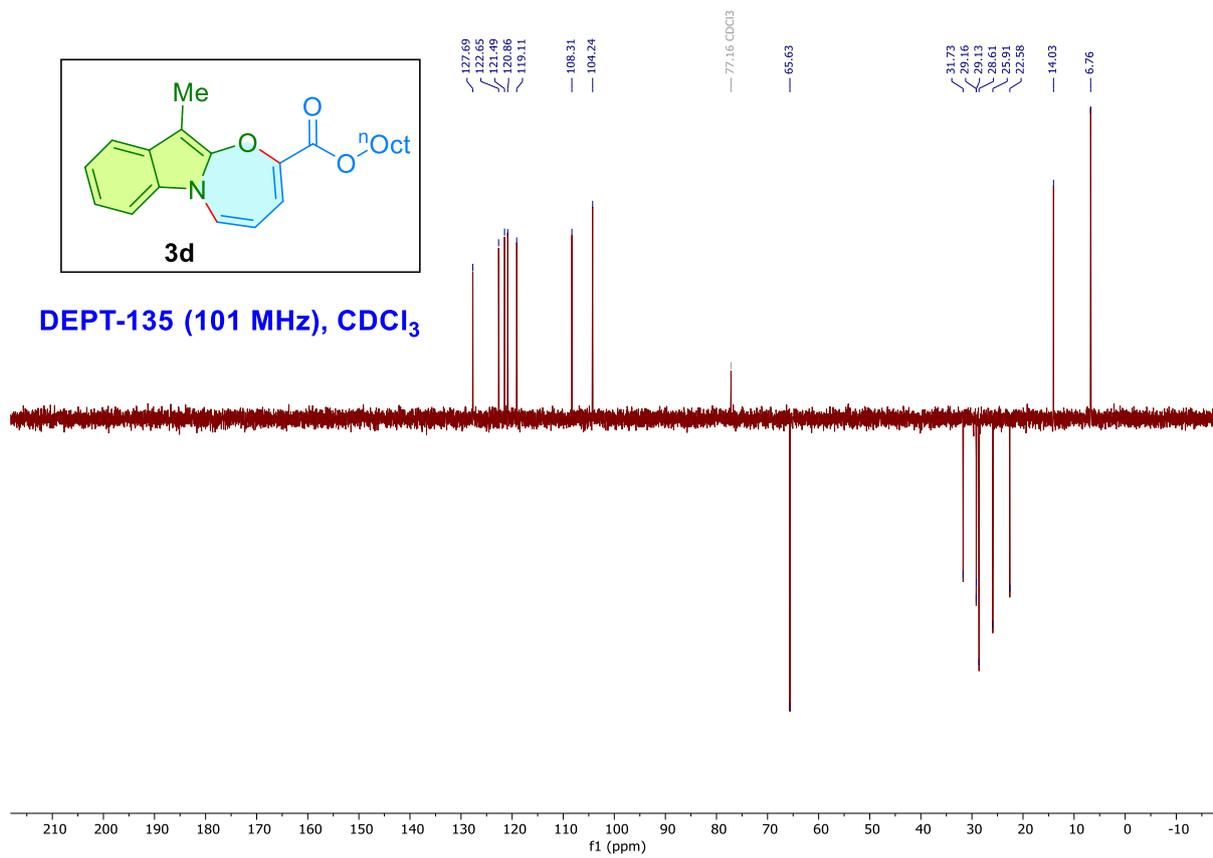


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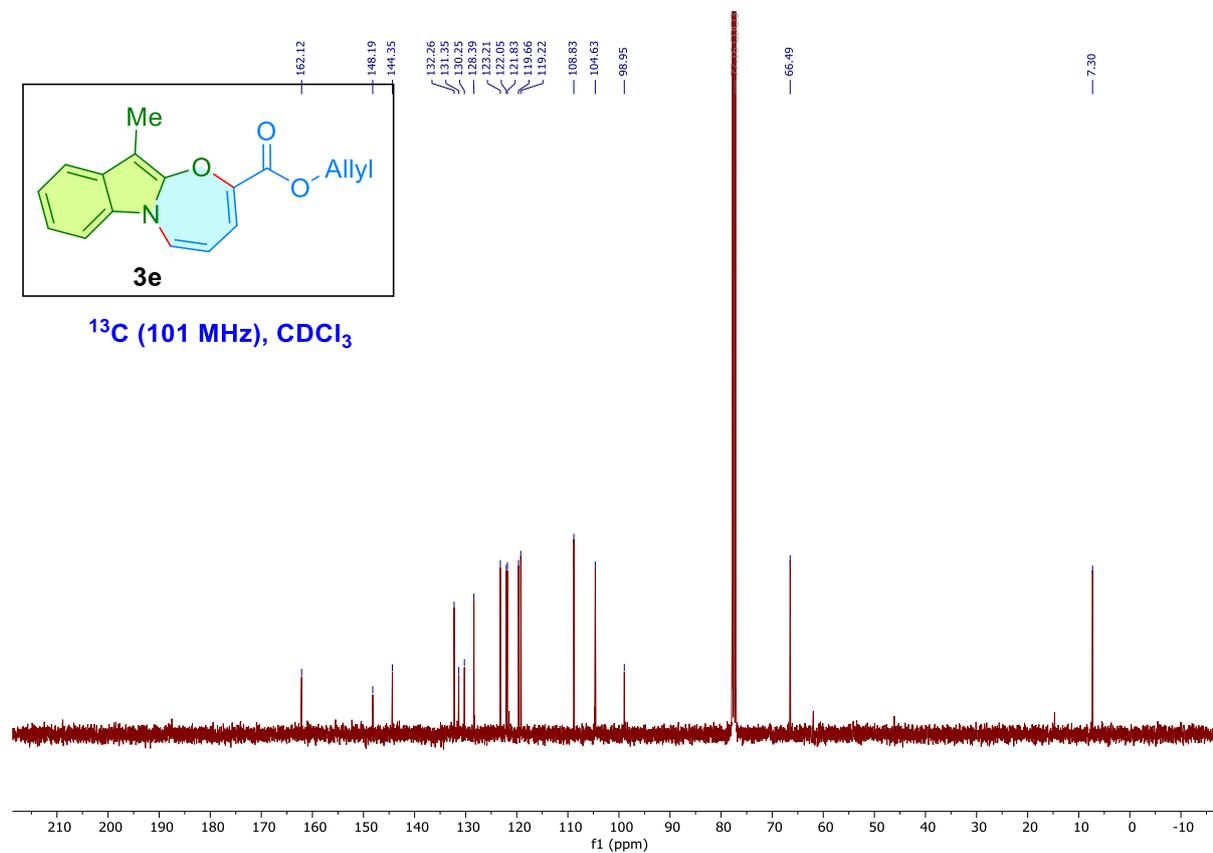
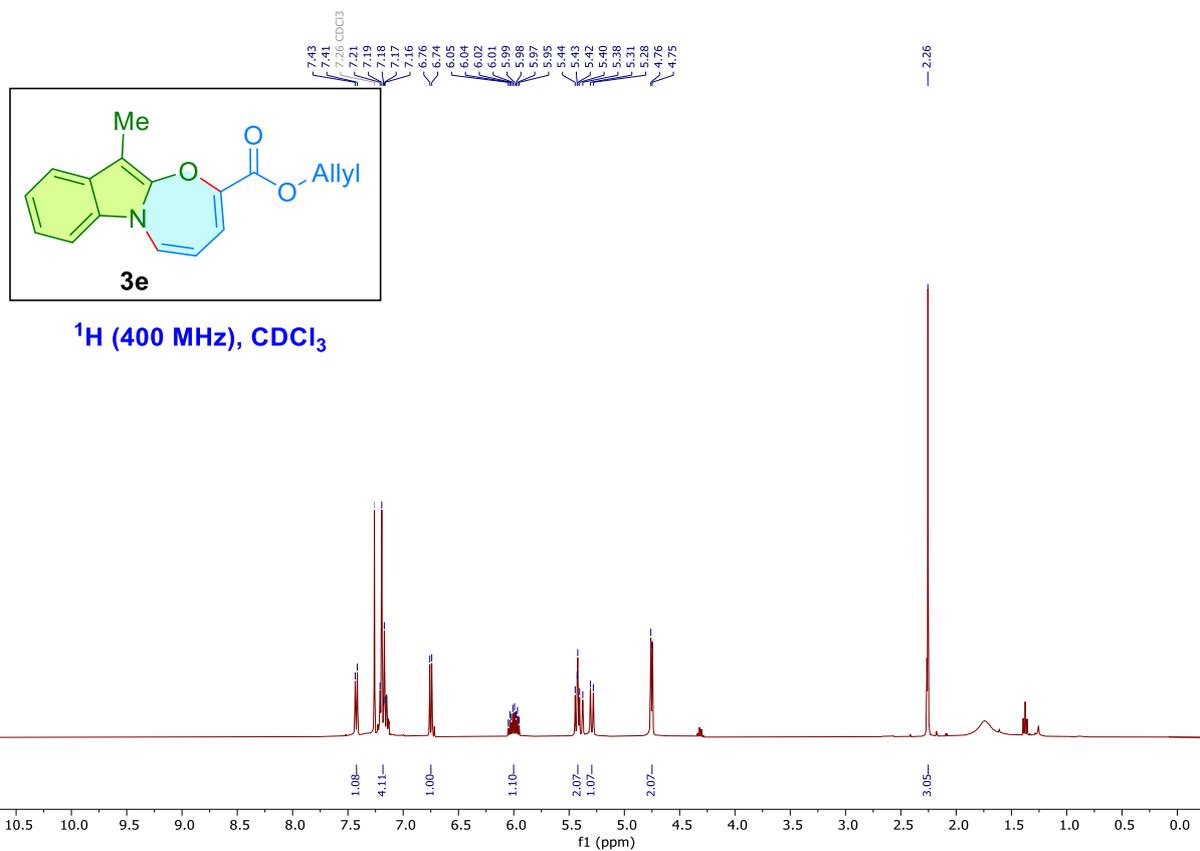




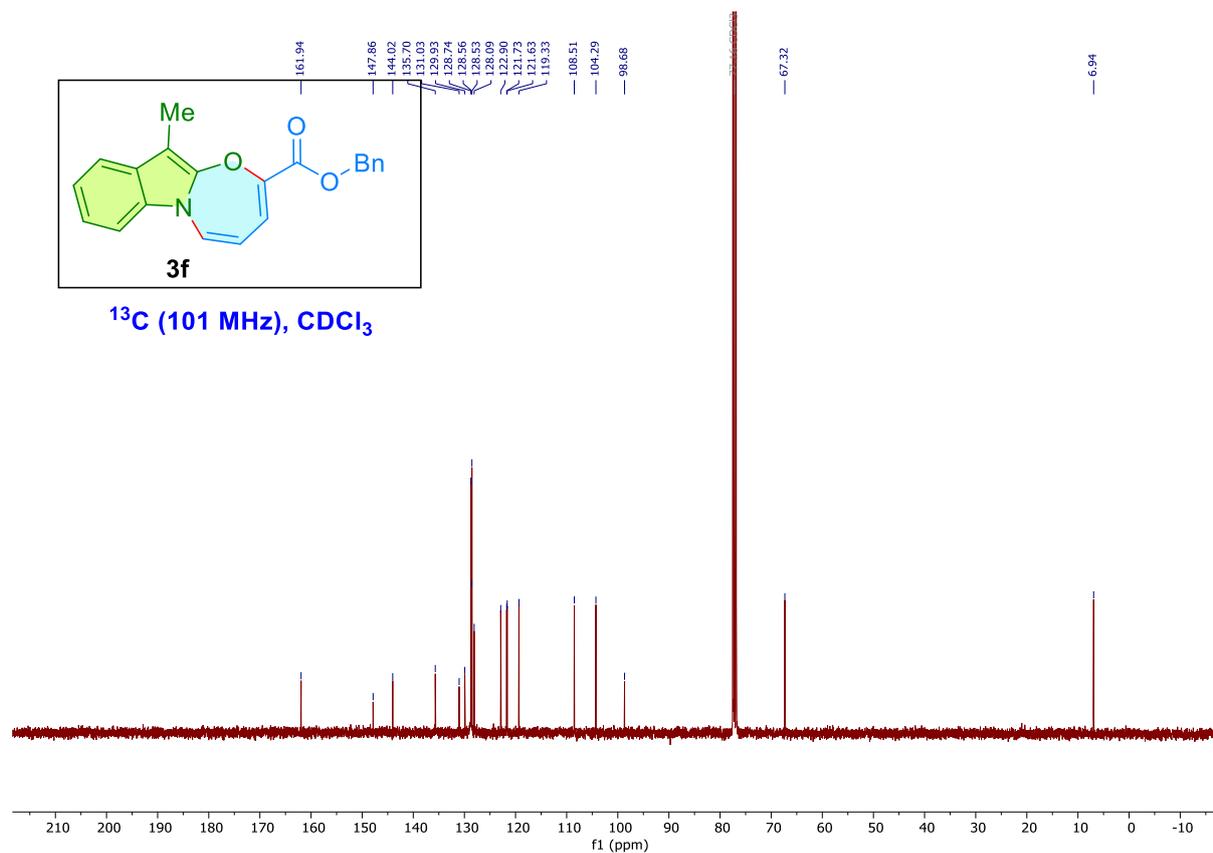
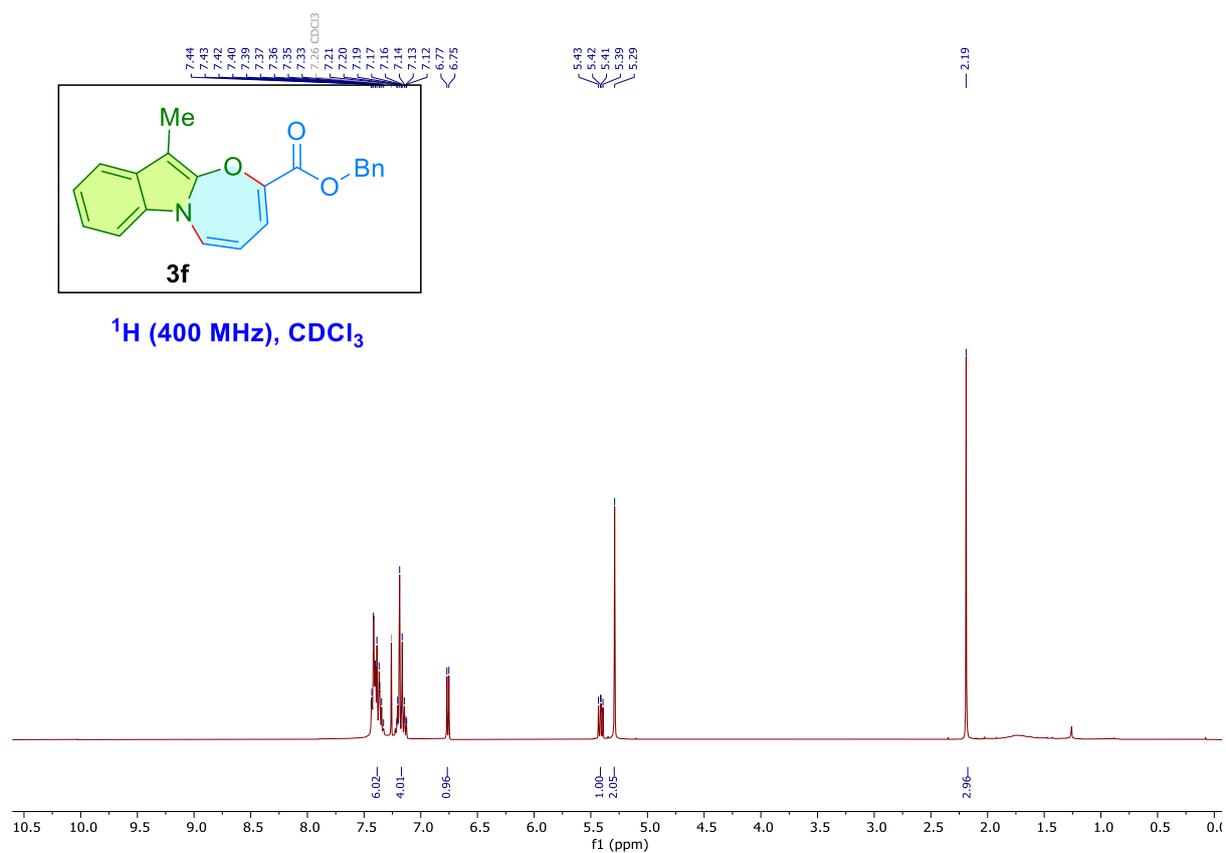
DEPT-135 (101 MHz), CDCl₃



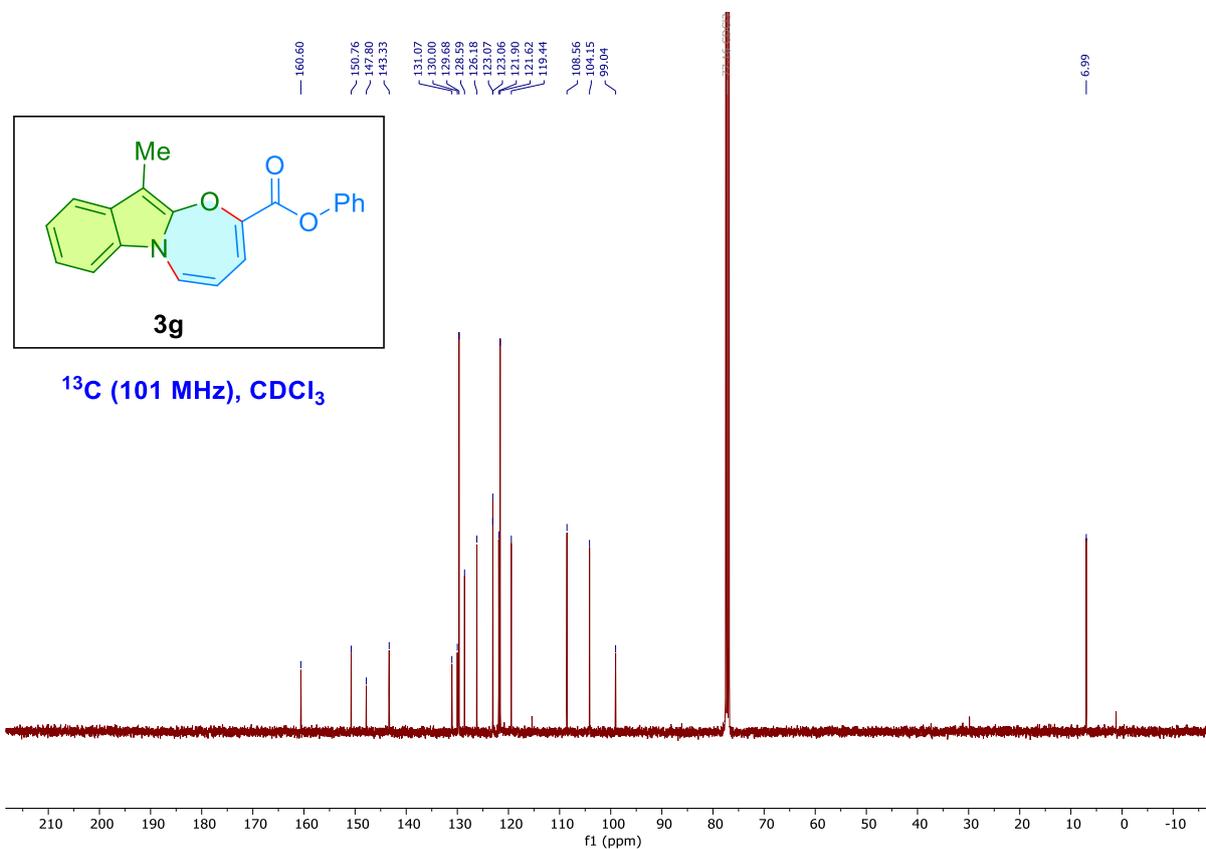
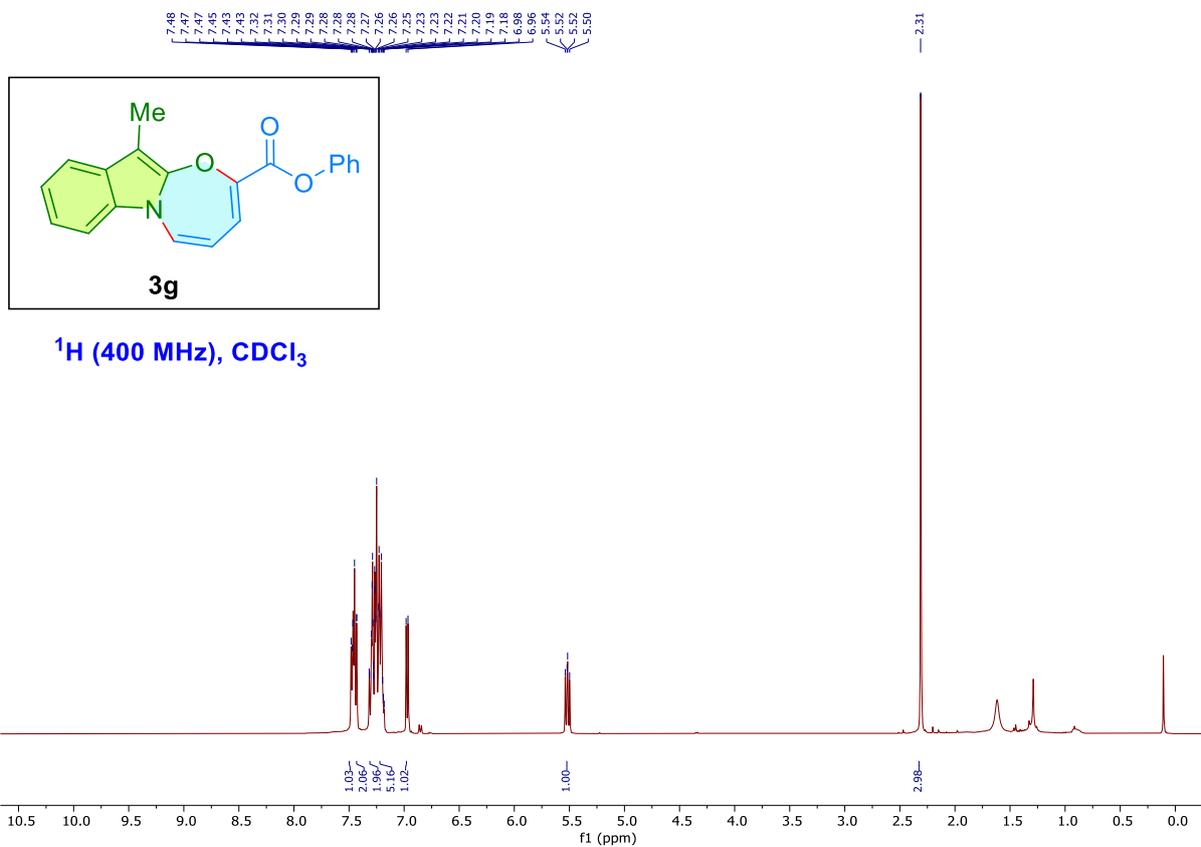
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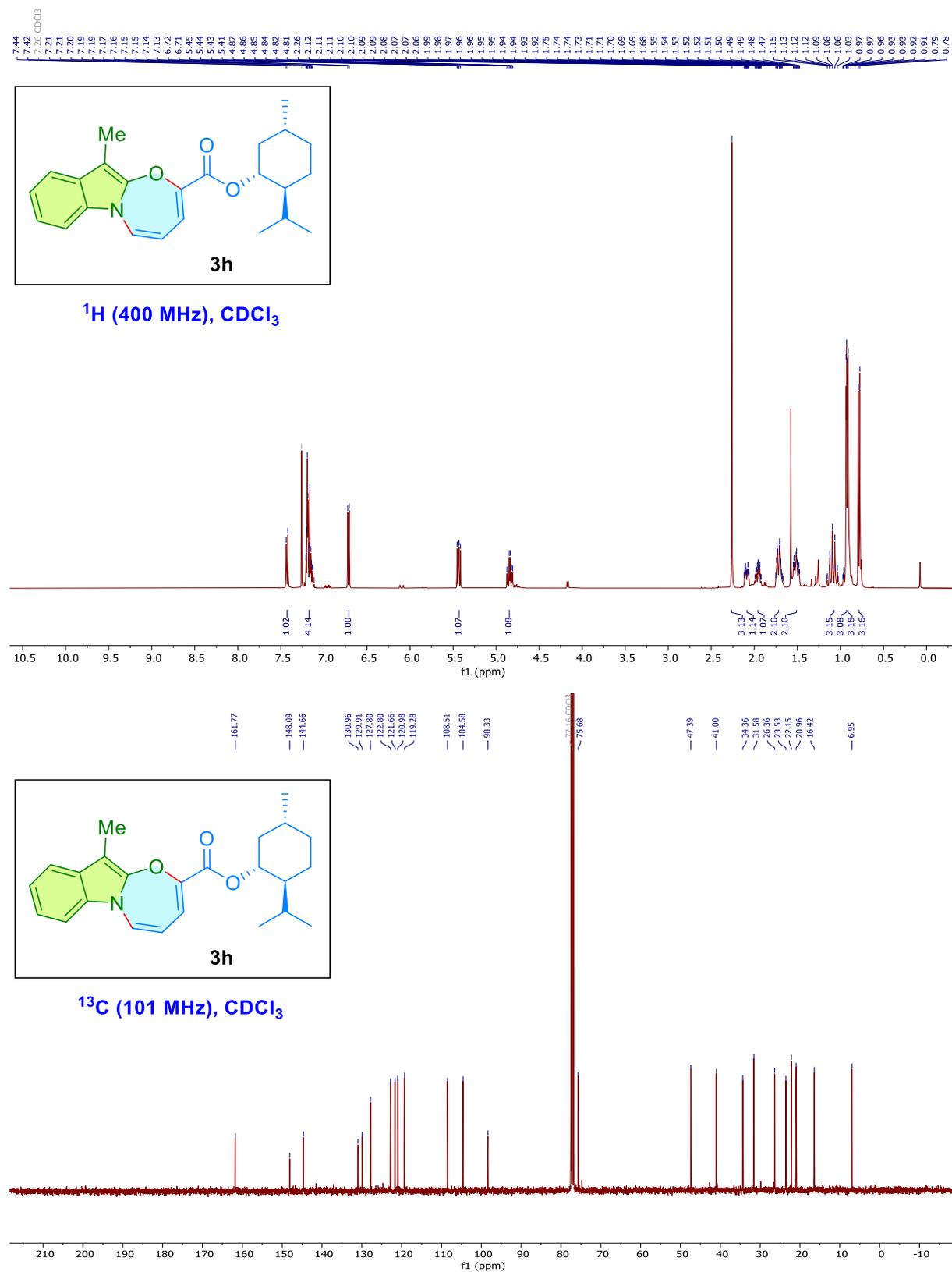
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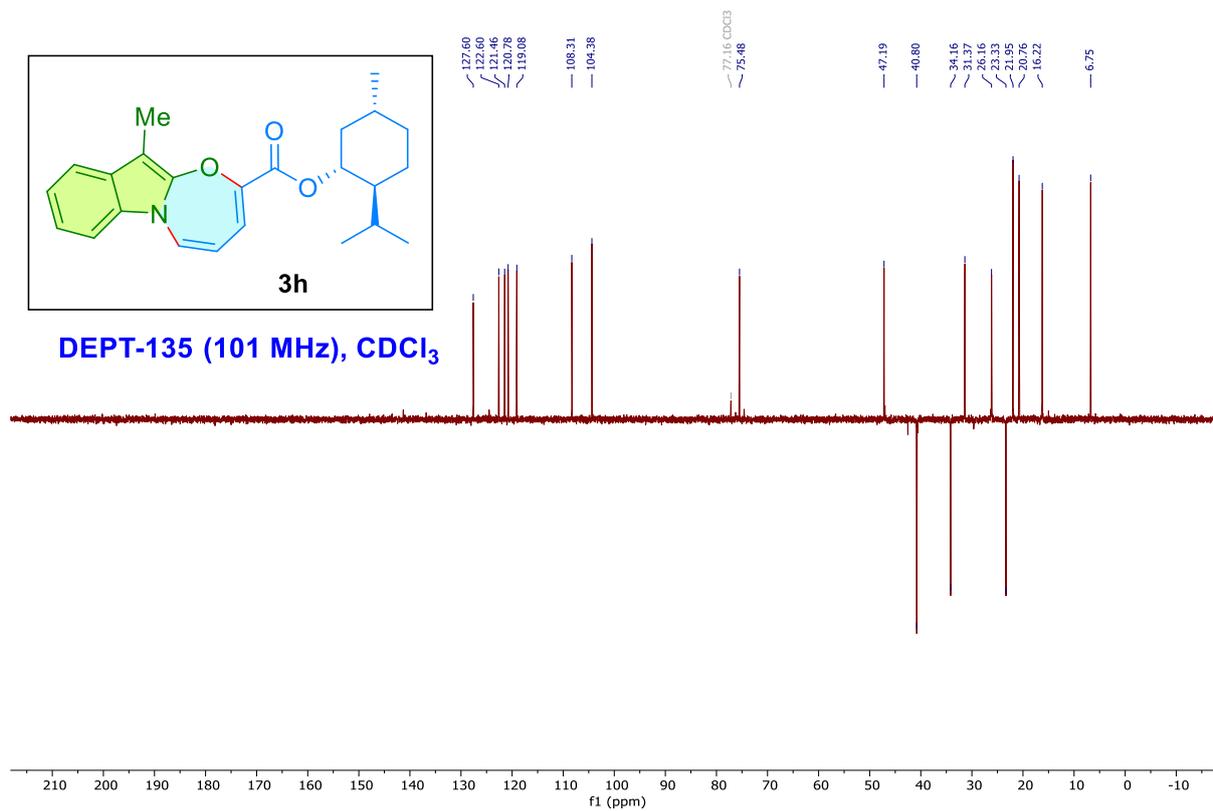


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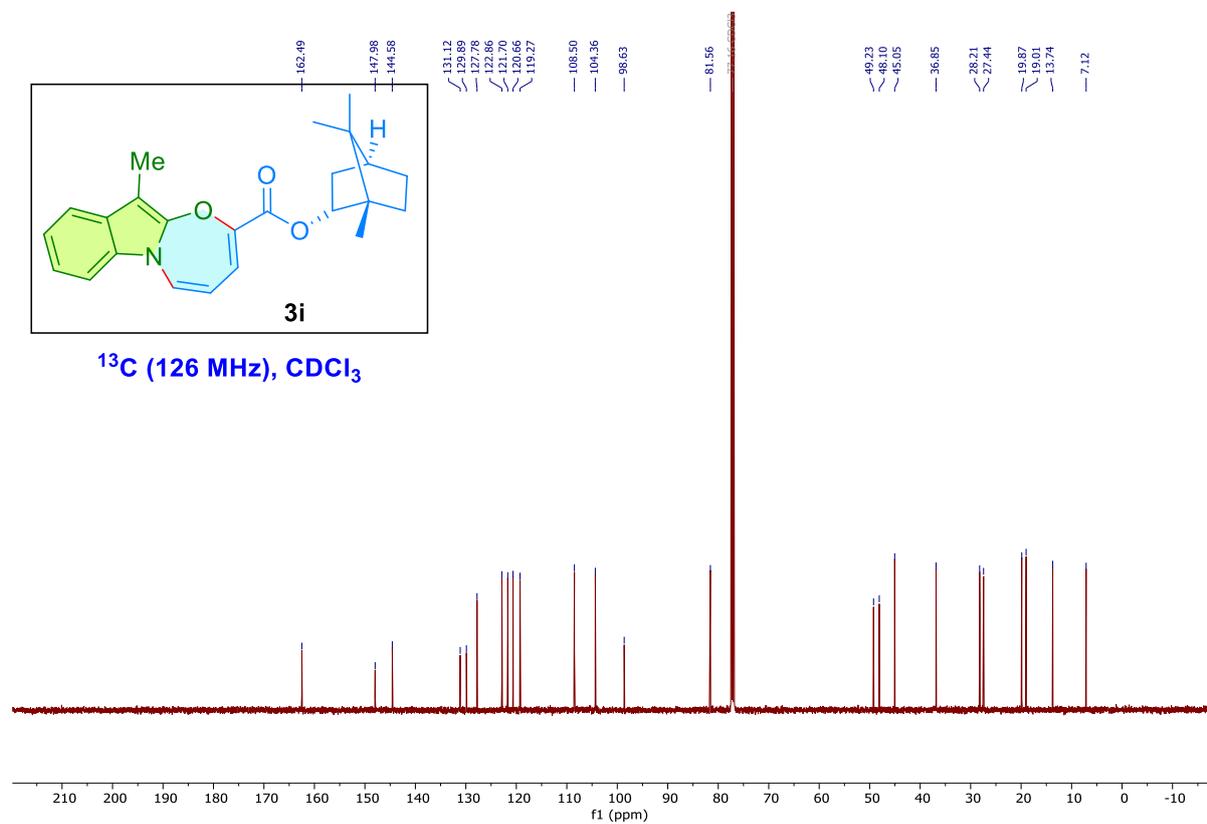
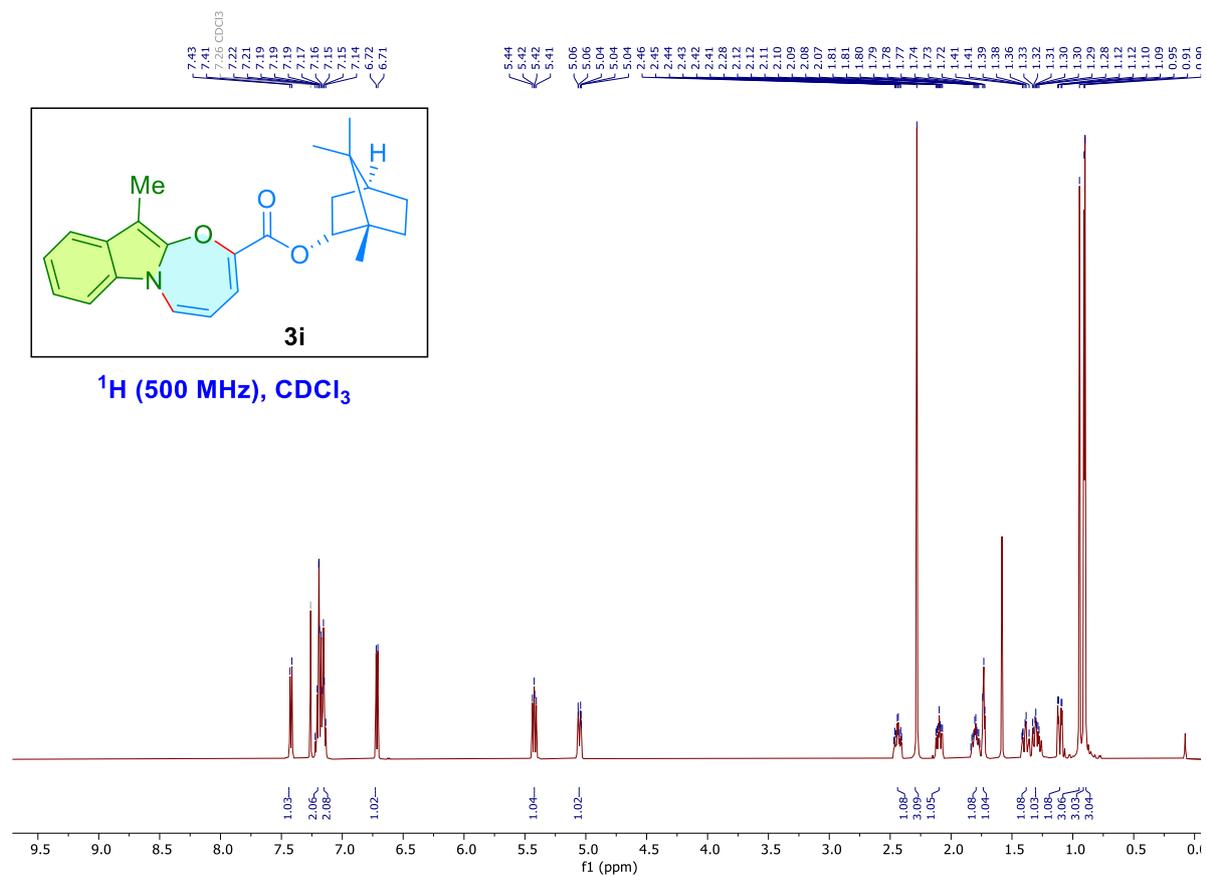


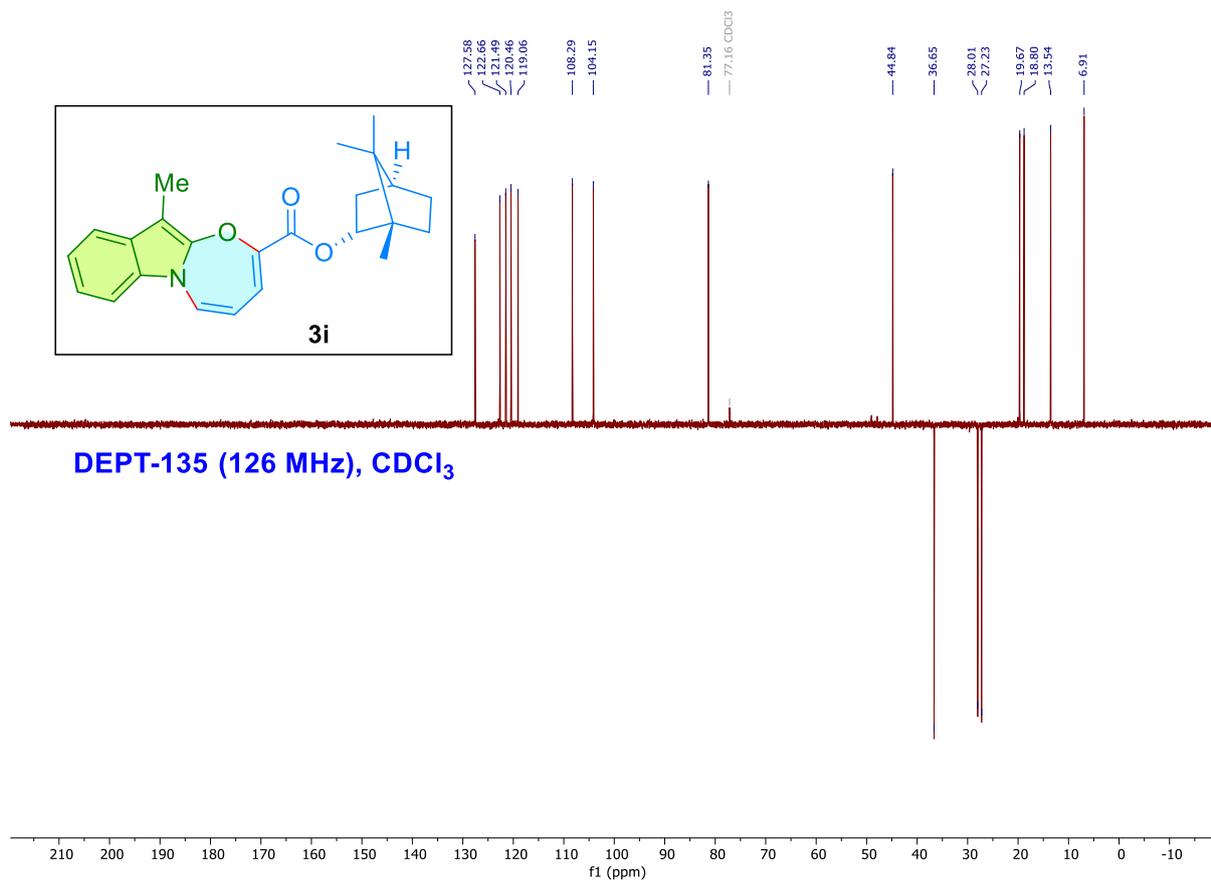
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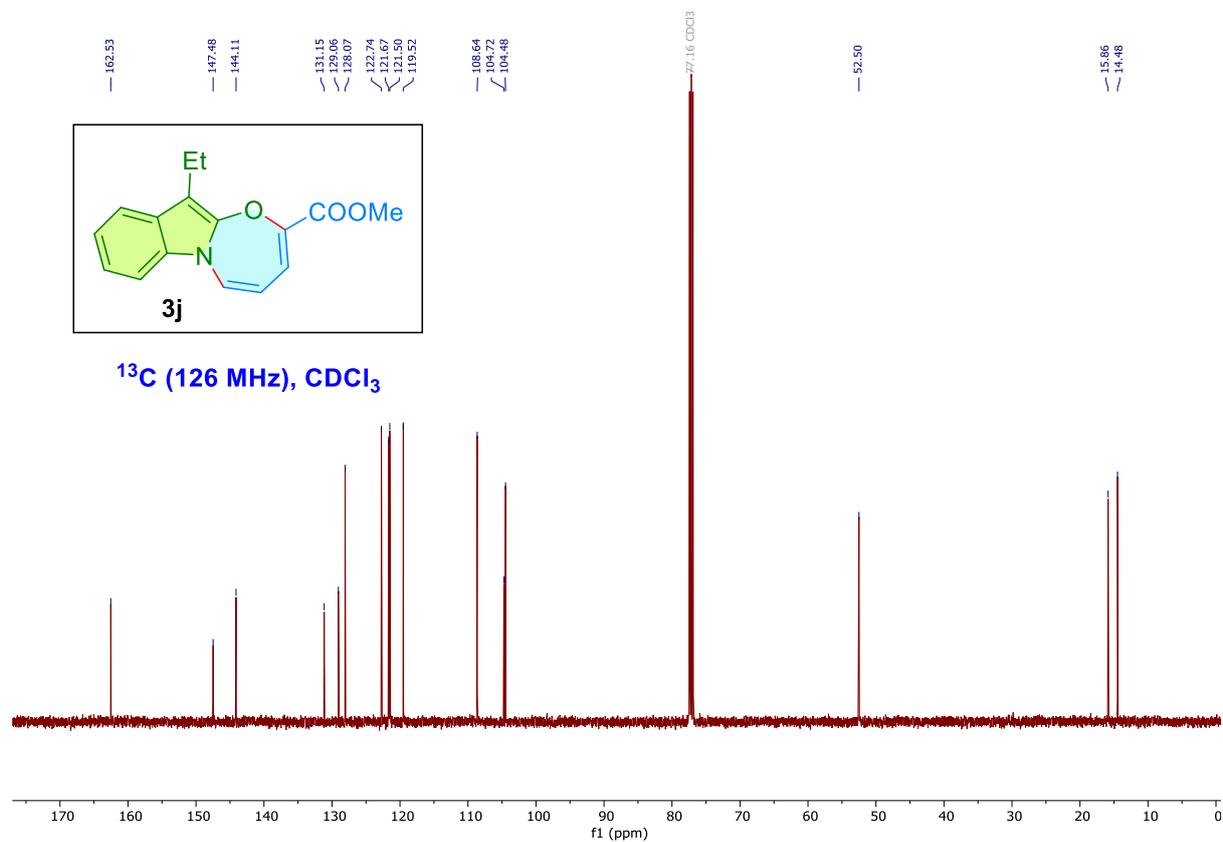
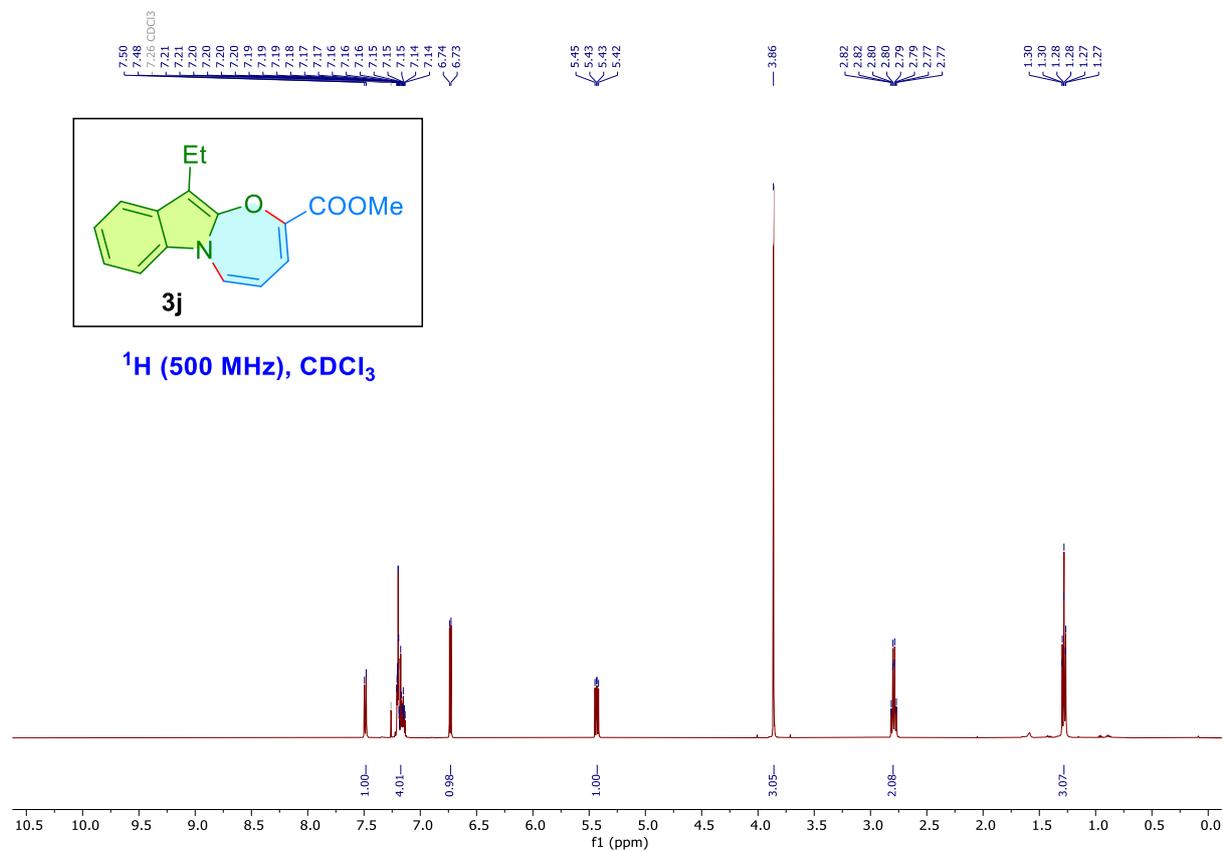


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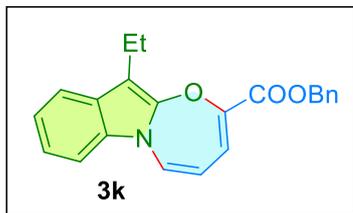




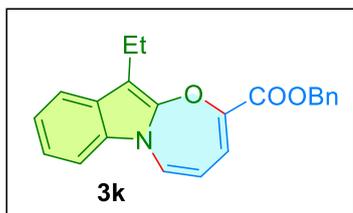
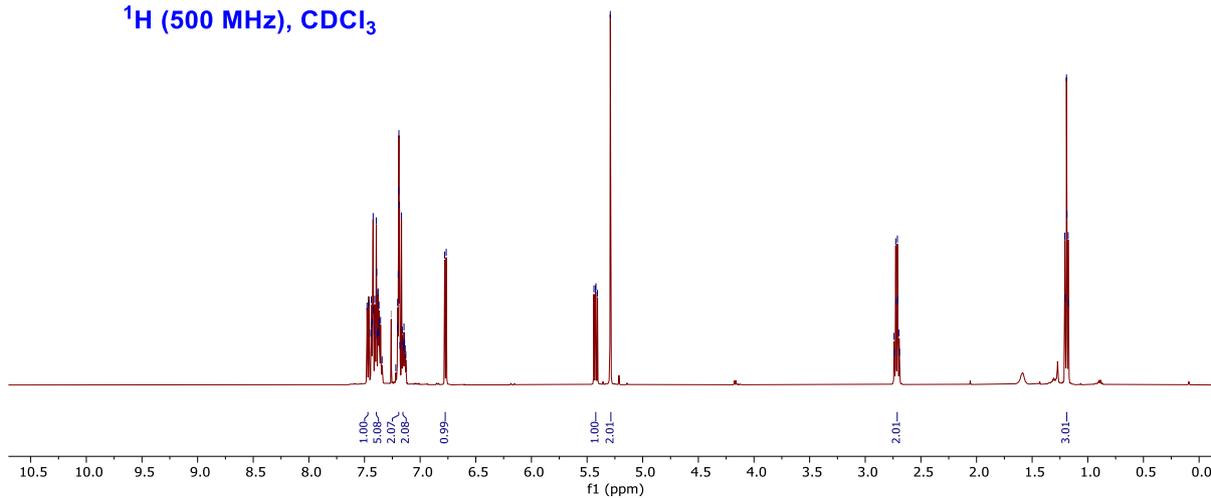
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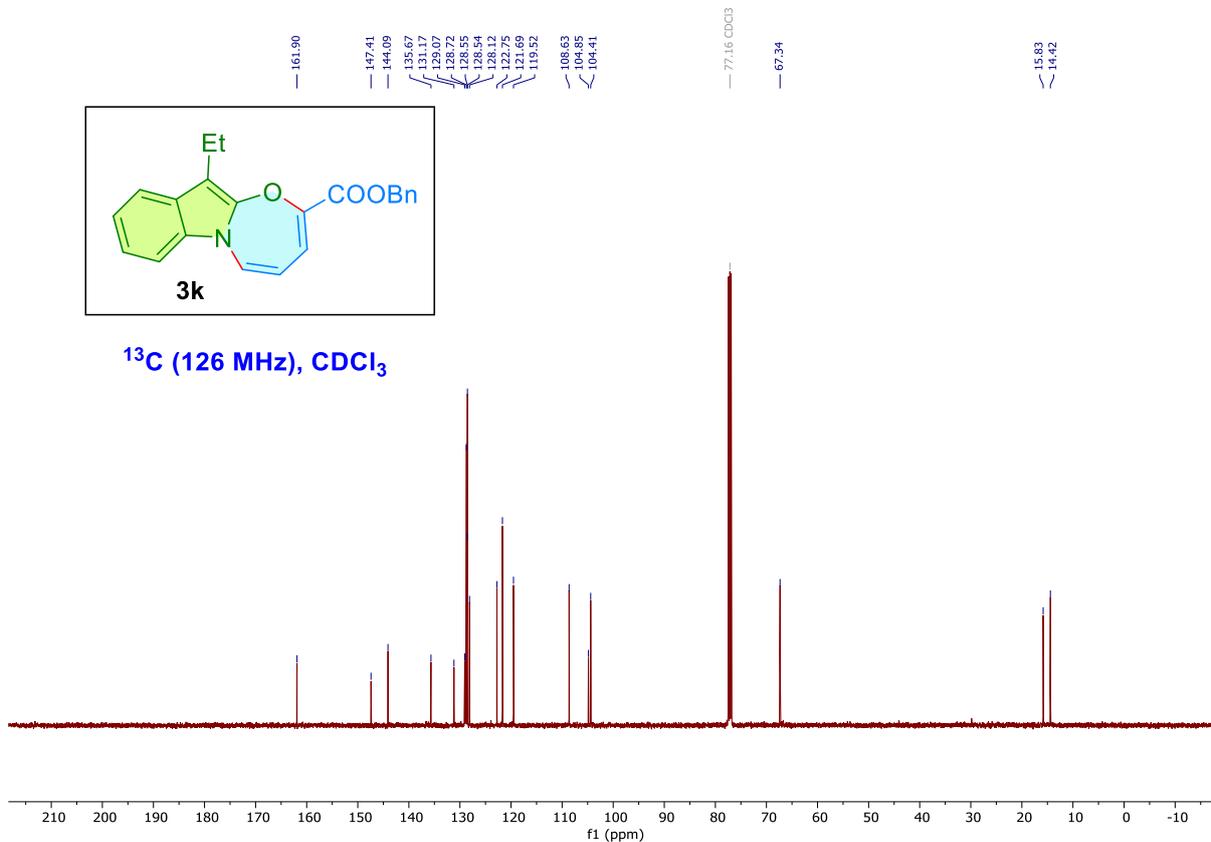
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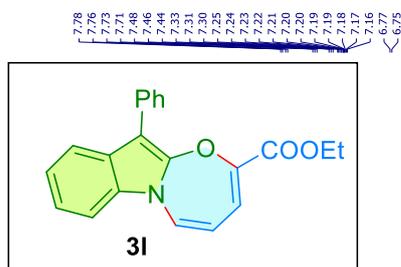
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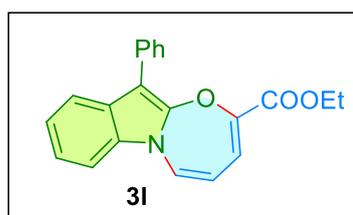
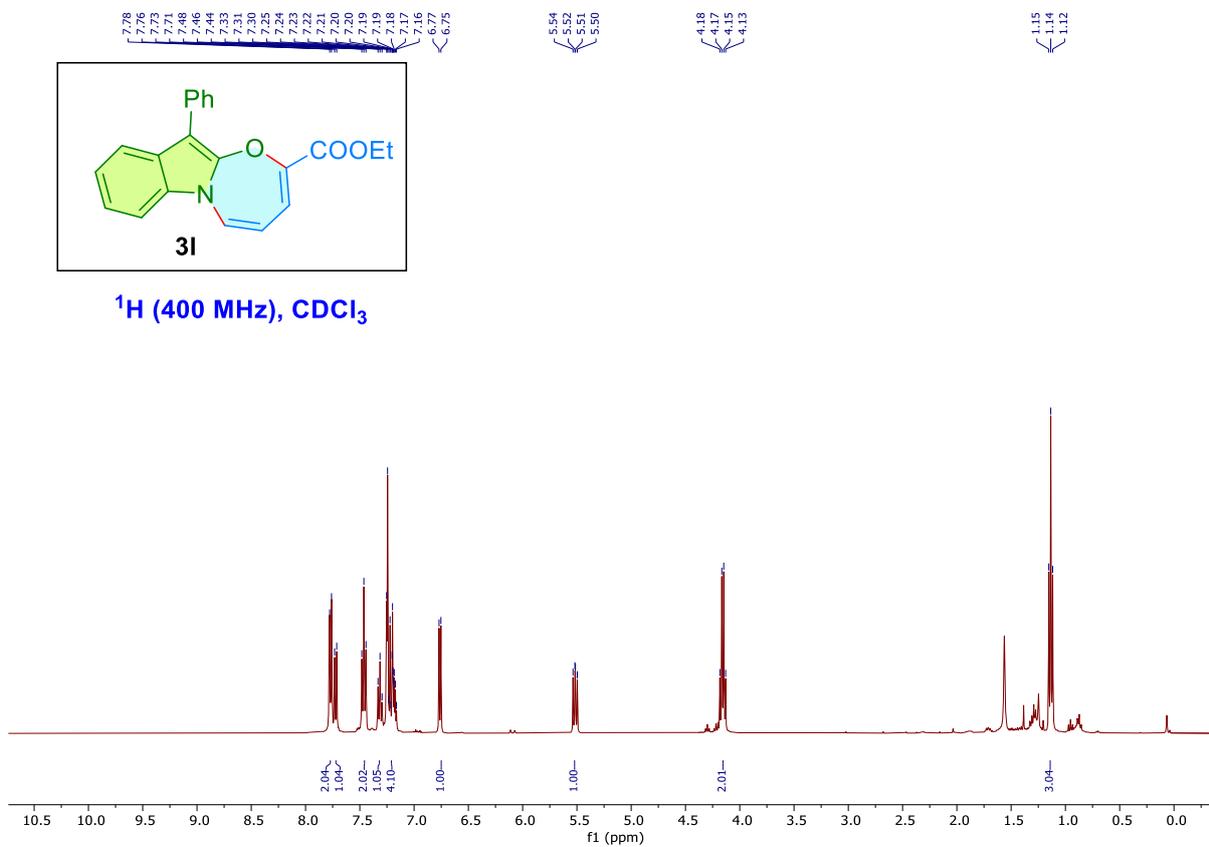
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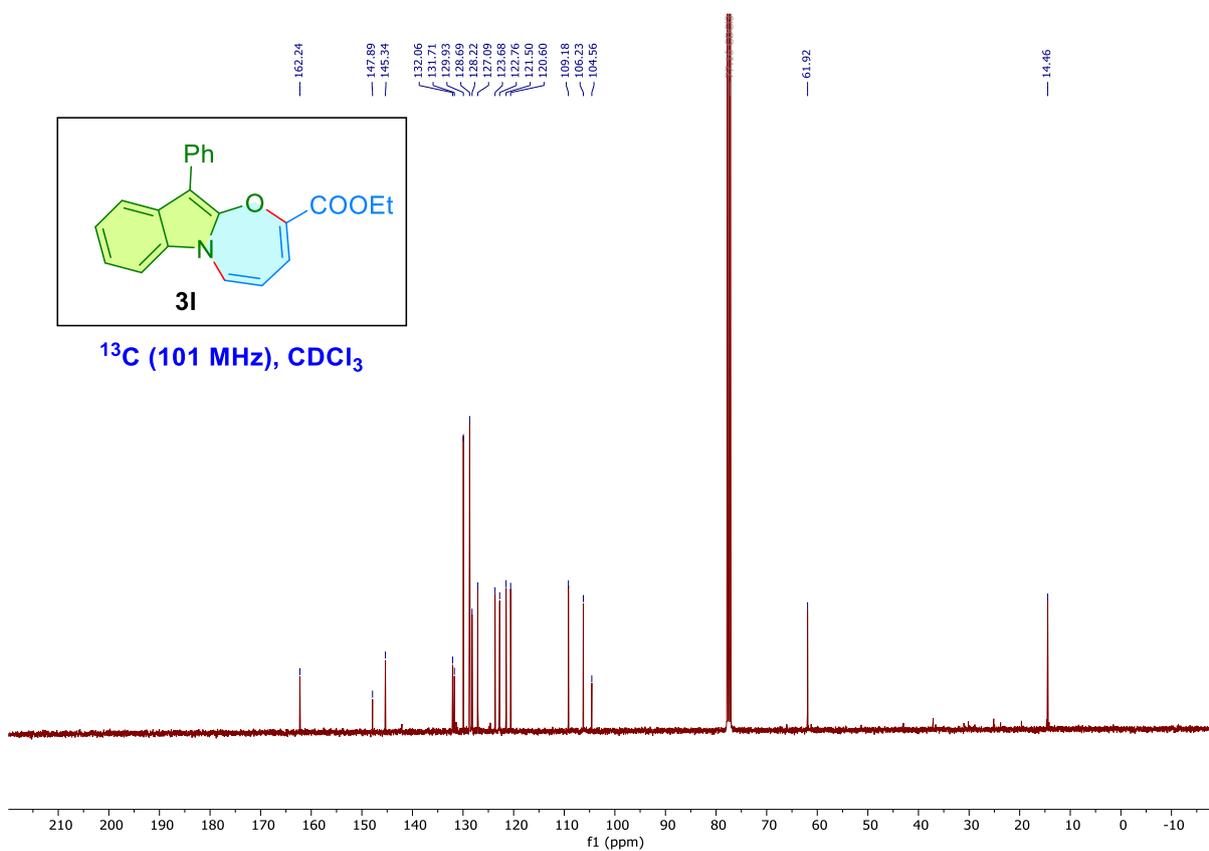
Links: [DETAILS](#) NMR



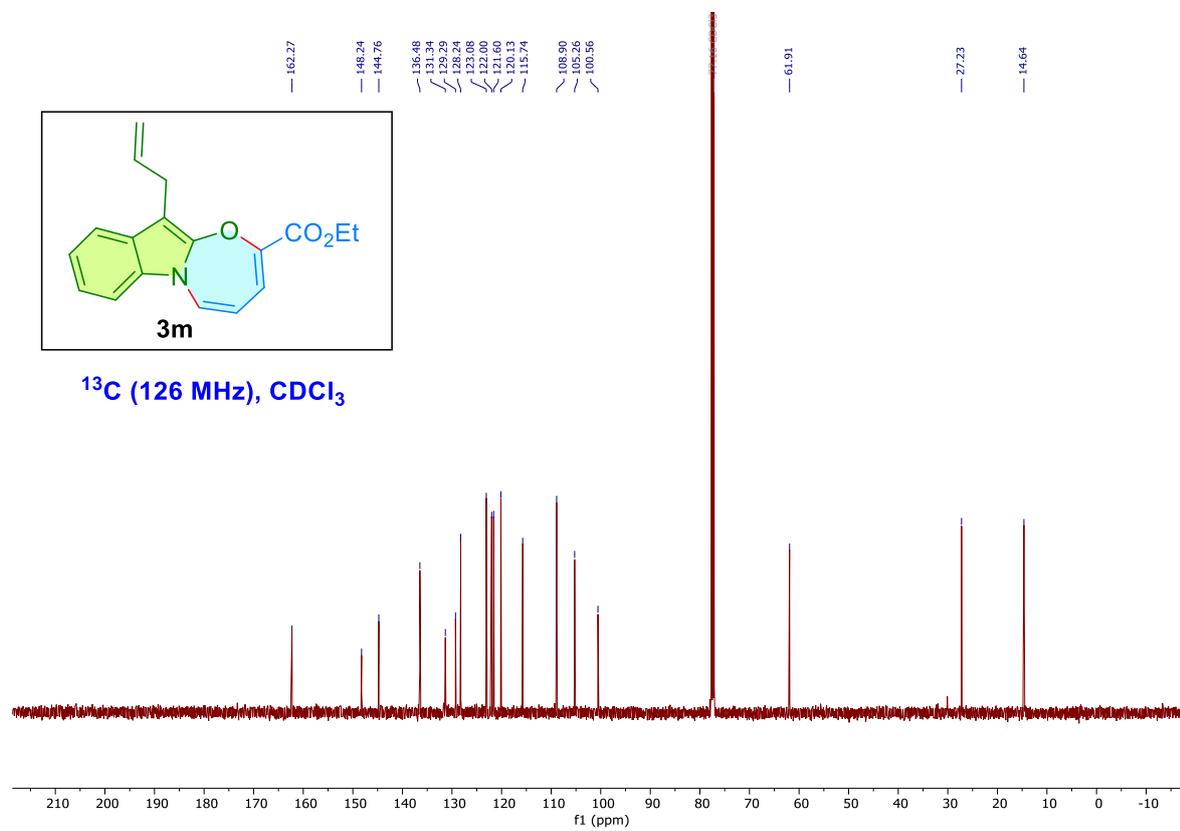
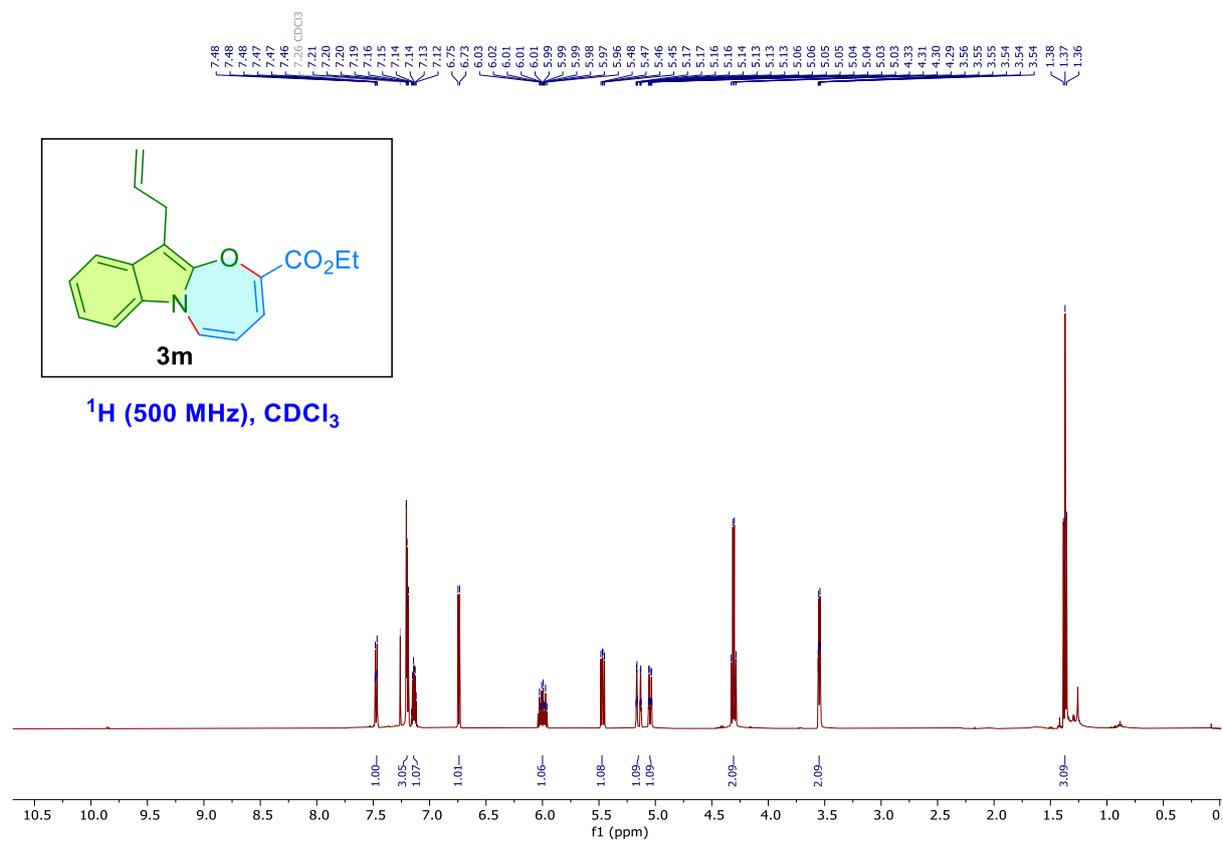
^1H (400 MHz), CDCl_3



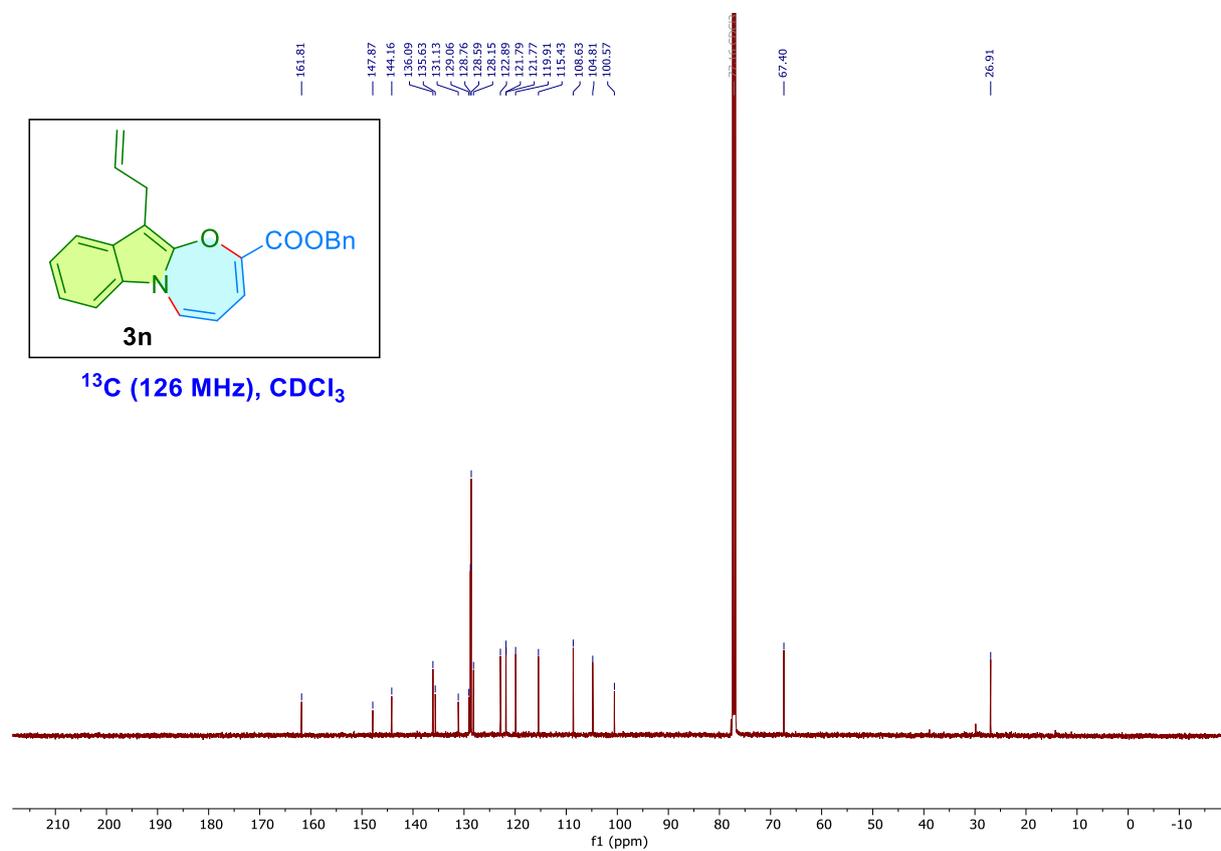
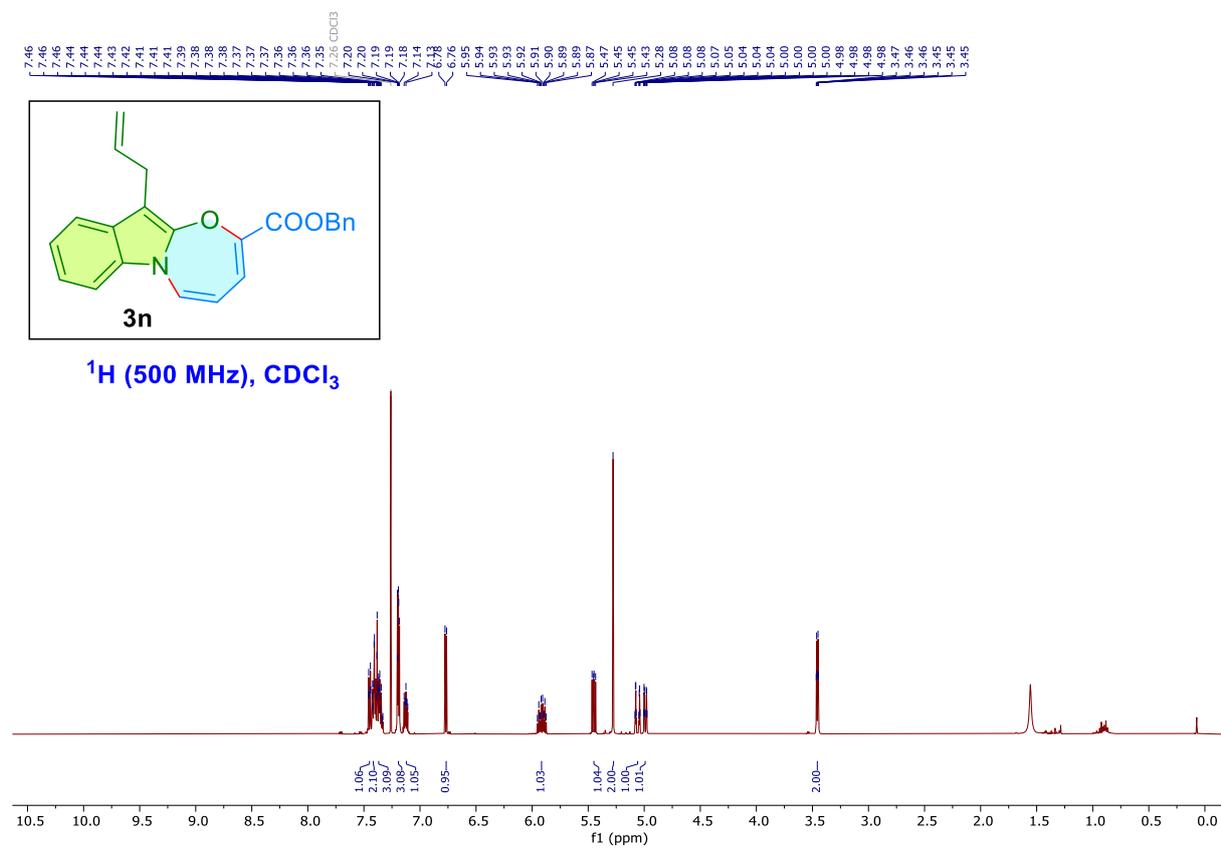
^{13}C (101 MHz), CDCl_3



Links: [DETAILS](#) [NMR](#)

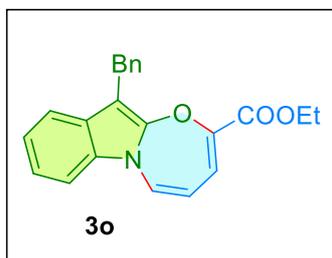


Links: [DETAILS](#) NMR

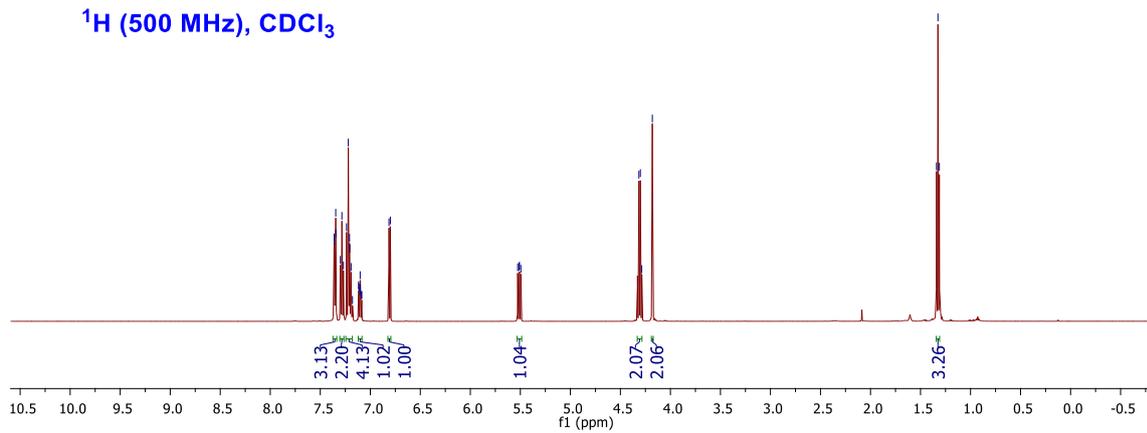


Links: [DETAILS](#) [NMR](#) [SCXRD](#)

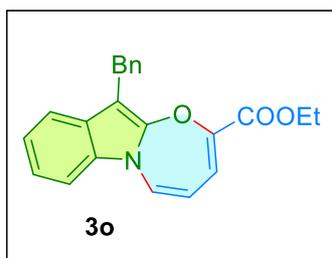
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7.36
7.35
7.34
7.30
7.28
7.27
7.24
7.22
7.21
7.21
7.19
7.18
7.12
7.11
7.11
7.10
7.10
7.09
7.09
6.81
6.80
5.53
5.51
5.51
5.50
4.31
4.30
4.29
4.18
1.34
1.33
1.31



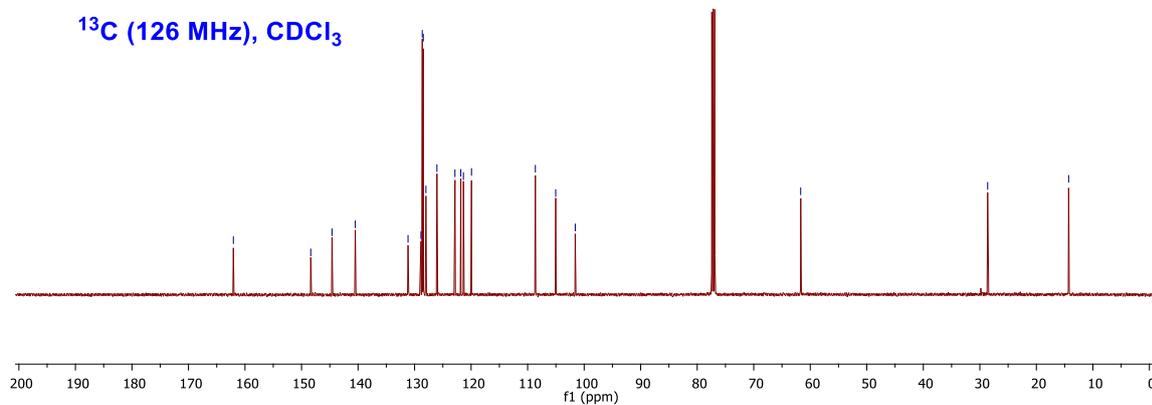
^1H (500 MHz), CDCl_3



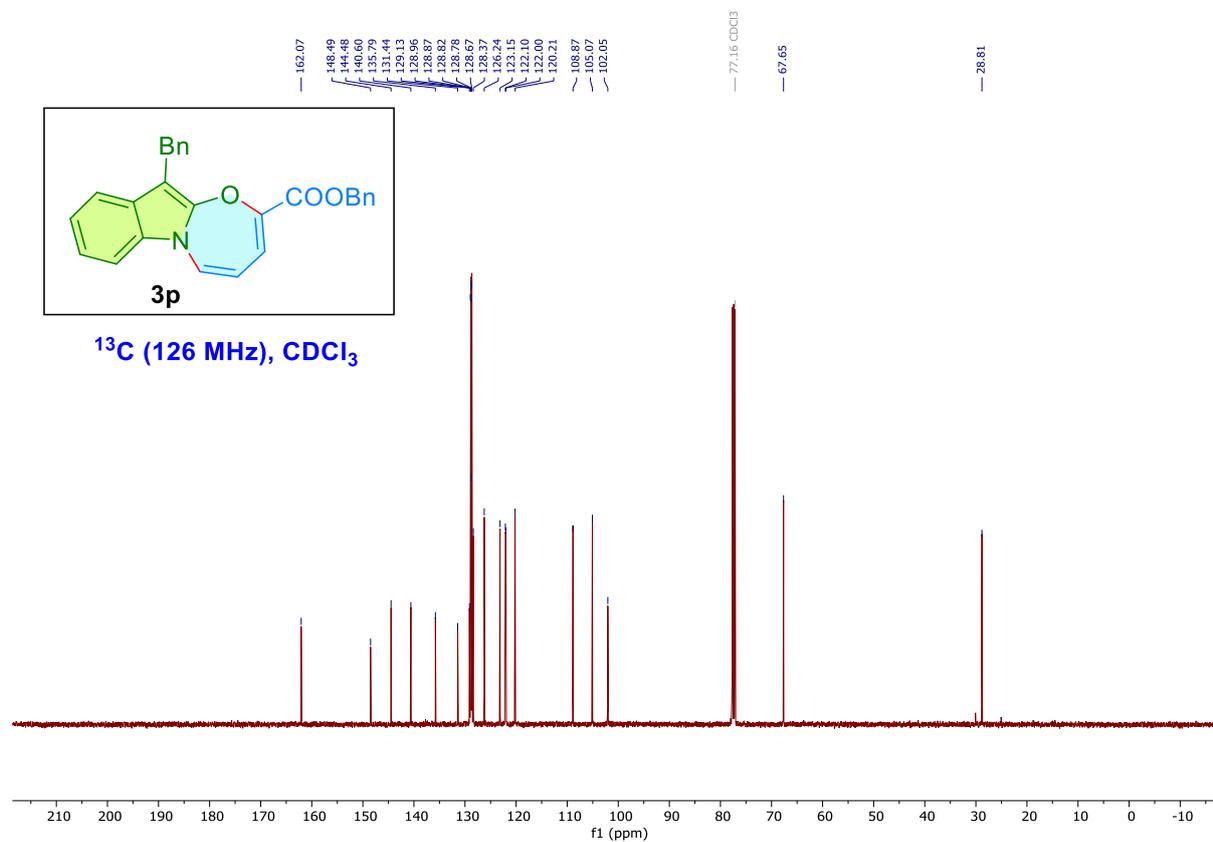
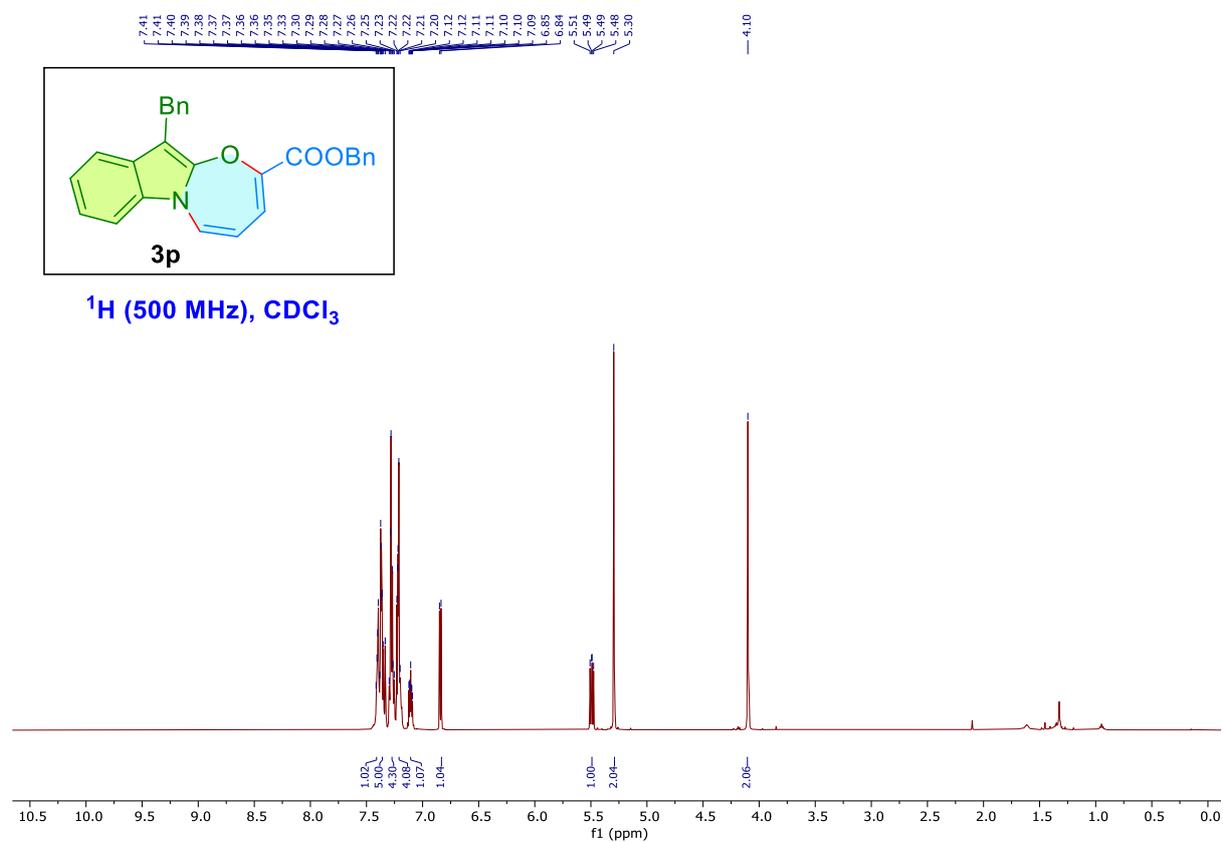
162.06
148.37
144.61
140.48
128.64
128.46
126.04
122.86
121.82
121.36
119.93
108.63
105.03
101.58
61.69
28.62
14.29



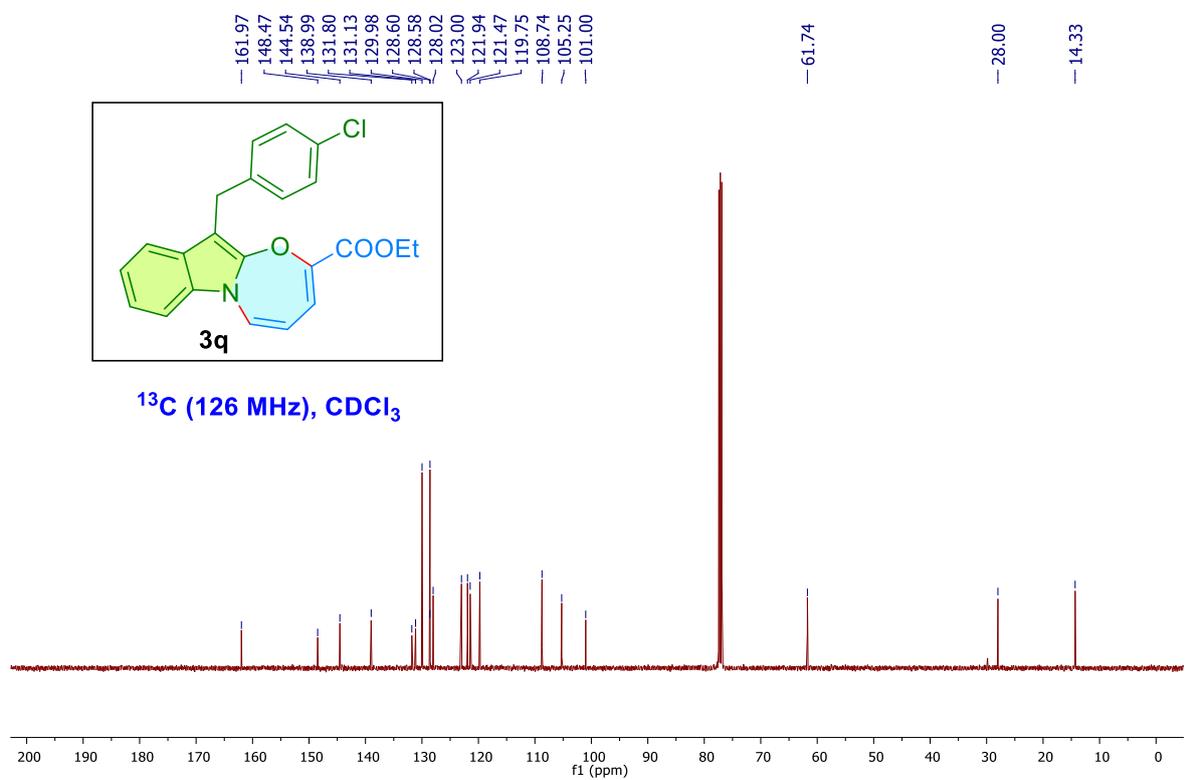
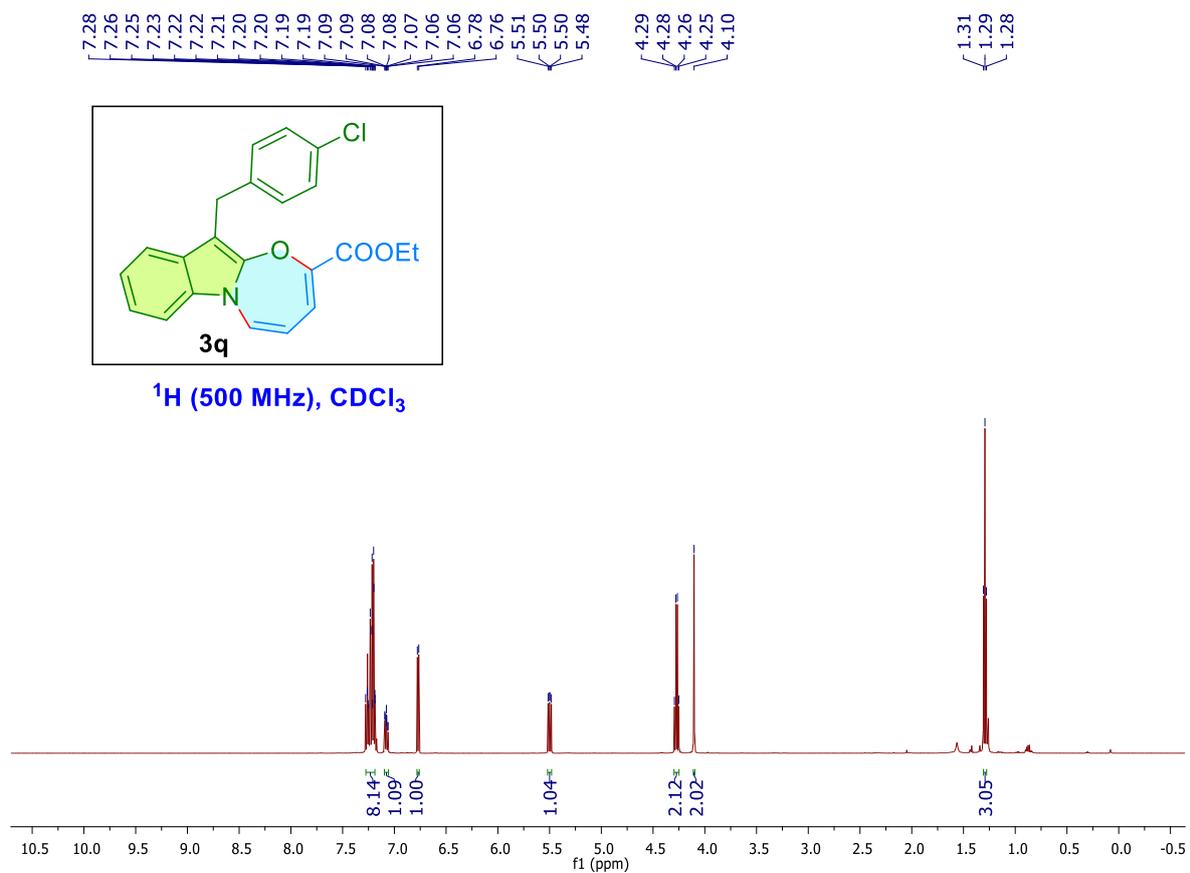
^{13}C (126 MHz), CDCl_3



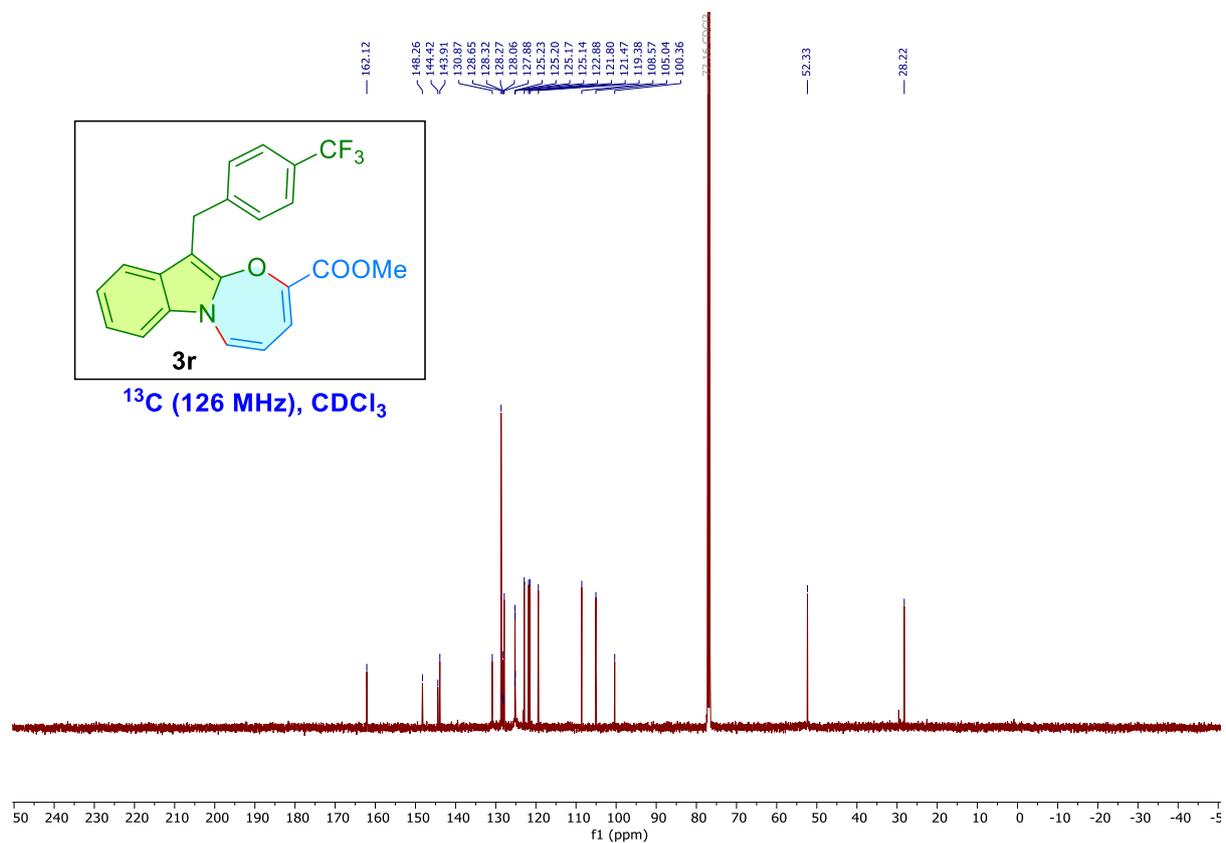
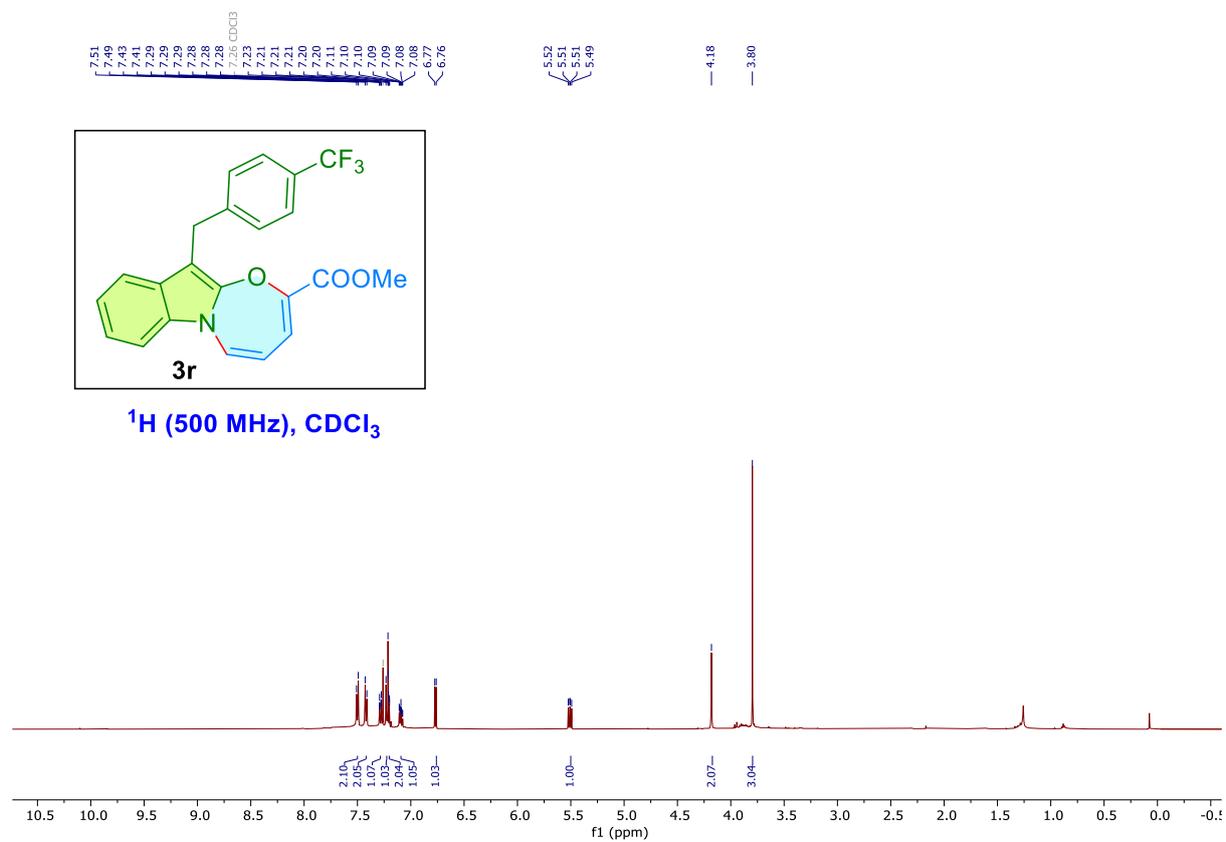
Links: [DETAILS](#) NMR



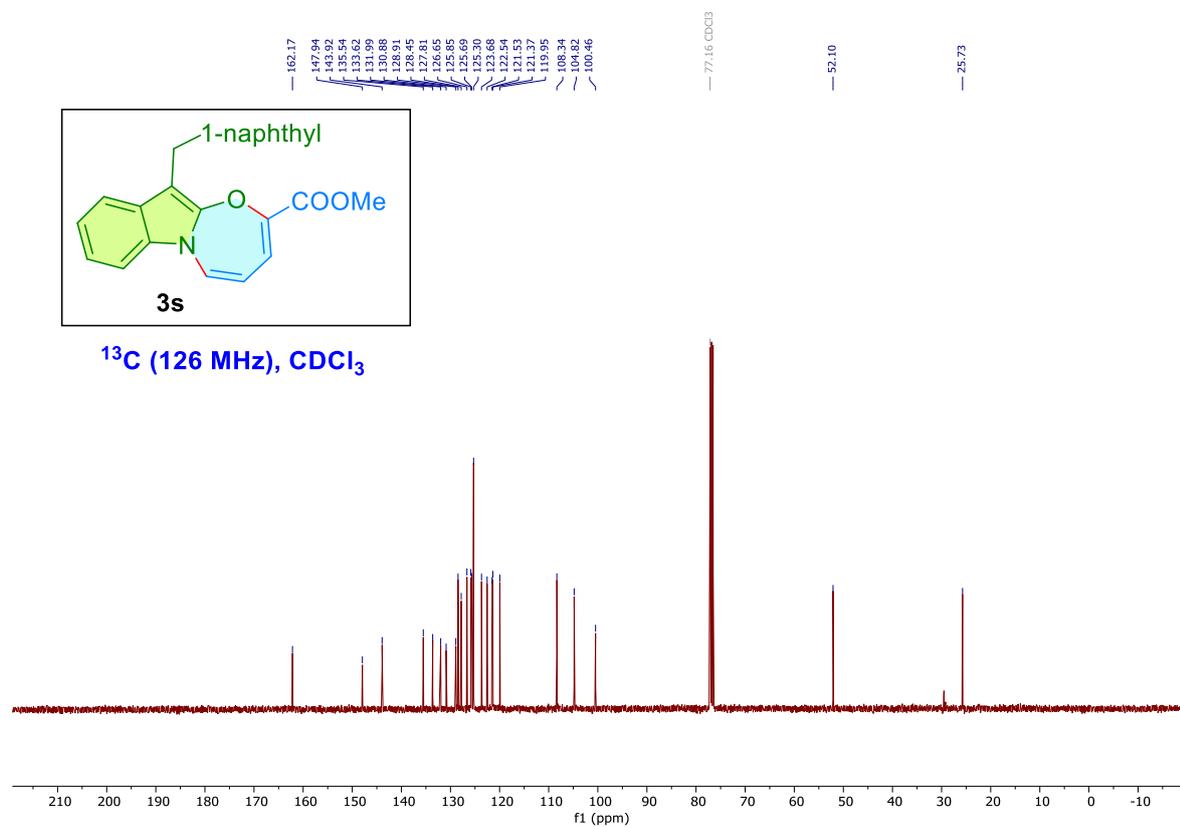
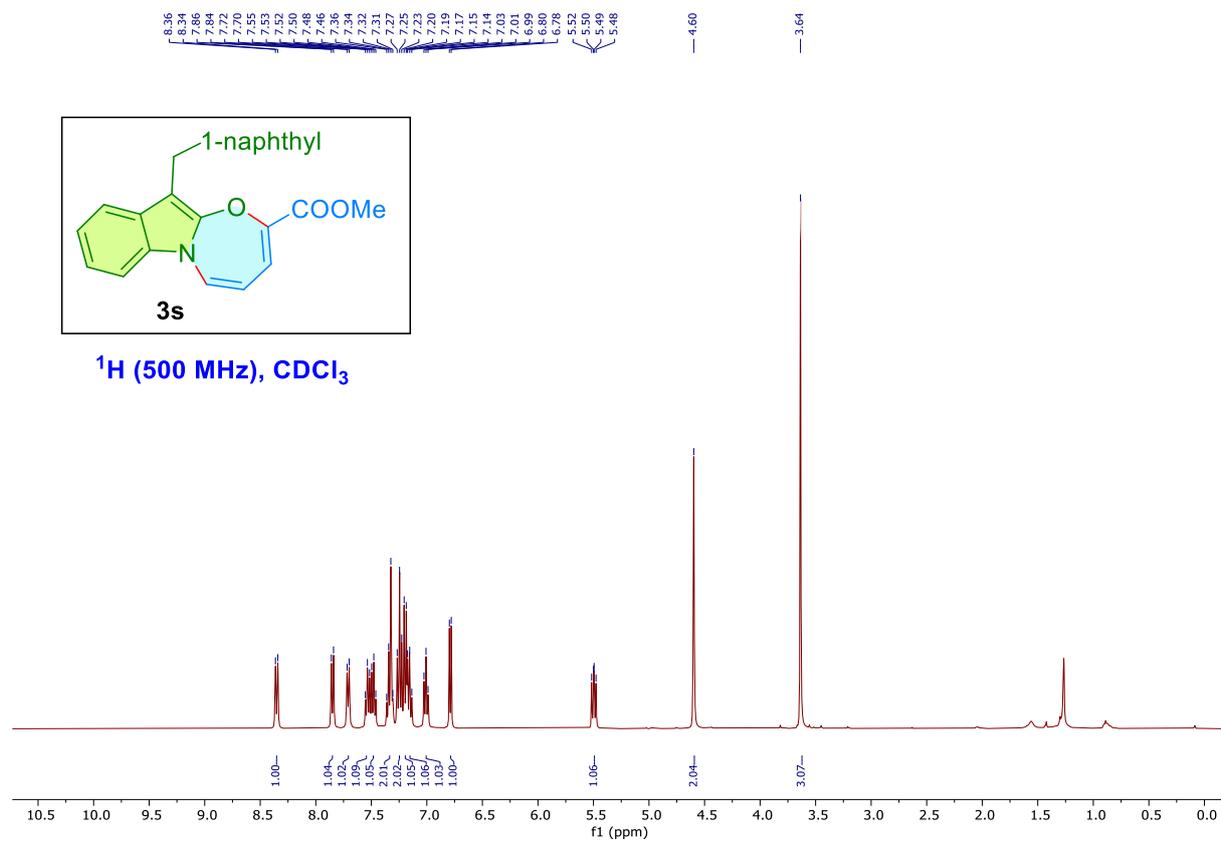
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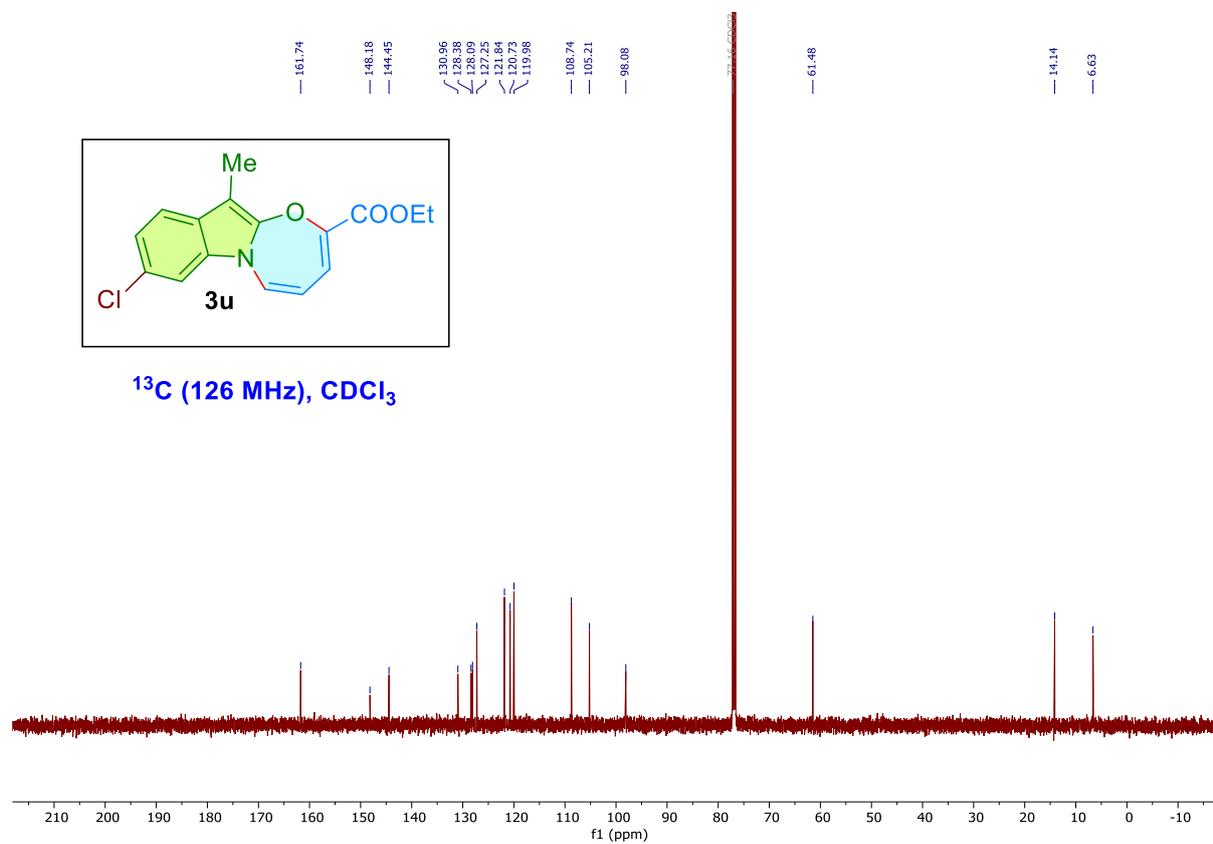
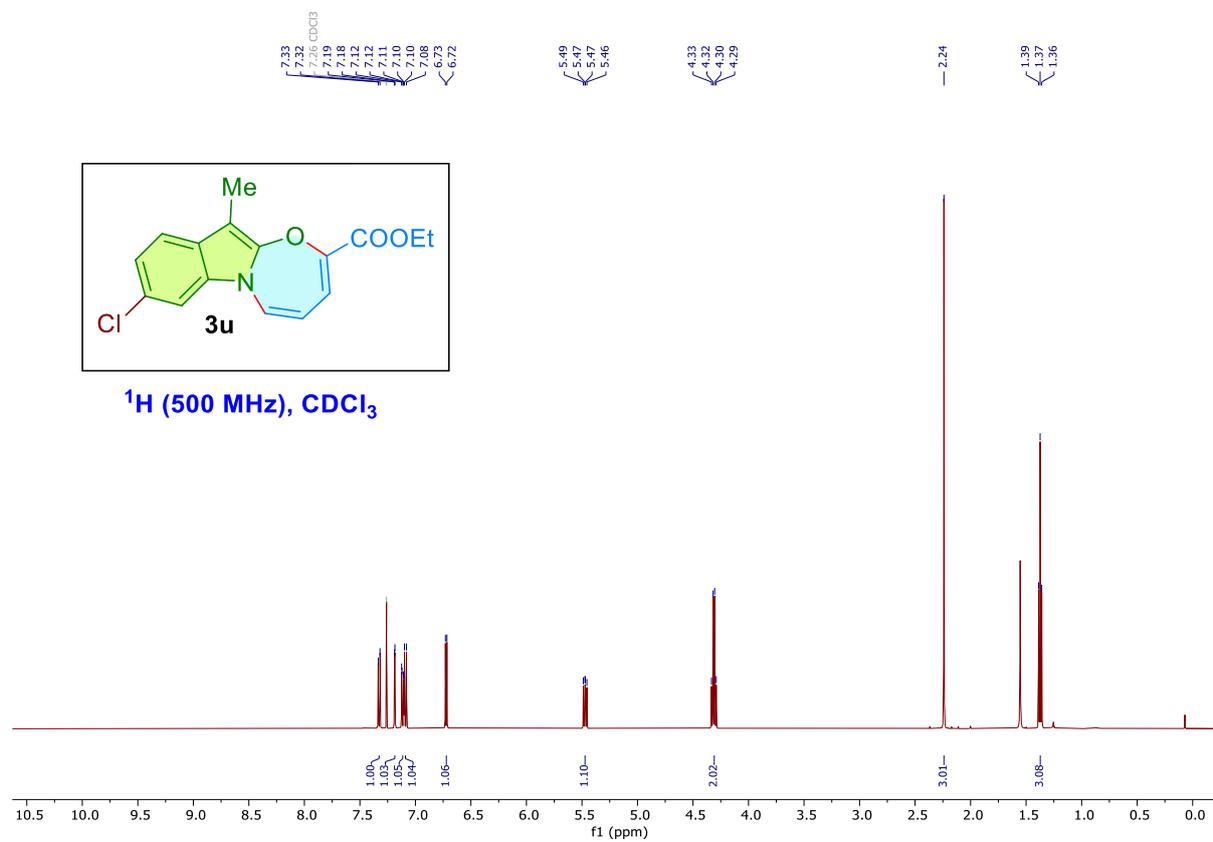
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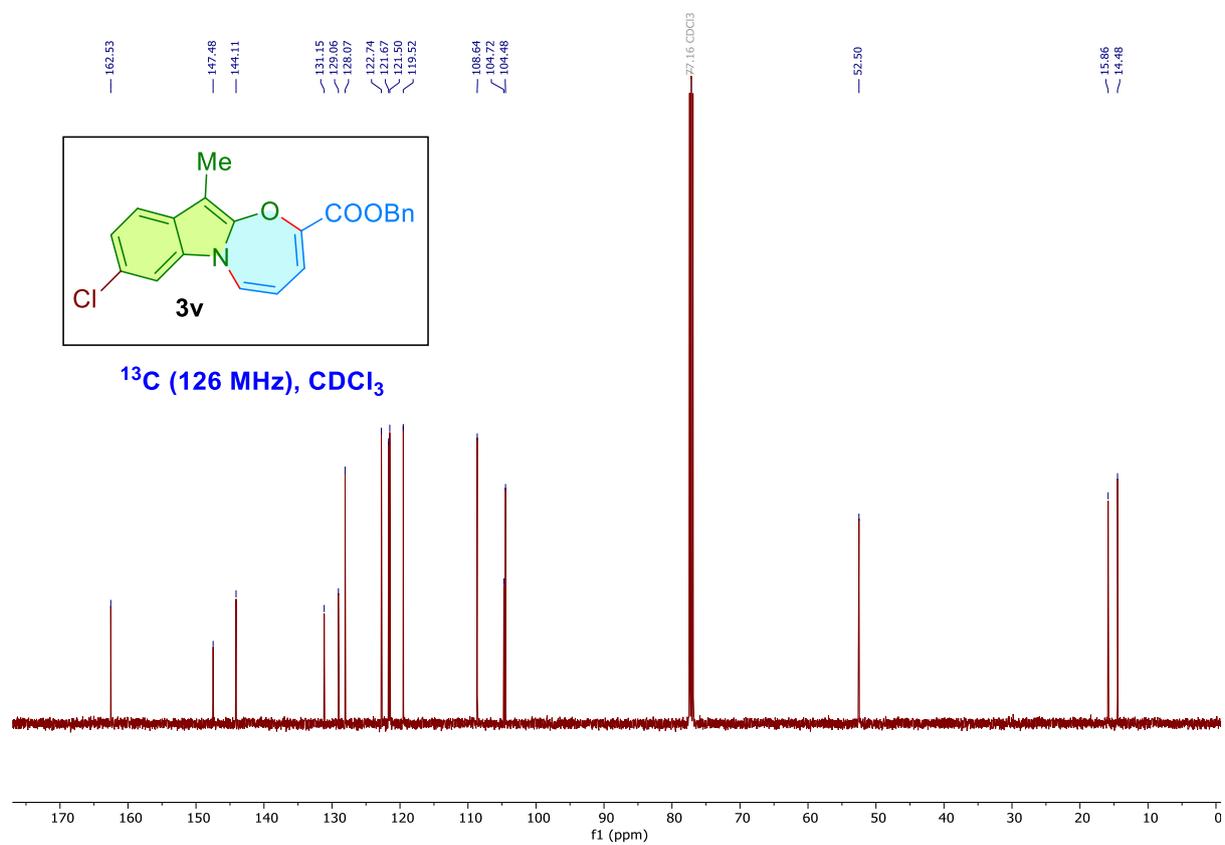
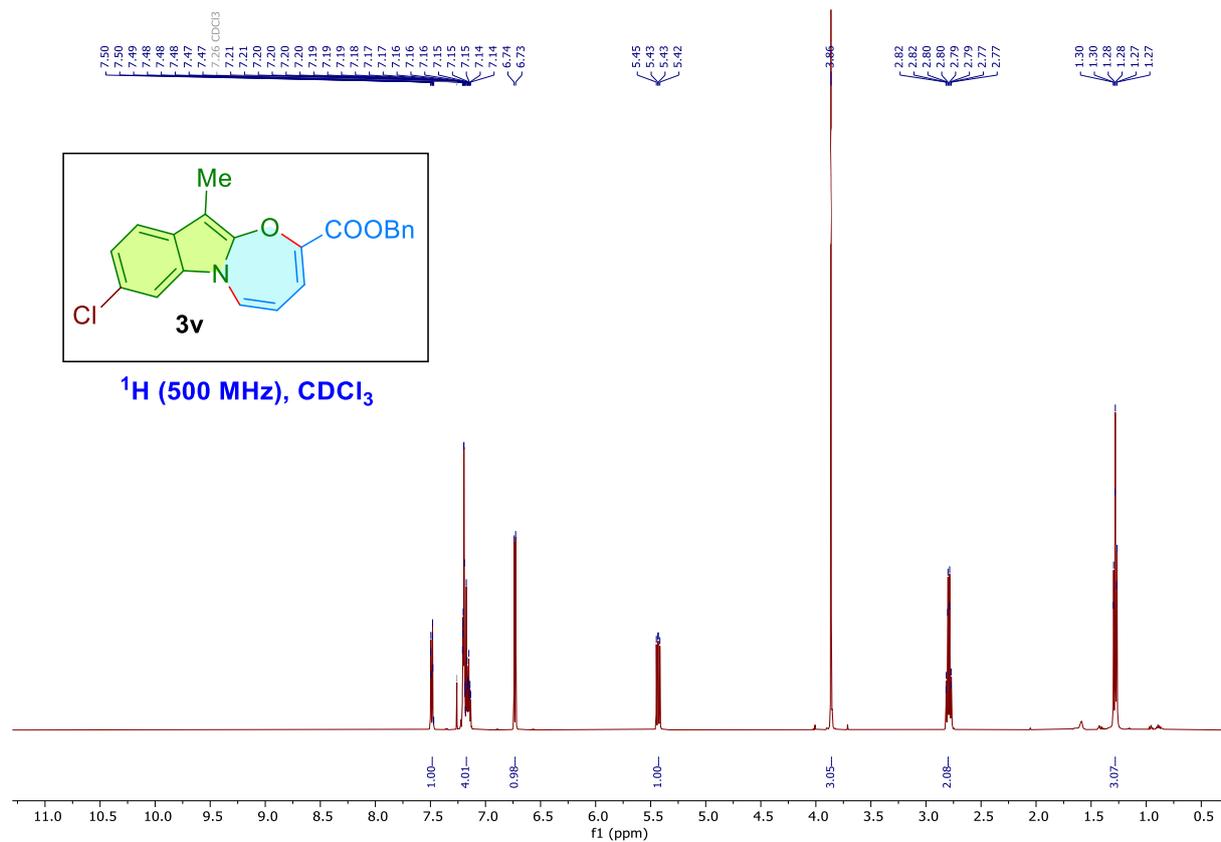
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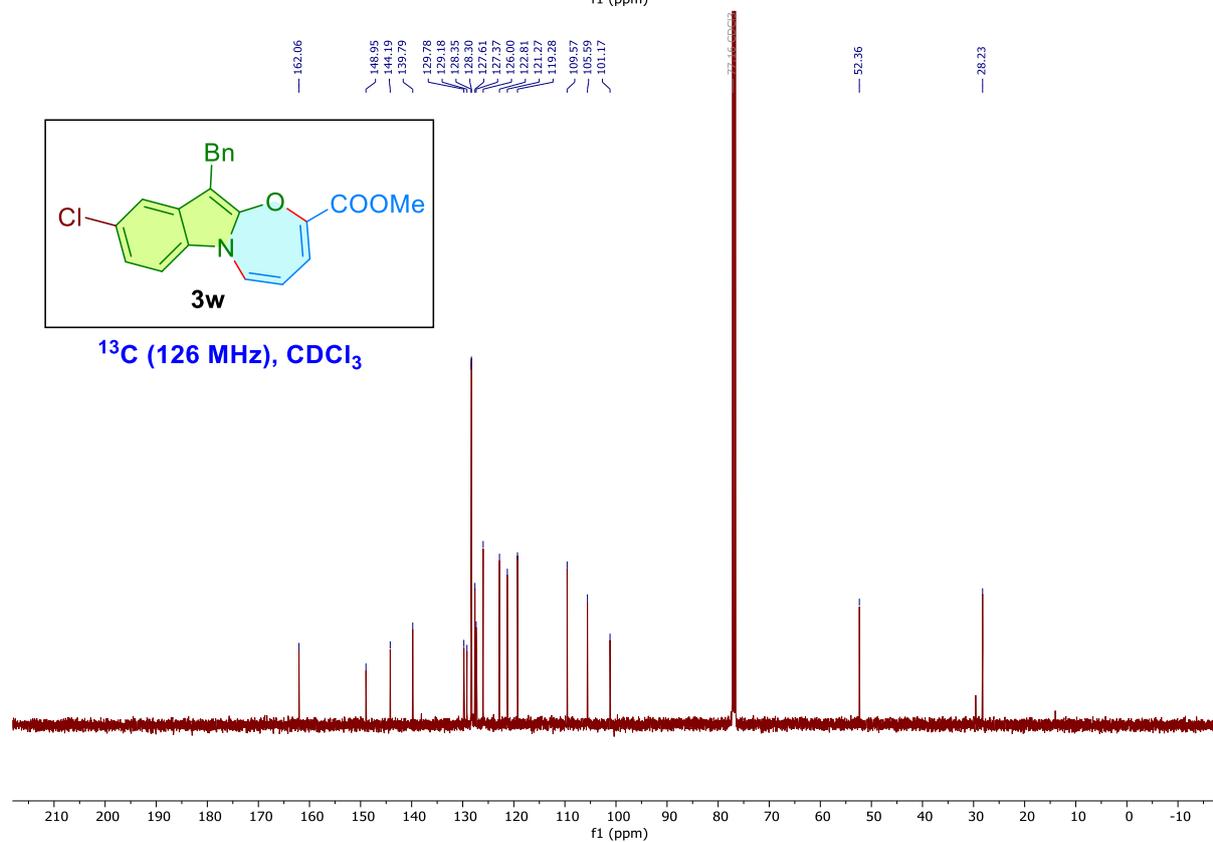
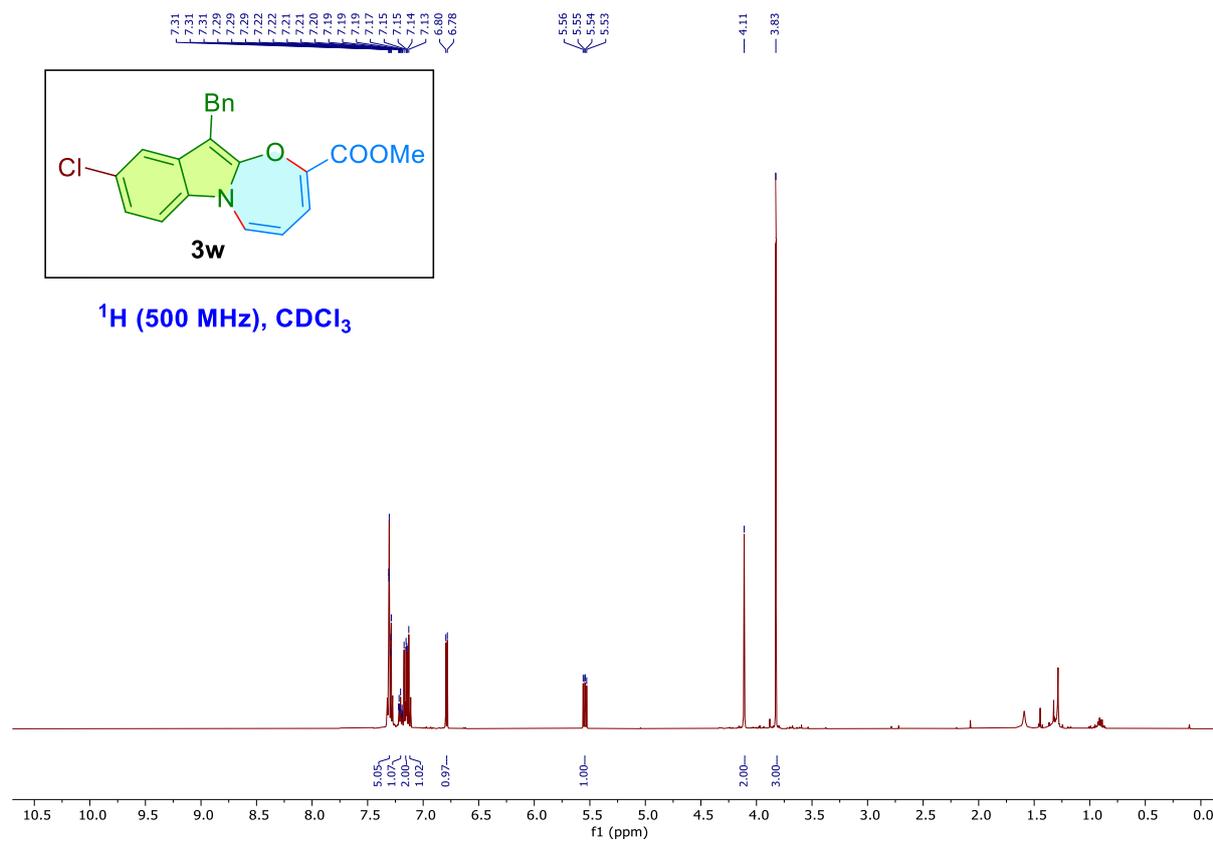
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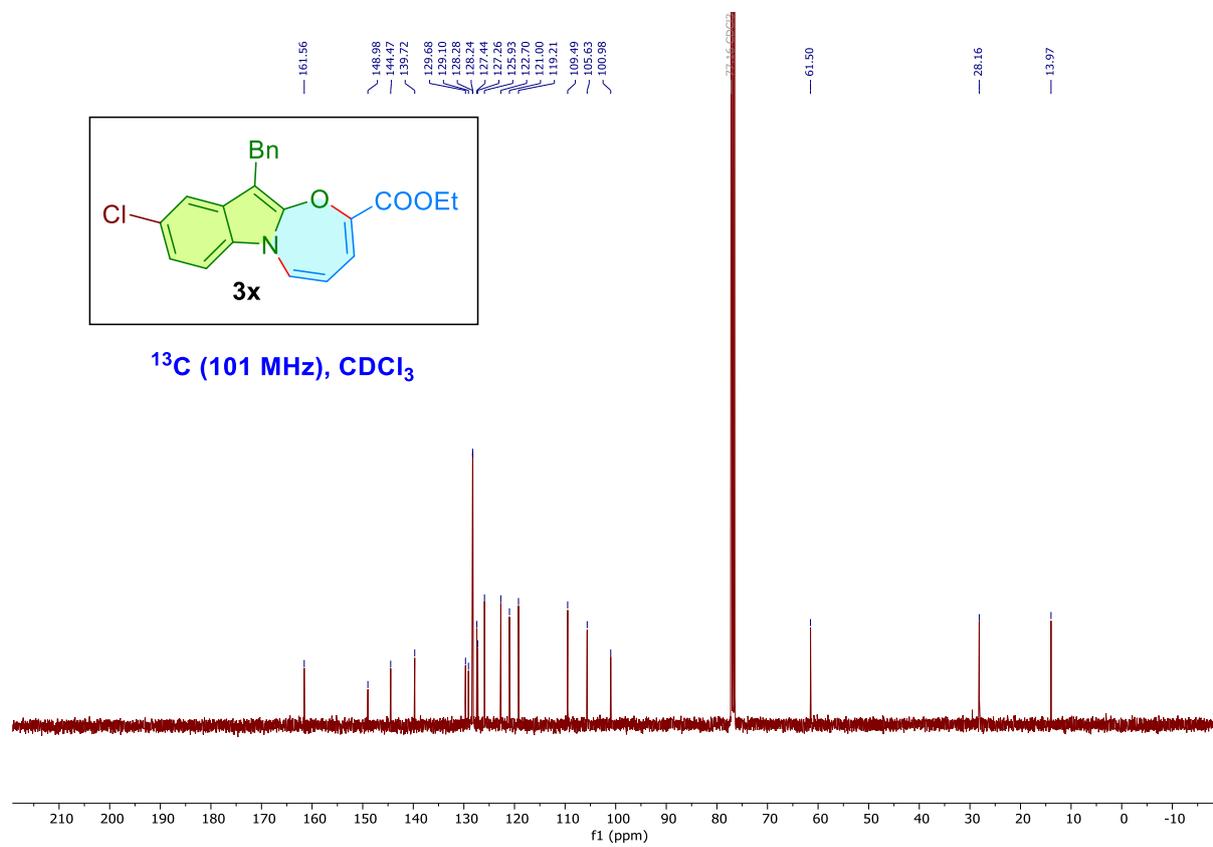
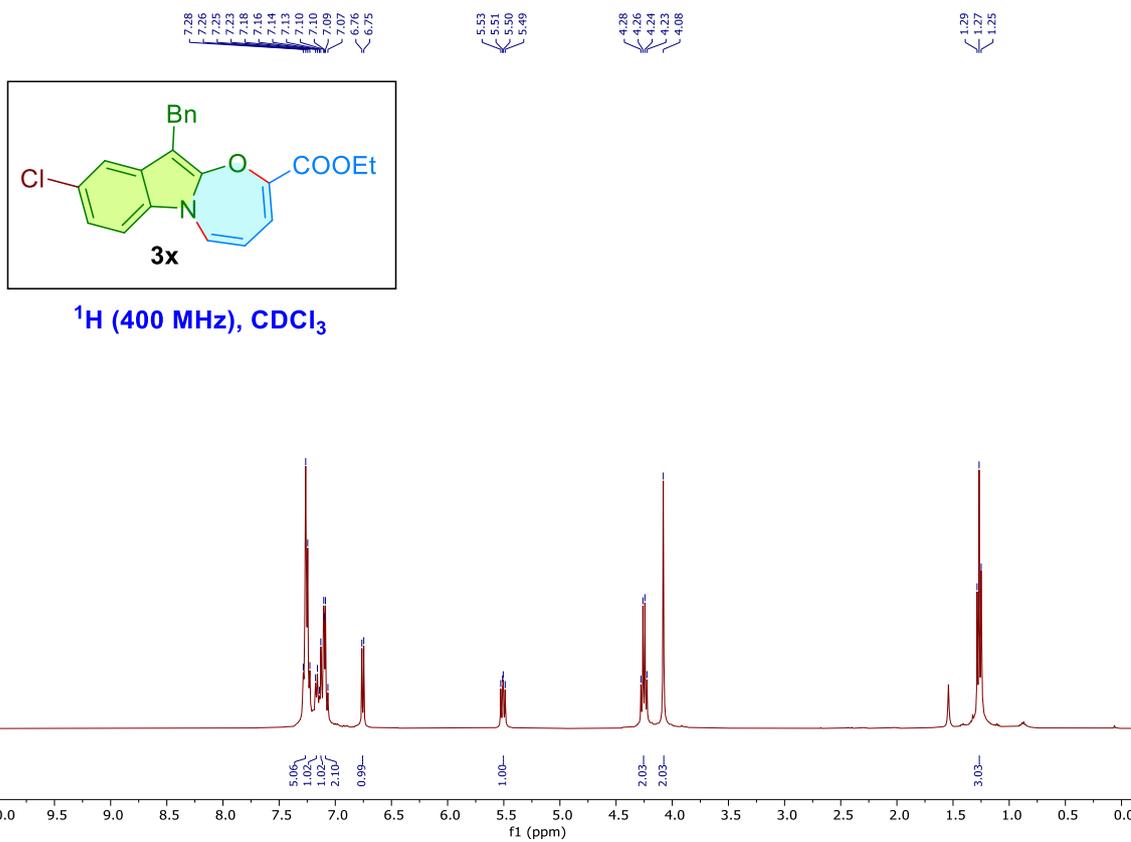
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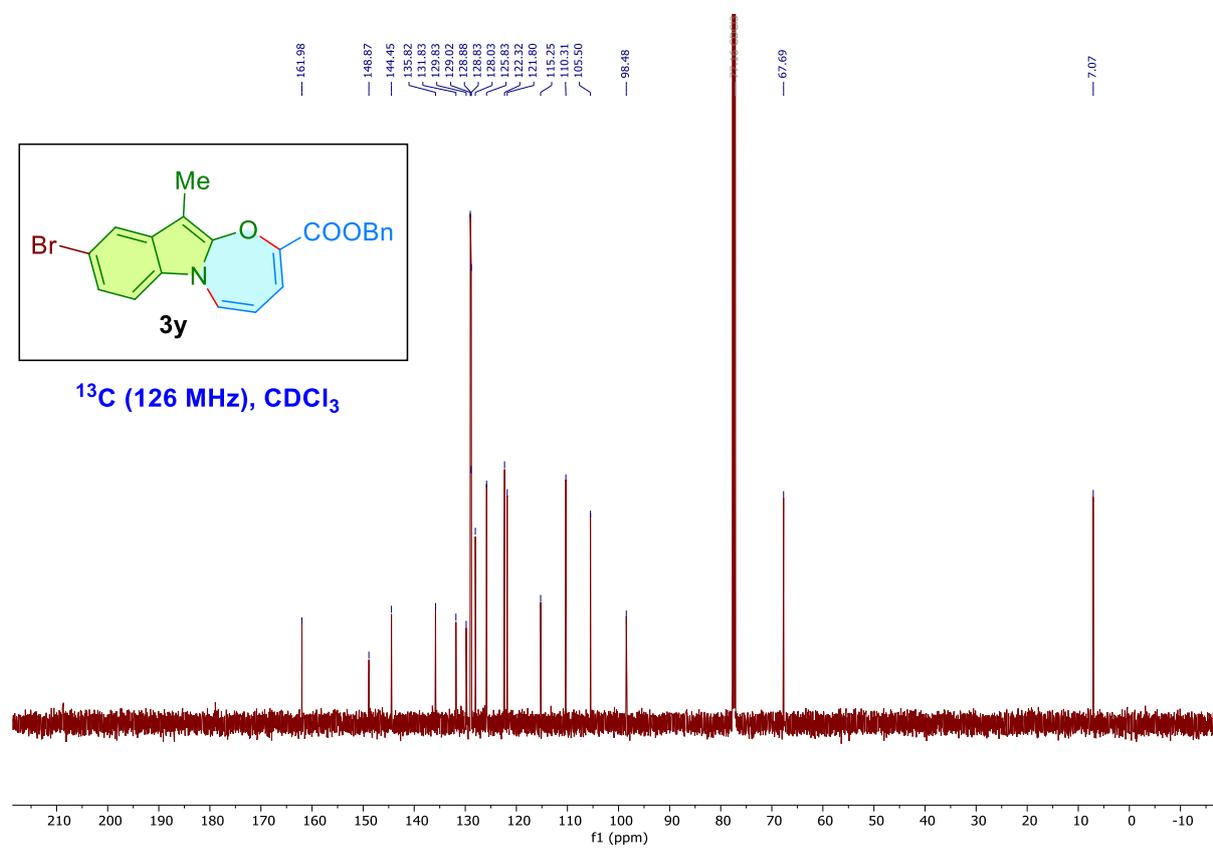
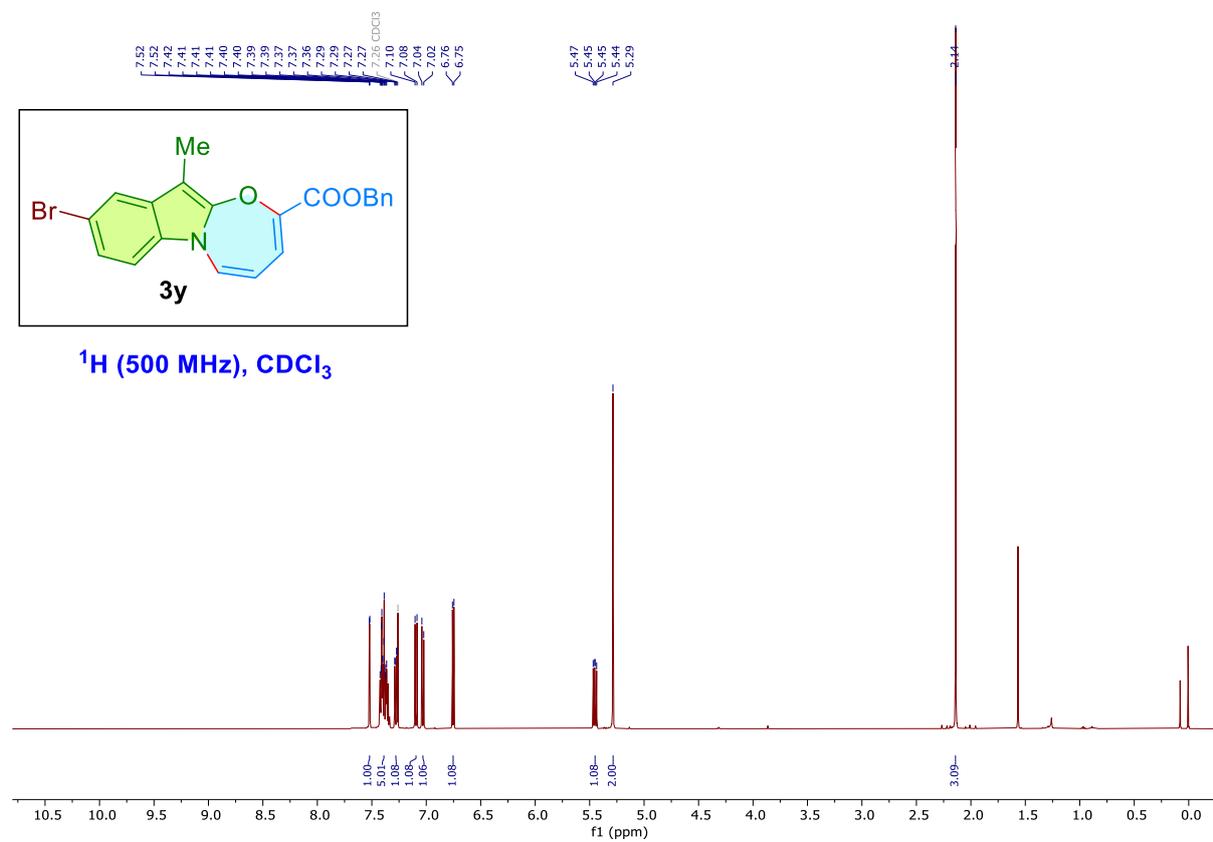
Links: [DETAILS](#) [NMR](#)



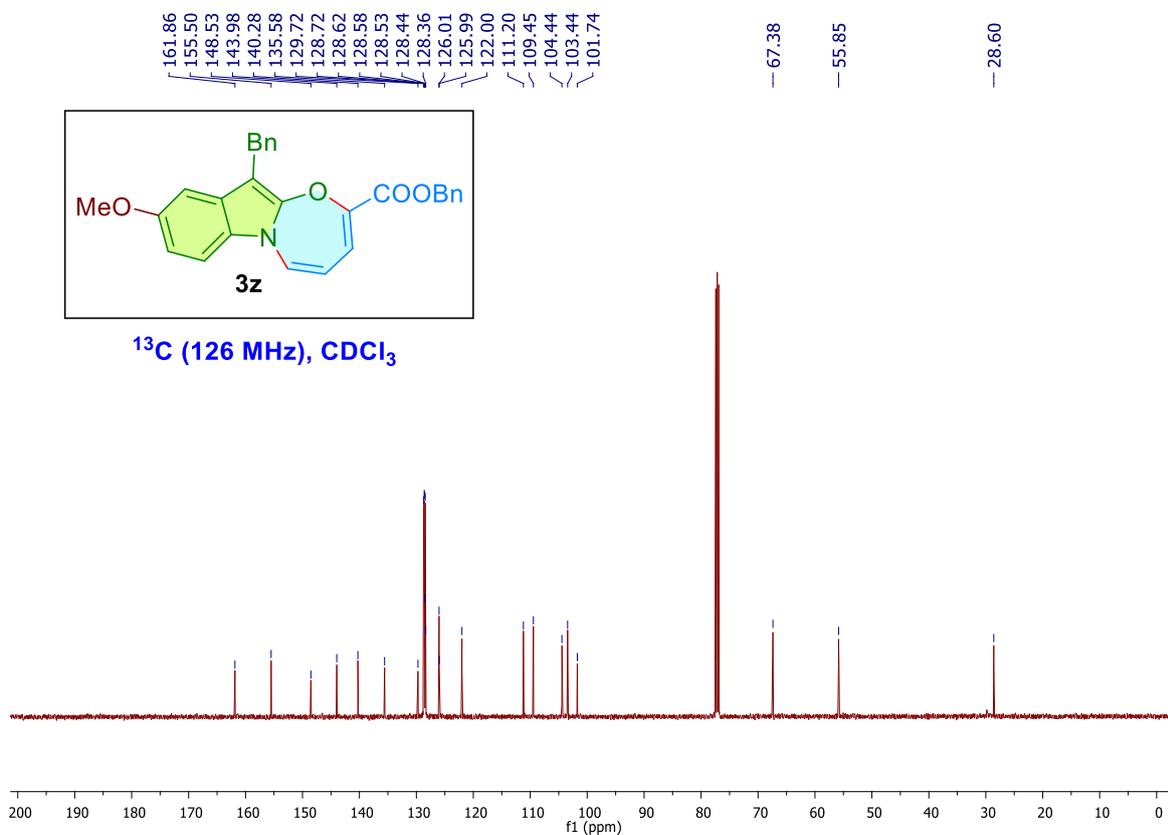
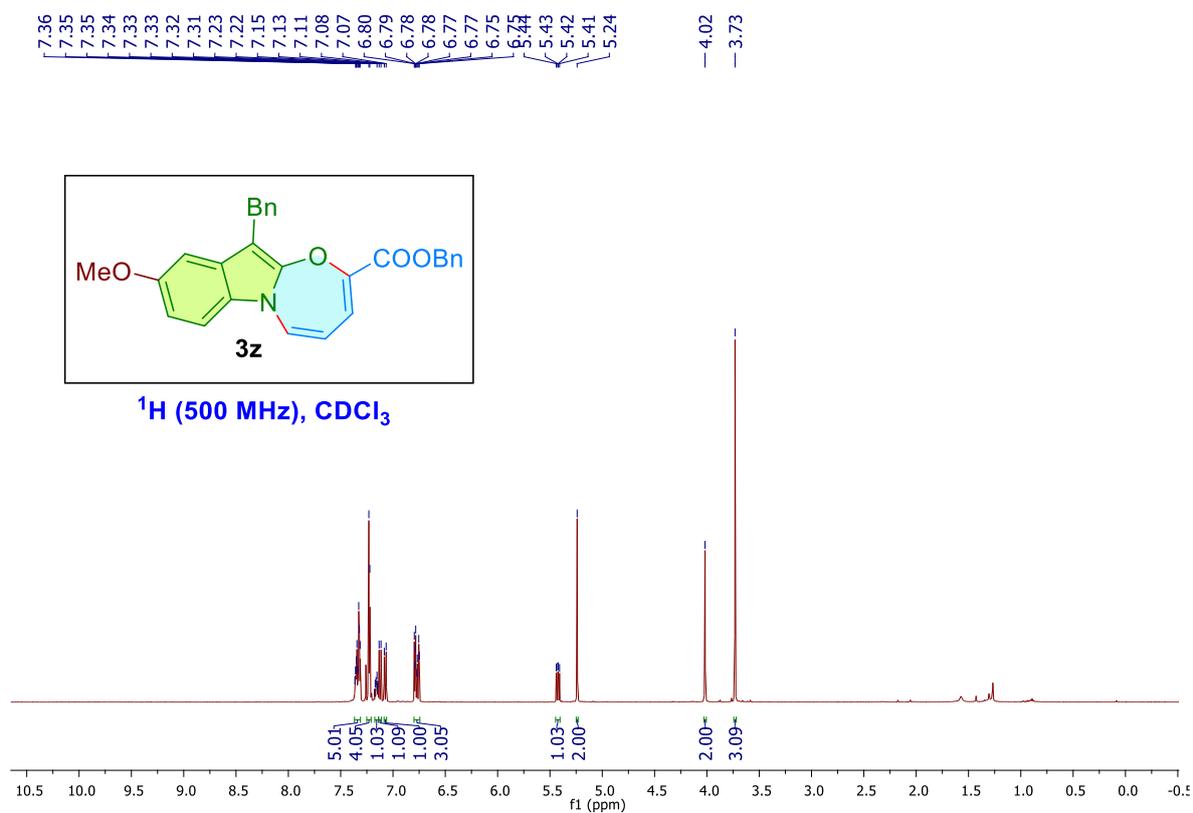
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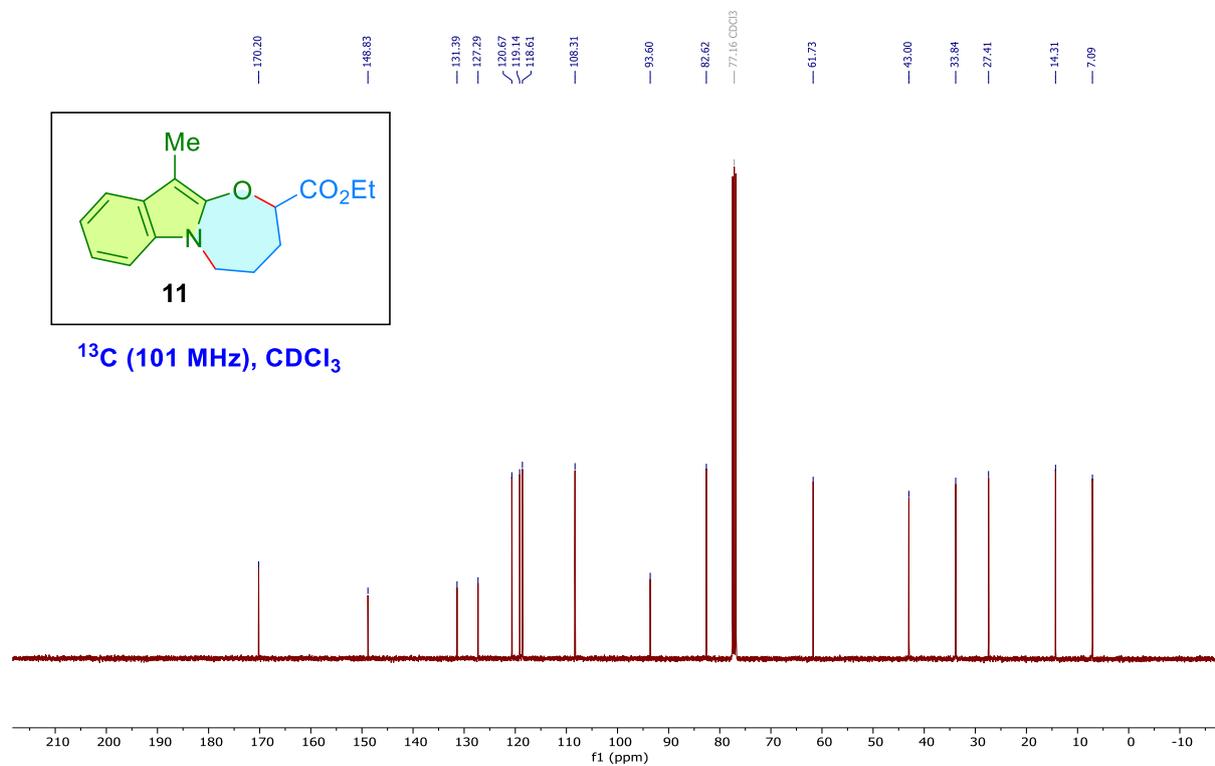
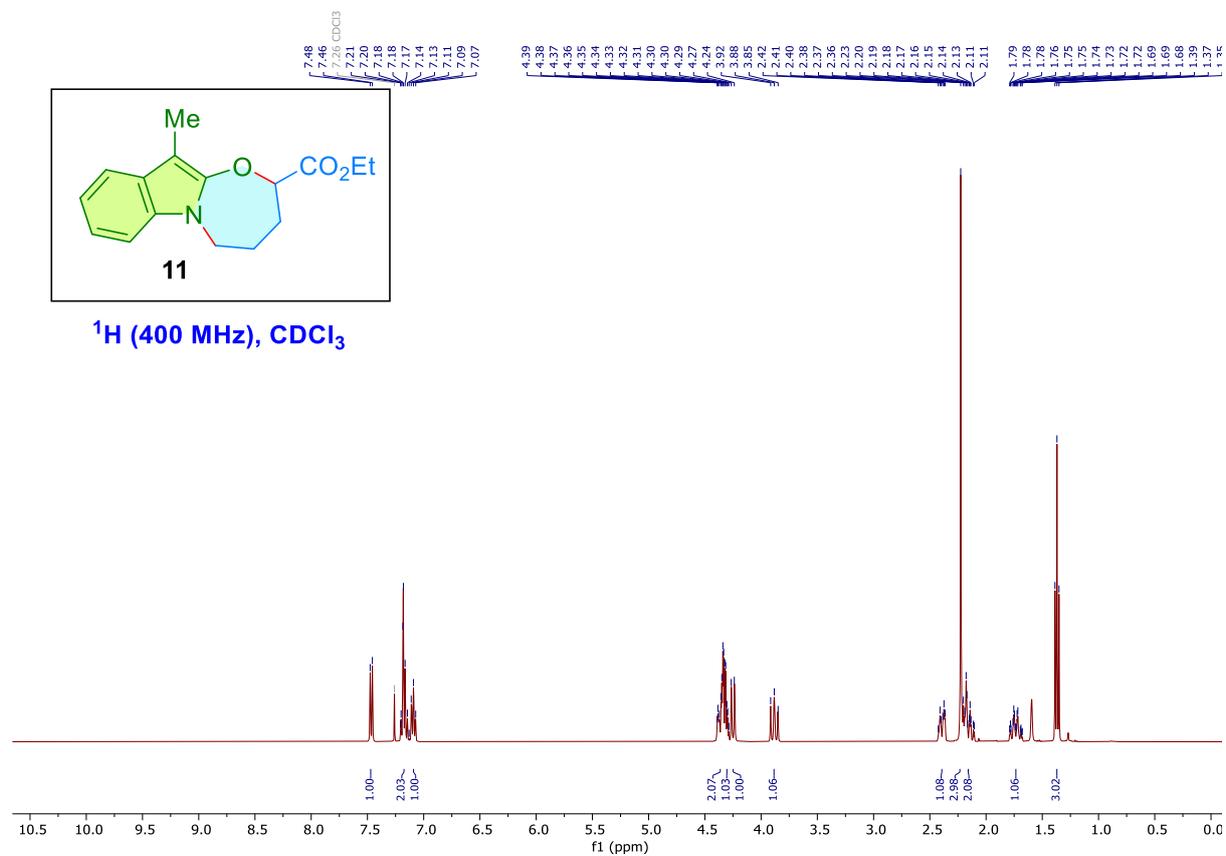
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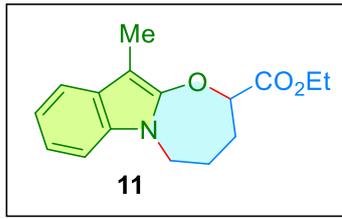


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Links: [DETAILS](#) [NMR](#) [SCXRD](#)





DEPT-135 (101 MHz), CDCl₃

