Electronic Supplementary Material (ESI) for ChemComm.

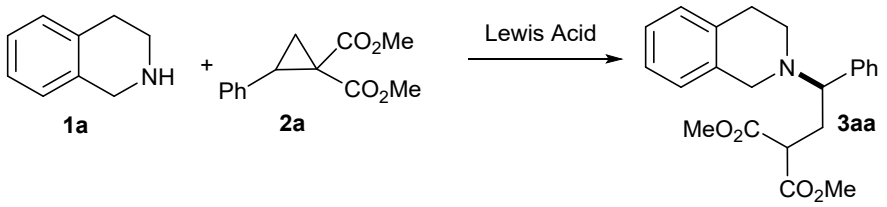
Supporting Information

Expedient $Ni(OTf)_2$/visible light photoredox-catalyzed annulation of donor-acceptor cyclopropanes with cyclic secondary amines

Table of Contents

General Information. 1,2,3,4-Tetrahydroisoquinoline (95%), N-benzylmethylamine (97%), $Cu(OTf)_2$ (98%), $Sc(OTf)_3$ (99%), $Bi(OTf)_3$, $Ni(OTf)_2$ (96%), $Yb(OTf)_3$ (99.99%), $Zn(OTf)_2$ (98%), Eosin Y (99%), rose bengal (95%), $[Ru(bby)_3]Cl_2•6H_2O$ (99.95%) and $Ru(bpy)_3(PF_6)_2$ (97%) were purchased from Aldrich and used as received. K_2CO_3, K_3PO_4, DABCO and NEt_3 were procured from Merck and used as received. Cyclopropanes,[1,2] 2,3,4,5-tetrahydro-1*H*-benzo[c]azepine[3] and N-phenylbenzylamine[4] were prepared according to the reported procedure. Merck silica gel G/GF254 plates used for analytical TLC. Rankem silica gel (60-120 mesh) was utilized for column chromatography. NMR spectra were recorded with Bruker Avance III 600, 500 and 400 MHz spectrometers using $CDCl_3$ as solvent and Me_4Si as an internal standard. Chemical shifts (δ) and spin-spin coupling constant (*J*) are reported in ppm and in Hz, respectively, and other data are reported as follows: s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, dd = doublet of doublets. Melting points were determined using a Büchi B-540 apparatus and are uncorrected. FT-IR spectra were collected on Perkin Elmer IR spectrometer. Q-Tof ESI-MS instrument (model HAB 273) was used for recording mass spectra. Optical rotations were determined using Rudolph autopol I polarimeter. HPLC analysis was carried out using Waters-2489 with Daicel Chiralcel AD-H column using *iso*-propanol and hexane as an eluent. Single crystal X-ray data was collected on a Bruker SMART APEX equipped with a CCD area detector using Mo/Kα radiation and the structure was solved by direct method using *SHELXL-16* (Göttingen, Germany).

Table S1: Optimization of Stereospecific Ring Opening of **2a** with **1a**[a]



Entry	Lewis acid (5 mol %)	Solvent	Yield (%)[b]
1	$Cu(OTf)_2$	$(CH_2Cl)_2$	23
2	$Sc(OTf)_3$	$(CH_2Cl)_2$	n.d.
3	$Bi(OTf)_3$	$(CH_2Cl)_2$	n.d.
4	$Ni(OTf)_2$	$(CH_2Cl)_2$	69
5	$Yb(OTf)_3$	$(CH_2Cl)_2$	35
6	$Ni(OTf)_2$	Toluene	91

7	$Ni(OTf)_2$	DMF	24
8	$Ni(OTf)_2$	1,4-Dioxane	32
9[c]	$Ni(OTf)_2$	Toluene	84
10	-	Toluene	n.d.

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), Lewis acid (5 mol %), solvent (2 mL), 6 h, 80 °C. [b]Isolated yield. [c]Reaction temperature 70 °C. n.d. = not detected.

Synthesis of 3aa. Amine **1a** (0.2 mmol, 26 mg), cyclopropane **2a** (0.24 mmol, 47 mg) and $Ni(OTf)_2$ (5 mol %, 3.5 mg) were stirred in toluene (2 mL) at 80 ^oC for 6 h. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. The reaction mixture was cooled to room temperature and purified on silica gel column chromatography using ethyl acetate and hexane as an eluent.

Synthesis of 4aa. Compound **3aa** (0.2 mmol, 74 mg) and eosin Y (2 mol %, 2.7 mg) were stirred in DMF (0.5 mL) for 3 h under 14 W white LED at ambient temperature. The progress of the reaction was monitored by TLC using ethyl acetate and hexane. The reaction was treated with CH_2Cl_2 (20 mL) and washed with water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave the residue that was purified over silica gel column chromatography using ethyl acetate and hexane as eluent to afford **4aa**.

General Procedure for the Synthesis of 4. Amine **1** (0.2 mmol), cyclopropane **2** (0.24 mmol) and $Ni(OTf)_2$ (5 mol %, 3.5 mg) were stirred in toluene (2 mL) at 80 ^oC for 6 h. The reaction was cooled to room temperature and passed through a short pad of silica gel to remove the Ni-catalyst and toluene using hexane followed by 2% ethyl acetate in hexane. Evaporation of the solvent gave a residue that was reacted with eosin Y (2 mol %, 2.7 mg) in DMF (0.5 mL) for 3 h under 14 W white LED at ambient temperature. The progress of the reaction was monitored by TLC using ethyl acetate and hexane. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave the residue that was purified on silica gel column chromatography using ethyl acetate and hexane as eluent to afford **4**.

Enantiospecific Annulative Coupling. Amine **1c/1g** (0.2 mmol) and cyclopropane **2a′/2a″** (0.24 mmol) were subjected to the above-described reaction conditions. The *ee* was determined using chiral HPLC analysis.

Scale-up Synthesis of 4aa. Amine **1a** (3 mmol, 399 mg), cyclopropane **2a** (3.6 mmol, 842 mg) and $Ni(OTf)_2$ (5 mol %, 53 mg) were stirred in toluene (2 mL) at 80 ^oC for 6 h. The reaction mixture was passed through a short pad of silica gel. Evaporation of the solvent gave a residue, which was reacted with eosin Y (2 mol %, 41 mg) in DMF (5 mL) for 3 h under 14 W white LED at ambient temperature. The progress of the reaction was monitored by TLC using ethyl acetate and hexane. The reaction was then treated with CH_2Cl_2 (50 mL) and washed with water (3 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave the residue that was purified over silica gel column chromatography using ethyl acetate and hexane as eluent to afford **4aa**.

Crystal Data and Structure Refinement

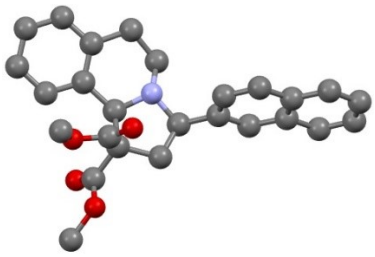


Figure S1. ORTEP diagram of dimethyl 3-(naphthalen-2-yl)-2,3,6,10b tetrahydropyrrolo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate **4al** (CCDC 2163965). H-Atoms omitted for clarity.

Identification code	**4al**
Empirical formula	'C26 H25 N O4'
Formula weight	415.47
Crystal habit, colour	Block /colourless
Crystal size, mm^3	0.32 x 0.25 x 0.24
Temperature, *T*/K	296 K
Wavelength, λ/Å	0.71073
Crystal system	'Monoclinic'
Space group	'P 21/c'

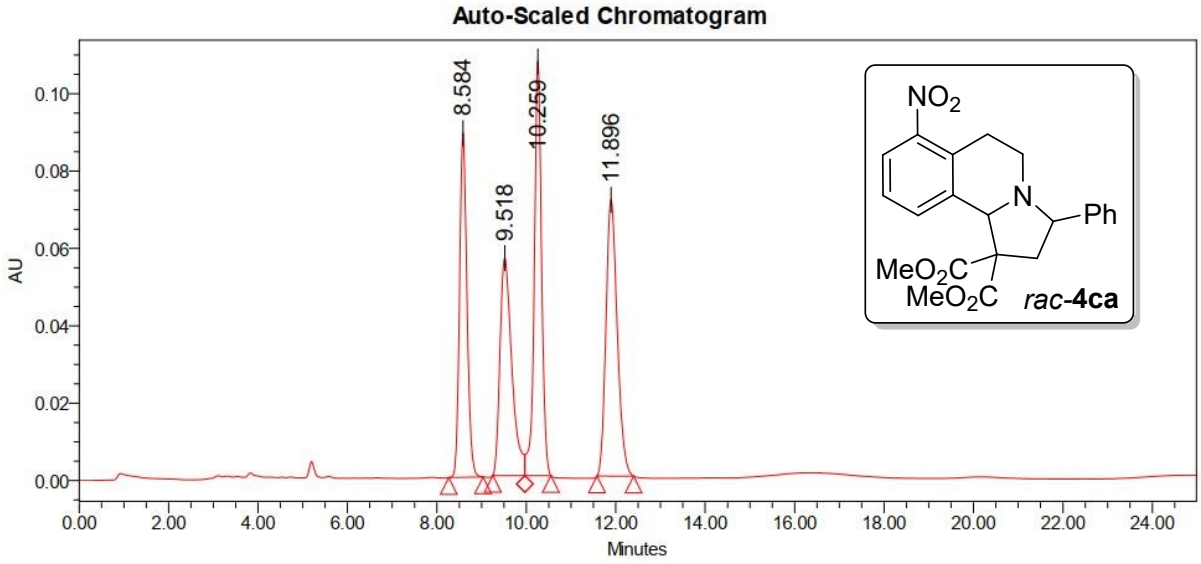
Unit cell dimensions	a = 15.1009(6) Å b = 7.6217(3) Å c = 19.2497(7) Å α = 90 β = 93.892(2) γ = 90
Volume, V/Å^3	2210.43(15)
Z	4
Calculated density, g cm^{-3}	1.248
Absorption coefficient, μ/mm^{-1}	0.084
F(000)	880.0
θ range for data collection	1.352 to 25.047°
Limiting indices	$-17 \leq h \leq 17$, $-9 \leq k \leq 9$, $-22 \leq l \leq 22$
Reflection collected / unique	3907/2799
Completeness to θ	100% (θ = 25.047°)
Absorption correction	None
Max. and min. transmission	0.975 and 0.980
Refinement method	'SHELXL-2014/7 (Sheldrick, 2014)'
Data / restraints / parameters	3907/0/282
Goodness–of–fit on F^2	1.060
Final R indices [I>2sigma(I)]	R1 = 0.0461, wR2 = 0.1055
R indices (all data)	R1 = 0.0695, wR2 = 0.1214

Detection of H_2O_2 in the Reaction Mixture[5]

The formation of H_2O_2 in the reaction mixture was detected in a typical reaction with $KMnO_4$.

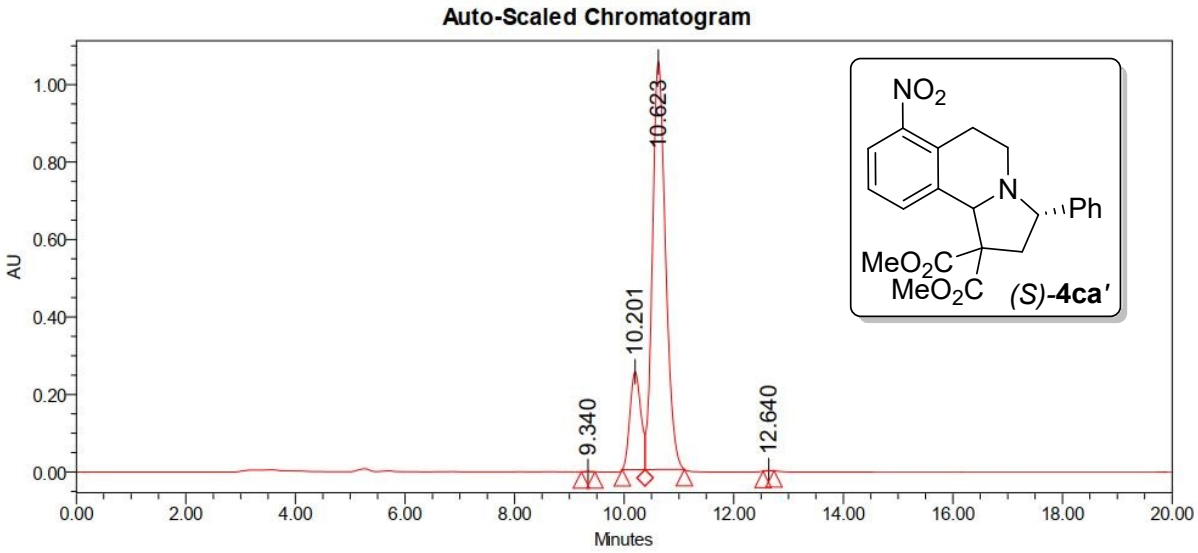
$$KMnO_4 + 3H_2O_2 \longrightarrow 2MnO_2 + 2KOH + 3O_2 + 2H_2O$$

HPLC Chromatograms



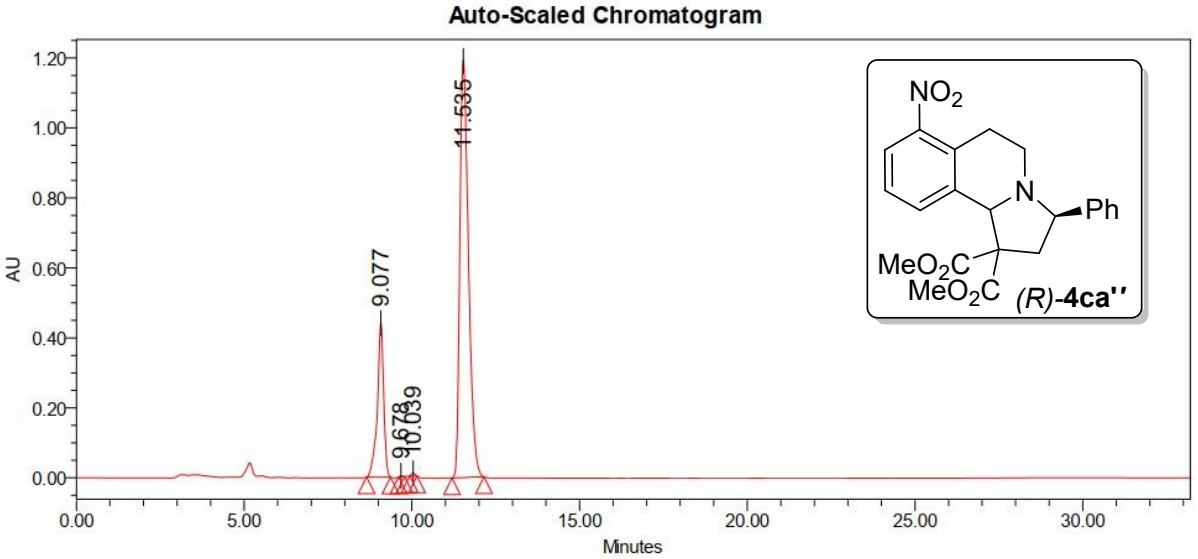
Peak Results

	Start Time (min)	End Time (min)	RT	Height (μV)	% Area
1	8.267	9.033	8.584	88978	22.67
2	9.250	9.967	9.518	56331	22.83
3	9.967	10.550	10.259	107659	26.87
4	11.583	12.400	11.896	71505	27.63



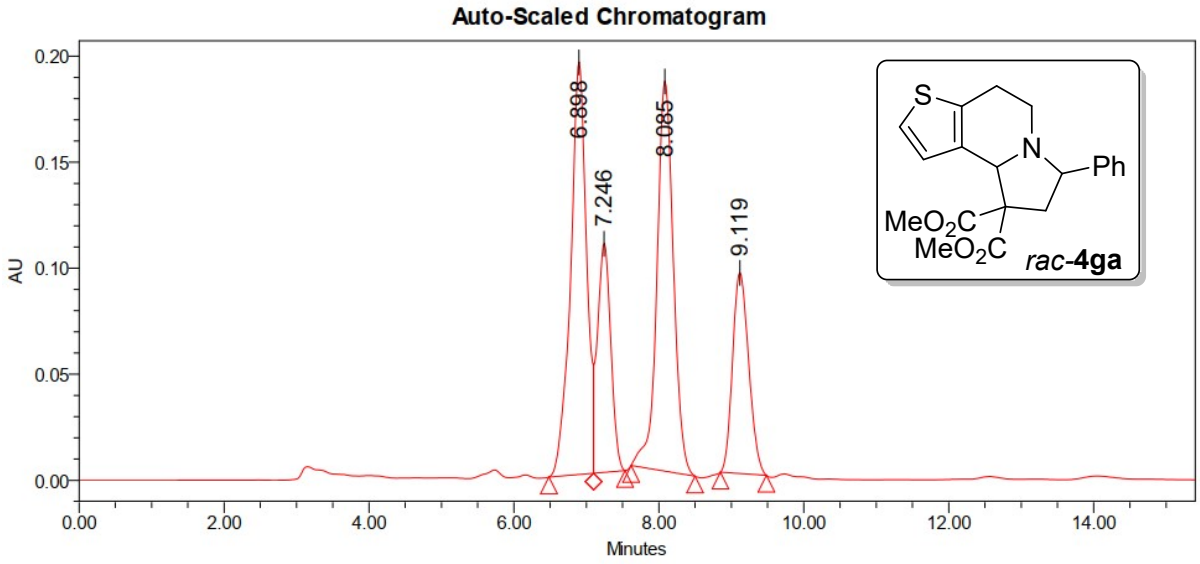
Peak Results

	Peak Codes	Start Time (min)	End Time (min)	RT	Height (μV)	% Area
1		9.217	9.467	9.340	1262	0.05
2		9.967	10.383	10.201	252783	16.70
3		10.383	11.100	10.623	1054997	83.21
4	I38	12.533	12.733	12.640	1079	0.04



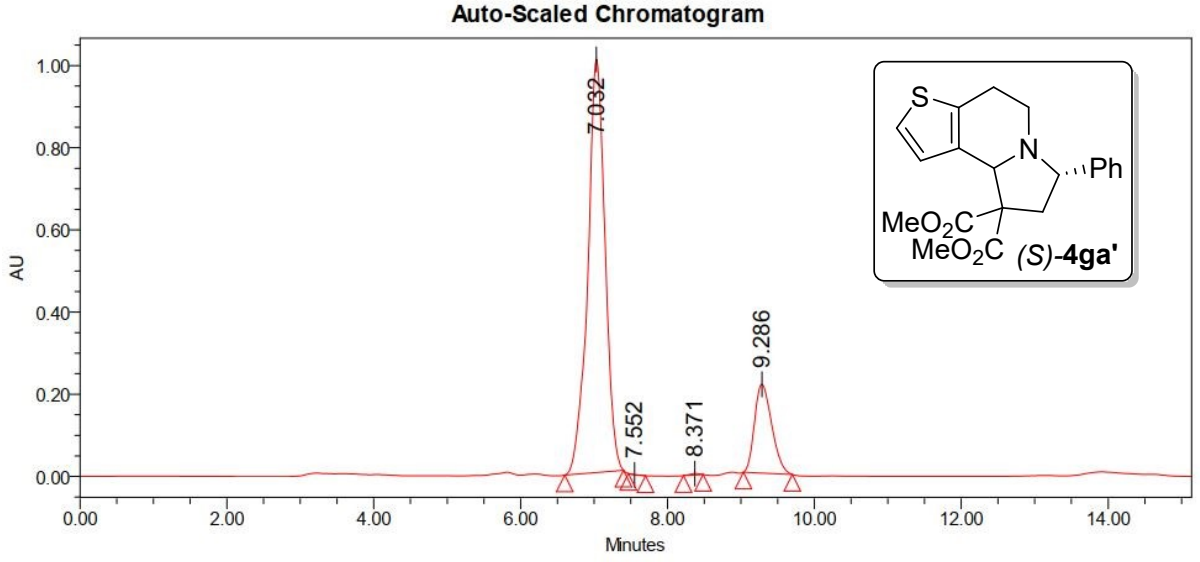
Peak Results

	Start Time (min)	End Time (min)	RT	Height (μV)	% Area
1	8.650	9.367	9.077	442495	21.37
2	9.600	9.783	9.678	3442	0.08
3	9.933	10.150	10.039	8568	0.23
4	11.200	12.150	11.535	1192245	78.33



Peak Results

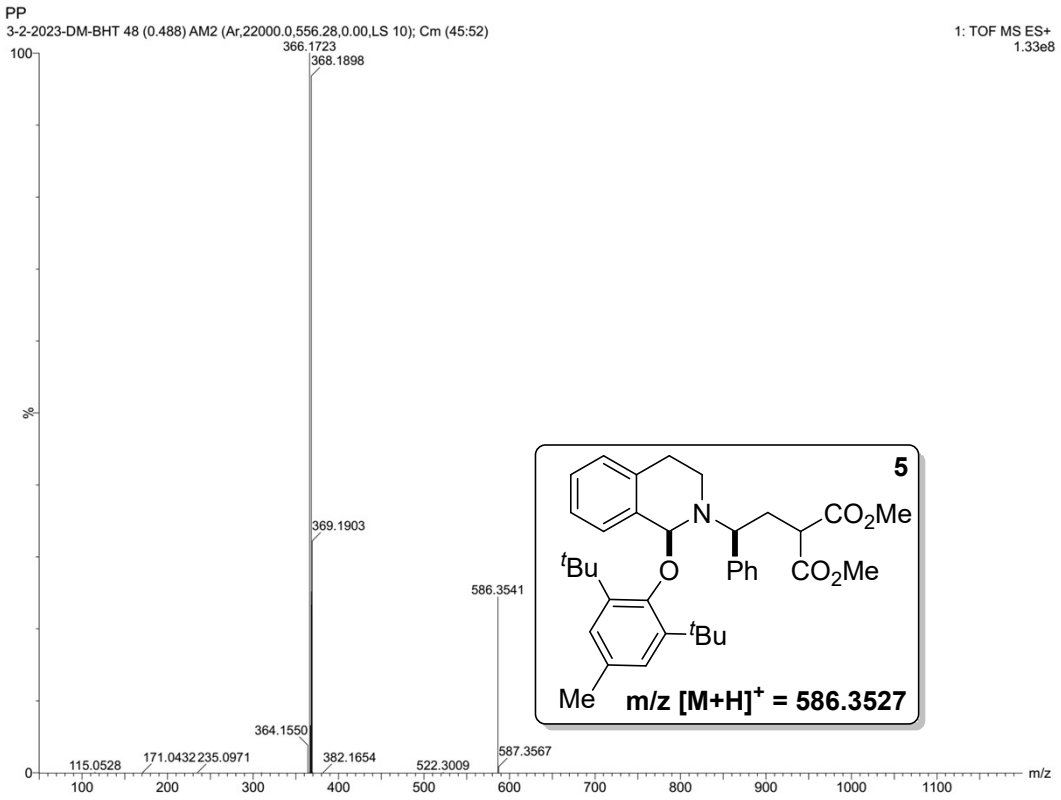
	Start Time (min)	End Time (min)	RT	Height (μV)	% Area
1	6.483	7.100	6.898	194598	33.85
2	7.100	7.533	7.246	108127	15.93
3	7.617	8.500	8.085	183949	33.36
4	8.850	9.483	9.119	94761	16.86



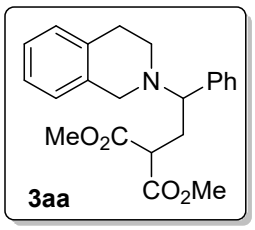
Peak Results

	Peak Codes	Start Time (min)	End Time (min)	RT	Height (μV)	% Area
1		6.600	7.400	7.032	1006043	82.20
2	I37	7.467	7.700	7.552	-1393	0.06
3	I37	8.217	8.483	8.371	3302	0.15
4		9.033	9.700	9.286	216581	17.59

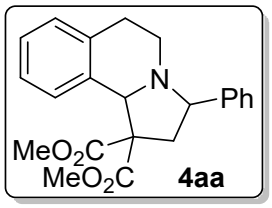
ESI-MS Spectrum of radical trapping experiment



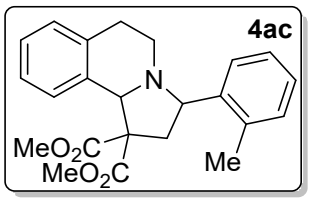
Characterization Data



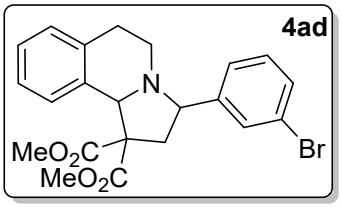
Dimethyl 2-(2-(3,4-dihydroisoquinolin-2(1H)-yl)-2-phenylethyl)malonate 3aa. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane; R_f = 0.47; thick liquid; yield 91% (66 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.0 Hz, 2H), 7.29-7.25 (m, 3H), 7.06-7.01 (m, 3H), 6.98-6.95 (m, 1H), 3.67-3.65 (m, 4H), 3.63-3.60 (m, 1H), 3.55 (s, 3H), 3.53-3.47 (m, 2H), 2.86-2.81 (m, 4H), 2.53-2.48 (m, 1H), 2.31-2.26 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.17, 170.11, 137.7, 135.3, 134.6, 128.7, 128.6, 128.3, 127.7, 126.7, 126.0, 125.5, 67.4, 52.6, 52.47, 52.45, 50.0, 47.6, 31.5, 29.4; FT-IR (Neat) 2951, 1749, 1731, 1495, 1434, 1346, 1196, 1150, 1099, 1029 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{26}NO_4$: 368.1856, found: 368.1868.



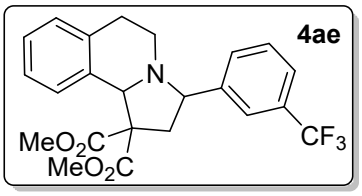
Dimethyl 3-phenyl-2,3,6,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1,1(5H) dicarboxy-late 4aa. Analytical TLC on silica gel, 1:49 ethyl acetate/hexane; R_f = 0.37; thick liquid; yield 90% (66 mg); 1.2:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48-7.44 (m, 4.51H), 7.41 (d, *J* = 7.5Hz, 1H), 7.35 (q, *J* = 7.0 Hz, 3.80H), 7.30-7.25 (m, 1.81H), 7.14-7.04 (m, 5.66H), 5.60 (s, 0.80H), 4.67-4.64 (m, 0.82H), 4.31 (s, 1H), 3.86 (s, 3H), 3.78 (s, 2.41H), 3.53 (t, *J* = 8.5 Hz, 1H), 3.44 (s, 3H), 3.12 (s, 2.42H), 3.06-3.00 (m, 1H), 2.92-2.87 (m, 2.75H), 2.81-2.70 (m, 3.91H), 2.65 (d, *J* = 15.5 Hz, 1H), 2.39 (d, *J* = 15.5 Hz, 0.80H), 2.32-2.27 (m, 1H), 2.20 (dd, *J* = 12.5, 10.5 Hz, 0.83H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 172.0, 171.0, 170.9, 143.0, 141.4, 137.3, 135.8, 135.6, 134.4, 128.7, 128.67, 128.63, 128.5, 128.27, 128.24, 127.7, 127.5, 127.4, 127.0, 126.5, 126.2, 125.6, 125.0, 70.1, 66.9, 65.9, 65.6, 65.5, 61.8, 52.9, 52.8, 52.1, 51.9, 46.3, 44.5, 43.7, 43.4, 30.2, 24.7; FT-IR (Neat) 2952, 1731, 1650, 1603, 1495, 1434, 1266, 1215, 1155, 1063, 1031 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{24}NO_4$: 366.1700, found: 366.1703.



Dimethyl 3-(o-tolyl)-2,3,6,10b-tetrahydropyrrolo[2,1-a]isoquino-line-1,1(5H)-dicarboxy-late 4ac. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.45; thick liquid; yield 58% (43 mg); 1:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 16.2, 7.8 Hz, 2H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 7.2 Hz, 1H), 7.17-7.15 (m, 2.11H), 7.11-7.02 (m, 9.74H), 6.98 (d, *J* = 7.2 Hz, 1H), 5.58 (s, 1H), 4.90-4.87 (m, 1H), 4.27 (s, 1H), 3.80 (s, 3H), 3.75 (t, *J* = 8.4 Hz, 1H), 3.70 (s, 3H), 3.35 (s, 3H), 3.04 (s, 3H), 2.91-2.89 (m, 1H), 2.83-2.65 (m, 6H), 2.60-2.55 (m, 2H), 2.34 (s, 3H), 2.29 (s, 3H), 2.26-2.20 (m, 2H), 1.91 (t, *J* = 12.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.0, 171.9, 171.1, 170.7, 140.8, 139.3, 137.3, 136.3, 136.2, 135.7, 135.6, 134.4, 130.3, 130.2, 128.7, 128.4, 128.3, 127.1, 126.99, 126.90, 126.8, 126.6, 126.59, 126.51, 126.2, 125.9, 125.5, 125.0, 69.8, 65.5, 65.1, 62.3, 61.7, 61.2, 53.0, 52.9, 52.2, 51.9, 46.4, 44.5, 42.1, 41.6, 30.1, 24.4, 19.5, 19.3; FT-IR (Neat) 2952, 1731, 1646, 1603, 1458, 1434, 1266, 1211, 1151, 1152, 1083 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{26}NO_4$: 380.1856, found: 380.1856.

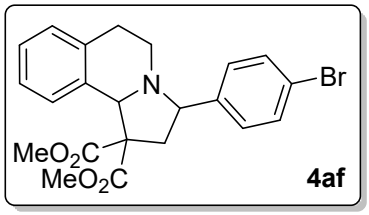


Dimethyl 3-(3-bromophenyl)-2,3,6,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4ad. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.41; thick liquid; yield 69% (61 mg); 1:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 12.0 Hz, 2H), 7.39 (d, *J* = 7.0 Hz, 1H), 7.35-7.30 (m, 5H), 7.14 (q, *J* = 8.0 Hz, 2H), 7.06-7.00 (m, 5H), 6.98 (d, *J* = 7.5 Hz, 1H), 5.50 (s, 1H), 4.57-4.54 (m, 1H), 4.23 (s, 1H), 3.79 (s, 3H), 3.71 (s, 3H), 3.43 (t, *J* = 8.0 Hz, 1H), 3.37 (s, 3H), 3.03 (s, 3H), 2.99-2.95 (m, 1H), 2.84-2.77 (m, 3H), 2.71-2.68 (m, 2H), 2.64 (d, *J* = 8.0 Hz, 2H), 2.59 (d, *J* = 16 Hz, 1H), 2.33 (d, *J* = 15 Hz, 1H), 2.27-2.22 (m, 1H), 2.07 (dd, *J* = 12.5, 10.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 171.7, 170.9, 170.6, 145.8, 144.1, 137.2, 135.6, 135.3, 134.1, 131.2, 130.8, 130.6, 130.33, 130.32, 130.2, 128.7, 128.5, 128.3, 127.0, 126.8, 126.6, 126.3, 126.1, 125.6, 125.1, 122.8, 122.7, 69.9, 66.1, 65.8, 65.5, 65.2, 61.7, 53.0, 52.9, 52.2, 51.9, 46.4, 44.6, 43.5, 43.2, 30.2, 24.7; FT-IR (Neat) 2952, 1732, 1649, 1601, 1568, 1475, 1434, 1265, 1214, 1154, 1069 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{22}H_{23}BrNO_4$: 444.0805, found: 444.0809.

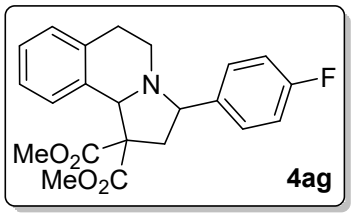


Dimethyl 3-(3-(trifluoromethyl)phenyl)-2,3,6,10b-tetrahydro-pyrrolo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4ae. Analytical TLC on silica gel, 1:13 ethyl acetate/hexane; R_f = 0.48; thick liquid; yield 63% (54 mg); 1.1:1 mixture of diastereomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.64 (m, 2.92H), 7.61 (d, *J* = 7.6 Hz, 0.90H), 7.47 (t, *J* = 8.0 Hz, 1.92H), 7.43-7.32 (m, 3.93H), 7.09-6.98 (m, 5.90H), 5.53 (s, 0.90H), 4.67-4.63 (m, 0.94H), 4.28 (s, 1H), 3.80 (s, 3H), 3.71 (s, 2.70H), 3.54 (t, *J* = 8.4 Hz, 1H), 3.38 (s, 3H), 3.04 (s, 2.69H), 3.01-2.94 (m, 1H), 2.84-2.70 (m, 5H), 2.66 (d, *J* = 8.4 Hz, 2H), 2.60-2.56 (m, 1.18H), 2.34-2.25 (m, 2.19H), 2.08 (dd, *J* = 12.8, 10.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 171.7, 170.9, 170.6, 144.4, 142.9, 137.2, 135.6, 135.2, 134.0, 131.5, 131.2 ($J_{C\text{-}F}$ = 6.6 Hz), 130.8, 129.2, 129.1, 128.8, 128.5, 128.3, 127.0, 126.6, 126.4, 125.7, 125.2, 125.0 ($J_{C\text{-}F}$ = 3.8 Hz), 124.6 ($J_{C\text{-}F}$ = 3.4 Hz), 124.4, 124.1, 123.0 ($J_{C\text{-}F}$ = 5.7 Hz), 69.9, 66.2, 65.8, 65.6, 65.3, 61.7, 53.0, 52.9, 52.2, 52.0, 46.4, 44.6, 43.5, 43.2, 30.2, 24.7; FT-

IR (Neat) 2954, 1732, 1650, 1603, 1436, 1328, 1267, 1200, 1163, 1122, 1073 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{23}F_3NO_4$: 434.1574, found: 434.1576.

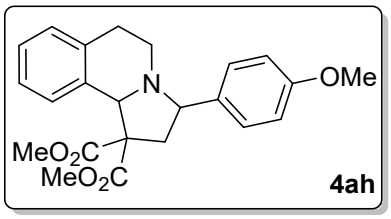


Dimethyl 3-(4-bromophenyl)-2,3,6,10b-tetrahydropyrrolo-[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4af. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.42; thick liquid; yield 73% (64 mg); 1.1:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.37 (m, 5H), 7.33-7.28 (m, 5H), 7.08-7.02 (m, 4H), 7.01-6.97 (m, 2H), 5.51 (s, 0.90H), 4.56-4.53 (m, 1H), 4.24 (s, 1H), 3.79 (s, 3H), 3.71 (s, 2.73H), 3.43 (t, *J* = 8.5 Hz, 1H), 3.36 (s, 3H), 3.03 (s, 2.74H), 2.99-2.92 (m, 1H), 2.82-2.66 (m, 5H), 2.63 (d, *J* = 8.5 Hz, 2H), 2.59-2.55 (m, 1H), 2.32 (d, *J* = 15.0 Hz, 1H), 2.26-2.21 (m, 1H), 2.08-2.03 (m, 1H).^{13}C NMR (150 MHz, $CDCl_3$) δ 172.8, 171.8, 170.9, 170.8, 142.1, 140.6, 137.2, 135.6, 135.2, 134.0, 131.79, 131.71, 129.9, 129.2, 128.7, 128.5, 128.2, 127.0, 126.6, 126.3, 125.6, 125.1, 121.5, 121.1, 69.8, 66.0, 65.7, 65.4, 64.9, 61.6, 53.09, 53.01, 52.3, 52.0, 46.3, 44.4, 43.5, 43.1, 30.1, 24.4; FT-IR (Neat) 2953, 1733, 1646, 1484, 1435, 1263, 1219, 1154, 1072, 1012 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{23}BrNO_4$: 444.0805, found: 444.0803.

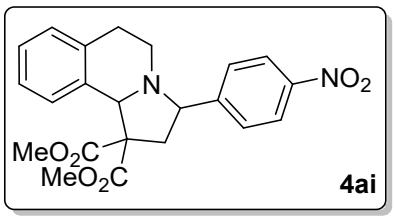


Dimethyl 3-(4-fluorophenyl)-2,3,6,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4ag. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.41; thick liquid; yield 74% (56 mg); 1:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47-7.43 (m, 5H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.16-7.10 (m, 4H), 7.09 (d, *J* = 7.2 Hz, 1H), 7.06-7.02 (m, 5H), 5.59 (s, 1H), 4.65-6.63 (m, 1H), 4.31 (s, 1H), 3.87 (s, 3H), 3.79 (s, 3H), 3.51 (t, *J* = 8.4 Hz, 1H), 3.44 (s, 3H), 3.11 (s, 3H), 3.05-3.00 (m, 1H), 2.92-2.83 (m, 3H), 2.79-2.63 (m, 5H), 2.39 (d, *J* = 15.0 Hz, 1H), 2.32-2.27 (m, 1H), 2.15 (dd, *J* = 12.6, 10.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.9, 171.9, 171.0, 170.9, 163.2 ($J_{C\text{-}F}$ = 27 Hz), 161.6 ($J_{C\text{-}F}$ = 26.4 Hz), 138.5 ($J_{C\text{-}F}$ = 2.25 Hz), 137.2, 137.1 ($J_{C\text{-}F}$ = 3.15 Hz), 135.7, 135.4, 134.1, 129.7 ($J_{C\text{-}F}$ = 7.8 Hz), 128.9 ($J_{C\text{-}F}$ = 7.95 Hz), 128.7, 128.5, 128.2, 127.0, 126.5, 126.3, 125.6, 125.0, 115.5 ($J_{C\text{-}F}$ = 13.05 Hz), 115.4 ($J_{C\text{-}F}$ = 12.9 Hz), 69.8, 66.0,

65.7, 65.4, 64.7, 61.6, 53.0, 52.9, 52.3, 52.0, 46.2, 44.3, 43.6, 43.3, 30.2, 24.4; FT-IR (Neat) 2953, 1731, 1649, 1603, 1509, 1435, 1266, 1222, 1156, 1083 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{23}FNO_4$: 384.1606, found: 384.1611.

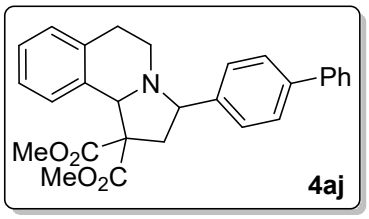


Dimethyl 3-(4-methoxyphenyl)-2,3,6,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4ah. Analytical TLC on silica gel, 1:14 ethyl acetate/hexane; R_f = 0.38; thick liquid; yield 69% (54 mg); 1:1 mixture of diastereomers; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.36 (m, 1H), 7.34-7.30 (m, 5H), 7.07-6.96 (m, 6H), 6.83-6.80(m, 4H), 5.51 (s, 1H), 4.54-4.50 (m, 1H), 4.22 (s, 1H), 3.79 (s, 3H), 3.73 (d, *J* = 2.0 Hz, 6H), 3.71 (s, 3H), 3.40 (t, *J* = 8.4 Hz, 1H), 3.36 (s, 3H), 3.03 (s, 3H), 2.98-2.91 (m, 1H), 2.85-2.77 (m, 3H), 2.72-2.54 (m, 5H), 2.31-2.27 (m, 1H), 2.23-2.16 (m, 1H), 2.12 (dd, *J* = 13.2, 10.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.0, 172.1, 171.1, 171.0, 159.2, 159.0, 137.2, 135.8, 135.5, 134.6, 134.3, 133.2, 129.3, 128.9, 128.7, 128.59, 128.50, 128.1, 126.9, 126.5, 126.2, 125.5, 125.0, 113.9, 69.9, 66.2, 65.6, 65.3, 64.7, 61.7, 55.4, 55.3, 53.0, 52.9, 52.2, 51.9, 46.1, 44.1, 43.6, 43.2, 30.1, 24.3; FT-IR (Neat) 2953, 1730, 1646, 1609, 1215, 1434, 1246, 1215, 1116, 1083, 1032 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{26}NO_5$: 396.1805, found: 396.1810.

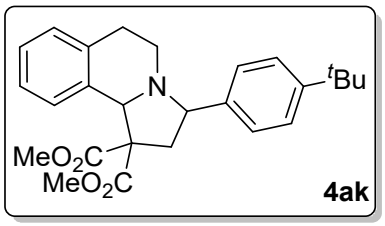


Dimethyl 3-(4-nitrophenyl)-2,3,6,10b-tetrahydropyrrolo-[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4ai. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane; R_f = 0.36; thick liquid; yield 62% (50 mg); 1.1:1 mixture of diastereomers; ^1H NMR (500 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 8.5, 5.5 Hz, 3.70H), 7.61 (d, *J* = 8.5 Hz, 3.71H), 7.41 (d, *J* = 7.0 Hz, 1H), 7.35 (d, *J* = 7.0 Hz, 1H), 7.10-6.99 (m, 6H), 5.54 (s, 0.90H), 4.74-4.71 (m, 0.90H), 4.32 (s, 1H), 3.80 (s, 3H), 3.71 (s, 2.70H), 3.62 (t, *J* = 8.0 Hz, 1H), 3.37 (s, 3H), 3.05 (s, 2.75H), 3.02-2.95 (m, 1H), 2.79-2.74 (m, 4H), 2.66-2.55 (m, 4H), 2.36-2.29 (m, 2H), 2.07(t, *J* = 11 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4, 171.4, 170.7, 170.5, 147.8, 147.6, 138.0, 136.9, 135.4, 133.7, 129.0, 128.8, 128.5, 128.3, 128.2, 127.16, 127.11, 126.8, 126.6, 125.8, 125.29, 125.25, 124.0, 123.9, 69.7, 65.83, 65.81, 65.6, 65.4, 61.7, 53.09,

53.01, 52.3, 52.0, 46.5, 44.9, 43.3, 43.0, 30.2, 24.8; FT-IR (Neat) 2951, 1728, 1604, 1519, 1434, 1344, 1267, 1156, 1065, 1034 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{23}N_2O_6$: 411.1551, found: 411.1555.

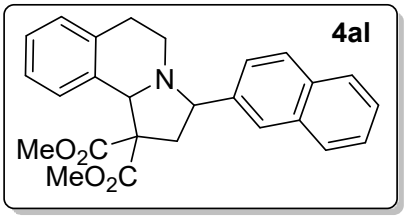


Dimethyl 3-([1,1'-biphenyl]-4-yl)-2,3,6,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4aj. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.38; colorless solid; mp 151-152 °C; yield 72% (63 mg); 1.2:1 mixture of diastereomers; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54-7.47 (m, 12H), 7.40-7.34 (m, 6H), 7.28-7.26 (m, 2H), 7.09-6.98 (m, 6H), 5.56 (s, 0.80H), 4.65-4.63 (m, 0.80H), 4.26 (s, 1H), 3.80 (s, 3H), 3.72 (s, 2.44H), 3.51 (t, *J* = 8.4 Hz, 1H), 3.38 (s, 3H), 3.05 (s, 2.40H), 3.01-2.97 (m, 1H), 2.90-2.85 (m, 3H), 2.76-2.71 (m, 3H), 2.68-2.65 (m, 1H), 2.60 (d, *J* = 15.6 Hz, 1H), 2.33 (d, *J* = 15.6 Hz, 0.83H), 2.28-2.24 (m, 1H), 2.16 (dd, *J* = 12.6, 10.2 Hz, 0.84H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.9, 172.0, 171.0, 170.9, 142.0, 141.07, 141.04, 140.6, 140.5, 137.3, 135.7, 135.5, 134.2, 129.7, 128.87, 128.84, 128.7, 128.6, 128.5, 128.2, 127.8, 127.4, 127.38, 127.33, 127.2, 127.1, 126.9, 126.7, 126.5, 126.2, 125.5, 125.0, 70.0, 66.5, 65.7, 65.5, 65.1, 61.7, 53.0, 52.9, 52.3, 52.0, 46.3, 44.4, 43.6, 43.2, 30.2, 24.4; FT-IR (Neat) 2952, 1729, 1651, 1487, 1433, 1380, 1263, 1212, 1136, 1065, 1040 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{28}H_{28}NO_4$: 442.2013, found: 442.2013.

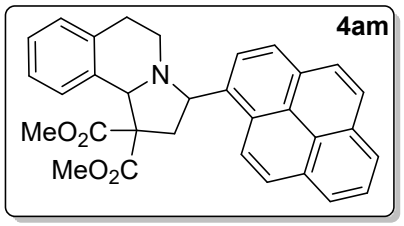


Dimethyl 3-(4-(tert-butyl)phenyl)-2,3,6,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4ak. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.42; thick liquid; yield 75% (63 mg); 1:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.5 Hz, 1H), 7.33-7.28 (m, 9H), 7.07-6.96 (m, 6H), 5.52 (s, 1H), 4.57-4.54 (m, 1H), 4.23 (s, 1H), 3.79 (s, 3H), 3.70 (s, 3H), 3.44 (t, *J* = 8.5 Hz, 1H), 3.36 (s, 3H), 3.04 (s, 3H), 3.00-2.93 (m, 1H), 2.87-2.81 (m, 3H), 2.73-2.66 (m, 3H), 2.64-2.54 (m, 2H), 2.31-2.27 (m, 1H), 2.23-2.18 (m, 1H), 2.15 (dd, *J* = 13.0, 10.0 Hz, 1H), 1.26 (d, *J* = 3.0 Hz, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 172.1,

171.1, 170.9, 150.6, 150.4, 139.8, 138.1, 137.4, 135.8, 135.7, 134.5, 128.7, 128.4, 128.2, 127.8, 127.1, 126.9, 126.4, 126.2, 125.58, 125.53, 125.4, 125.0, 70.1, 66.6, 65.8, 65.6, 65.1, 61.9, 52.9, 52.8, 52.1, 51.9, 46.2, 44.5, 43.6, 43.4, 34.67, 34.64, 31.5, 30.3, 24.6; FT-IR (Neat) 2954, 1732, 1650, 1604, 1434, 1265, 1215, 1155, 1111, 1084, 1018 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{26}H_{32}NO_4$: 422.2326, found: 422.2326.

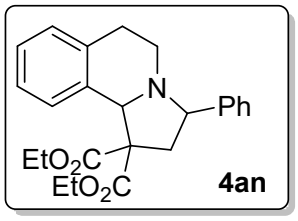


Dimethyl 3-(naphthalen-2-yl)-2,3,6,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4al. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.37; colourless solid; mp 62-63 °C; yield 73% (60 mg); 1.2:1 mixture of diastereomers; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 0.91H), 7.79-7.74 (m, 7H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 0.90H), 7.42-7.35 (m, 5.80H), 7.10-6.98 (m, 6H), 5.60 (s, 0.80H), 4.77-4.73 (m, 0.89H), 4.30 (s, 1H), 3.80 (s, 3H), 3.71 (s, 2.44H), 3.63 (t, *J* = 8.4 Hz, 1H), 3.40 (s, 3H), 3.06 (s, 2.46H), 2.99-2.94 (m, 1H), 2.89-2.82 (m, 3H), 2.78-2.67 (m, 4H), 2.58 (d, *J* = 15.6 Hz, 1H), 2.33-2.20 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.9, 172.0, 171.0, 170.9, 138.9, 137.3, 135.8, 135.5, 134.4, 133.6, 133.48, 133.41, 133.3, 128.8, 128.6, 128.5, 128.4, 128.3, 127.93, 127.91, 127.85, 127.81, 127.3, 127.0, 126.5, 126.4, 126.3, 126.1, 126.0, 125.9, 125.7, 125.6, 125.4, 125.1, 70.1, 67.0, 65.9, 65.76, 65.74, 61.9, 52.9, 52.8, 52.2, 51.9, 46.3, 44.5, 43.5, 43.2, 30.2, 24.7; FT-IR (Neat) 2952, 1732, 1648, 1434, 1267, 1213, 1067 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{26}H_{26}NO_4$: 416.1856, found: 416.1858.

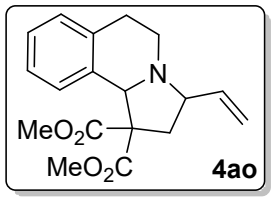


Dimethyl 3-(pyren-1-yl)-2,3,6,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1,1(5H)-dicar-boxylate 4am. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.34; thick liquid; yield 75% (73 mg); 1.2:1 mixture of diastereomers; ^1H NMR (500 MHz, $CDCl_3$) δ 8.53 (s, 0.73H), 8.47 (d, *J* = 9.5 Hz, 1H), 8.41 (d, *J* = 8.0 Hz, 0.94H), 8.29 (s, 1H), 8.15 (dd, *J* = 8.0, 2.5 Hz, 1.90H), 8.11-8.09 (m, 3.86H), 8.05 (dd, *J* = 9.0, 3.0 Hz, 2H), 8.00-7.96 (m, 4H), 7.94-7.90 (m, 2H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.42 (d, *J* = 6.5 Hz, 1H), 7.12-7.01 (m, 6H), 5.80-5.77 (m, 0.84H), 5.76 (s, 0.80H), 4.59 (s, 1H), 4.52 (s,

1H), 3.84 (s, 3H), 3.68 (s, 2.42H), 3.40 (s, 3H), 3.13 (s, 2.49H), 3.10-3.04 (m, 1.81H), 2.99-2.85 (m, 6H), 2.62 (d, *J* = 16.0 Hz, 1H), 2.37-2.29 (m, 2H), 2.17 (t, *J* = 12.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.0, 171.8, 171.3, 170.9, 137.5, 136.7, 135.8, 135.7, 134.4, 131.55, 131.52, 130.8, 130.7, 130.5, 129.3, 129.2, 128.8, 128.6, 128.5, 127.7, 127.68, 127.65, 127.63, 127.3, 127.0, 126.9, 126.6, 126.4, 126.0, 125.9, 125.68, 125.65, 125.5, 125.26, 125.24, 125.20, 125.09, 125.06, 125.02, 123.8, 123.1, 122.6, 70.2, 65.9, 62.2, 61.7, 53.1, 52.9, 52.3, 52.0, 46.5, 44.9, 43.2, 43.1, 30.2, 24.7; FT-IR (Neat) 2950, 1727, 1643, 1433, 1267, 1200, 1157, 1083, 1066 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{32}H_{28}NO_4$: 490.2013, found: 490.2017.

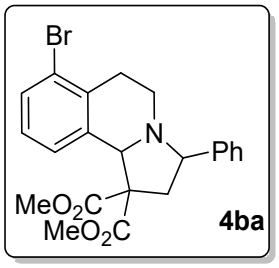


Diethyl 3-phenyl-2,3,6,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4an. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.36; thick liquid; yield 78% (61 mg); 1.1:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50-7.46 (m, 6H), 7.35-7.32 (m, 3.86H), 7.29-7.25 (m, 2.45H), 7.14-7.03 (m, 5.92H), 5.58 (s, 0.90H), 4.67-4.64 (m, 1H), 4.38-4.20 (m, 5H), 3.96-3.85 (m, 1.82H), 3.68-3.62 (m, 1H), 3.55-3.44 (m, 2H), 3.05-2.98 (m, 1H), 2.93-2.87 (m, 3H), 2.81-2.77 (m, 3H), 2.69-2.61 (m, 1.93H), 2.40 (d, *J* = 15.5 Hz, 1H), 2.32-2.27 (m, 1H), 2.20 (dd, *J* = 13.0, 10.0 Hz, 1H), 1.33 (t, *J* = 7.0 Hz, 2.71H), 1.26 (t, *J* = 7.0 Hz, 3H), 0.91 (t, *J* = 7.0 Hz, 2.71H), 0.85 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.5, 171.5, 170.7, 170.4, 143.1, 141.6, 137.3, 135.8, 135.7, 134.5, 128.63, 128.62, 128.61, 128.48, 128.44, 128.2, 127.7, 127.55, 127.50, 127.4, 126.4, 126.2, 125.6, 124.9, 69.8, 66.7, 65.7, 65.6, 65.3, 61.8, 61.7, 61.6, 61.24, 61.22, 46.1, 44.6, 43.5, 43.4, 30.3, 24.8, 14.2, 14.1, 13.7, 13.5; FT-IR (Neat) 2933, 1727, 1651, 1603, 1495, 1455, 1367, 1262, 1214, 1189, 1094, 1061, 1031 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{28}NO_4$: 394.2013, found: 394.2023.

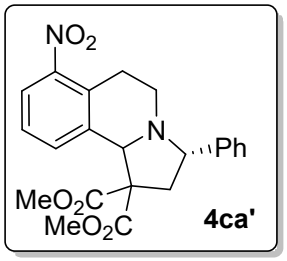


Dimethyl 3-vinyl-2,3,6,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4ao. Analytical TLC on silica gel, 1:19 ethyl acetate/hexane; R_f = 0.32; thick liquid; yield 45% (28 mg); 2.4:1 mixture of diasteroisomers; ^{1}H NMR (500 MHz,

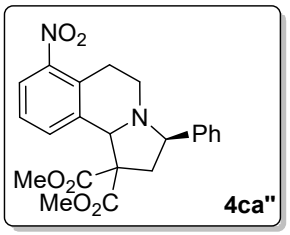
$CDCl_3$) δ 7.35 (d, *J* = 6.5 Hz, 1H), δ 7.27 (d, *J* = 7.5 Hz, 0.43H), 7.06-7.00 (m, 3.51H), 6.98 (d, *J* = 6.0 Hz, 1H), 5.81-5.74 (m, 0.53H), 5.68-5.61 (m, 1H), 5.32 (s, 1H), 5.23 (d, *J* = 17 Hz, 1H), 5.17 (d, *J* = 10.5 Hz, 0.49H), 5.11 (d, *J* = 10.5 Hz, 1H), 4.12 (s, 0.42H), 3.94-3.90 (m, 1H), 3.78 (s, 1.30H), 3.74 (s, 3H), 3.33 (s, 1.34H), 3.14-3.11 (m, 0.45H), 3.05-3.03 (m, 1H), 3.02 (s, 3H), 3.01-2.97 (m, 0.50H), 2.95-2.92 (m, 0.48H), 2.80-2.65 (m, 3H), 2.61 (d, *J* = 5.5 Hz, 0.44H), 2.59 (d, *J* = 5.5 Hz, 0.47H), 2.53-2.47 (m, 1H), 2.41-2.38 (m, 1H), 2.30-2.35 (m, 0.53H), 2.07 (dd, *J* = 13.0, 9.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 172.1, 171.1, 170.9, 140.2, 138.4, 136.9, 135.5, 135.0, 134.4, 128.7, 128.4, 128.2, 126.8, 126.5, 126.3, 125.5, 125.1, 118.5, 117.4, 70.0, 65.9, 65.7, 65.5, 65.0, 62.1, 52.99, 52.93, 52.2, 51.9, 46.0, 44.3, 40.6, 40.1, 29.9, 25.2; FT-IR (Neat) 2951, 1728, 1642, 1493, 1453, 1433, 1352, 1253, 1206, 1146, 1112, 1087, 1008 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{18}H_{22}NO_4$: 316.1543, found: 316.1548.



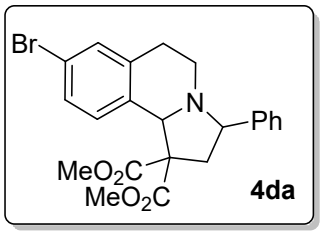
Dimethyl 7-bromo-3-phenyl-2,3,6,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4ba. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.42; thick liquid; yield 72% (63 mg); 1.6:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.38 (m, 3.80H), 7.35-7.32 (m, 3H), 7.29-7.25 (m, 4H), 7.23-7.20 (m, 2H), 6.95 (q, *J* = 8.0 Hz, 1.73H), 5.49(s, 0.60H), 4.55-4.52 (m, 0.62H), 4.21 (s, 1H), 3.79 (s, 3H), 3.70 (s, 1.84H), 3.44 (t, *J* = 8.5 Hz, 1H), 3.37 (s, 3H), 3.08 (s, 1.80H), 2.90-2.76 (m, 3H), 2.73-2.67 (m, 5.61H), 2.60 (d, *J* = 12.5 Hz, 0.65H), 2.22-2.14 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 171.9, 170.8, 170.7, 142.4, 141.0, 138.4, 137.0, 136.8, 135.6, 130.8, 130.3, 128.7, 128.6, 128.1, 127.8, 127.6, 127.4, 127.2, 126.7, 126.3, 126.1, 125.1, 124.7, 70.0, 66.7, 65.9, 65.7, 65.4, 61.8, 53.0, 52.9, 52.3, 52.0, 46.1, 44.0, 43.9, 43.3, 31.5, 24.7; FT-IR (Neat) 2952, 1729, 1651, 1561, 1435, 1261, 1204, 1178, 1150, 1061, 1025 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{23}BrNO_4$: 444.0805, found: 444.0808.



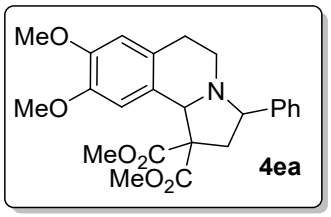
Dimethyl (3*S*,10b*R*)-7-nitro-3-phenyl-2,3,6,10b-tetrahydropyrrolo-[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4ca′. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane; R_f = 0.37; thick liquid; yield 65% (53 mg); 1.8:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79-7.73 (m, 3.14H), 7.47-7.45 (m, 3.19H), 7.36 (q, *J* = 7.0 Hz, 3.18H), 7.32-7.25 (m, 3.85H), 5.66 (s, 0.55H), 4.68-4.65 (m, 0.60H), 4.34 (s, 1H), 3.88 (s, 3H), 3.79 (s, 1.70H), 3.56 (t, *J* = 8.5 Hz, 1H), 3.45 (s, 3H), 3.30-3.25 (m, 1H), 3.18 (s, 1.70H), 3.10-3.04 (m, 0.65H), 2.99-2.95 (m, 1H), 2.93-2.86 (m, 1.73H), 2.82-2.78 (m, 1.66H), 2.75-2.69 (m, 2.34H), 2.28-2.22 (m, 1.69H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.7, 171.7, 170.5, 170.2, 149.8, 149.4, 142.1, 140.7, 138.8, 137.5, 133.2, 132.8, 132.2, 131.4, 128.8, 128.7, 128.09, 128.05, 127.8, 127.4, 125.7, 125.6, 123.1, 122.5, 69.7, 66.6, 66.0, 65.5, 65.4, 62.1, 53.2, 53.1, 52.4, 52.2, 45.4, 43.5, 43.4, 43.2, 27.9, 21.5; FT-IR (Neat) 2953, 1730, 1656, 1525, 1434, 1349, 1265, 1209, 1127, 1064, 1027 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{23}N_2O_6$: 411.1551, found: 411.1562. $[\alpha]_D^{25}$ = +50.00 (c = 0.02, CH_2Cl_2); HPLC analysis: *ee* for major diastereomer = >99% [Daicel CHIRALCEL AD-H column, hexane/iPrOH = 92:8, flow rate: 1 mL/min, λ = 254 nm, t_R= 10.62 min (major), 12.64 min (minor)].



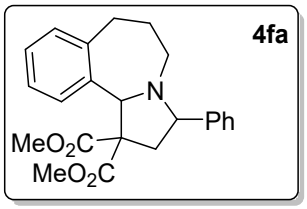
Dimethyl (3R,10bR)-7-nitro-3-phenyl-2,3,6,10b-tetrahydropyrro-lo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4ca′′. $[\alpha]_D^{25}$ = -95.00 (c = 0.02, CH_2Cl_2); HPLC analysis: *ee* for major diastereomer = >99% ee [Daicel CHIRALCEL AD-H column, hexane/iPrOH = 92:8, flow rate: 1 mL/min, λ = 254 nm, t_R= 11.53 min (major), 10.03 min (minor)].



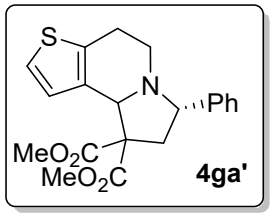
Dimethyl 8-bromo-3-phenyl-2,3,6,10b-tetrahydropyrrolo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4da. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.39; thick liquid; yield 71% (62 mg); 1.2:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.37 (m, 3.73H), 7.29-7.26 (m, 4H), 7.25-7.19 (m, 4H), 7.18-7.15 (m, 4H), 5.44 (s, 0.80H), 4.57-4.54 (m, 0.81H), 4.14 (s, 1H), 3.78 (s, 3H), 3.70 (s, 2.44H), 3.45 (t, *J* = 8.5 Hz, 1H), 3.39 (s, 3H), 3.12 (s, 2.41H), 2.97-2.90 (m, 1H), 2.83-2.78 (m, 2.90H), 2.72-2.60 (m, 4H), 2.55-2.51 (m, 1H), 2.30-2.26 (m, 0.87H), 2.22-2.10 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 171.9, 170.8, 170.6, 142.7, 141.2, 139.7, 138.3, 134.6, 133.5, 131.5, 131.2, 130.0, 128.9, 128.7, 128.6, 128.2, 128.1, 127.8, 127.6, 127.3, 120.4, 120.2, 69.6, 66.7, 65.7, 65.6, 65.2, 61.7, 53.0, 52.9, 52.3, 52.0, 45.9, 44.2, 43.5, 43.2, 30.1, 24.7; FT-IR (Neat) 2952, 1729, 1648, 1592, 1482, 1434, 1264, 1212, 1150, 1120, 1092, 1030 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{23}BrNO_4$: 444.0805, found: 444.0804.



Dimethyl 8,9-dimethoxy-3-phenyl-2,3,6,10b-tetrahydropyrrolo-[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 4ea. Analytical TLC on silica gel, 3:7 ethyl acetate/hexane; R_f = 0.32; thick liquid; yield 56% (47 mg); 1.4:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50-7.46 (m, 3.51H), 7.36 (q, *J* = 7.0 Hz, 3.66H), 7.30-7.28 (m, 1.37H), 7.07 (d, *J* = 10.5 Hz, 1.75H), 6.57 (d, *J* = 8.5 Hz, 1.72H), 5.50 (s, 0.70H), 4.66-4.63 (m, 0.74H), 4.23 (s, 1H), 3.86 (s, 2.70H), 3.84 (d, *J* = 5.5 Hz, 10.22H), 3.78 (s, 2.10H), 3.53 (t, *J* = 8.5 Hz, 1H), 3.47 (s, 3H), 3.20 (s, 2.13H), 3.00-2.94 (m, 1H), 2.90-2.72 (m, 6.80H), 2.57 (d, *J* = 14.5 Hz, 1H), 2.31-2.19 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 181.0, 171.0, 170.1, 170.0, 148.5, 147.29, 147.26, 146.9, 142.7, 137.7, 132.4, 128.76, 128.73, 128.5, 128.3, 127.77, 127.76, 127.0, 126.3, 126.0, 117.2, 114.5, 111.1, 109.3, 67.4, 64.1, 59.8, 56.1, 56.0, 55.9, 52.9, 52.7, 52.5, 51.9, 50.0, 47.7, 46.8, 41.8, 35.6, 34.7, 31.7, 31.4, 28.9, 25.3; FT-IR (Neat) 2925, 1732, 1642, 1602, 1514, 1454, 1434, 1342, 1276, 1213, 1090, 1025 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{28}NO_6$: 426.1911, found: 426.1915.

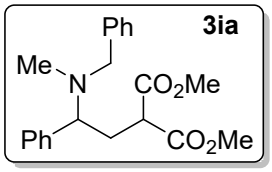


Dimethyl 3-phenyl-2,3,5,6,7,11b-hexahydro-1H-benzo[c]pyrrolo-[1,2-a]azepine-1,1-dicarboxylate 4fa. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.34; thick liquid; yield 63% (47 mg); 2.8:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49-7.46 (m, 3H), 7.43-7.39 (m, 1.14H), 7.36-7.31 (m, 2.81H), 7.28 (t, *J* = 7.5 Hz, 1.18H), 7.17-7.15 (m, 0.77H), 7.13-7.11 (m, 1.73H), 7.10-7.07 (m, 0.54H), 7.03-7.02 (m, 1H), 5.80 (s, 0.35H), 4.80 (s, 1H), 4.50-4.47 (m, 0.37H), 3.79 (s, 3H), 3.75-3.69 (m, 2.25H), 3.66-3.62 (m, 1H), 3.24 (s, 3H), 3.16 (s, 1.04H), 3.12-3.09 (m, 0.33H), 3.06-3.02 (m, 0.40H), 2.83 (dd, *J* = 13.0, 9.0 Hz, 1H), 2.72-2.68 (m, 1.35H), 2.66-2.60 (m, 0.46H), 2.48-2.37 (m, 3.66H), 2.15 (dd, *J* = 13.0, 9.0 Hz, 0.41H), 1.90-1.82 (m, 0.48H), 1.77-1.69 (m, 1.19H), 1.51-1.46 (m, 2H); ^{13}C NMR (150MHz, $CDCl_3$) δ 172.5, 171.5, 171.4, 170.9, 143.0, 142.5, 140.8, 139.1, 138.5, 136.9, 130.37, 130.31, 129.6, 129.0, 128.6, 128.5, 128.0, 127.69, 127.68, 127.5, 127.1, 126.1, 125.8, 76.3, 71.6, 67.2, 64.47, 64.42, 63.3, 52.9, 52.8, 52.2, 52.1, 44.9, 43.5, 43.3, 41.6, 31.5, 30.6, 28.2, 23.6; FT-IR (Neat) 2950, 1731, 1637, 1493, 1449, 1434, 1356, 1265, 1228, 1199, 1095, 1060 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{26}NO_4$: 380.1856, found: 380.1860.

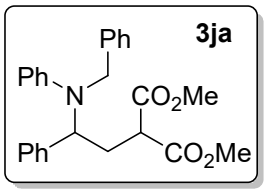


Dimethyl (7*S*,9a*S*)-7-phenyl-4,7,8,9a-tetrahydrothieno[2,3-g]indolizine-9,9(5H)-dicar-boxylate 4ga′. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.36; thick liquid; yield 68% (50 mg); 1.4:1 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.5 Hz, 2H), 7.38 (d, *J* = 7.5 Hz, 1.43H), 7.28 (q, *J* = 7.5 Hz, 3.68H), 7.23-7.19 (m, 1.73H), 6.95-6.94 (m, 2.58H), 6.85 (d, *J* = 5.5 Hz, 1H), 5.37 (s, 0.70H), 4.50-4.47 (m, 0.70H), 4.02 (s, 1H), 3.76 (s, 3H), 3.71 (s, 2.13H), 3.49 (t, *J* = 9.0 Hz, 1H), 3.42 (s, 3H), 3.29 (s, 2.12H), 2.92-2.83 (m, 3H), 2.81-2.47 (m, 6.90H), 2.26-2.21 (m, 1H), 2.16-2.12 (m, 0.74H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.3, 171.7, 170.9, 170.4, 142.7, 141.7, 136.1, 136.0, 133.2, 133.0, 128.68, 128.65, 128.2, 127.7, 127.5, 127.4, 126.5, 126.4, 121.2, 121.0, 68.5, 66.5, 64.6, 64.3, 64.2, 61.1, 52.9, 52.8, 52.3, 52.2, 46.5, 44.7, 43.0, 42.4, 26.2, 21.0; FT-IR (Neat) 2950, 1730, 1494, 1434, 1334, 1228, 1198, 1153, 1109, 1028 cm^{-1};

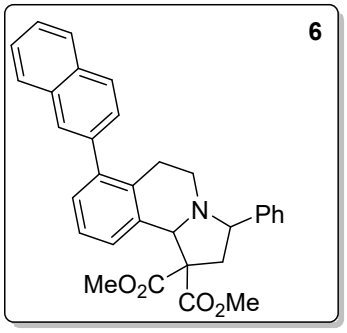
HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{22}NO_4S$: 372.1264, found: 372.1271. $[\alpha]_D^{25}$ = -80.00 (c = 0.02, CH_2Cl_2); HPLC analysis: *ee* for major diasteromer = 99% [Daicel CHIRALCEL AD-H column, hexane/iPrOH = 95:5, flow rate: 1 mL/min, λ = 254 nm, t_R= 07.03 min (major), 08.37 min (minor)].



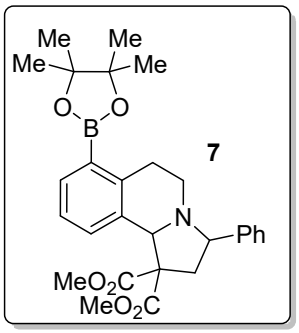
Dimethyl 2-(2-(benzyl(methyl)amino)-2-phenylethyl)malonate 3ia. Analytical TLC on silica gel, 1:20 ethyl acetate/hexane; R_f = 0.32; thick liquid; yield 58% (41 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (t, *J* = 8.0 Hz, 2H), 7.22-7.20 (m, 5H), 7.15 (d, *J* = 7.5 Hz, 3H), 3.65 (s, 3H), 3.60 (s, 3H), 3.59-3.54 (m, 2H), 3.41 (d, *J* = 13.0 Hz, 1H), 3.25 (d, *J* = 13.5 Hz, 1H), 2.66-2.60 (m, 1H), 2.23-2.18 (m, 1H), 1.97 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3, 170.1, 139.7, 137.5, 129.0, 128.9, 128.3, 128.2, 127.6, 127.0, 65.2, 59.2, 52.61, 52.60, 49.6, 36.9, 31.4; FT-IR (Neat) 2952, 1751, 1734, 1494, 1453, 1435, 1263, 1202, 1153, 1062, 1028 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{21}H_{26}NO_4$: 355.1856, found: 355.1846.



Dimethyl 2-(2-(benzyl(phenyl)amino)-2-phenylethyl)malonate 3ja. Analytical TLC on silica gel, 1:20 ethyl acetate/hexane; R_f = 0.39; thick liquid; yield 75% (62 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.17 (m, 5H), 7.14-7.03 (m, 7H), 6.77 (d, *J* = 8.4 Hz, 2H), 6.68 (t, *J* = 7.2 Hz, 1H), 5.06 (t, *J* = 7.6 Hz, 1H), 4.26-4.13 (m, 2H), 3.62 (s, 3H), 3.58 (s, 3H), 3.57-3.55 (m, 1H), 2.55 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 169.8, 149.4, 139.4, 139.2, 129.1, 128.6, 128.4, 127.9, 127.7, 127.0, 126.6, 118.7, 116.3, 61.0, 52.77, 52.72, 50.0, 49.1, 31.1; FT-IR (Neat) 2955, 1733, 1596, 1501, 1454, 1436, 1331, 1271, 1222, 1152 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{26}H_{28}NO_4$: 418.2013, found: 418.2010.



Dimethyl 7-(naphthalen-2-yl)-3-phenyl-2,3,6,10b-tetrahydro-pyrrolo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 6. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.43; thick liquid; yield 84% (82 mg); 1:1.2 mixture of diastereomers; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80-7.75 (m, 6H), 7.70 (d, *J* = 16.5 Hz, 2H), 7.48 (dd, *J* = 7.0, 2.5 Hz, 1H), 7.44-7.40 (d, *J* = 6.9 Hz, 10H), 7.38 (d, *J* = 8.5 Hz, 1H), 7.27 (q, *J* = 7.5 Hz, 4H), 7.21 (d, *J* = 7.5 Hz, 2H), 7.17-7.14 (m, 2.93H), 7.11 (d, *J* = 7.5 Hz, 0.90H), 5.67 (s, 1H), 4.69-4.65 (m, 1H), 4.33 (s, 0.81H), 3.83 (s, 2.44H), 3.73 (s, 3H), 3.46 (s, 2.41H), 3.12 (s, 3H), 2.91-2.83 (m, 2H), 2.77-2.73 (m, 3H), 2.70-2.66 (m, 2H) 2.61-2.56 (m, 1H), 2.38 (d, *J* = 17.0 Hz, 1H), 2.23 (d, *J* = 16.0 Hz, 1H), 2.15-2.09 (m, 2H); ^{13}C NMR (150MHz, $CDCl_3$) δ 173.1, 171.9, 171.1, 171.0, 143.0, 141.8, 141.2, 139.5, 138.8, 136.2, 135.5, 134.8, 133.7, 133.4, 133.3, 132.46, 132.40, 128.67, 128.62, 128.3, 128.19, 128.15, 128.13, 128.08, 128.05, 127.966, 127.961, 127.93, 127.89, 127.81, 127.7, 127.6, 127.58, 127.56, 127.4, 126.4, 126.3, 126.2, 126.0, 125.9, 125.3, 125.0, 70.6, 66.8, 66.2, 66.1, 65.5, 62.0, 53.0, 52.9, 52.3, 52.1, 46.3, 44.6, 43.9, 43.4, 29.7, 23.3; FT-IR (Neat) 2951, 1731, 1650, 1587, 1334, 1271, 1204, 1060 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{32}H_{30}NO_4$: 492.2169, found: 492.2169.



Dimethyl 3-phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3,6,10b-tetrahydro-pyrrolo[2,1-a]isoquinoline-1,1(5H)-dicarboxylate 7. Analytical TLC on silica gel, 1:24 ethyl acetate/hexane; R_f = 0.44; colorless solid; mp 150-151°C; yield 70% (68 mg); 1.4:1 mixture of diastereomers; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (t, *J* = 7.6 Hz, 1.72H), 7.46-7.39 (m, 5H), 7.29-7.25 (m, 3.70H), 7.22-7.18 (m, 1.71H), 7.05 (q, *J* = 7.6 Hz, 1.79H), 5.56 (s, 0.71H), 4.59 (dd, *J* = 10.0, 5.6 Hz, 0.71H), 4.26 (s, 1H), 3.79 (s, 3H),

3.70 (s, 2.12H), 3.43 (t, J = 8.4 Hz, 1H), 3.34 (s, 3H), 3.04-3.01 (m, 4H), 2.91-2.78 (m, 4H), 2.73-2.67 (m, 3H), 2.64-2.59 (m, 1H), 2.21-2.10 (m, 2H), 1.25 (d, J = 2.4 Hz, 9.27H), 1.23 (s, 11.09H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.1, 172.1, 171.1, 170.9, 143.7, 142.8, 142.3, 141.5, 135.0, 134.5, 134.2, 133.9, 131.1, 129.9, 128.69, 128.64, 128.60, 128.5, 128.29, 128.20, 127.7, 127.5, 124.6, 124.1, 83.57, 83.51, 70.5, 66.9, 66.1, 65.9, 65.3, 62.0, 52.98, 52.90, 52.2, 52.0, 46.4, 44.4, 43.7, 43.3, 30.5, 29.8, 29.7, 25.06, 25.02, 25.01, 24.9, 23.7; FT-IR (Neat) 2953, 2928, 1732, 1586, 1435, 1353, 1271, 1207, 1143, 1062 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{28}H_{35}BNO_6$: 492.2552, found: 492.2543.

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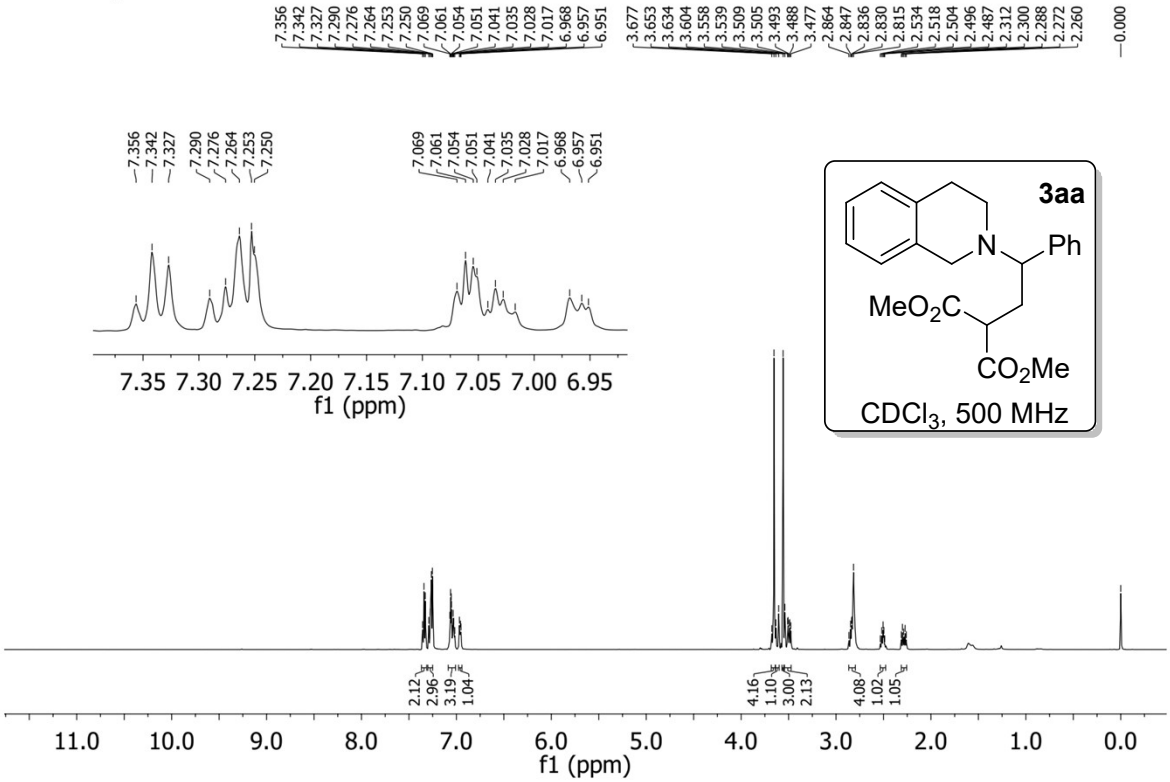
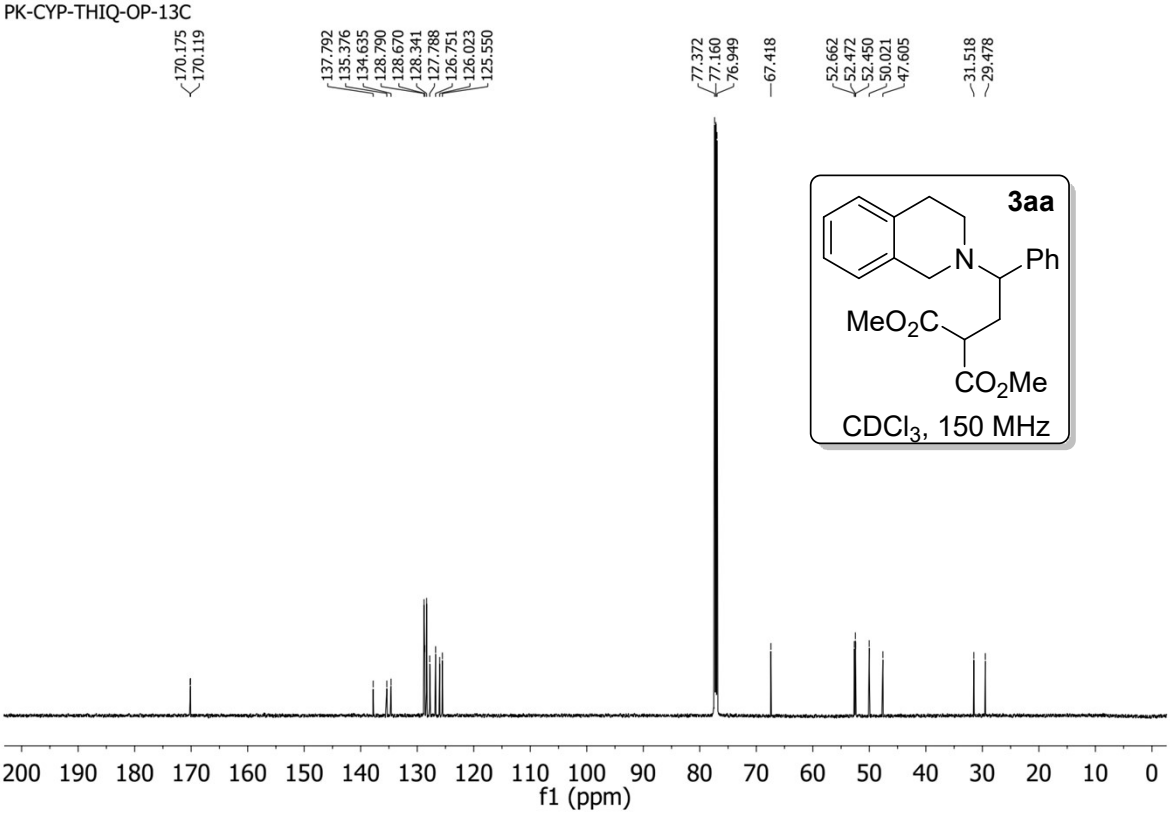
2. For preparation of chiral cyclopropane, see: K. Sapeta and M. A. Kerr, *J. Org. Chem*., 2007, **72**, 8597.
3. F. H. Darras, B. Kling, J. Heilmann and M. Decke, *ACS Med. Chem. Lett*., 2012, **11**, 914.
4. X. Ling, Y. Xiong, R. Huang, X. Zhang, S. Zhang and C. Chen, *J. Org. Chem*., 2013, **78**, 5218.
5. Y. Sun, H. Liu, X. Tan, Z. Li, Y. Du, A. Zheng, X. Liu and N. Peng, *RSC Adv*., 2019, **9**, 1889.

NMR (^{1}H and ^{13}C) Spectra

PK-CYP-THIQ-OP-1H



PK-CYP-THIQ-OP-13C



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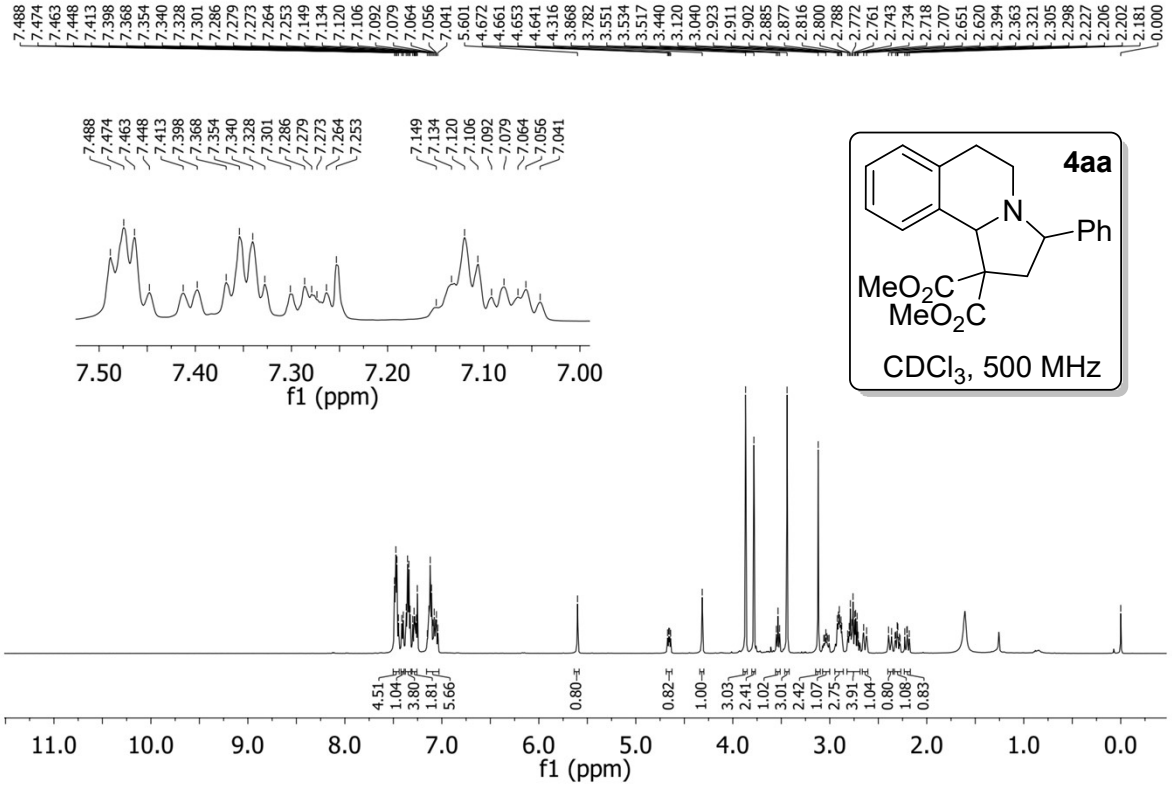

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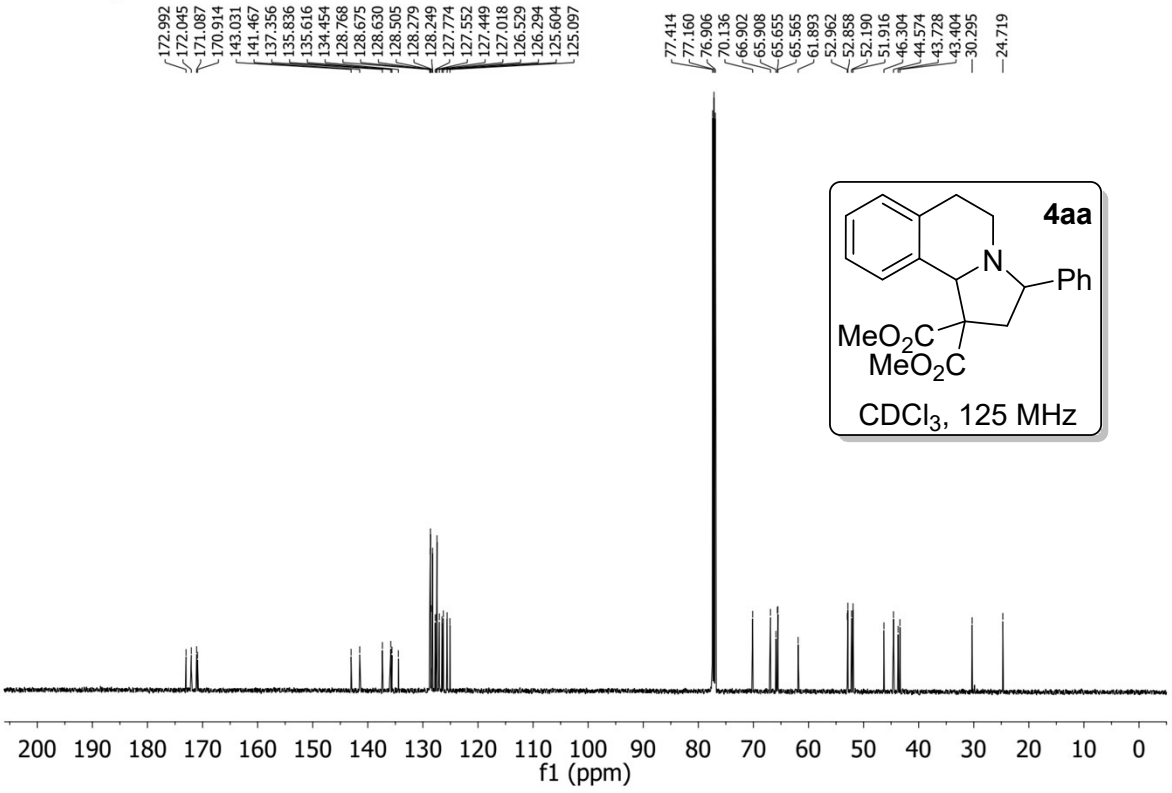

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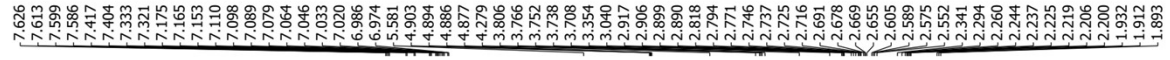

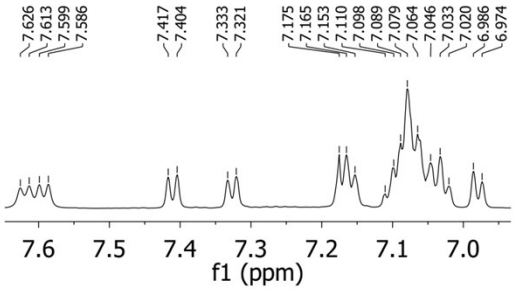

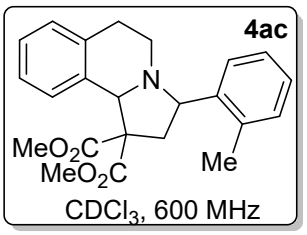

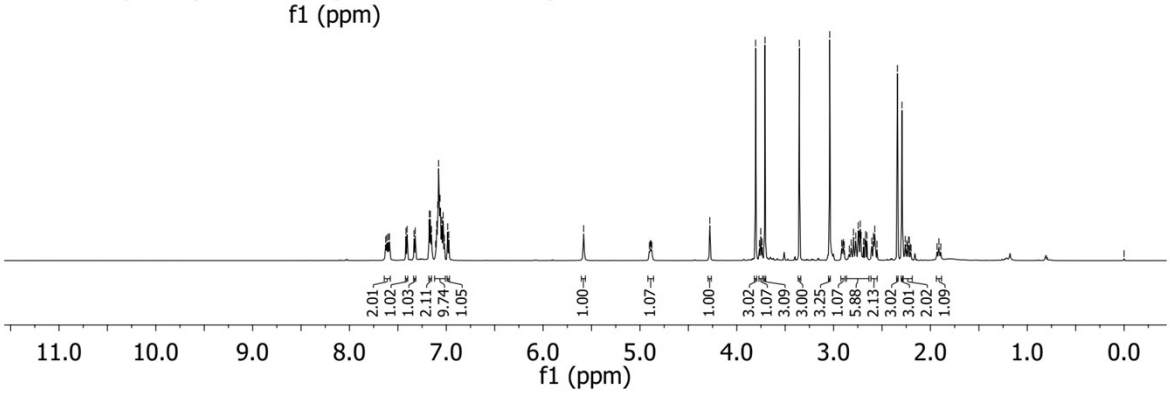

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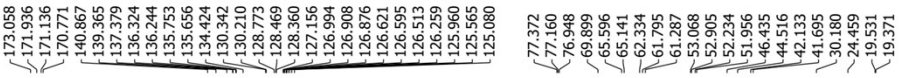

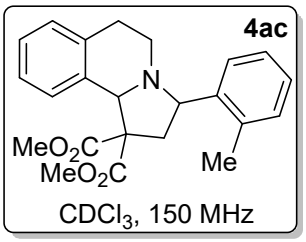

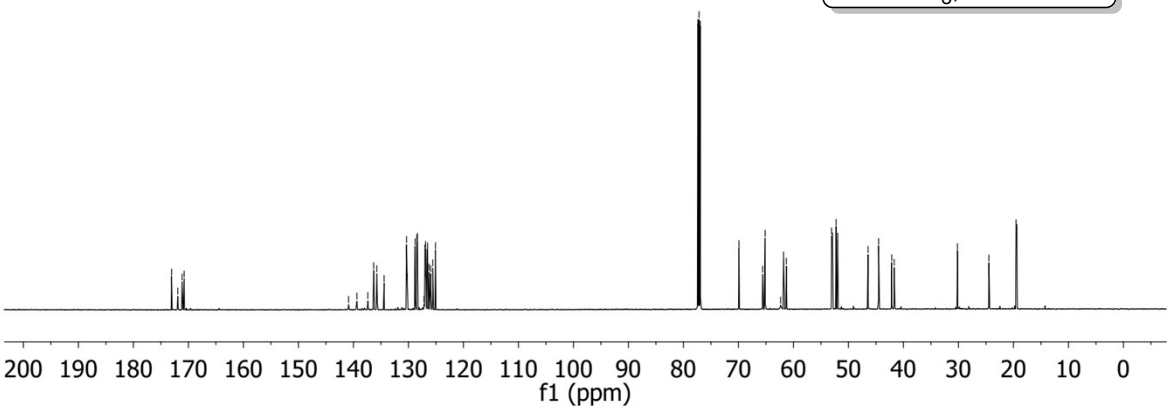

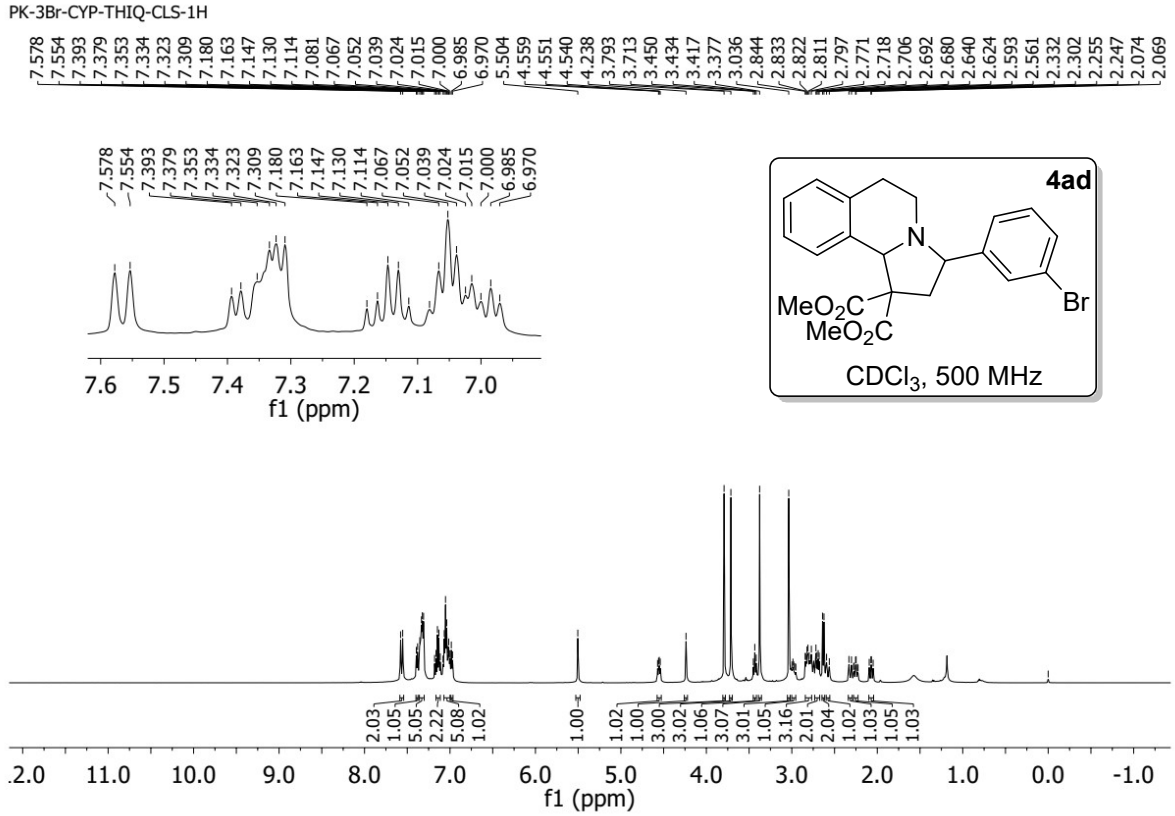
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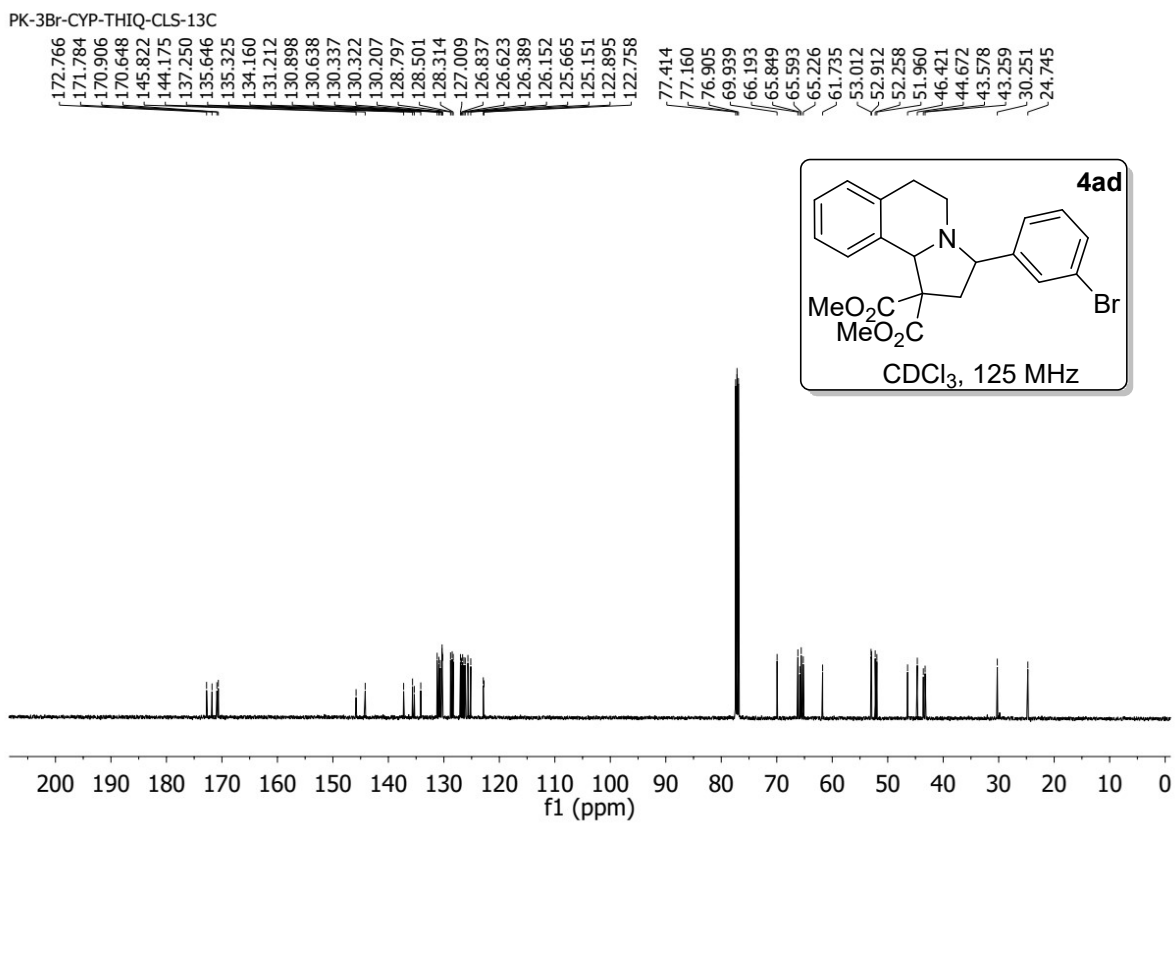
MeO2C
Br
CDCl3, 500 MHz
f1 (ppm)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f1 (ppm)

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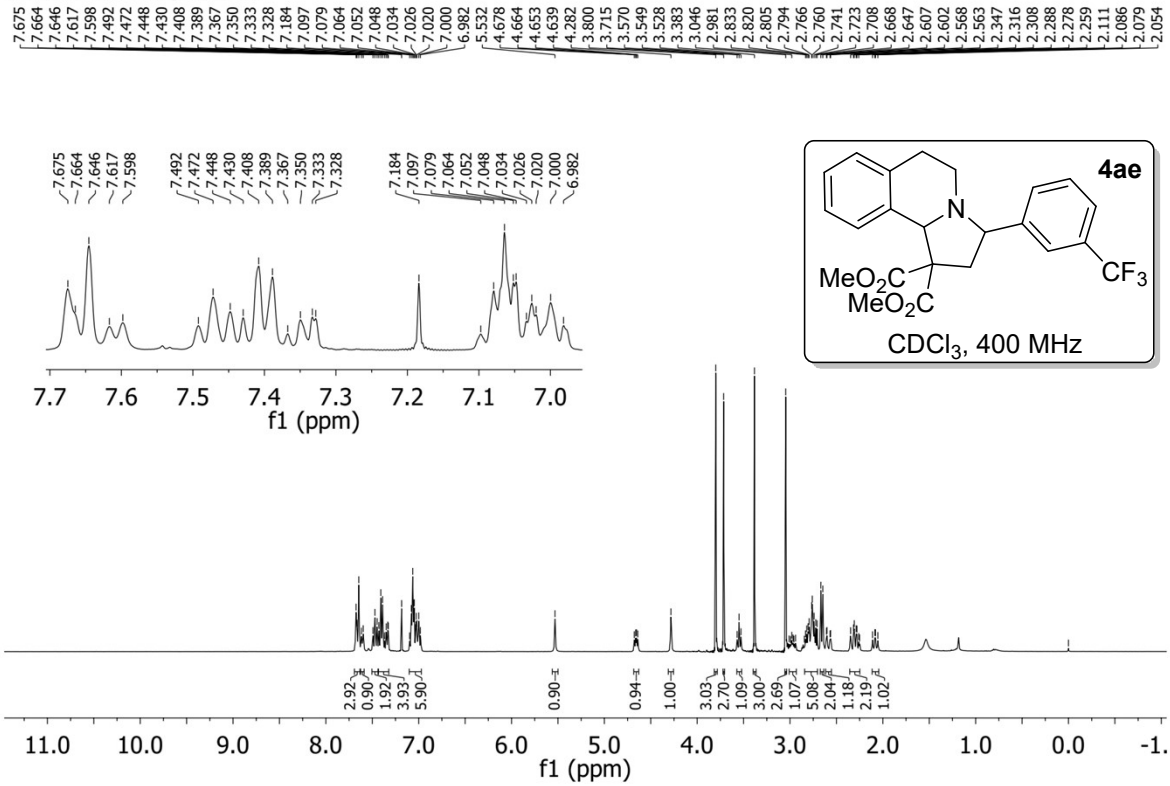

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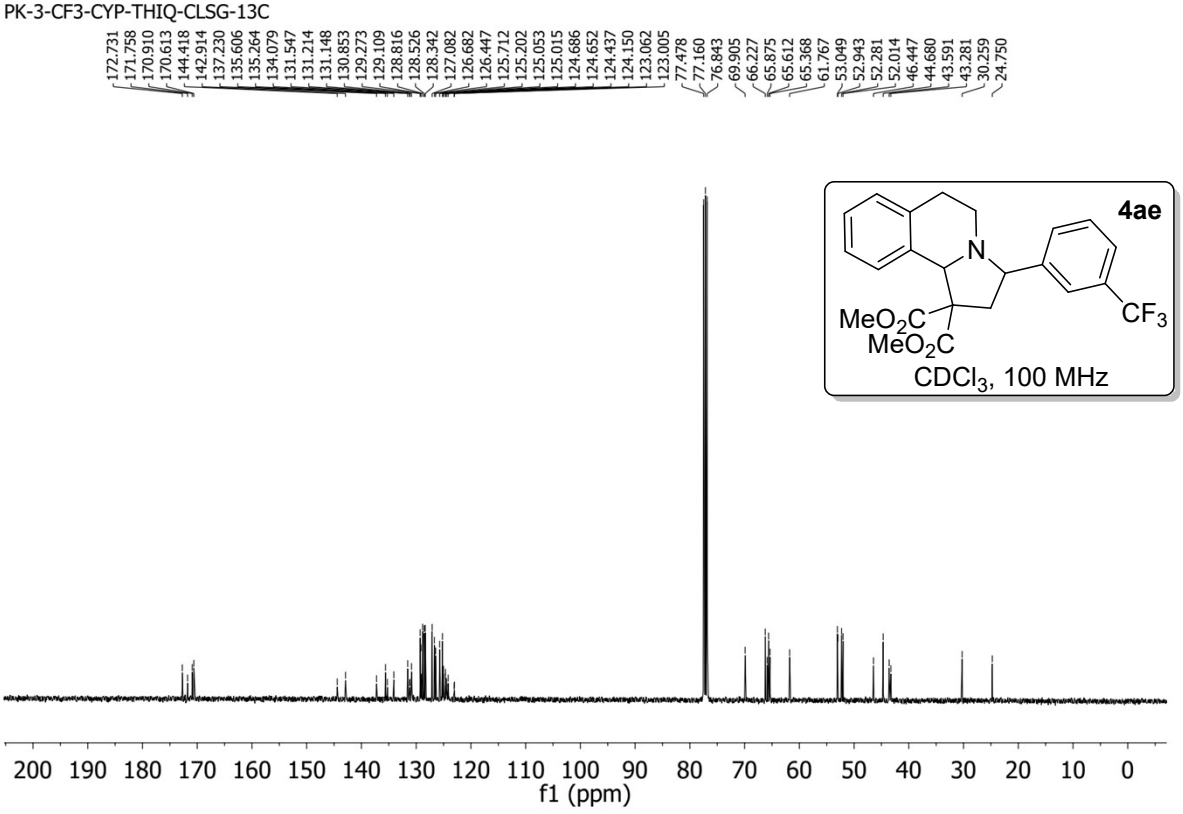

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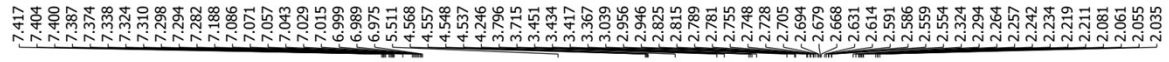

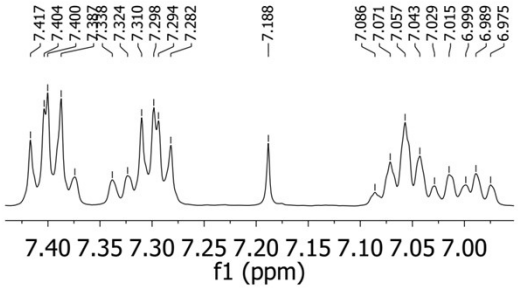

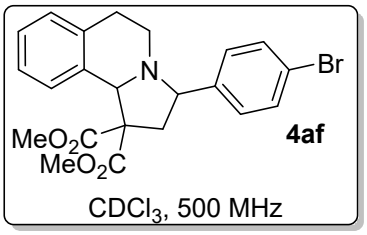

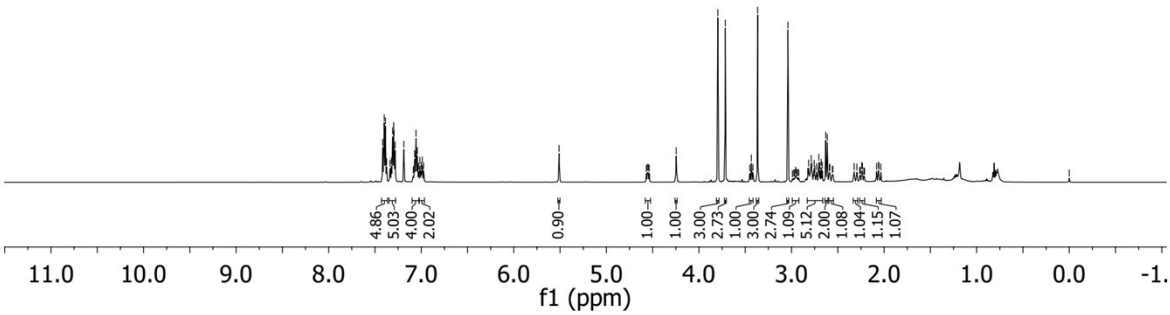

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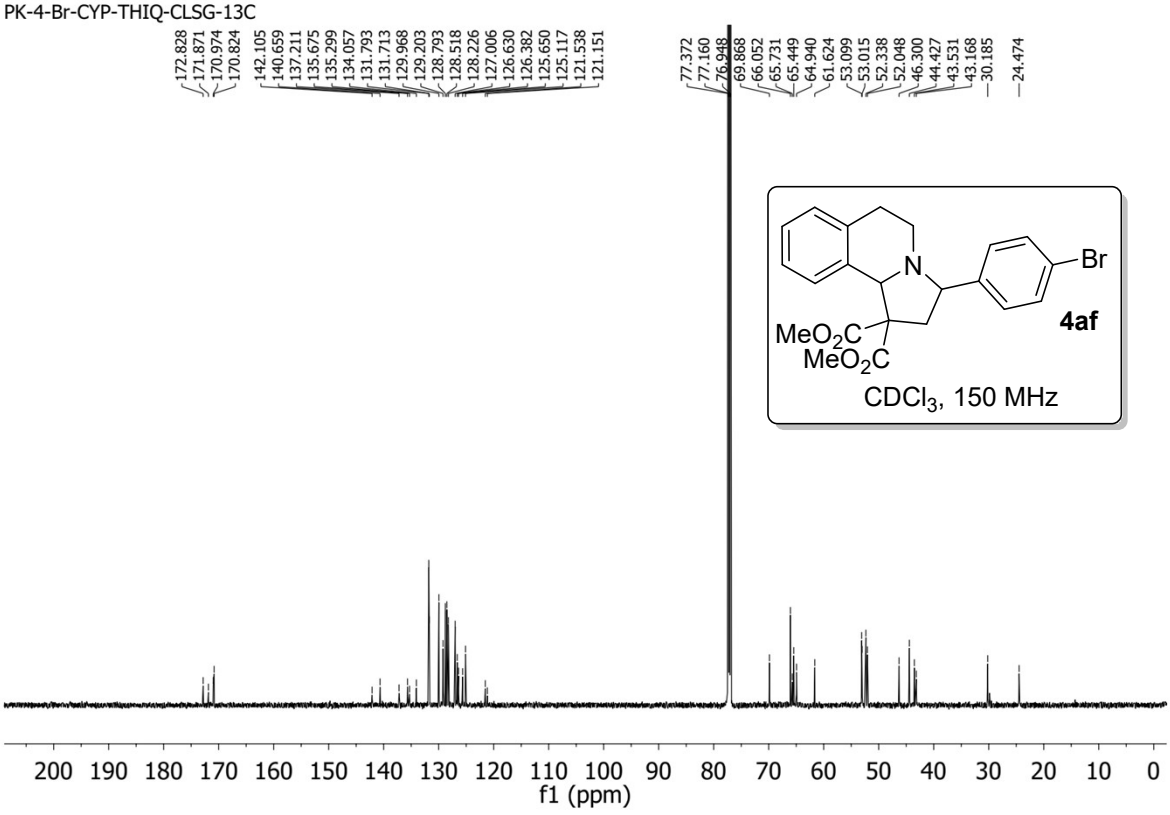

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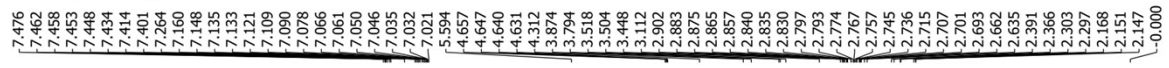

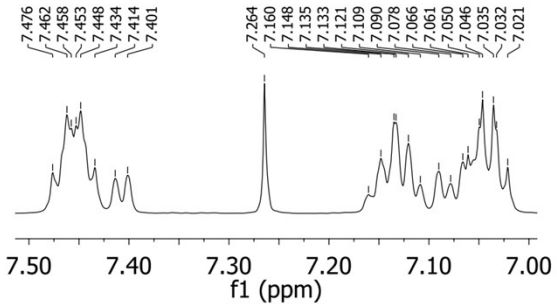

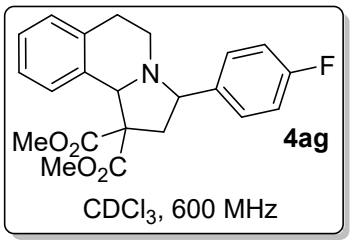

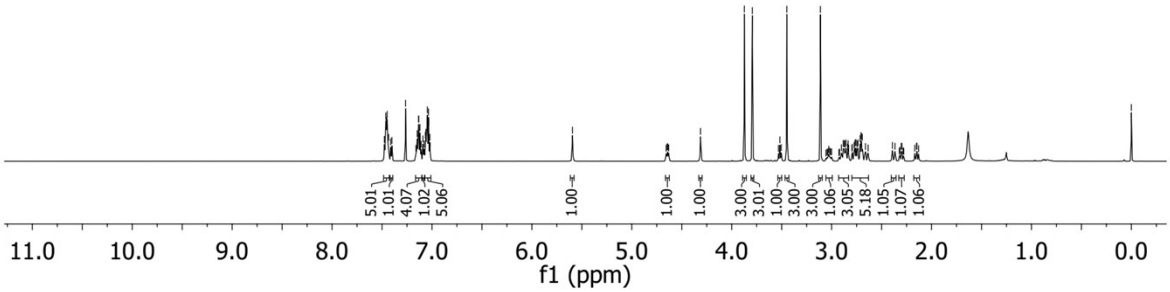

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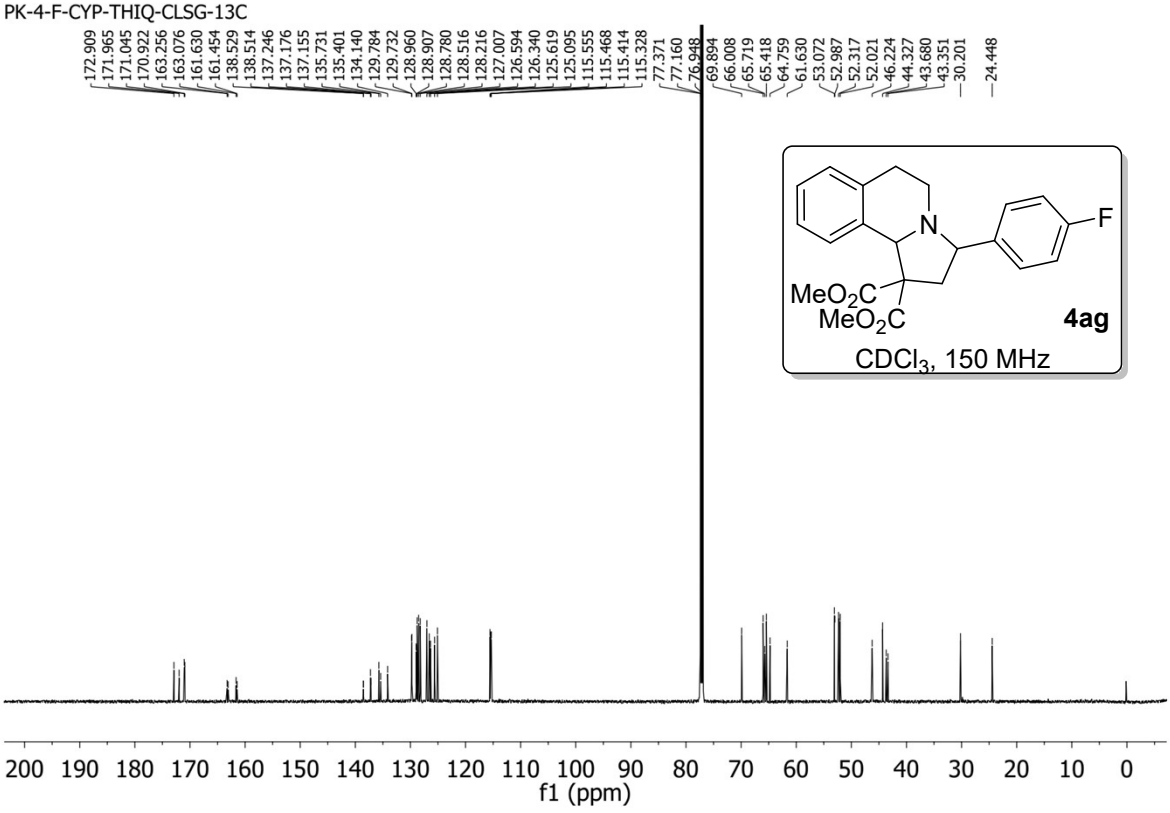

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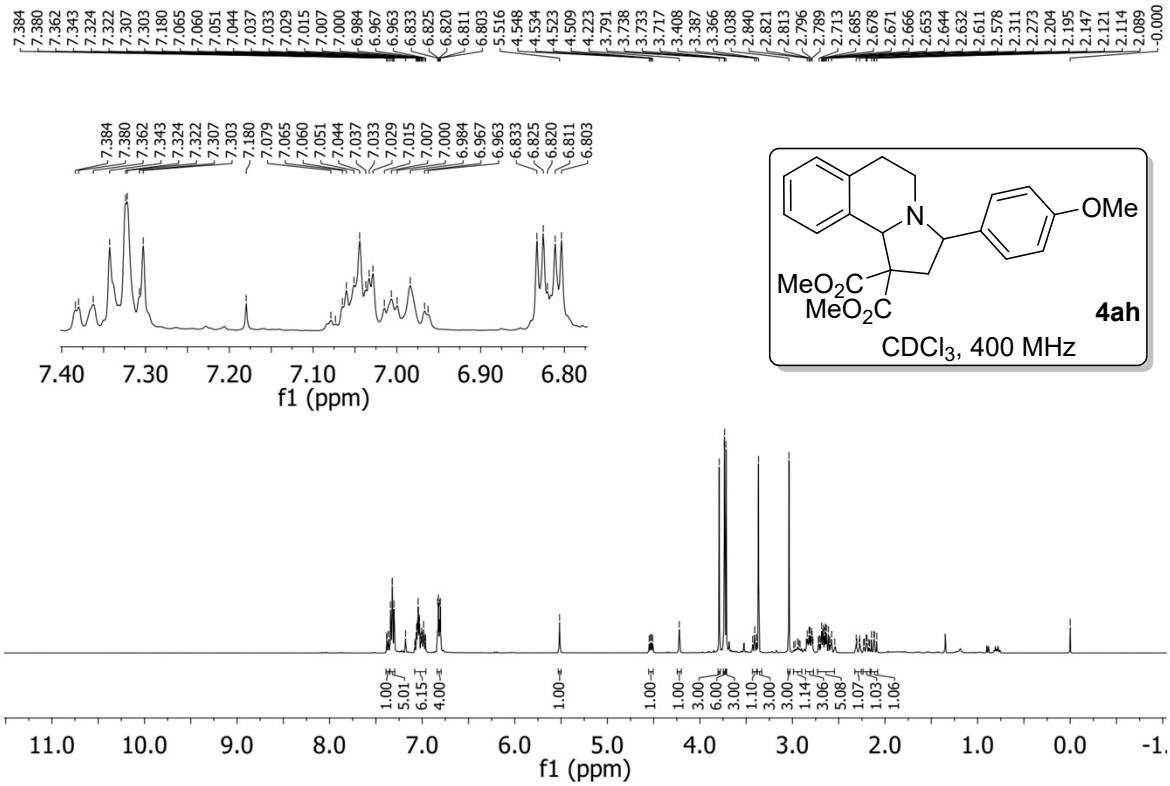

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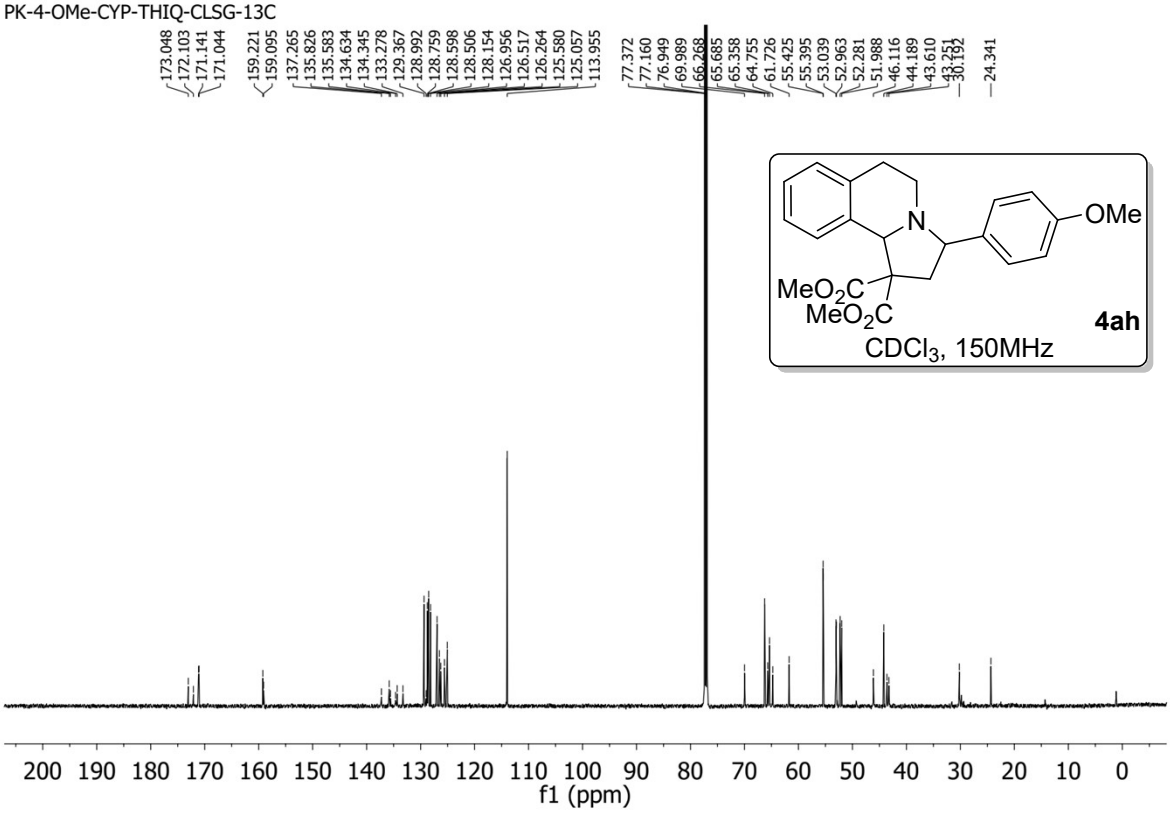

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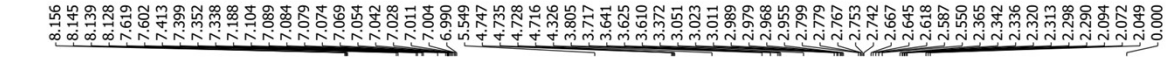

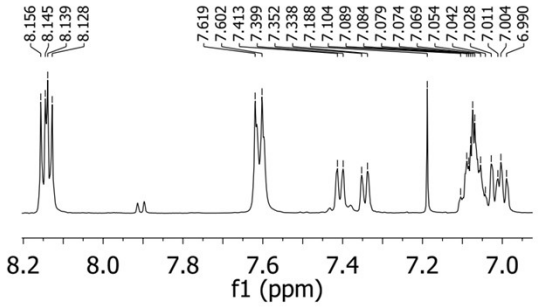

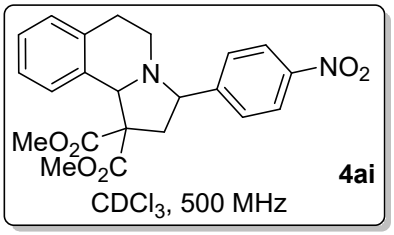

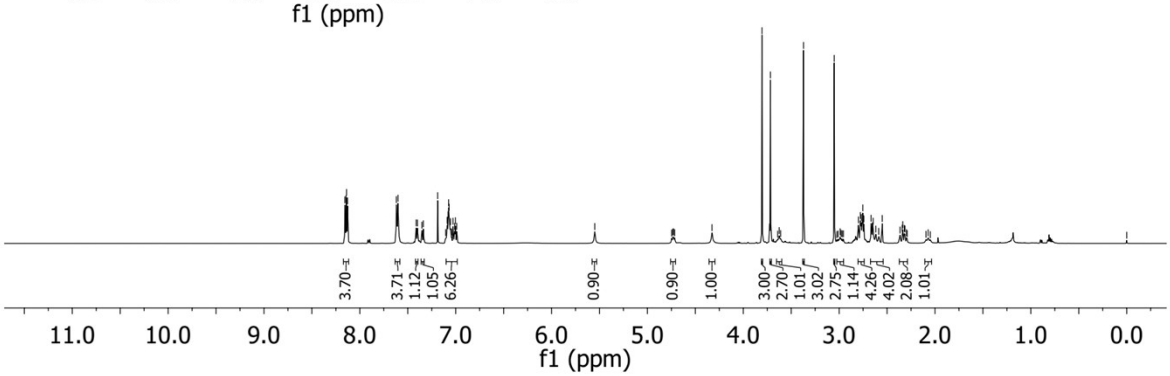

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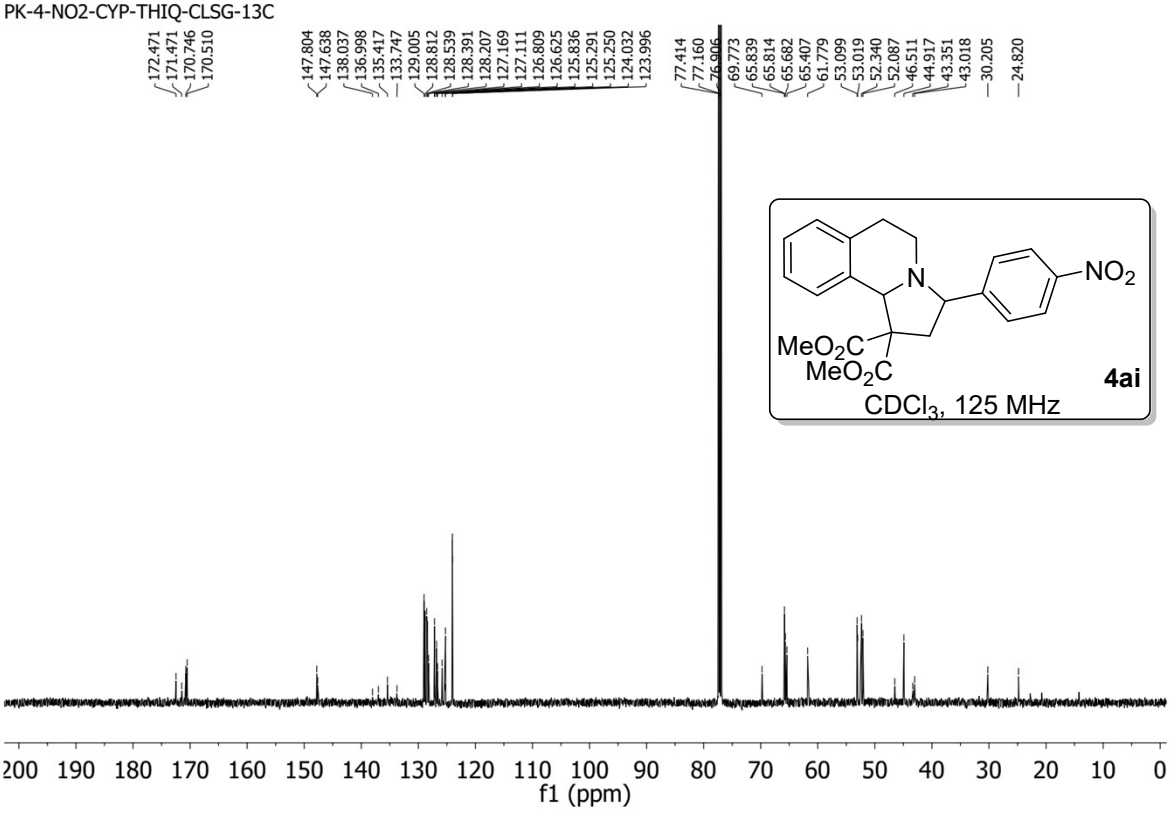

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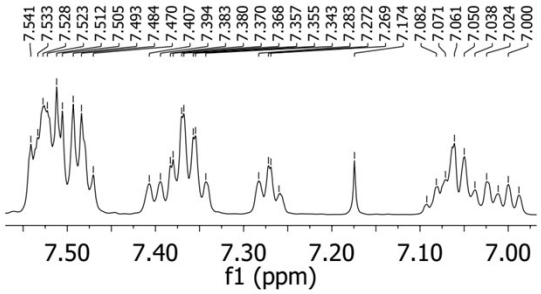

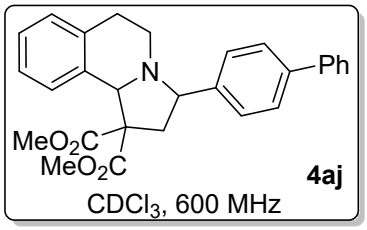

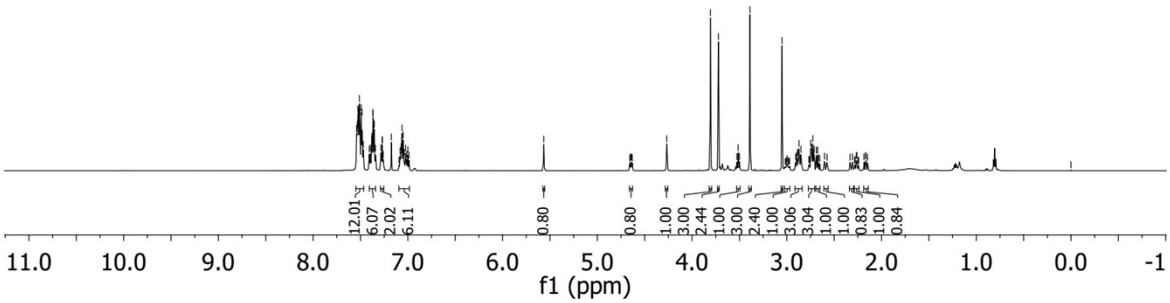

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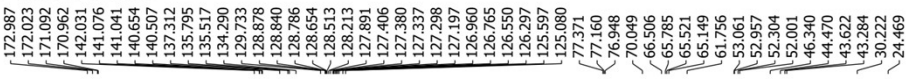

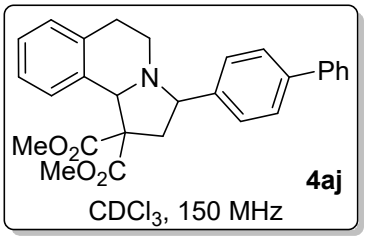

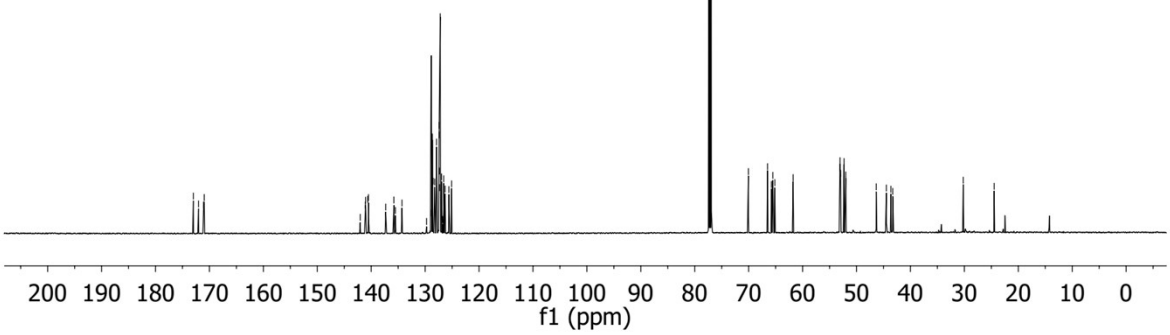

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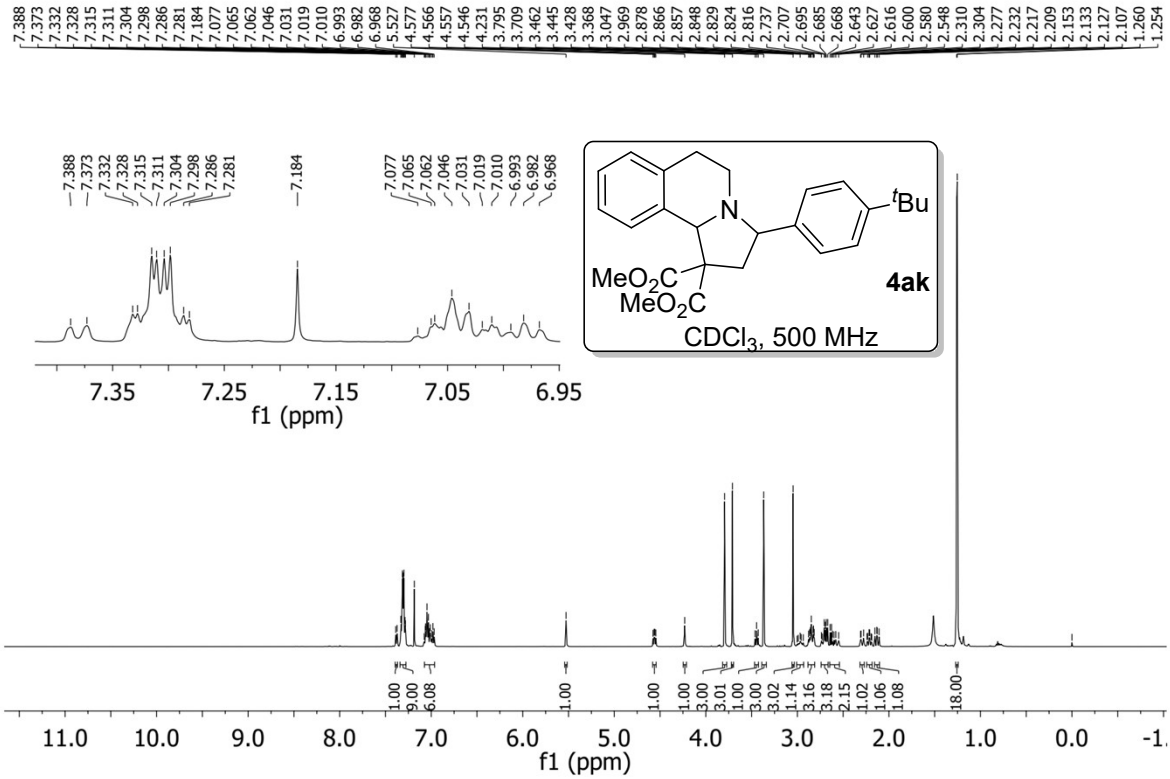

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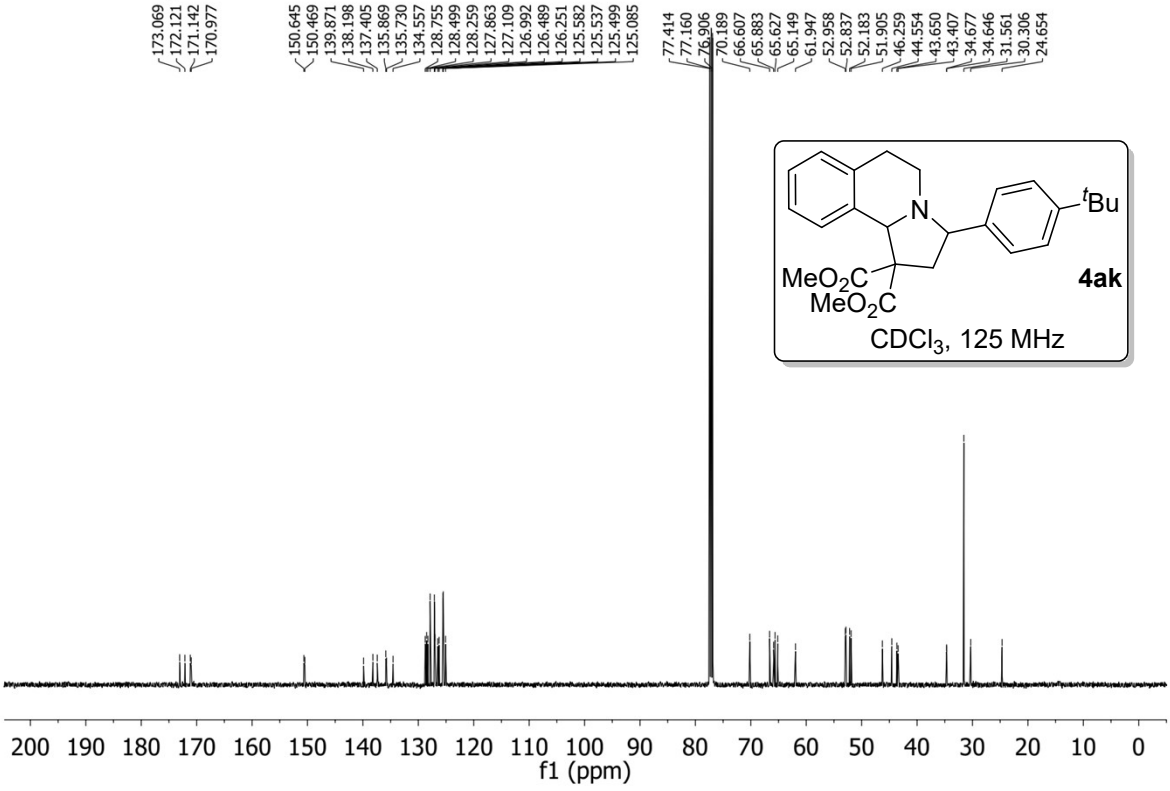

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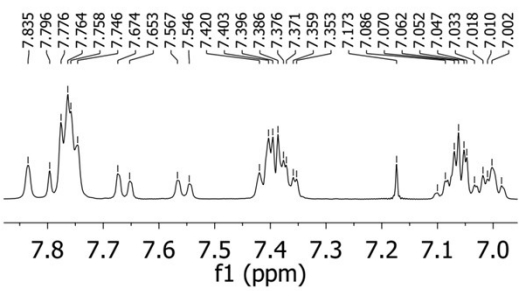
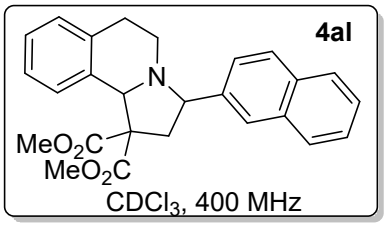
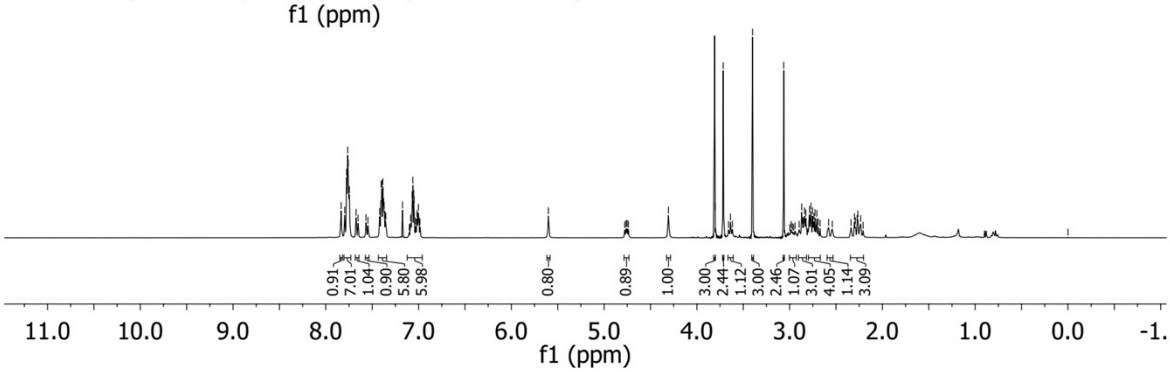
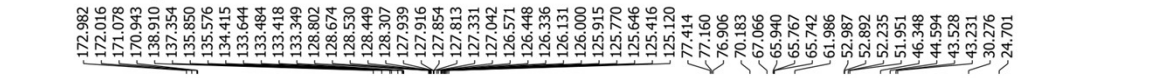
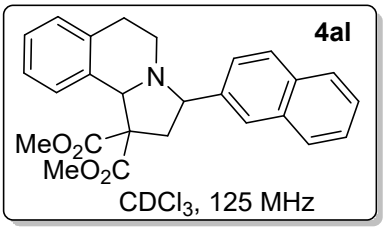




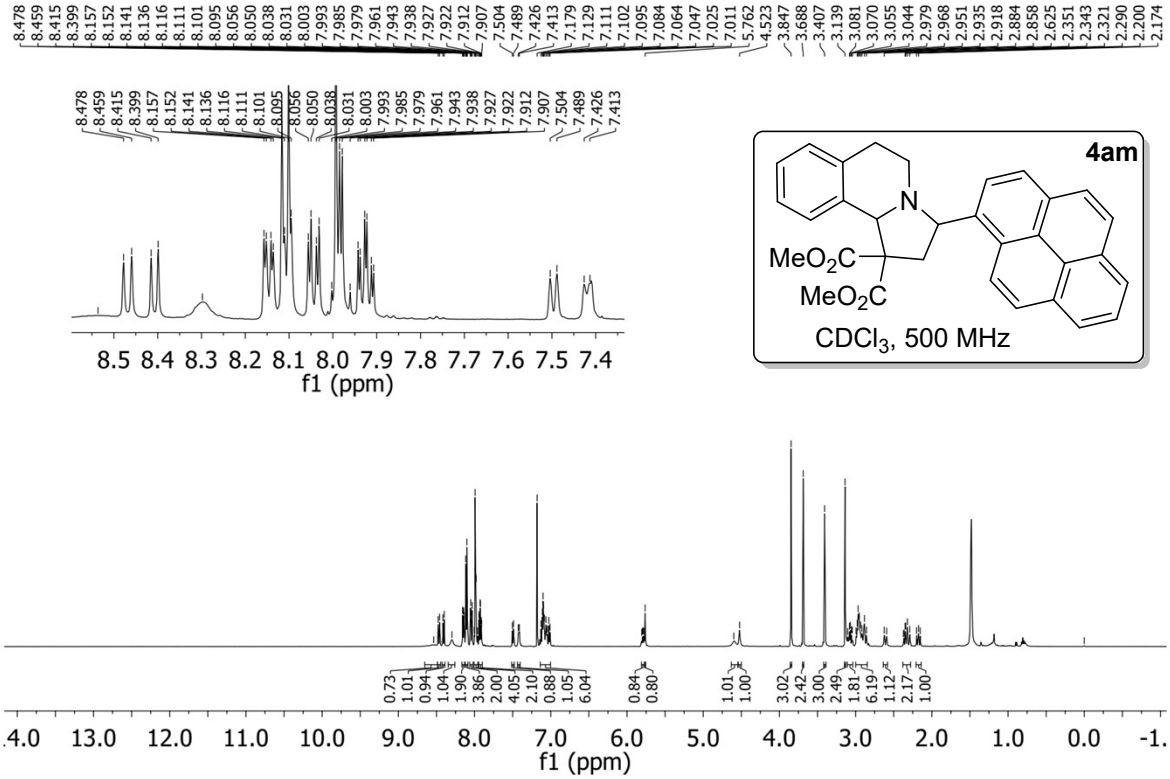


PK-NAP-CYP-THIQ-CLSG-13C

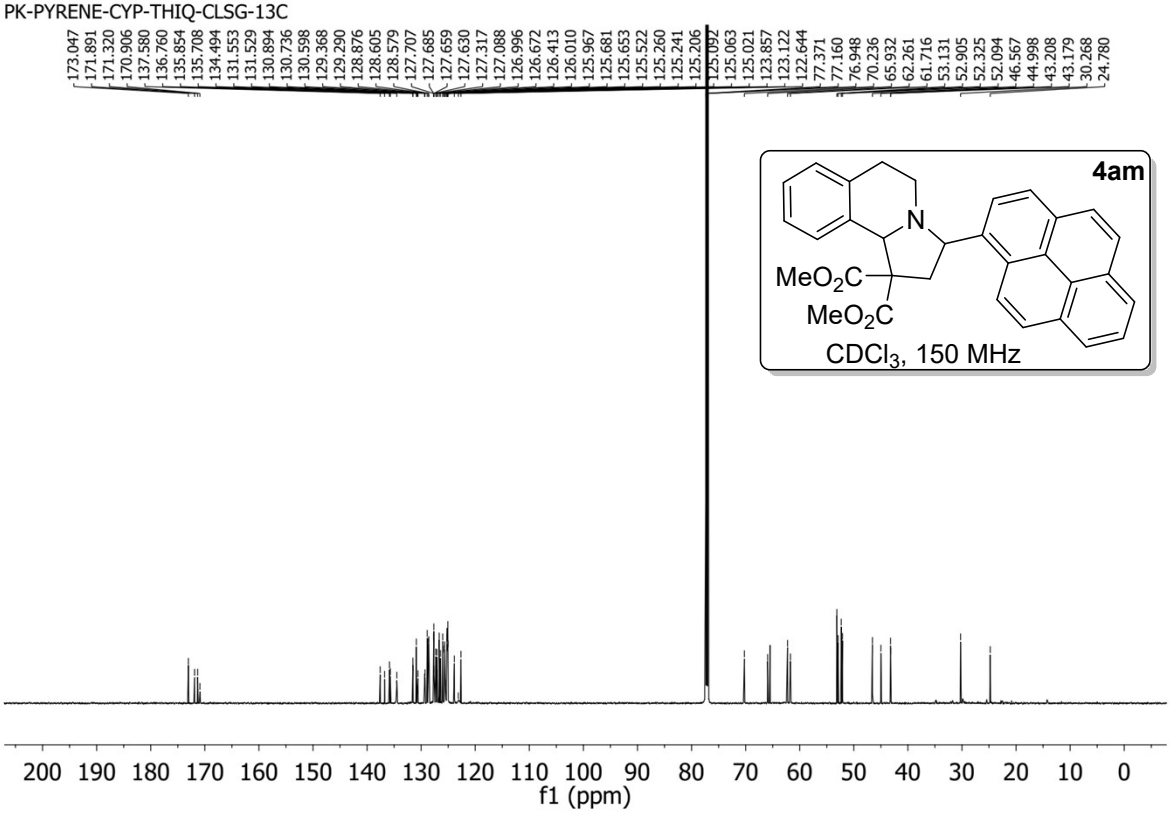




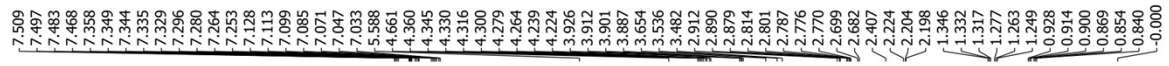
PK-PYRENE-CYP-THIQ-CLSG-1H

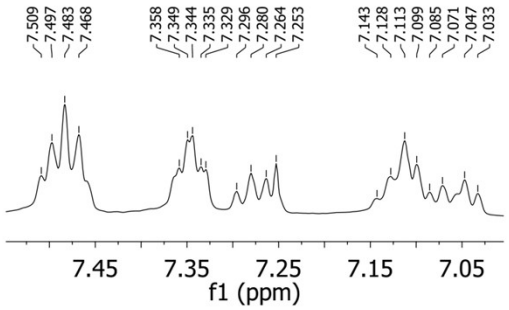


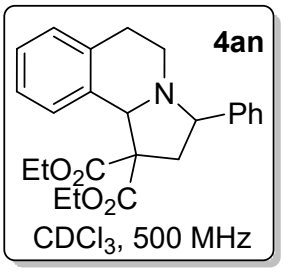
PK-PYRENE-CYP-THIQ-CLSG-13C

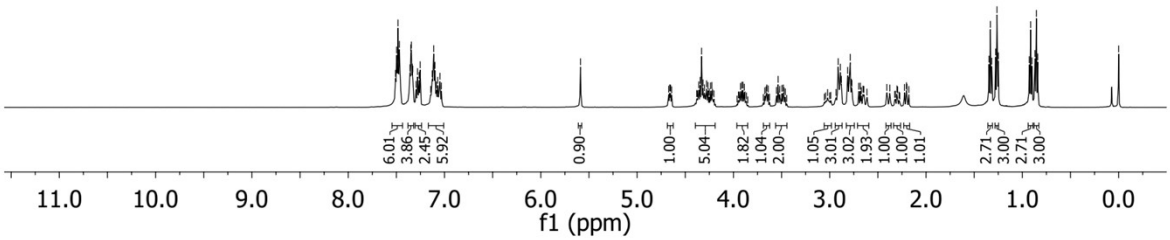


PK-Et-CYP-THIQ-CLSG-1H

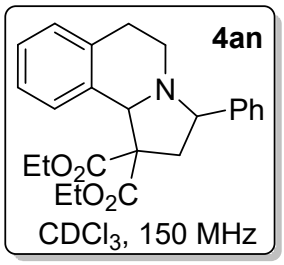


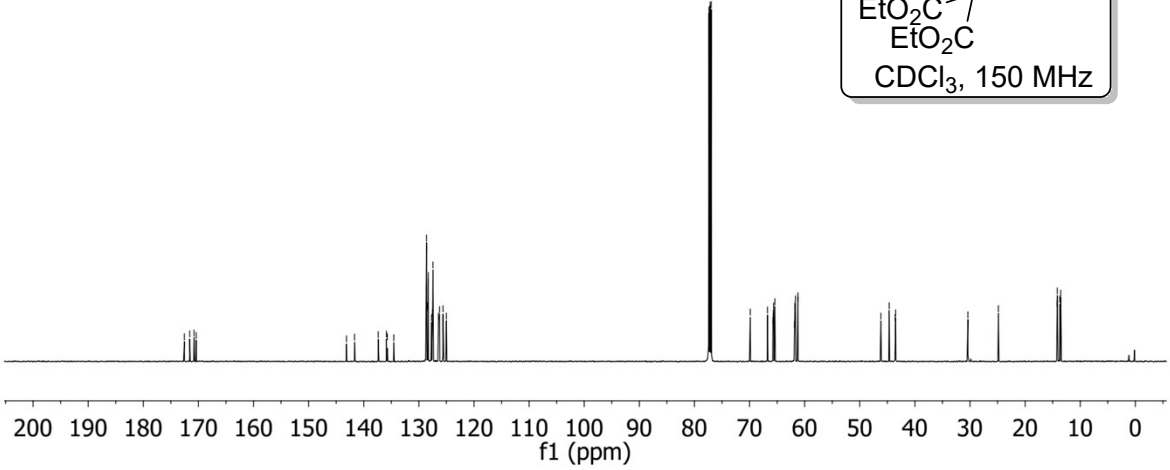


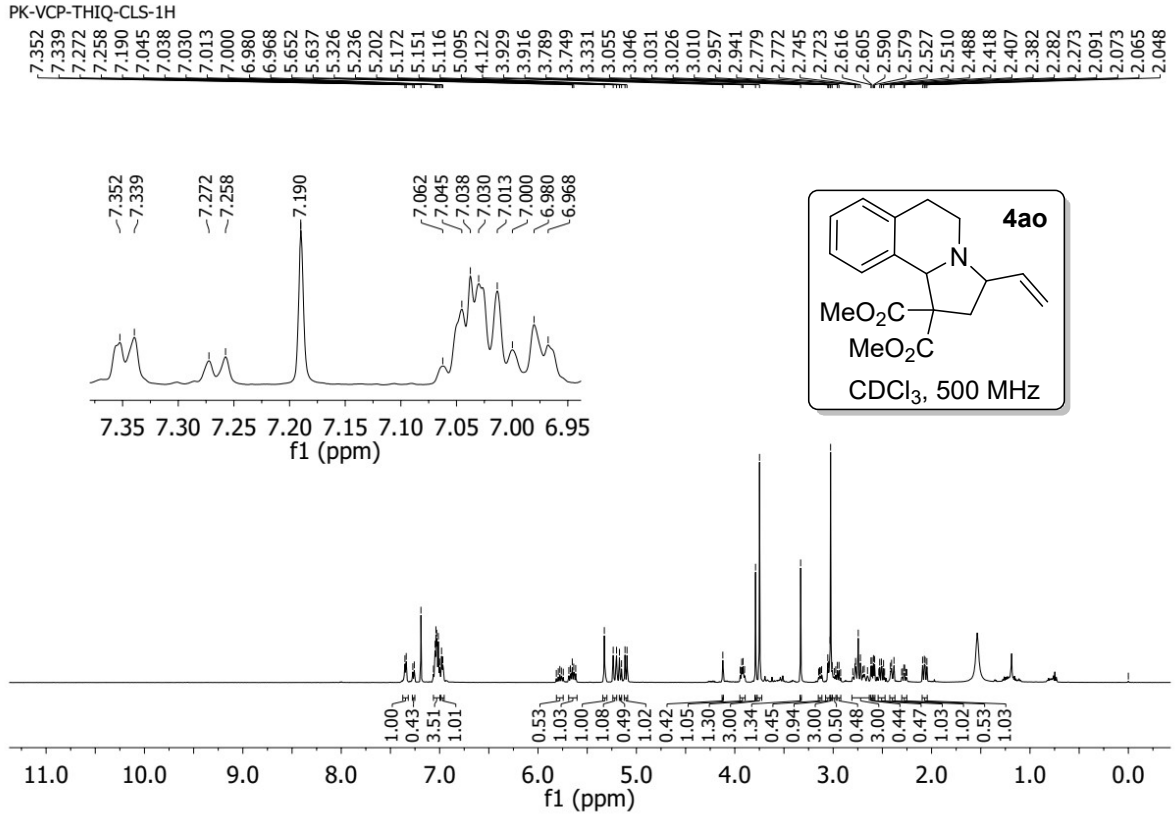


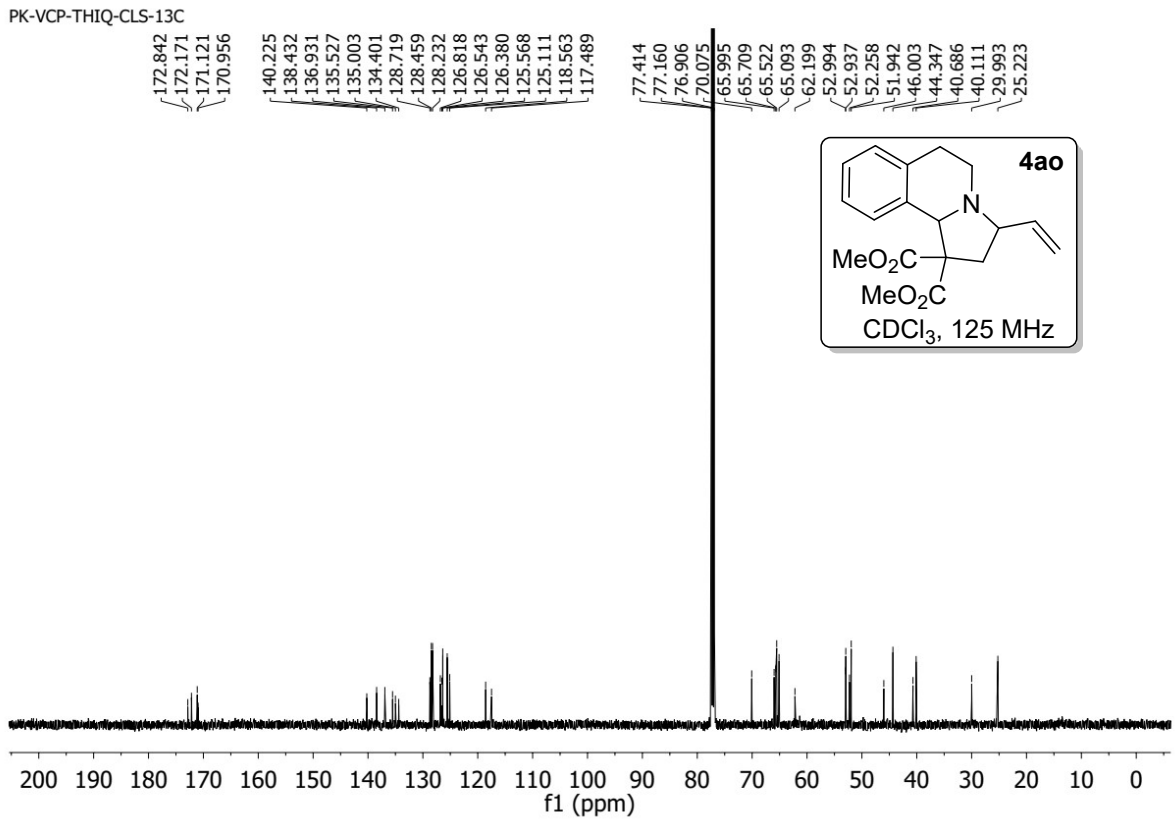


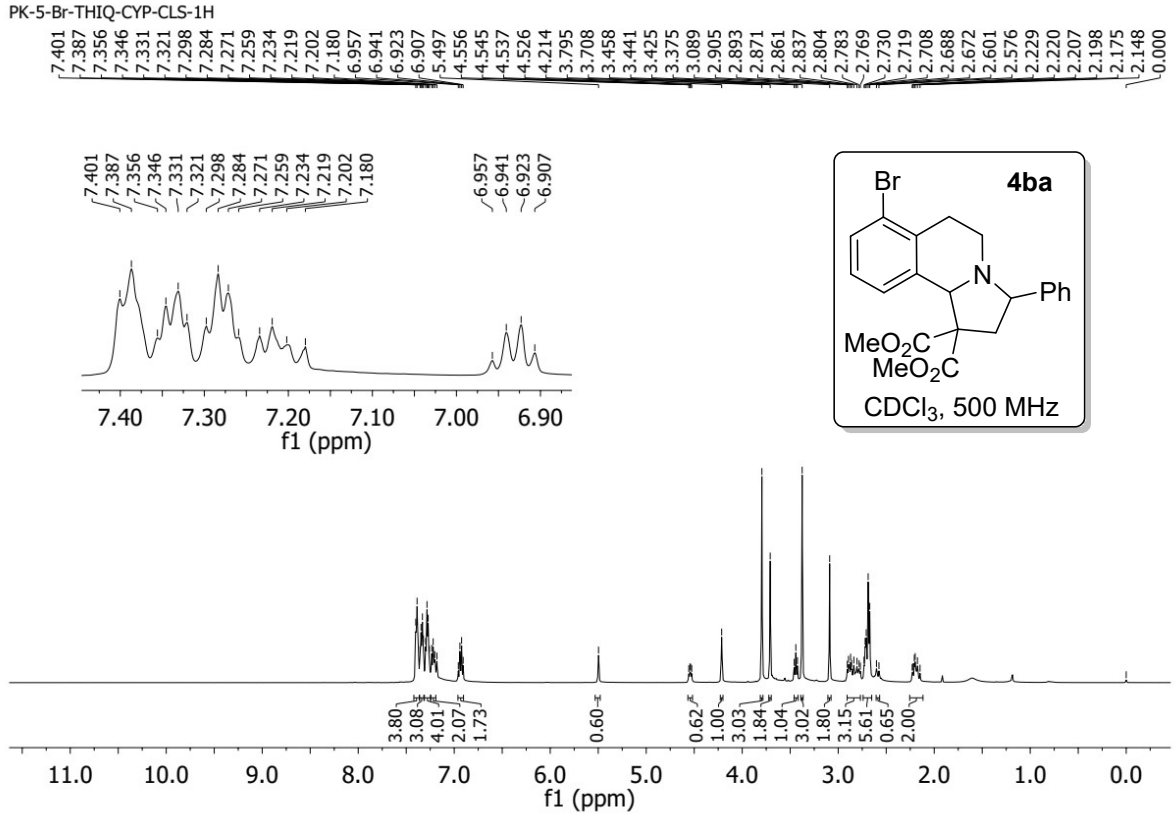
PK-Et-CYP-THIQ-CLSG-13C

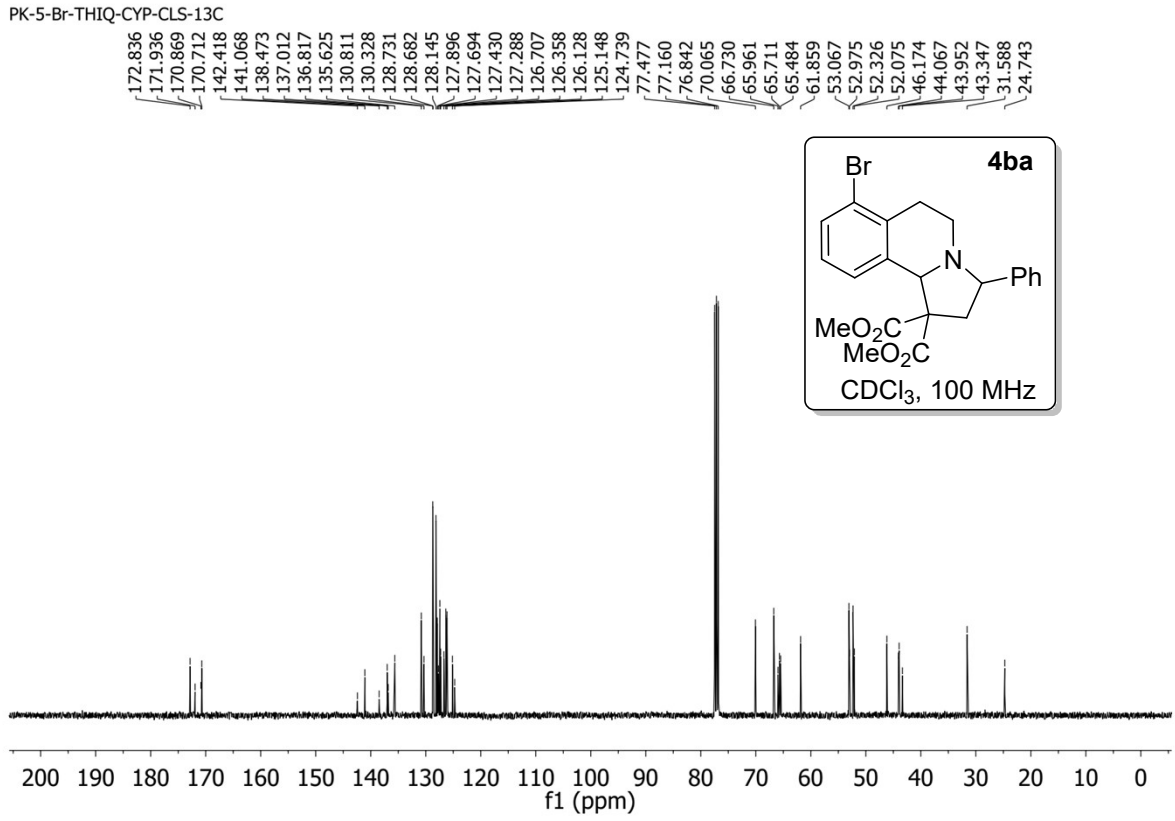




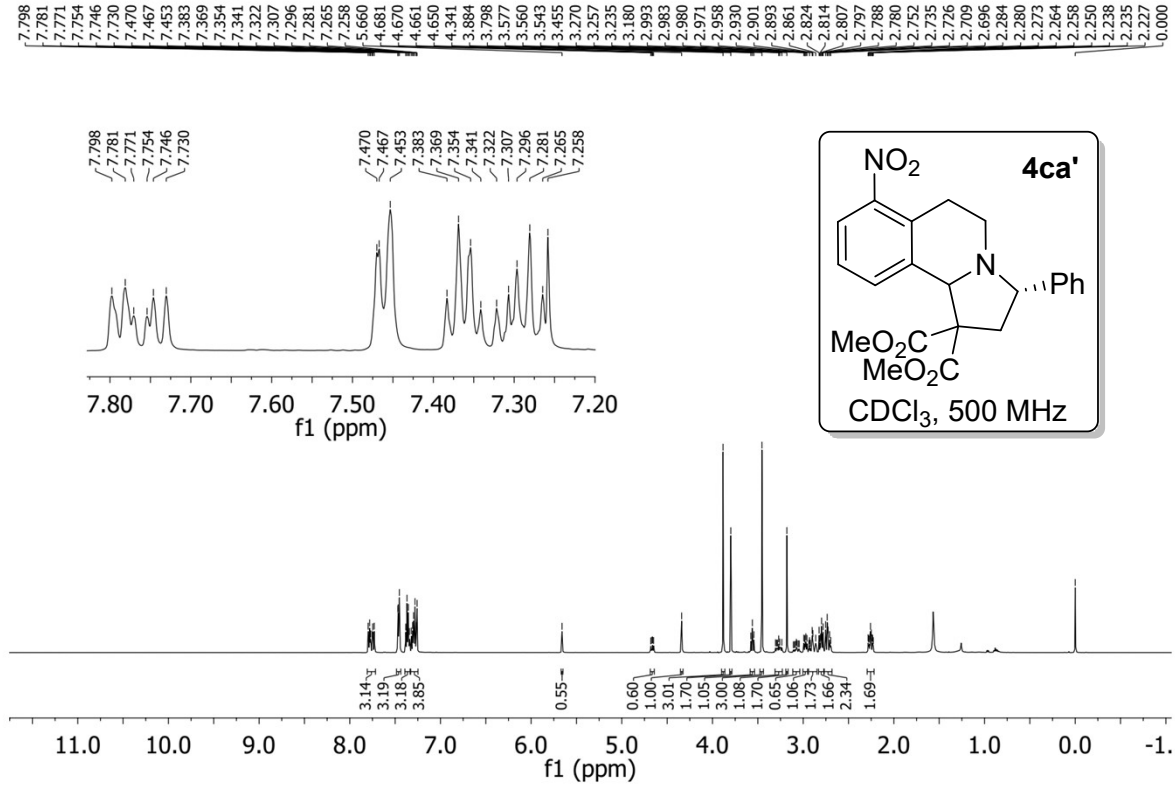

PK-VCP-THIQ-CLS-1H
4ao
MeO2C
MeO2C
CDCl3, 500 MHz
f1 (ppm)


PK-VCP-THIQ-CLS-13C
4ao
MeO2C
MeO2C
CDCl3, 125 MHz
f1 (ppm)

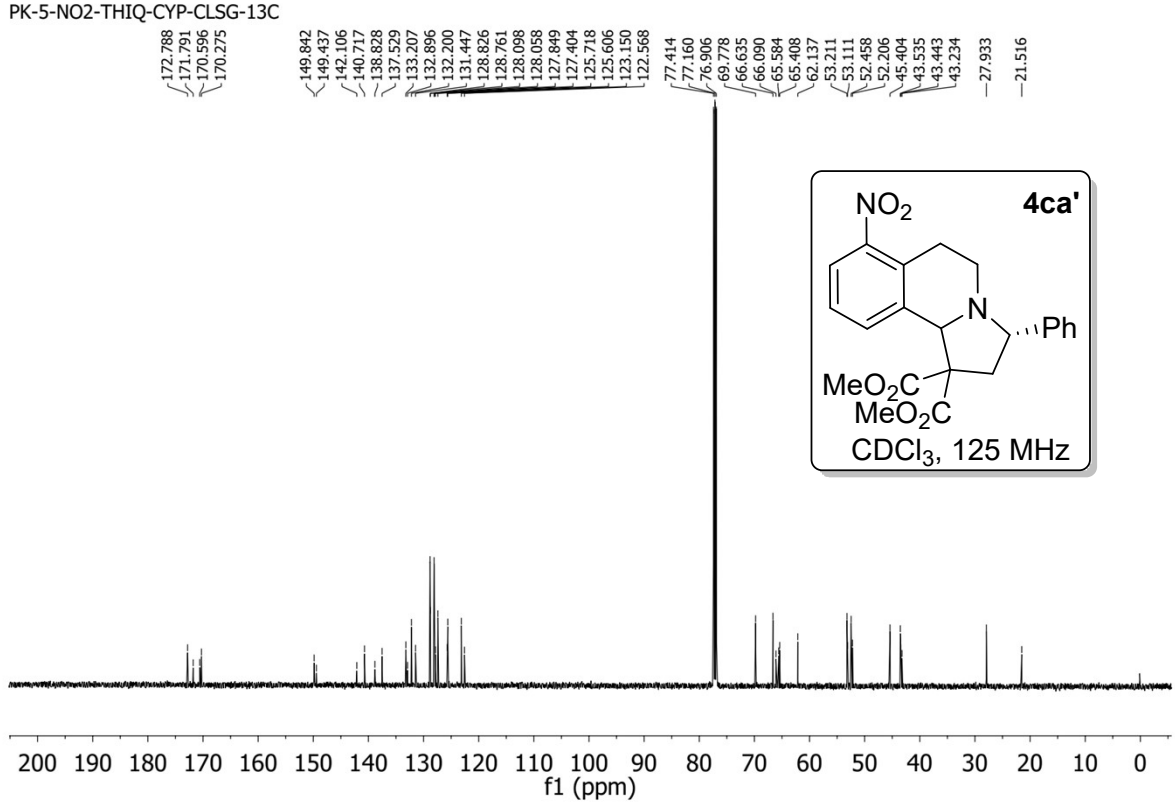

PK-5-Br-THIQ-CYP-CLS-1H
Br
4ba
N
Ph
MeO2C
MeO2C
CDCl3, 500 MHz
f1 (ppm)


PK-5-Br-THIQ-CYP-CLS-13C
Br
4ba
N
Ph
MeO2C
MeO2C
CDCl3, 100 MHz
f1 (ppm)

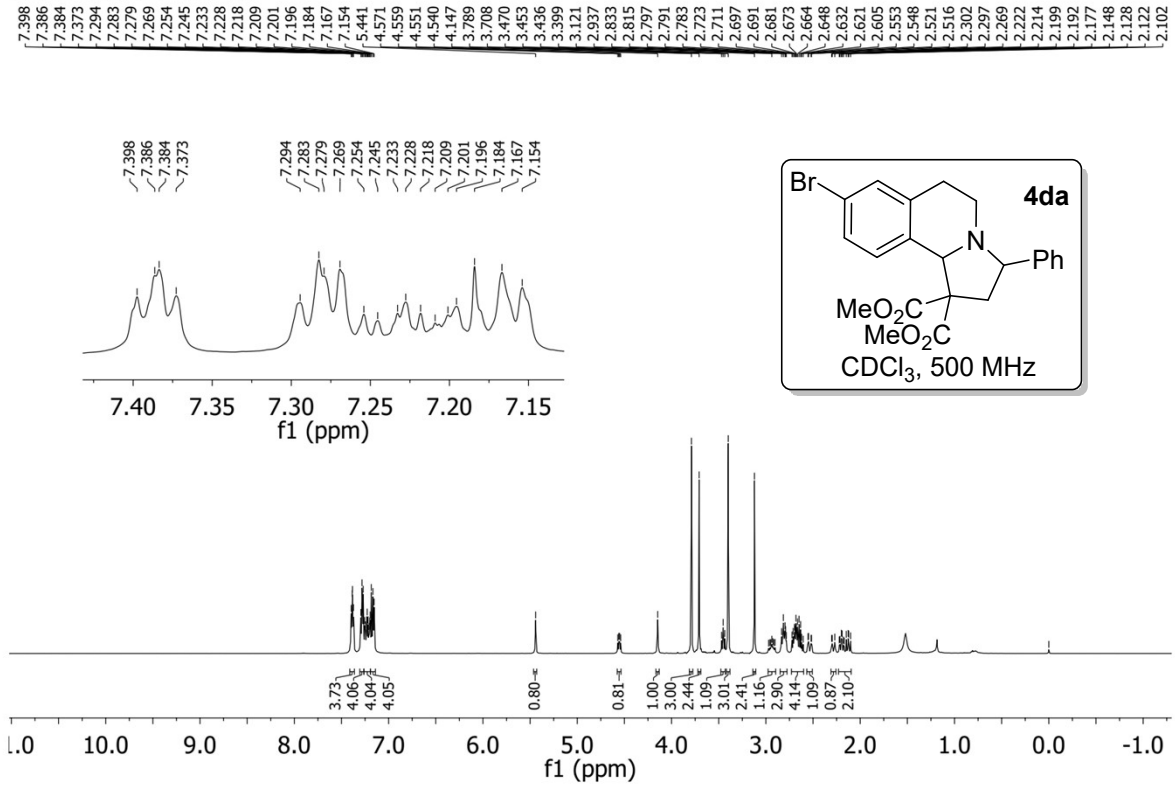
PK-5-NO2-THIQ-CYP-CLSG-1H



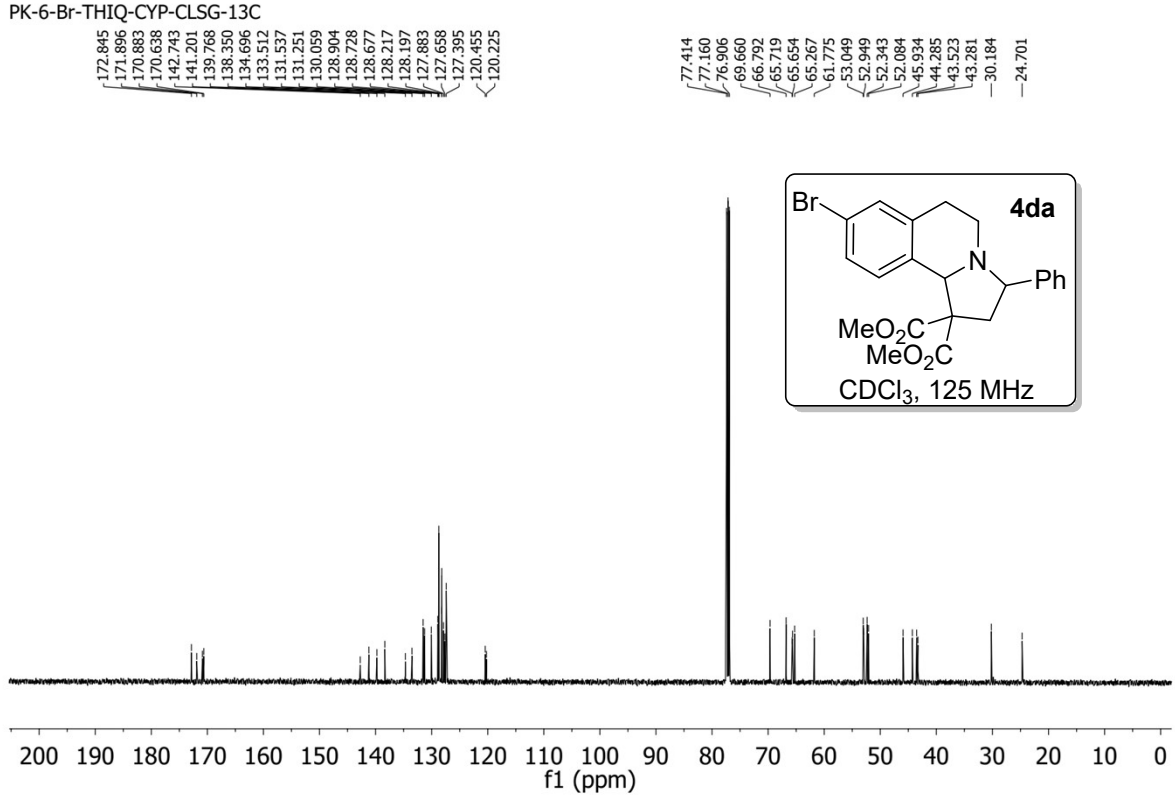
PK-5-NO2-THIQ-CYP-CLSG-13C



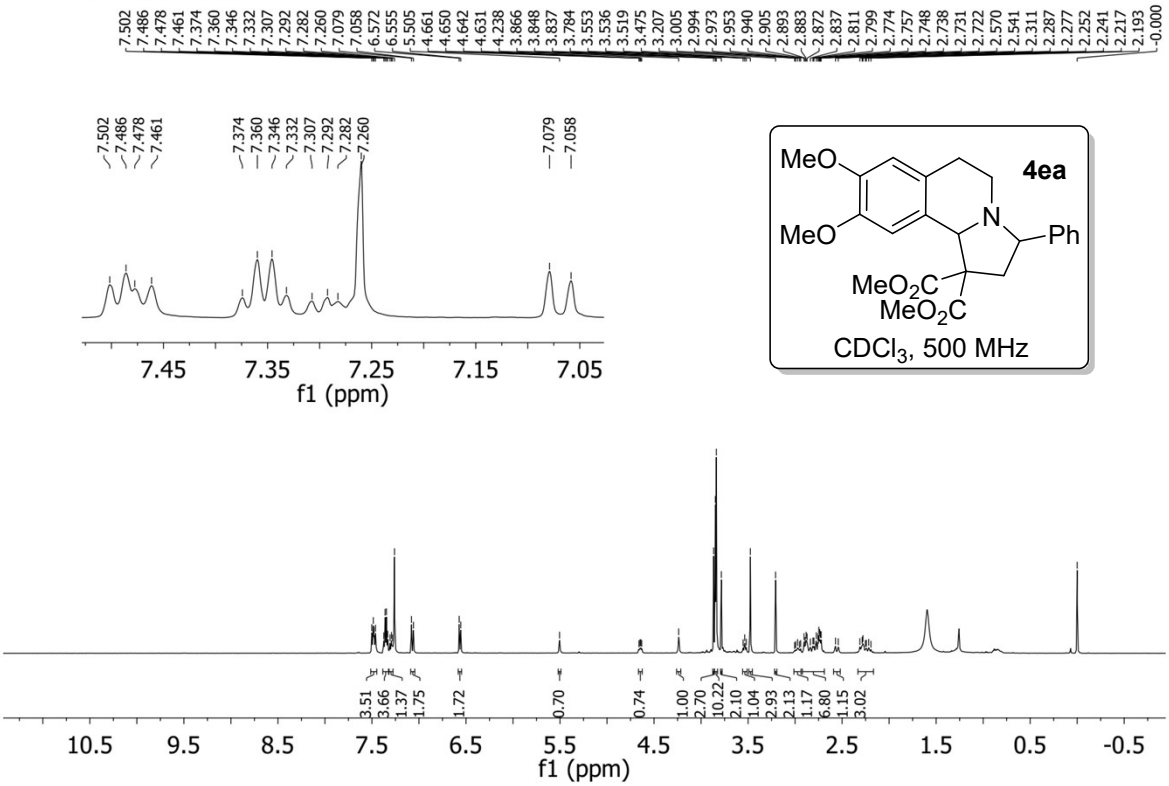
PK-6-Br-THIQ-CYP-CLSG-1H



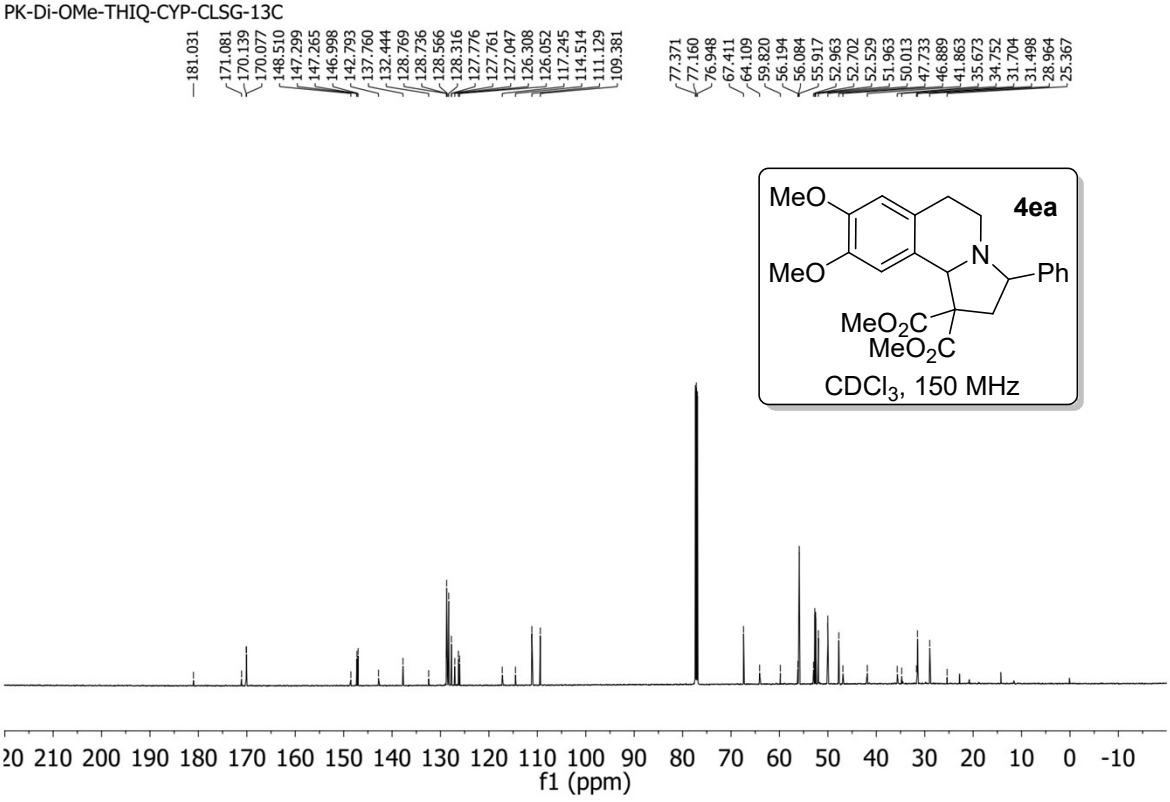
PK-6-Br-THIQ-CYP-CLSG-13C



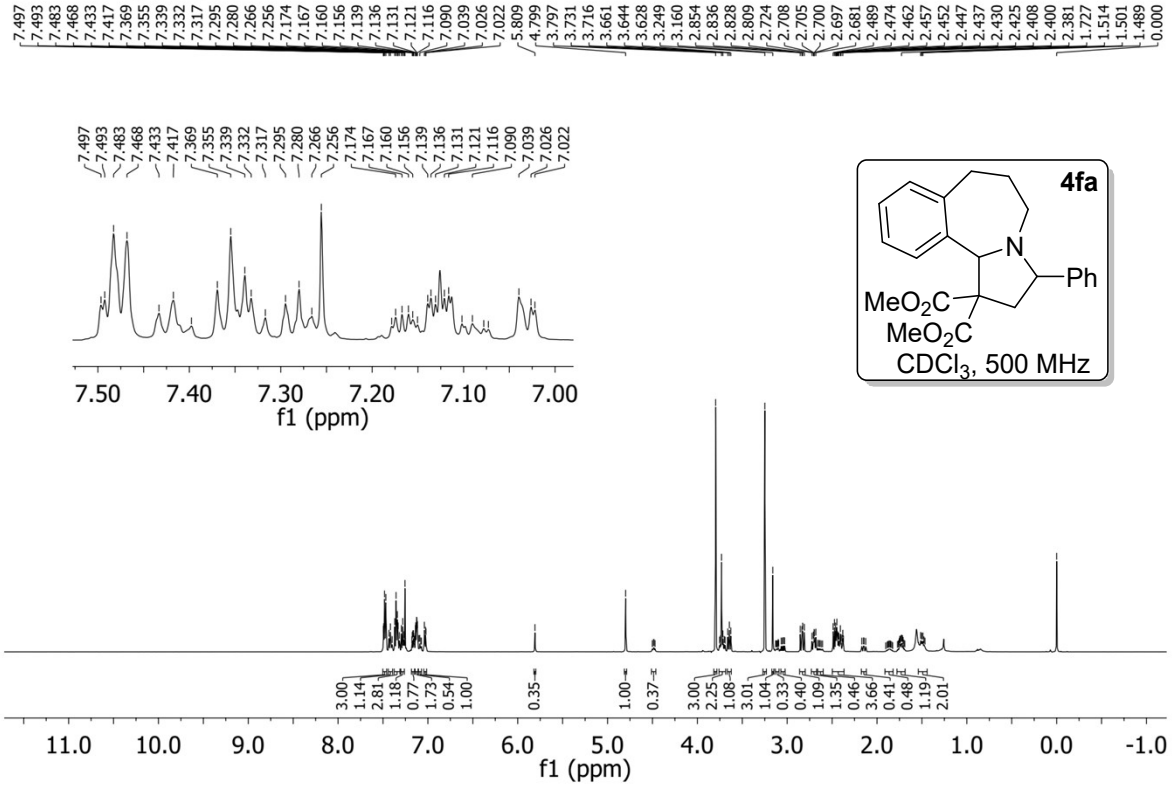
PK-Di-OMe-THIQ-CYP-CLSG-1H



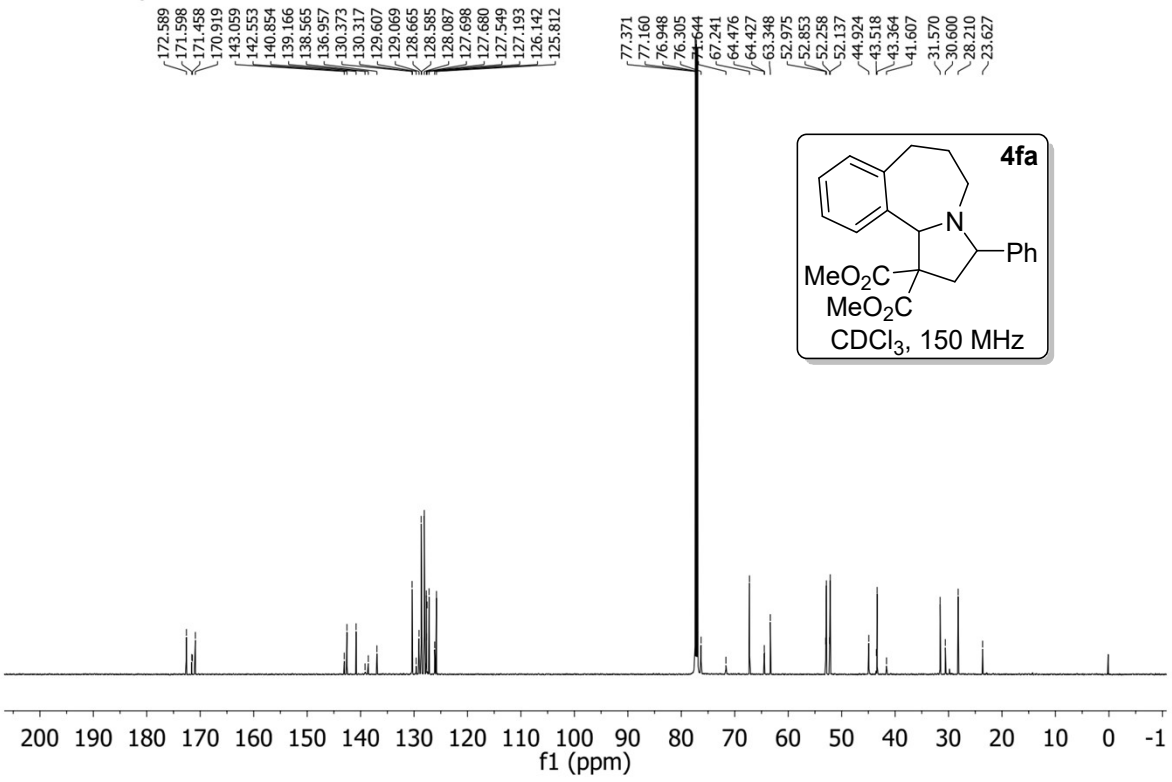
PK-Di-OMe-THIQ-CYP-CLSG-13C



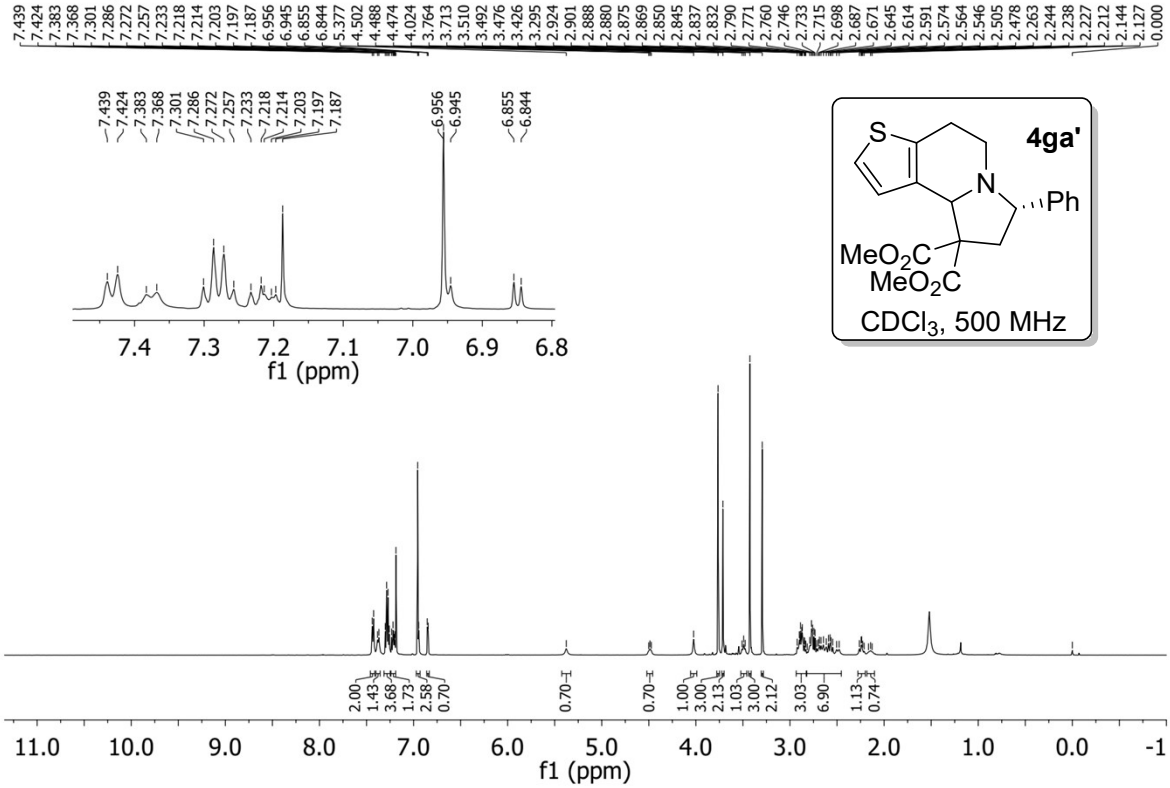
PK-7-MEM-THIQ-CYP-CLSG-1H



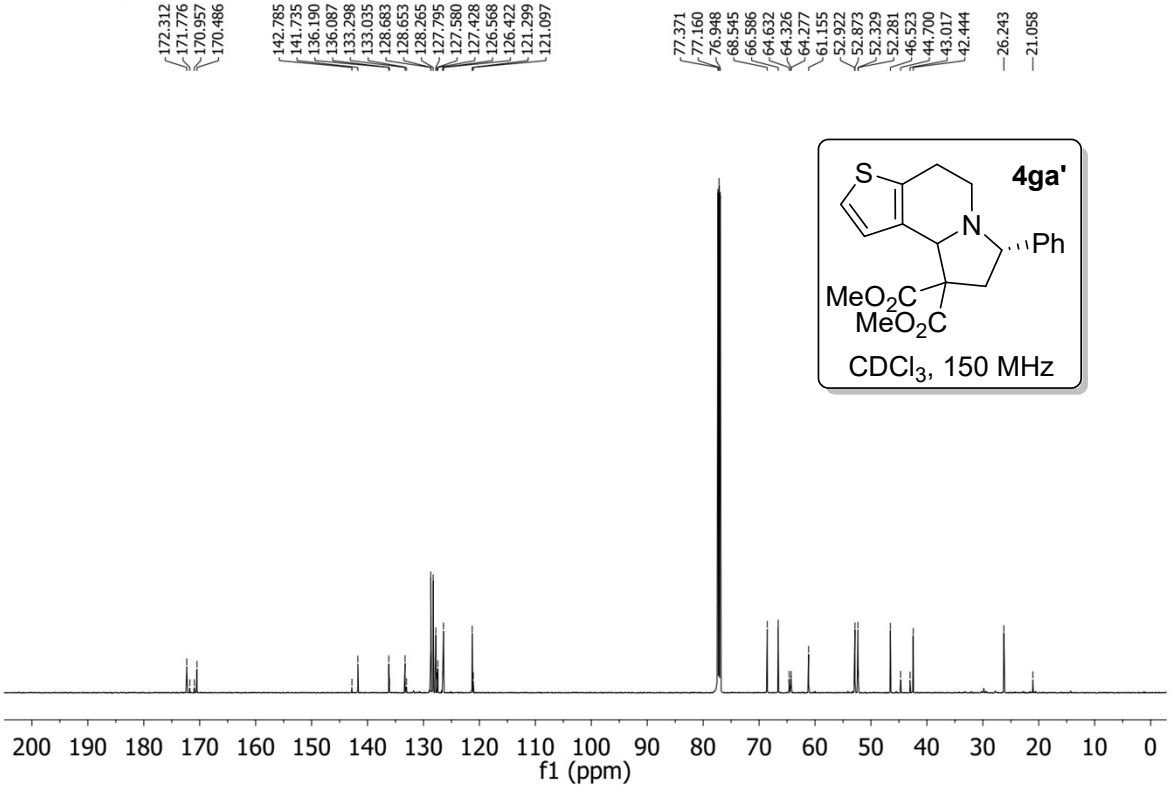
PK-7-MEM-THIQ-CYP-CLSG-13C

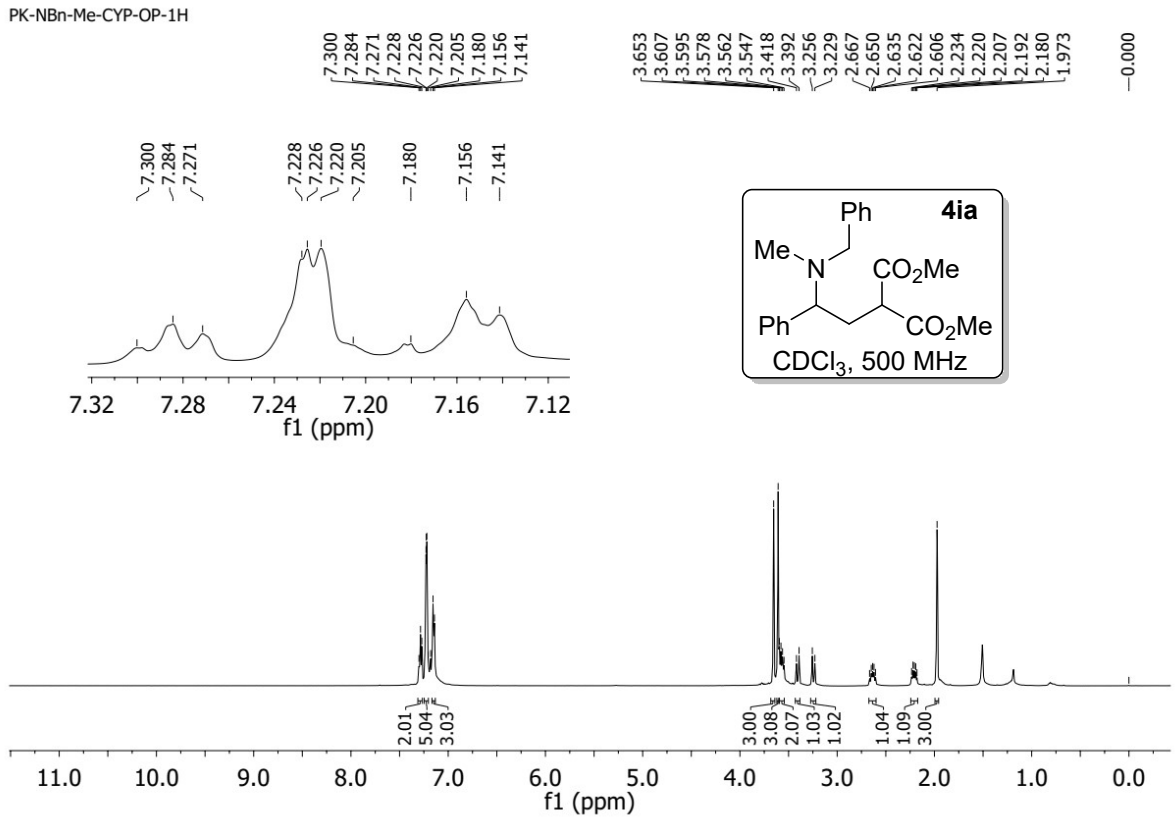


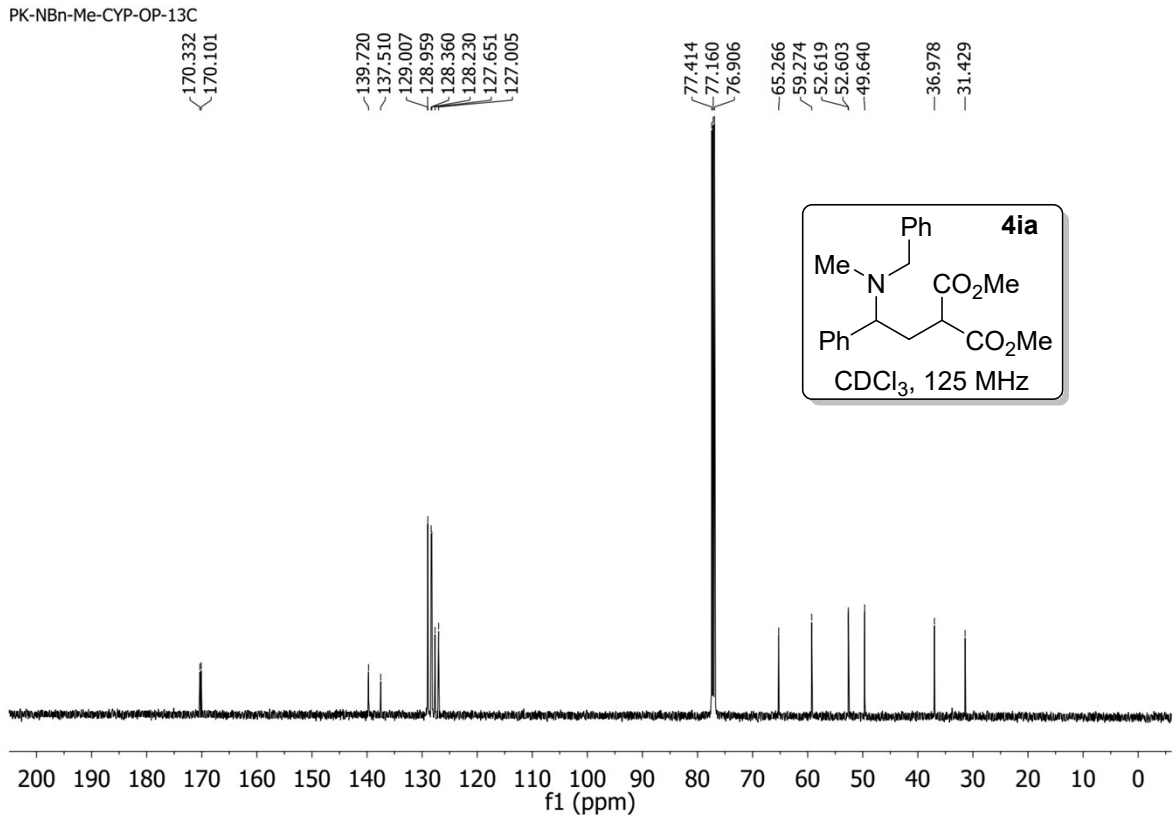
PK-THP-THIQ-CYP-CLSG-1H



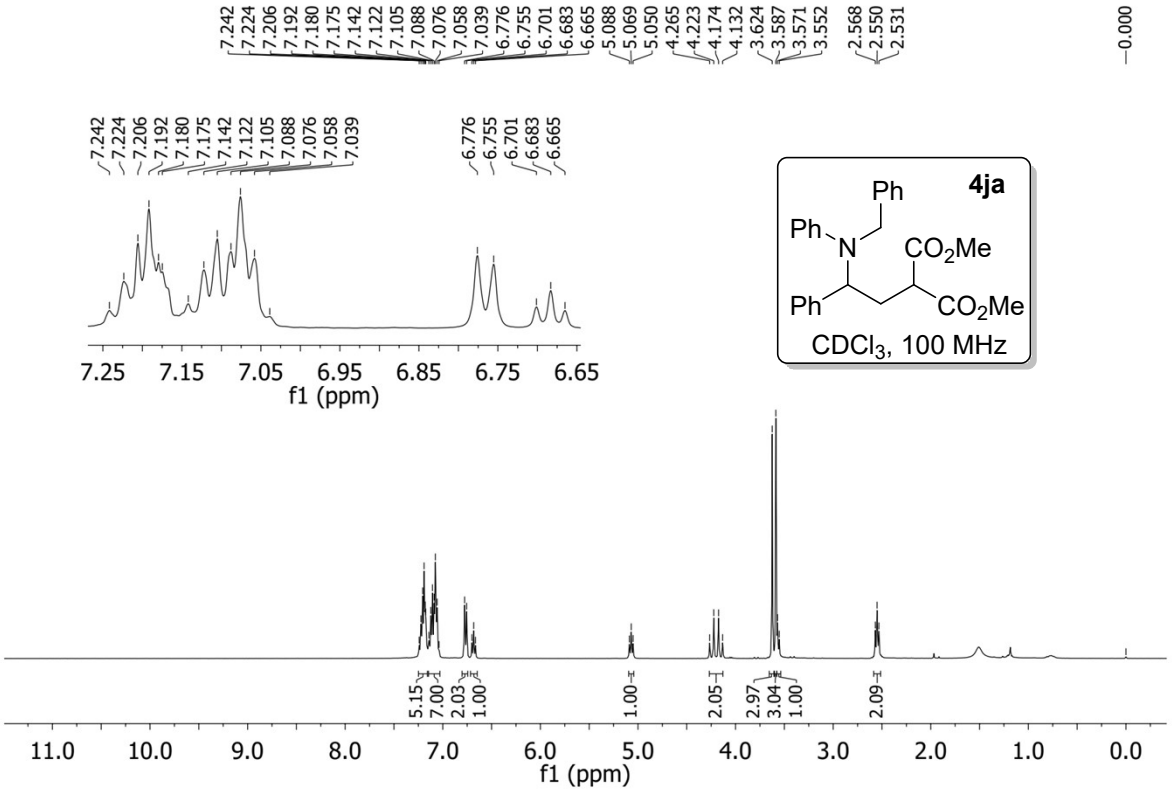
PK-THP-THIQ-CYP-CLSG-13C




PK-NBn-Me-CYP-OP-1H
7.300
7.284
7.271
7.228
7.226
7.220
7.205
7.180
7.156
7.141
3.653
3.607
3.595
3.578
3.562
3.547
3.418
3.392
3.256
3.229
2.667
2.650
2.635
2.622
2.606
2.234
2.220
2.207
2.192
2.180
1.973
0.000
Ph
4ia
Me
N
CO2Me
Ph
CO2Me
CDCl3, 500 MHz
2.01
5.04
3.03
3.00
3.08
2.07
1.03
1.02
1.04
1.09
3.00
f1 (ppm)


PK-NBn-Me-CYP-OP-13C
170.332
170.101
139.720
137.510
129.007
128.959
128.360
128.230
127.651
127.005
77.414
77.160
76.906
65.266
59.274
52.619
52.603
49.640
36.978
31.429
Ph
4ia
Me
N
CO2Me
Ph
CO2Me
CDCl3, 125 MHz
f1 (ppm)

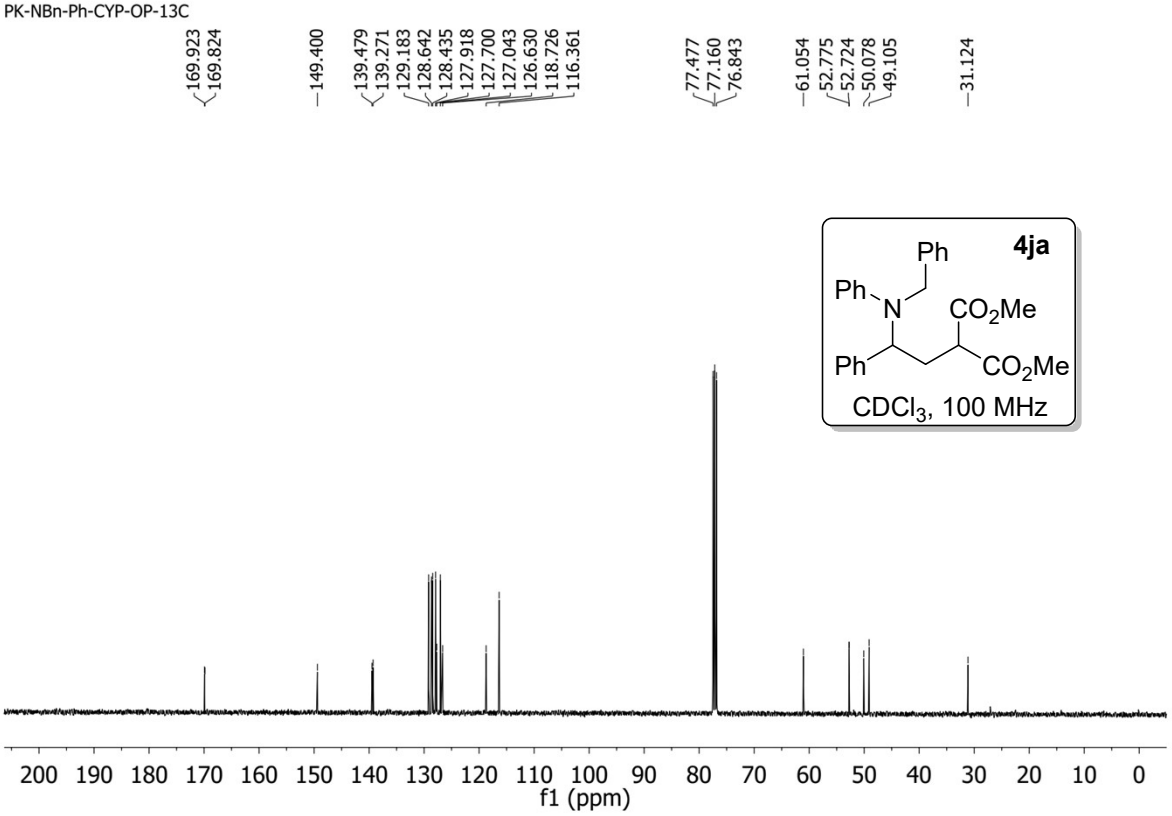
PK-NBn-Ph-CYP-OP-1H



4ja

$CDCl_3$, 100 MHz

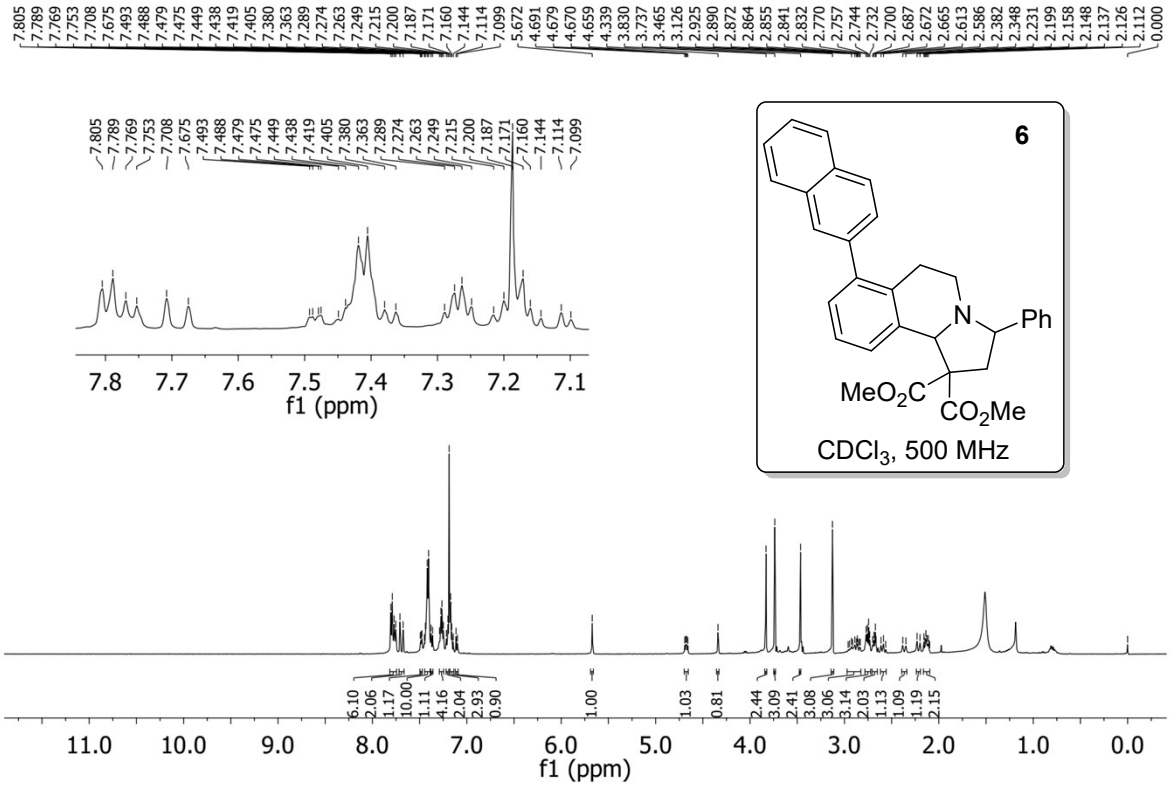
PK-NBn-Ph-CYP-OP-13C



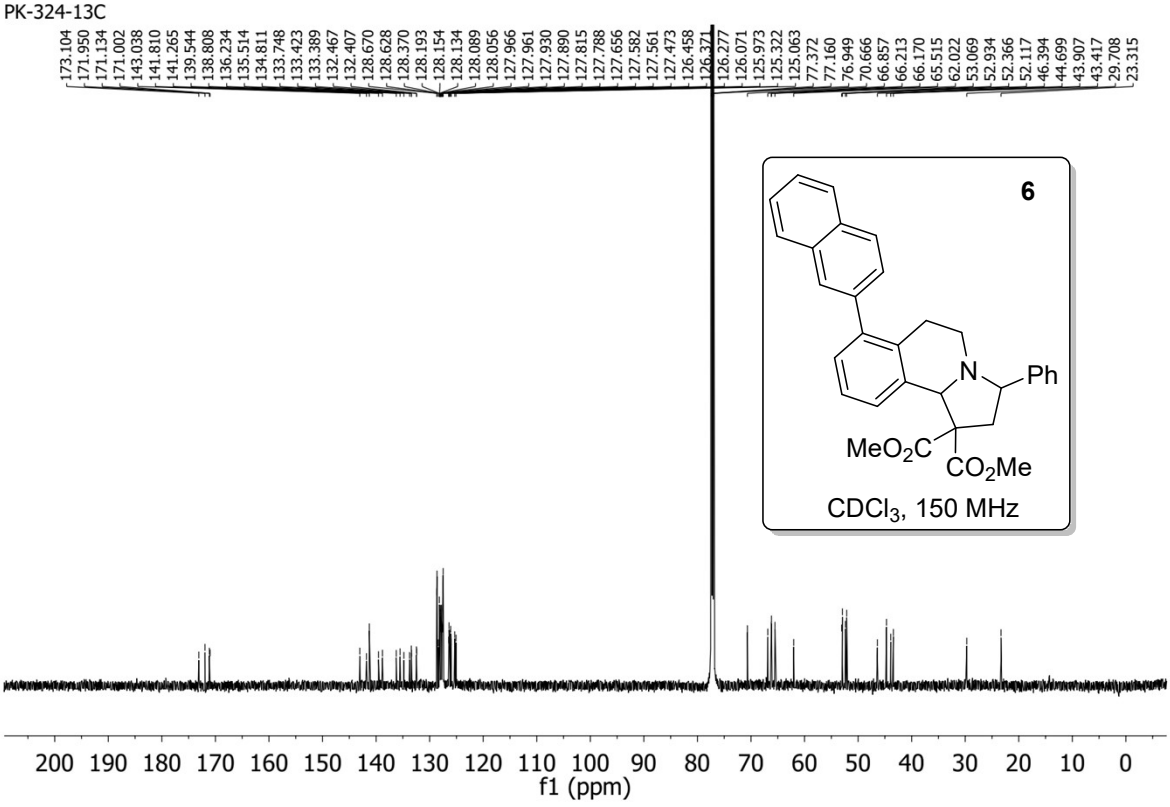
4ja

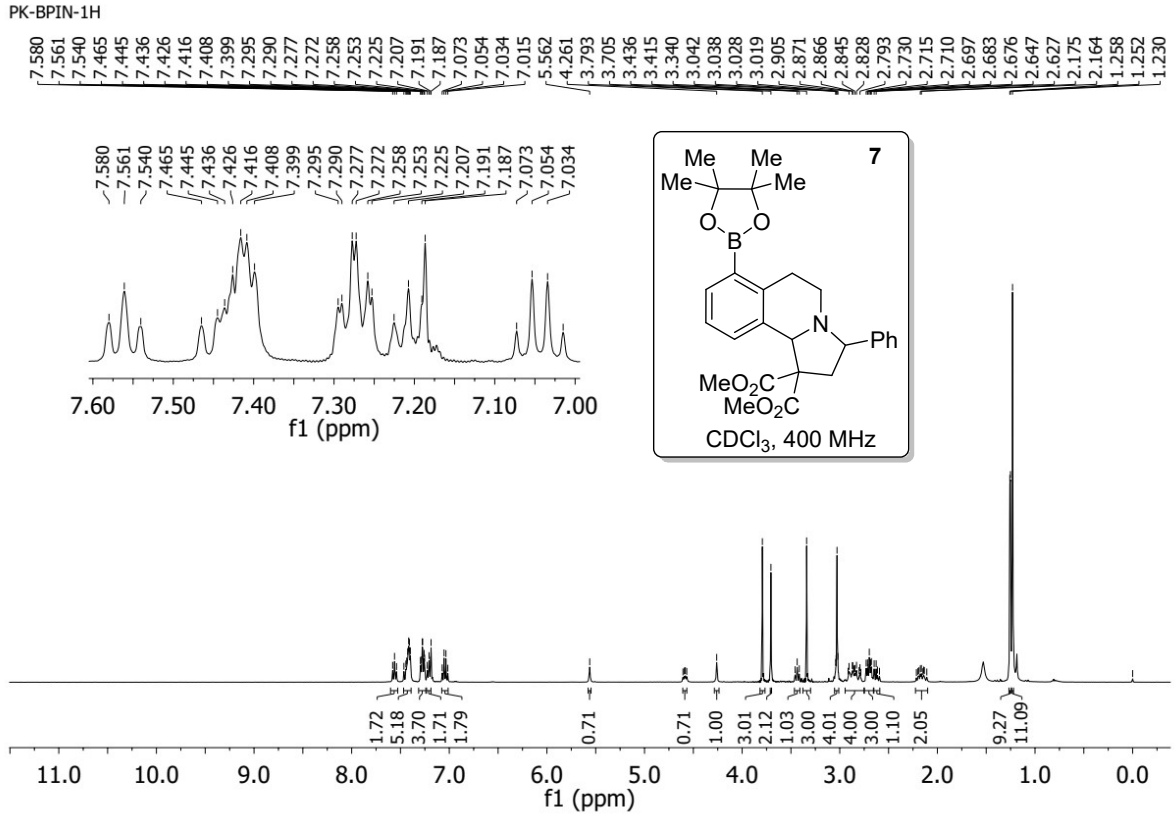
$CDCl_3$, 100 MHz

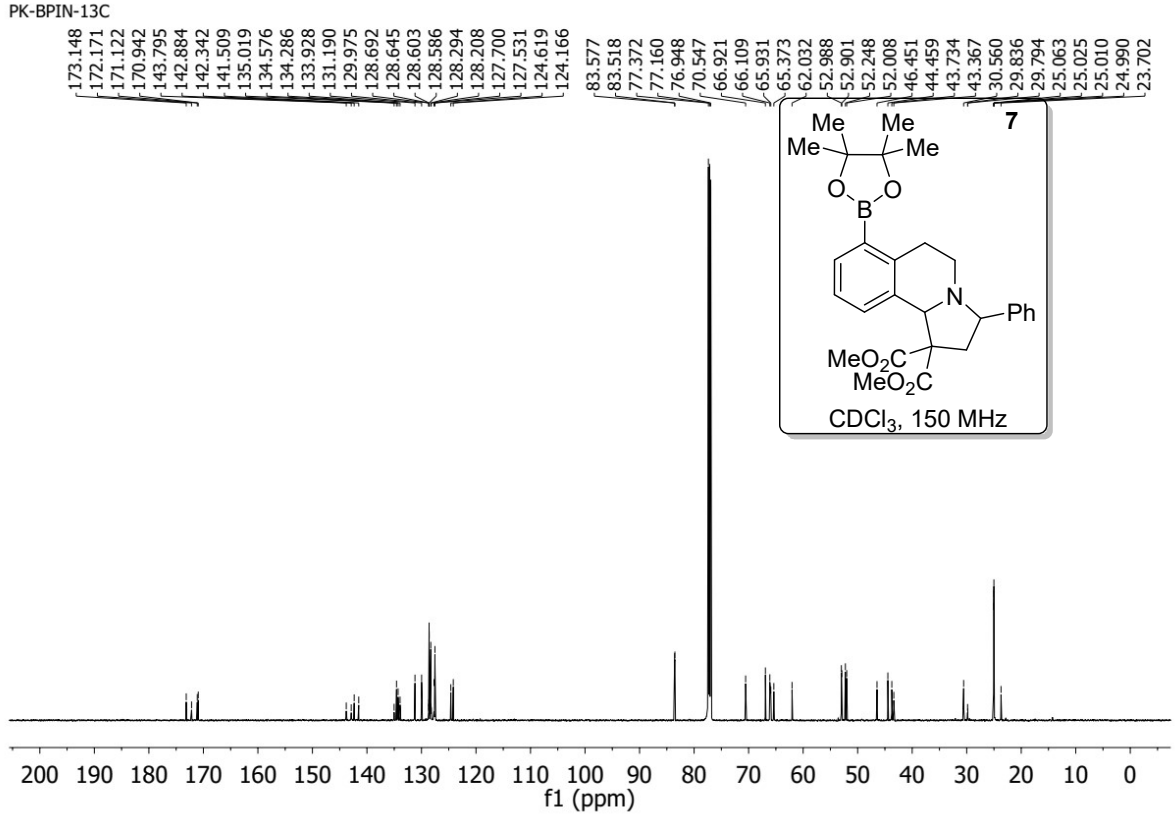
PK-324-1H



PK-324-13C




PK-BPIN-1H
7
CDCl3, 400 MHz
f1 (ppm)


PK-BPIN-13C
7
CDCl3, 150 MHz
f1 (ppm)